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Abstracts of Speakers

S1
What is synaptic and intrinsic plasticity?

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Ever since the discovery of synaptic plasticity, it is an attractive model for learning and memory because growing evidence suggests that behavioral performance leads to synaptic changes in the brain. Therefore, we often think that plasticity induced by non-invasive brain stimulation (NIBS) in humans is also caused by synaptic plasticity. However, synaptic plasticity is not a sole mechanism of such changes in our brain. Intrinsic plasticity, a change in the intrinsic excitability of the neuron, also plays a critical role in shaping adaptive changes. Both synaptic and intrinsic plasticity therefore may underlie exactly how our brain changes as a function of experience. I will introduce several animal studies in which intrinsic plasticity has been linked to modification of synaptic plasticity and vice versa. Both plasticity neuronal signature may be implicated in what we observed with NIBS technique.
Abstracts of Speakers

S2
Synaptic and intrinsic property (axonal) plasticity in the human motor cortex

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The neural plasticity is one main mechanism to support the flexibility of human brain. There are several stimulation methods to induce plastic changes in human brain. We have used quadripulse stimulation (QPS) to study the plasticity in the human brain. In this talk, we will show some intrinsic property plastic changes in addition to the synaptic plastic changes induced by QPS.

Synaptic plasticity by QPS

In QPS, a burst consisting of four monophasic pulses is given every five seconds for 30 minutes. After QPS, motor evoked potentials (MEPs) to TMS are bidirectionally modulated depending on the interval of magnetic pulses in one burst. Short interval QPS (QPS5; interval of 5ms) potentiates and longer interval QPS (QPS50; interval of 50ms) depresses MEPs to TMS. Their physiological characteristics, bidirectional modulation, dependence on the interval of pulses, spatial specificity are all compatible with the synaptic plasticity reported previously. We conclude that QPS is able to induce neuronal plasticity in human brain. These all are consistent with long term potentiation (LTP)/long term depression (LTD) of synaptic efficacy.

Intrinsic property or axonal plasticity by QPS

In some situations, axonal excitability changes are also induced in association with synaptic plasticity in animal experiments. We studied whether axonal plasticity is also induced in the human motor cortex in QPS over M1. To evaluate axonal plastic changes of the corticospinal tracts (CSTs), we used transcranial high voltage electric stimulation (TES) of M1 which is considered to activate CST axons directly. Namely, MEPs to TES were measured before and after QPS, and the time courses of their sizes were investigated. MEPs to TES were depressed after QPS5 in contrast to LTP of MEPs to TMS. QPS50 potentiated MEPs to TES even though MEPs to TMS were depressed. We consider that the changes in MEPs to TES is produced by axonal plastic changes of CST axon hillocks because QPS induced no changes in MEPs to brainstem stimulation of CSTs.

Conclusion

QPS may induce homeostatic plastic changes in the CST axons and synaptic plastic changes at the synapses between the facilitatory motor cortical interneurons and CST neurons, simultaneously. The axonal plasticity should also be considered when we interpret the plasticity induction studies in humans.
Abstracts of Speakers

S3
Experiments into readiness for action - Bereitschaftspotential

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Question

In 1964 my mentor Hans Helmut Kornhuber (1928-2009) and I recorded brain activity in the EEG preceding willful (volitional) actions. The term readiness potential was offered but Bereitschaftspotential (BP) was preferred (a German word in the English language). The BP was not a serendipitous discovery - we were actively searching for signs of self-active intention and will.

Methods

The method of reverse averaging was developed in 1964. Simple movements (rapid flexions of the forefinger) have to be monophasic. Using wrist extention and flexion in one flick of the hand is not good, since this employs 2 movements instead of one.

Results

We found the BP in 1964. The full paper was published in 1965 in Pfluegers Arch. - a citation classic.

In 1978 another citation classic appeared [3] with the important finding that the supplementary motor area, SMA is active prior to willful actions and the activation of motor cortex (M1, BA4).

In 1981 together with Weinberg and Brickett the MEG equivalent of the BP, the Bereitschaftsfield, was first recorded.

In 1984 we used visual tracking movements and found evidence that the frontal cortex is starting and supervising the tracking but not executing it, delegating this to the ‘expert systems’ visual cortex and M1, Lang et al. [4].

In 2002 [5] and 2003 [6] the term Bereitschafts-BOLD effect was coined by Cunnington et al. in event-related fMRI studies.

Conclusions

The 1st component of the BP (BP1 or BP{\text{early}}) is generated by the SMA proper, the pre-SMA and also the C(cingulate)MA. The 2nd component (BP2 or BP{\text{late}}) is generated by M1. Against previous belief, the intentional activity is not travelling directly from the SMA to M1 but runs via the motor loop. This means that the formation of will has already taken place in the frontal lobe, and the preparation for movement is initially handed over to unconscious routine processes of the basal ganglia which do the groundwork for M1. M1 gives the last command [1]. During BP1 we do not yet consciously perceive our own motor planning, but during BP2 we do. From this observation Libet [2] concluded that we do not have free will in the initiation of the action (BP1) but only in its control (BP2). Yet we [1] show that consciousness is not a prerequisite for free will. There are conscious and unconscious agendas in the brain. Thus, free will is involved in control and initiation.

References

Abstracts of Speakers


References


S4
Generator mechanism of BP and its clinical application
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Since discovery of the slow negative electroencephalographic (EEG) activity preceding self-initiated movement by Kornhuber and Deecke in 1964, various source localization techniques in normal subjects and epicortical recording in epilepsy patients have disclosed the generator mechanisms of each identifiable component of the movement-related cortical potentials (MRCPs). Regarding simple movements, the initial slow segment of BP (early BP) begins about 2 s before the movement onset in the pre-supplementary motor area (pre-SMA) with no movement site-specificity and in the SMA proper with some somatotopic organization, and shortly thereafter in the lateral premotor cortex bilaterally with relatively clear somatotopy. About 400 ms before the movement onset, the steeper negative slope (late BP) occurs in the contralateral primary motor cortex (M1) and lateral premotor cortex with precise somatotopy. Both early and late BPs are influenced by complexity of the movements while late BP is influenced by discreteness of finger movements. Volitional motor inhibition or muscle relaxation is preceded by BP which is quite similar to that preceding voluntary muscle contraction. Regarding movements used for daily living such as grasping and reaching, BP starts from the parietal cortex, more predominantly of the dominant hemisphere. BP has been applied for investigating pathophysiology of various movement disorders. Early BP is smaller in patients with Parkinson disease, probably reflecting the deficient thalamic input to SMA. BP is smaller or even absent in patients with lesion in the dentato-thalamic pathway. Since BP does not occur before involuntary movements, BP is used for detecting the participation of the ‘voluntary motor system’ in the generation of apparently involuntary movements in patients with psychogenic movement disorders.
S5
Movement-related desynchronisation and resting state sensorimotor networks

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Preparation for a voluntary movement is not only accompanied by the “Bereitschaftspotential” (BP) and the pre-movement desynchronisation (ERD) of central alpha and beta band rhythms but also by a concomitant heart rate (HR) deceleration. The intimate connection between brain and heart was enunciated by Claude Bernard over 150 years ago (Darwin 1999, pp. 71-72, originally published 1872) and is based on central commands projecting to cardiovascular neurons in the brain stem and modulating the HR. One interesting question is why these BP, ERD and HR changes start already some seconds prior to movement onset? It has been documented that the resting state sensorimotor network can oscillate at ~0.1 Hz observed in EEG, NIRS-HbO2/Hb and fMRI-BOLD signals (Vanhatalo et al. PNAS 2004, Sasai et al. Neuroimage 2011). This suggests that the ongoing brain activity can display slow/ultraslow excitability fluctuations in the range of ~10 s and voluntary movements are most likely initiated if the excitability in resting state sensorimotor networks reaches a specific threshold. Remarkable is that a close coupling can exist between cerebral and cardiovascular ~0.1 Hz oscillations.
Abstracts of Speakers

S6
Motor and sensory conduction in inflammatory and hereditary neuropathies

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Nerve electrophysiology plays an important role in establishing the presence of peripheral disease. In inflammatory neuropathies such as Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy, electrodiagnostic classification can be challenging. Patients with Guillain-Barré syndrome can present with nerve conduction changes that rapidly reverses in the early phase of the disease, making serial studies of increasing importance.

The inherited neuropathies, in particular Charcot-Marie-Tooth disease is associated with more than 50 genetic mutations. Ascertaining which genetic analyses to perform can prove challenging to treating clinicians. More recently, a practical approach utilizing neurophysiological characteristics along with knowledge of the family pedigree has proven useful in targeting the responsible genetic mutation.

In this talk, Dr Shahrizaila will discuss the patterns of sensory and motor conduction seen in the common inflammatory and inherited neuropathies, including the value of serial studies in Guillain-Barré syndrome.
Abstracts of Speakers

S7
Nerve function studies of pelvic floor

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Normal pelvic floor function requires the integrity of extensive neurologic circuitry of the central and peripheral nervous systems supplied by the somatic and autonomic nervous systems.

Electrodiagnostic medicine is assuming now an increasing role in the diagnosis and management of pelvic floor disorders. Urodynamic and anorectal manometric studies help with electrodiagnosis to provide functional assessment of the pelvic floor and its neural control.

Nerve function studies of the pelvic floor can be divided into four main parts, covering:

Pudendal nerve conduction studies.

Sacral reflexes: which are reflex contractions of striated muscle structures in the pelvic floor which occur in response to stimulation of the perineum or genital region. They are useful in studying lower motor neuron lesions affecting pelvic floor function. Different forms of sacral reflexes have been described: pudendo anal reflex, urethral anal reflex, bladder anal reflex and Bulbo-cavernous reflex.

Cortical and visceral evoked potentials: Cortical and spinal responses can be obtained from pudendal nerve stimulation, or bladder stimulation.

Electromyography: to assess the integrity of innervations in pelvic floor muscles
Abstracts of Speakers

S8
Clinical application of a novel motor unit number estimation method - Motor Unit Number Index MUNIX

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“Motor Unit Number Index“ (MUNIX) is a new electrophysiologic method to track motor neuron loss over time in neuromuscular diseases like amyotrophic lateral sclerosis (ALS). This new method has several advantages, but also some limitations. Compared to other motor unit number estimation (MUNE) techniques, MUNIX is easy and quickly performed, non-invasive and applicable to several muscles in an adequate amount of time. This allows to exam a whole set of muscles in different regions which should be more accurate to reflect disease progression in comparison to only one single muscle. However, patient’s cooperation and accurately and carefully performed standard neurographic procedures are required and technical features have to be kept in mind to give reliable results. The available literature demonstrates a good inter- and intra-rater reproducibility in healthy volunteers and ALS patients. In ALS patients longitudinal data (to be published) suggests that decline of MUNIX exceeds other markers of disease progression like the functional rating scale ALSFRS-R. This supports the concept that MUNIX is capable to detect early motor neuron loss before clinical symptoms like weakness and atrophy and therefore functional deterioration occurs. This makes this method a favourable candidate as a sensitive biomarker in longitudinal ALS trials and other progressive neuromuscular disorders.
S9
Ultrasound in Complementing Nerve Entrapment Syndrome Diagnosis and Therapeutic Decision-Making

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Clinical examination and electrodiagnostic testing remain the gold standards for diagnosis of entrapment neuropathies, including carpal tunnel syndrome and ulnar neuropathy at the elbow. Unfortunately, these modalities provide little insight into the anatomical causes of nerve compression, adversely impacting treatment decisions and leading to unnecessary exploratory surgery and delays in treatment. Until recently, imaging has been neglected in the assessment of peripheral nerve disease. Neuromuscular ultrasound (NMUS) now offers a non-invasive and reliable method for evaluating the structural changes of entrapment neuropathies, providing appropriate guidance for therapy. NMUS can assist in the diagnosis of entrapment neuropathy, typically demonstrating nerve enlargement at or near sites of compression. The etiology of nerve entrapment is revealed in many cases, particularly with ulnar neuropathy at the elbow and fibular neuropathy at the fibular head. Additionally, NMUS is helpful in improving our understanding of the pathophysiology of these common conditions. NMUS is now a standard aspect of evaluating peripheral nerve entrapment in electrodiagnostic laboratories that offer imaging. Ongoing research suggests that it may become an essential element in the evaluation of peripheral nerve disease.
S10
High resolution sonography in the evaluation of the peripheral nervous system in polyneuropathies

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Clinical, laboratory and electrodiagnostic studies were the mainstay in the diagnosis of polyneuropathy. A new additional tool, namely high-resolution sonography of the peripheral nervous system allows nerves to be readily visualised and to assess their morphology. In this lecture we review the literature on its clinical application in polyneuropathy. Several polyneuropathies have been studied by means of ultrasound: Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies, chronic inflammatory demyelinating polyneuropathy, Guillain-Barré syndrome, multifocal motor neuropathy, paraneoplastic polyneuropathy, leprosy and diabetic neuropathy. The most prominent reported pathological changes described are nerve and fascicle enlargement, increased hypo-echogenicity and increased intraneural vascularisation. Sonography seems to reveal intriguingly different patterns of nerve enlargement between inflammatory neuropathies, axonal and inherited polyneuropathies. New prospective studies with standardised protocols for nerve sonography, clinical and electrodiagnostic testing are ongoing to determine the diagnostic and prognostic role of nerve sonography in both inherited and acquired polyneuropathies.
Neurophysiological assessment of muscle membrane properties

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Muscle fibers, like nerve fibers, are complex electrical organs, in which the accurate control of membrane potential, and the interplay of multiple voltage-dependent ion channels, have essential roles in normal physiological function. Recently, using lessons learnt from nerve excitability studies, effective protocols for clinical assessment of muscle membranes have been devised, using direct muscle stimulation and recording, and inferring activity-dependent changes in membrane potential from changes in conduction velocity. Like superexcitability in nerve, supernormality following a conditioning stimulus is highly sensitive to changes in resting potential. A late phase of supernormality is related to potassium accumulation in the t-tubules, and measurements made within a 10-minute recording can distinguish several different kinds of ion channel dysfunction. This symposium will review the basics of this new technique, demonstrate the recording technique and discuss its potential roles in the diagnosis of muscle disorders and providing new insights into their pathophysiology.
Consciousness is the state of being aware of an external object or something within oneself and has an enormous impact on the life of the individual. Philosophers since the time of Descartes and Locke have struggled to comprehend its meaning and fortunately neuroscience now focuses on understanding the neural correlates of consciousness.

Seizures may arise from cortex and rapidly spread to the reticular formation causing an alteration of consciousness. Generalized seizures are now known as associated with disruption of the default state network, including the frontoparietal association cortices. Subcortical contribution through activation of thalamocortical structures and striate nuclei are also important to produce impaired consciousness in generalized seizures.

Alteration of consciousness is difficult to define, both theoretically and practically. Impairment of consciousness may frequently be observed during a seizure which markedly impact on the quality of life of the epileptic patient. Thus epilepsy creates an excellent model to explore the consciousness and seizures recorded with long-term video-EEG studies are of extreme importance.

Seizure semiology is an important clue but not always significantly different between so called absence seizures and focal seizures consisting mainly of alteration in consciousness. The constituent functions of consciousness examined during the seizures may include the orientation to the examiner, intentional behavior demonstrated by speech, and postictal memory.

We evaluated the semiologic characteristics of video-recorded seizures consisting mainly of an alteration in consciousness (absence/dialeptic seizures) in a large series of patients with focal versus generalized epilepsies in a comparative design. The lack of aura, presence of blinking, high seizure frequency, shorter seizure duration, besides family history of epilepsy and resistance to therapy point towards generalized epilepsy.

Neuropsychological and neurophysiological studies suggested that the consciousness is neither an emergent property of the brain as a whole nor a function of a single center. Rather, the neuronal correlate of consciousness consists of different interacting neural networks. In that sense epilepsy may provide vital leads to some mechanisms of consciousness.
Abstracts of Speakers

S14
A survey of clinical pathophysiology and neuropharmacology of somatosensory high frequency oscillations

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Electrical stimulation of upper limb nerves allows to evoke on the contralateral fronto-parietal scalp regions a train of 600 Hz wavelets. Earlier experiments demonstrated that these High-Frequency oscillations (HFOs) are influenced by arousal-related structures. To elucidate their putative generators, as well as their functional meaning, we have thus far performed three types of studies. 1) Analysis of HFO modifications after acute administration of cholinergic and GABAergic drugs. These studies confirmed the strict relationship between HFOs and arousal-related structures, whereas their relationship with GABAergic circuitries remains still unsolved. 2) Analysis of HFO modifications in neurological diseases which involve cortical excitability, such as epilepsy and migraine. These studies strongly suggested that early HFOs, giving origin from the thalamus, probably act as a buffer which tends to compensate abnormal changes of the cortical excitability. 3) Analysis of HFO modifications in healthy subjects after manipulation of stimulus presentation. These studies strongly suggest that HFOs do not undergo habituation but are involved in sensitization mechanisms, and that they play probably a role in the very early processing of novel stimuli. In conclusion, our experience reinforces the view that somatosensory HFOs represent a somatosensory arousal system, the main aim of which is the very early selection of relevant somatosensory stimuli.
S15
Sensitivity and validity of MEG source localization in focal epilepsy: dependencies on source size and location

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Source localization in focal epilepsy implies dipole localization of interictal spikes in the most studies. There are two aspects of this approach that could be challenged: first the fact that interictal spikes do not necessarily represent the "source" of epilepsy, i.e. the area where the seizures starts or, in the context of epilepsy surgery, the area that needs to be removed in order to render a patient seizure free. Second, modeling the source of an interictal spike by the current source dipole model might not be valid. Even if the dipole model would be valid, the sensitivity of source localization of interictal spikes as a non-invasive replacement of intracranial EEG monitoring, the current gold standard, remains to be specified.

In this study MEG registrations of interictal spikes are compared to interictal spikes in the intracranial EEG of the same patients. The seizure onset zone (SOZ) is known as well. A simulation model for extended sources is set up, and the sensitivity of MEG for sources of different location and extent is evaluated. Dipole localization of simulated extended sources is performed.

It is found that sensitivity of MEG varies for different brain regions. This sensitivity can be explained by source depth, source extent and source location. Depending on location, a larger source extent does not necessarily imply greater MEG sensitivity. Dipole modeling of extended sources can result in differences of more than 1 cm between the dipole position and the center of the extended source. Finally, SOZ, intracranial interictal spike location and MEG interictal spike localization may coincide, but not all valid MEG source localizations indicate the SOZ.
Diagnostic Utility of TMS

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Transcranial magnetic stimulation has demonstrated or potential clinical utility in several neurological disorders. In amyotrophic lateral sclerosis, measurement of central motor conduction time (CMCT) can detect upper motor neuron involvement. The sensitivity may be increased by combining with other parameters such as the motor threshold, silent period duration or by using the triple stimulation method (TST). CMCT measurement may also be used to detect myelopathy. In multiple sclerosis, TMS measures such as motor threshold, CMCT, TST and silent period may also be used to detect clinically silent lesions and may have prognostic implications. In facial nerve disorders, TMS combined with peripheral stimulation may be used to localize the facial nerve lesion and help to determine the cause of facial palsy. CMCT and TMS measures of transcallosal inhibition may help to distinguish different parkinsonian syndromes. An form of cortical inhibition known as short-latency afferent inhibition may assist in the diagnosis of Alzheimer's disease, Parkinson's dementia and mild cognitive impairment, and may play a role in predicting the response to treatment as well as monitoring disease progression.
S17
Utility of TMS in Prediction of Disability Progression in Multiple Sclerosis

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Assessing disease course and prognosis of MS is challenging for multiple reasons, among them: (1) there are three main disease course types (relapsing remitting, secondary progressive, and the much rarer primary progressive form); (2) lesions are by definition multiple in time and location; (3) pathological lesions may be clinically silent; (4) pathological patterns of MS lesions differ; (5) inflammatory processes as identified by imaging may represent tissue destruction as well as healing; (6) while important aspects of pathomechanisms have been described, etiology is still unknown; (7) the disease evolves in most cases over many years, which may also imply changes of diagnostic and therapeutic standards. However, the common cause of clinical manifestations and disability consists in an alteration of impulse generation and propagation in the CNS.

TMS allows studying measures of threshold, conduction velocity, the number of functioning upper motor neurons and of the modulatory input to the corticospinal tract. These measures proved to correlate with clinical outcome in cross-sectional and in longitudinal studies. Multimodal evoked potentials assess several systems simultaneously, and therefore, give a broader impression of clinical and subclinical affection of the CNS than does TMS alone. Their results correlate with prediction of clinical disability over two and up to 20 years in prospective studies, even when recorded in the early phase of the disease.

These results support a role for TMS combined with other modalities of evoked potentials in the identification of patient groups at high risk for development of disability. Inclusion of additional techniques for assessment of evoked potentials or of procedures allowing characterization of impulse propagation in CNS connections that are inaccessible to direct stimulation may allow to further increase the predictive value of electrophysiological testing, with the ultimate goal of achieving a reliable prognosis on an individual base.

(Supported by the Swiss National Science Foundation; SPUM 33CM30_140338, and the Swiss Multiple Sclerosis Society)
S18
Changes in neuromuscular axonal excitability in benign cramps-fasciculation syndrome

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The cramp-fasciculation syndrome, occurring without weakness or atrophy, is generally regarded as a benign, non-progressive disorder. The responsible mechanisms are poorly understood. In general, there is a long debate on the both spinal and peripheral mechanisms.

To clarify whether in cramp-fasciculation syndrome an abnormal excitability of motor axons may contribute to the pathophysiology of the disease, we carried out a threshold tracking study on the median nerve of patients and compared our results to controls. A total of 35 individuals were studied, fifteen patients with a cramp-fasciculation syndrome and 20 healthy volunteers as a normal control group.

Axonal excitability studies were performed in cramp-FS patients without current treatment on motor axons in vivo. In all patients any other known origin of muscle cramps was excluded. The patients had normal conduction velocity. The median nerve was stimulated at the wrist and compound muscle action potentials were recorded from M. abductor pollicis brevis. Threshold tracking techniques were used to record strength-duration time constant, threshold electrotonus, current/threshold relationship and recovery cycle.

In threshold electrotonus patients showed a smaller peak in response to depolarizing and to hyperpolarizing currents (-70 %, -100 %). In the recovery cycle patients had less superexcitability at 7 ms interstimulus interval. Consistently with the threshold electrotonus results the current threshold relation reflects an inward rectification.

Our results show a hyperexcitability of motor nerves in benign cramp-fasciculation syndrome. The main result indicates an enhanced inward rectification which is mainly due to I\textsubscript{N}, I\textsubscript{h}, is known to regulate the spiking frequency. A higher spiking frequency may enhance the probability of suffering from fasciculations and muscle cramps.
S19
CIP and CIM

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Neurological complications of severe critical illness and sepsis are critical illness polyneuropathy (CIP), critical illness myopathy (CIM). Both present with an ICU acquired muscular weakness and combinations of both are frequent. Weaning problems may be often the first symptoms at the intensive care unit. Electrophysiological assessment plays a major role in early diagnosis as the critically ill patients often cannot be adequately neurologically examined. In this review the disease entities, pathophysiological concepts, and current diagnostic possibilities such as nerve conduction studies, classical electromyography, and direct muscle stimulation are discussed. Early diagnosis is most important as it improves the therapeutic regime in the ICU setting. Moreover, the differentiation between CIM and CIP has prognostic implications as the prognosis of CIP in its longtime course is more harmful. New promising diagnostic tools are skin biopsies to assess small nerve fiber impairments and muscle ultrasound to evaluate muscle structure, muscle wasting, and spontaneous activity (supported by the Center of Sepsis Control&Care (CSCC), funded by the German Federal Ministry of Education and Research (BMBF) grant no. 01 E0 1002.).
Deep brain stimulation in experimental and clinical dementia-related disorders

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Memory loss is the key symptom of dementia-related disorders, including the prevalent Alzheimer’s disease (AD). To date, pharmacological treatments for AD have limited and short-lasting effects. Therefore, researchers are investigating novel therapies such as deep brain stimulation (DBS) to treat memory impairment and to reduce or stop the progression of it. Clinical and preclinical studies have been performed and stimulations of the fornix, entorhinal cortex and nucleus basalis of Meynert have been carried out. The results of these studies suggest that DBS has the potential to enhance memory functions in patients and animal models. The mechanisms underlying memory enhancement may include the release of specific neurotransmitters and neuroplasticity. Some authors suggest that DBS might even be disease-modifying. Nevertheless, it is still premature to conclude that DBS can be used in the treatment of AD, and the field will wait for the results of ongoing clinical trials.
NIBS and memory enhancement: refining research towards therapeutic applications

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Transcranial magnetic stimulation has been traditionally viewed as a cognitive interference method; yet cumulating evidence that this technique can also enhance cognitive function stems from early studies. More recently, investigations employing other methods such as transcranial direct current stimulation have clearly shown that NIBS can be used to improve memory function, in young and elder healthy subjects and in patients with conditions implying memory impairments. In general the beneficial effects of NIBS on memory performance are short-lasting, but methodological variations such as simulating over multiple sessions or days are being investigated towards extending the effects. In parallel, studies coupling NIBS with neuroimaging techniques have allowed us to increase our knowledge about the possible neurophysiologic mechanisms that mediate positive gains of memory, including rapid functional reorganizations of brain networks that may counteract initial disruptions. These findings as well as the possibility of using subject-specific or condition-specific imaging information should strengthen the usage of NIBS on memory enhancement for therapeutical applications.
Abstracts of Speakers

S22  
Logic reasoning

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**Question**

Abstract reasoning abilities, or fluid intelligence (Gf), can be improved by 40Hz transcranial alternating current stimulation (tACS) applied to the left middle frontal gyrus (MFG) [1]. Anyway, why gamma-tACS might induce enhancement of logical reasoning via modulation of working memory (WM) processes, or via increased cortical excitability [2], or as a function of individual differences in Gf [3] are still debated questions.

**Methods**

To address these issues we conducted two experiments, both implementing a Gf task, composed by randomly presented “Relational” and “Logical” visuo-spatial matrices, and a WM task (change localization). 24 participants underwent Gf and WM tasks while receiving gamma (40hz), theta (5hz) and sham tACS on the left MFG. Another 24 participants underwent the same tasks by receiving a low-frequency transcranial Random Noise Stimulation (tRNS) instead of theta-tACS, using the same electrodes montage.

The relationship between accuracy [ACC] and response time [RT] with the predictors of interest, i.e. tACS (sham/5/40Hz) or tRNS, and kind of test (LOGIC, RELATIONS and WM) was investigated through repeated measurements ANCOVA models including gender, age, Gf-WM tasks order and tACS/tRNS conditions order as covariates. Moreover, potential individual differences in the response to tACS have been explored through a partial correlation analysis computed between the individual Gf improvements and baseline performance of the entire sample (n=48).

**Results**

In line with previous data [1], gamma-tACS reduced the time taken to correctly solve LOGIC matrices with no effect neither for RELATIONS trails RT nor for ACC levels in general, without speed-accuracy trade off effects. Additionally, no modulation of the WM task was observed in both experiments, and the pattern of Gf modulation was consistent with gamma-tACS but not tRNS enhancing of Gf. Finally, subjects with relatively lower Gf abilities at baseline showed a significantly greater improvement with gamma-tACS.

**Conclusions**

These findings support the functional relevance of gamma-band activity within the left MFG in high-loading Gf tasks. Individuals with slower RTs on sham benefit more from exogenously induced gamma oscillations (possibly due to suboptimal endogenous gamma oscillations), making the obtained finding an intriguing achievement for neuro-rehabilitation purposes.

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Noninvasive brain stimulation techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are increasingly used in rehabilitation of perceptual and cognitive disorders resulting from brain injury. One such neurological condition is cortical blindness, where non-invasive brain stimulation has been informative not only in terms or revealing some of the neural processes which are important for visual perception to arise, but also in the restitution of visual functions. In particular when combined with behavioural rehabilitation therapies, brain stimulation offers new possibilities for treatments aimed at the recovery of visual functions. These developments will be reviewed in this talk.
Combining EEG and transcranial alternating current stimulation

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Transcranial alternating current stimulation (tACS) is a relatively recent method to stimulate the brain with weak sinusoidal currents. It has been demonstrated that tACS can modulate perception as well as other cognitive processes. To assess the immediate effects of tACS on brain activity, recording of EEG or would be desirable at the time of stimulation. Unfortunately, however, the electric current flow caused by tACS introduces a relatively strong artefact in electrophysiological measurements. One way to circumvent the artefact is to record EEG before and after tACS in order to assess the after-effects. Using this approach, we were able to demonstrate that tACS at individuals’ EEG alpha frequency is able to modulate the amplitude of EEG alpha oscillations for a duration of at least 30 minutes after the end of tACS. In addition, we will introduce a novel procedure for removal of the artefact and will show an evaluation of its validity. Using the latter approach, we were able to demonstrate that tACS at 10 Hz is able to entrain individuals’ EEG alpha rhythm to 10 Hz and to enhance its amplitude.
Abstracts of Speakers

S25
Closed Loop DBS: from pathophysiology to bedside technology

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Despite their proven therapeutic efficacy in several neurological disorders, especially Parkinson’s disease, conventional deep brain stimulation (DBS) systems can be further implemented to maximize treatment benefits. In particular, because current open-loop DBS strategies based on fixed stimulation settings leave motor fluctuations partly uncontrolled, research has focused on developing novel "closed-loop" or "adaptive" DBS (aDBS) systems. aDBS consists of a closed-loop model designed to capture and analyze a control variable reflecting the patient’s clinical condition to elaborate new stimulation parameters and send them to an "intelligent" implanted stimulator. One important problem in developing an aDBS system is choosing the ideal control variable for feedback. Available experimental and clinical data support the advantages of neurosignal-controlled aDBS that uses local field potentials (LFPs) as a control variable. The available aDBS technology already warrants ongoing trials to assess the clinical impact of closed loop DBS systems in patients with Parkinson's disease.
Abstracts of Speakers

S26
Language processing: Insights from MEG and fMRI

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Magnetoencephalography (MEG) detects the spatiotemporal progression of neural current flow via the associated magnetic field, whereas functional magnetic resonance imaging (fMRI) localizes neural-activity-related oxygen consumption (blood-oxygen-level-dependent signal, BOLD). Within each imaging modality, activation patterns are fairly reproducible, even in high-level cognitive tasks such as language processing. MEG-fMRI comparison of low-level sensory and motor processing has suggested similarity of activated areas. However, we now know that the MEG and fMRI activation views of cognitive functions do not always agree. This talk discusses combined MEG-fMRI studies of basic language processing: word reading, spoken word perception and picture naming (word production). Autonomous analysis of the MEG evoked responses and BOLD fMRI contrasts showed both functional and spatial differences, most markedly in reading. Part of the explanation for the different activation views could be that activation changes at the various nodes of cognitive networks may be picked up differently by electrophysiological (MEG) and haemodynamic (fMRI) imaging measures.
S27
Language and non-invasive brain stimulation
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Recent studies have reported enhanced performance on specific cognitive tasks in patients with several types of neurological diseases (Alzheimer - AD, stroke) after receiving non-invasive brain stimulation (NIBS), i.e., repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS). Studies have shown evidence of plastic changes, even in severely affected areas.

In AD patients, the NIBS-induced partial recovery of language abilities, may be due to a strengthening of the synaptic activity of the surviving neurons in the stimulated network. The same phenomenon can be observed in stroke patients after a lesion to an adjacent area or when connected areas become ‘silent’ due to diaschisis and lesion-induced effects that result in silent synapses. NIBS might induce a gradual readjustment of an area that remains intact but “functionally” suppressed due to a steady reduction in synaptic strength. Therefore, these data support the idea that brain stimulation-induced changes in synaptic strength are an essential step toward the recovery of function. Additionally compensatory networks may be recruited or rebalanced to accomplish the impaired function.

NIBS could be used to strengthen or modify a network that is specific to a diminished cognitive function. Studies have suggested that the best way to perpetrate this strengthening is to stimulate the area and activate the network supporting the specific function. This approach can be achieved by combining exogenously induced plasticity (i.e., NIBS) with a specific training-induced plasticity (i.e., cognitive training). In part, this approach resembles the one used to improve motor performance in patients with hemiplegia. If NIBS is applied when the system is in a given functional state, it will enhance and strengthen the specific distributed functional cortico-cortical (or subcortical) network that is active rather than inducing a non-specific arousal or activation of the system.

The potential for inducing a slowing down of the cognitive decline or even a behavioural improvement in AD or Stroke patients, and the further possibility that these effects become long-lasting, are intriguing, and NIBS study’s results could lead to the development of a new therapeutic approach.
Abstracts of Speakers

S28
Oscillatory brain networks in movement disorders: an insight from combined MEG and intracranial recordings.

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1
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Deep Brain Stimulation (DBS) surgery affords a unique opportunity to record local field potentials (LFP) from sub-cortical structures in awake humans. Combining such recordings with MEG makes it possible to characterise the oscillatory connectivity of DBS targets with the rest of the brain and look at modulation of oscillatory activity and connectivity by tasks and medication. Our analysis of combined LFP-MEG recordings in Parkinson’s Disease (PD) patients with electrodes in the subthalamic nucleus (STN) revealed two distinct resting oscillatory networks: a temporoparietal-brainstem network coherent with the STN in the alpha (7 - 13 Hz) band and a predominantly frontal network coherent in the beta (15 - 35 Hz) band. In addition, we found an increase in high-gamma (60-90 Hz) coherence between the STN and sensorimotor areas during movement with concurrent suppression of coherence in the alpha network. Both alpha and gamma effects were enhanced by dopamine and correlated with clinical improvement. Our more recent results suggest that these networks are not an exclusive feature of STN and PD but are also present in other subcortical structures and other disorders. Our efforts to understand the role of these networks in health and disease will be the subject of my presentation.
A universal constraint on the evolution of brains is that the nervous system’s computational power is limited by its energy supply. By devising an energy budget for the grey matter of the mammalian CNS, I will explain how key design features of the brain are partly determined by the energy supply the brain receives as oxygen and glucose, and how matching of brain energy supply to brain energy use underpins BOLD functional magnetic resonance imaging. I will examine why the white matter uses less energy than the grey matter, and whether myelination really saves energy. I will present a simple account of how information flow through synapses relates to the energy used by the synapses and show that this explains why synapses are unreliable transmitters of information. I will outline why the primary locus of control of the brain’s energy supply, and hence of the generation of BOLD fMRI signals, is in capillaries rather than arterioles.
S30
Fishing for epilepsy genes: Modeling epileptic encephalopathies in zebrafish

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There is growing recognition that novel insights into the etiology and treatment of epileptic encephalopathies will be gained through animal models with experimental alterations in neurological development, leading to the subsequent emergence of clinically relevant behaviors. Over the last decade, the zebrafish (*Danio rerio*) has emerged as a promising *in vivo* model for epilepsy research. The key advantages of zebrafish include the small size and rapid, *ex utero* development of their embryos and larvae, which furthermore exhibit a rich behavioral repertoire that is amenable to both genetic and pharmacological manipulation. Importantly, homologues for about 85% of the known epilepsy genes can be found in the zebrafish genome, underscoring its use as a relevant genetic model organism for human epilepsies. Our laboratory has been developing both genetic and pharmacological epilepsy models in zebrafish, and using these for both the activity profiling of known anti-epileptic drugs, and for the identification of novel small molecules with anti-epileptic activity. Unpublished data from our laboratory show that antisense knockdown of the zebrafish ortholog of *SCN1A* phenocopies Dravet syndrome (severe infantile myoclonic epilepsy). Larvae display spontaneous seizure-like behavior at the developmental stage equivalent to the first year of life in humans, are hyperthermia-sensitive, and respond to anti-epileptic drugs in the same manner as human patients. Furthermore, knockdown in zebrafish of *chd2*, a novel gene also found mutated in 3 patients with Dravet-like symptoms, demonstrated a delay in the onset of seizure-like behavior, similarly to patients in which seizures appeared after the first year of life. Taken together, the progress in this area underscores the potential of zebrafish as a promising *in vivo* bioassay for the functional analysis of novel human disease candidate genes.
Abstracts of Speakers

S31
Brain-computer interface and neuroimaging diagnosis in disorders of consciousness

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In a seminal paper¹, teams from Liège and Cambridge showed the possibility to detect “command following” in patients with disorders of consciousness with fMRI, independent of any motor pathway. This novel technique could help reducing the possible misdiagnosis rate in patients with disorders of consciousness², often suffering severe motor disabilities, provide motor-independent evidence of command following and even, in some cases, permit communication. This last point enables the diagnosis of patients with functional locked-in syndrome (LIS; i.e., fully aware but paralyzed and mute) or non-behavioral minimally conscious state (MCS)³. In the original paper, a patient diagnosed as being in vegetative state/unresponsive wakefulness syndrome was instructed to “imagine playing tennis” and “walking through her house” during an fMRI session. This patient displayed similar brain activations compared to control subjects for both tasks. A few months after the study, the patient behaviorally evolved into MCS. In a follow up study⁴ including 54 patients, 5 were able to willfully modulate their brain activity. One of them was even able to answer simple questions using one task for “yes” and the other for “no”. Building upon this work, more recent research has investigated patients’ abilities to generate “P3-potential” responses to auditory EEG evoked potential BCI paradigms⁵,⁶,⁷,⁸. One of these BCI paradigms enabled our team to establish the correct diagnosis of a complete LIS patient previously behaviorally diagnosed as being comatose⁷. These promising results have paved the way for a new application for Brain-computer Interface (BCI): detecting consciousness in patients with disorders of consciousness. They also illustrated the challenges we are facing.

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Abstracts of Speakers

S32
Role of coma induction in the treatment of refractory status epilepticus

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Status epilepticus (SE) that does not respond to an initial treatment with benzodiazepines and an antiepileptic drug is called refractory status epilepticus (RSE). This develops in about 1/3 of patients with SE and bears a high morbidity and mortality; however, almost no evidence is available to support the choice of specific therapeutic strategies. In this context, the balance between the aim of controlling ongoing seizures on the one side, and the risk of treatment-related side-effects on the other, is a challenging issue. While etiology and age represent the major independent SE outcome predictors, existing studies are controversial regarding the prognostic role of SE treatment, particularly coma induction.

Most expert guidelines recommend tailoring the therapeutic management to the underlying biological background of each patient. Focal RSE without major consciousness impairment should be approached initially without coma; conversely, a rapid escalation towards pharmacological coma and EEG-monitored seizure control appears mandatory in generalized-convulsive forms. For this purpose, midazolam, propofol or barbiturates represent the most popular compounds; however, again, there are no clear data to orient clinicians regarding the optimal extent of EEG suppression and the duration of coma. If RSE continues despite the first coma treatment, several additional options may come into play, such as other anesthetics, further antiepileptic drugs, immunomodulatory agents, ketogenic diet, electroconvulsive treatment, or hypothermia.

One particular SE form occurs in comatose survivors of cardiac arrest. In this setting, given the very high risk of poor outcome, it is often difficult to identify those patients who deserve an antiepileptic treatment; moreover, patients are already in coma. Recent observations suggest that the subgroup of subjects showing SE only after return to normothermia, displaying a background EEG reactivity, preserved cortical somatosensory evoked potentials, and brainstem reflexes, may reach good clinical outcomes if their SE is treated.
The electroencephalogram (EEG) reflects brain electrical activity. A flat (isoelectric) EEG, which is usually recorded during very deep coma, is considered to be a turning point between a living brain and a deceased brain. Therefore the isoelectric EEG constitutes, together with evidence of irreversible structural brain damage, one of the criteria for the assessment of brain death. By using EEG recordings in humans on the one hand, and on the other hand double simultaneous intracellular recordings in the cortex and hippocampus, combined with EEG, in cats, we demonstrate that a novel brain phenomenon is observable in both humans and animals during coma that is deeper than the one reflected by the isoelectric EEG, and that this state is characterized by brain activity generated within the hippocampal formation. This new state was induced either by medication applied to postanoxic coma (in human) or by application of high doses of anesthesia (isoflurane in animals) leading to an EEG activity of quasi-rhythmic sharp waves which we propose to call ν-complexes (Nu-complexes). Simultaneous intracellular recordings in vivo in the cortex and hippocampus (especially in the CA3 region) demonstrate that ν-complexes are first generated in the hippocampus and are subsequently transmitted to the cortex. The genesis of a hippocampal ν-complex depends upon another hippocampal activity, known as ripple activity, which is not overtly detectable at the cortical level. Based on our observations, we propose a scenario of how self-oscillations in hippocampal neurons can lead to a whole brain phenomenon during coma.
The triple stimulation technique (TST) is a collision method that combines transcranial and peripheral nerve stimuli. Three stimuli are given in sequence as to cause two collisions that synchronize the response evoked initially by the transcranial stimulus. Practical implementation of the TST has been substantially simplified by use of dedicated software. The TST circumvents the phase cancellation phenomenon and variability of size of the responses encountered with standard motor evoked potentials (MEPs). By doing so, it allows an accurate quantification of the proportion of motor units of a target muscle that are activated by transcranial stimulation. This proportion, which is close to 100% in healthy subjects, is reduced in disorders affecting cortico-spinal conduction. In patients the TST is two to three times more sensitive than conventional MEPs to disclose deficits of cortico-spinal conduction caused by central conduction block, lesions of axons or of motor neurons. This is especially important since in disorders affecting the central nervous system, conduction deficits are nearly three times more frequent than central motor conduction slowing detected by MEPs. The TST, which further allows quantifying the amount of repetitive discharges evoked by transcranial stimuli, may be used for research and clinical purposes. In disorders affecting the cortico-spinal tract, the method is a useful diagnostic tool that enables follow-up studies and evaluation of treatments.
**S35**  
The triple stimulation technique (TST) in amyotrophic lateral sclerosis (ALS)

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Clinical signs of upper motor neuron (UMN) loss in ALS may sometimes be ambiguous, and masked by the effects of lower motor neuron (LMN) loss. Conventional motor evoked potentials (MEPs) are reduced in ALS, but contribution of LMN loss to this amplitude reduction is often difficult to assess.

The TST circumvents the problem caused by LMN loss, by relating a TST test curve to a TST control curve. The resulting TST amplitude ratio reflects solely conduction within the central motor pathway, while influences of LMN loss are eliminated. At the same time, the TST control curve allows an estimate of the LMN integrity.

We applied TST in 86 abductor digiti minimi muscles (ADM) of 48 ALS patients and in 7 abductor hallucis muscles (AH) of 6 ALS patients. In ADM, the TST disclosed and quantified central conduction failures attributable to UMN loss in 38 sides of 24 patients (subclinical in 15 sides), whereas conventional MEPs detected abnormalities in only 18 sides of 12 patients (subclinical in 2 sides). In AH, the TST revealed central conduction failures in 3 sides of 6 patients, whereas conventional MEPs were abnormally reduced in only 1 side. The increased sensitivity of the TST to detect UMN dysfunction was particularly observed in early cases. In sides with clinical UMN syndromes, the TST response size (but not the central motor conduction time) correlated with the muscle weakness.

We conclude that the TST is a sensitive method to detect UMN dysfunction in ALS. It allows a quantitative estimate of the UMN loss, which is related to the functional deficit. Newer studies have shown that the TST measure also correlates to the abnormality of the corticospinal tract as seen in diffusor tensor imaging. The TST has a considerable impact on diagnostic certainty in many ALS patients and may be used to follow the disease progression and therapeutic trials.
S36
The triple stimulation technique (TST) in multiple sclerosis (MS)

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In MS, the cortico-spinal tract is frequently affected and impaired motor performance is a major cause of disability. Whereas central motor conduction time (CMCT) is easily and reliably measured by motor evoked potentials (MEPs), their sensitivity to detect central motor conduction deficit (CMCD) is rather poor. TST overcomes this disadvantage of MEPs and allows for accurate quantification of CMCD. In a study on 141 MS patients we could show that CMCD measured by TST correlated well with the clinical motor deficit, independently of disease duration and MS type (acute relapsing-remitting versus primary or secondary chronic progressive). In contrast, increase of CMCT did not correlate with clinical motor deficit neither with disease duration, but was found to be a hallmark of chronic progressive MS. Using TST also allowed quantification of Uhthoff's phenomenon, which is thought to reflect a temperature dependent conduction block. Temperature-induced changes of CMCD correlated well with self-assessment of temperature vulnerability of patients and their walking performance. Temperature alterations did not significantly affect CMCT, but the extent of baseline prolongation of CMCT did influence temperature vulnerability, since marked Uhthoff's phenomenon occurred almost exclusively in patients with abnormally prolonged CMCT. Performing TST before and after methylprednisolone treatment for acute exacerbations in MS confirmed decrease of CMCD in parallel to improvement of clinical motor deficit, probably due to partial resolution of central conduction block. However, in patients suffering from exacerbations of primary progressive MS, methylprednisolone treatment was neither associated with significant decrease of CMCD nor with relevant clinical improvement.
Beta Activity in the human EEG

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Beta (15-30 Hz) activity is well recognised in recordings of cortical activity in the human, particularly over motor cortical areas. It is attenuated prior to and during voluntary movement and rebounds following movement. Here I will consider the functional relevance of this activity. A recent theory argues that it promotes the status quo, which, in the motor system, generally means postural muscular activity. The same theory postulates that the suppression of beta activity frees the cortex to engage in more focal, dynamic and information-rich activities so that novel processing is facilitated. Within the motor system, this generally means that new voluntary movements can be effectively made. Excessive synchronisation that is poorly reactive, as in Parkinson’s disease, compromises movement, but at times this state can be beneficial, as when an inappropriate prepotent response has to be suppressed. Indeed, transcranial alternating current stimulation at 20 Hz can impair or improve motor performance in healthy subjects, depending on the precise details of the task.

But how might this potential function of beta also explain the beta rebound that follows movement? I will present evidence that the degree of beta rebound relates to the error made in the corresponding movement. An accurate movement is followed by greater beta rebound, as the existing processing is reinforced. However, inaccurate movements are followed by weaker rebound, consistent with the need to revise the recent motor program.
One of the major unresolved questions is how information can be integrated and how coherent functional states can be established in distributed brain networks. It has been suggested that this problem may be solved in the temporal domain. The basic assumption is that synchronization of neuronal discharges can serve for the integration of distributed neurons into cell assemblies and that this process may underlie the selection of relevant signals. In particular, it has been suggested that fast oscillations at gamma-band frequencies (>30 Hz) may help to entrain spatially separate neurons into synchrony and, thus, may promote the dynamic coordination of neuronal populations. Furthermore, it has been hypothesized that gamma-band interactions may predominate if sensory or motor systems are ready to process novel information, for example when a ‘Go’ signal is expected, a change in a sensory stimulus, or if an unknown novel stimulus is expected to occur. I will discuss supportive evidence for these hypotheses from human EEG and MEG studies, demonstrating a role of gamma-band oscillations in processing of coherent sensory stimuli, in semantic priming and perceptual selection.
Abstracts of Speakers

S39
Motor Evoked Potential Monitoring in both brain and spine Tumor Surgery: Updates and Impact on modern tumor surgery approaches

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Motor evoked potentials (MEPs) describe a time-locked response to follow transcranial (TES) or direct cortical (DCS) applied electric stimulation, which preferentially activates fast conducting axons of the corticospinal tract (CT) and is now widely used for intraoperative neuromonitoring of the motor pathways.

In supratentorial surgery especially in brain surgery, the location of activation of the CT is critical. Experience from vascular cerebral surgery supported evidence that moderate anodal suprathreshold TES as well as anodal direct cortical stimulation, activates the corticospinal tract close to the axon hillock at the border between the grey and the white matter. DCS remains the most focal stimulation possible and thus is favorable used for tumor removal within the vicinity of the motor cortex. MEPs became focus of neurooncological strategies for optimized glioma resection. Combining DCS-MEPs and monopolar cortical/subcortical stimulation mapping techniques in supratentorial tumor surgery as well as combination with intraoperative imaging could achieve supramarginal resection. The proposed subcortical stimulation motor threshold of 2 mA for safe resection has to be confirmed with regard to tumor type and precise location of stimulation.

As been shown in cerebral aneurysm surgery, the ability to detect pure motor hemiparesis in carotid endarterectomy was more recently shown in a multicenter study.

In spine surgery, presence or disappearance ("all-or-nothing" principle) of MEP amplitude criteria is commonly accepted: the presence of any MEPs is related to unaffected motor function or transient paresis, with the exception of radiculopathy. In cervical and thoracic intramedullary spinal cord surgery, the additional implementation of the D-wave helps to distinguish between permanent and transient motor deficit: D-wave preservation is always followed by a recovery of motor function. The latter seems to be applicable in supratentorial surgeries alike.

In summary, MEPs are specific and sensitive for the assessment of the motor cortex and the corticospinal tract. In supratentorial tumor surgery MEPs are increasingly becoming a tool for “functional” guided resection strategies.
Abstracts of Speakers

S40
Intraoperative Neurophysiological Monitoring in Pediatric Neurosurgery: A focus on the sacral system

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Introduction

Intraoperative neurophysiologic monitoring (IOM) is nowadays extensively used in Pediatric Neurosurgery and tethered cord surgery is one of the most useful application. Our goal is to describe and discuss the standard IOM techniques used during tethered cord surgery, in the light of our clinical experience over the past ten years.

Material and Methods

Neurophysiological mapping of the conus-cauda is performed through direct stimulation of these structures and bilateral recording from segmental target muscles. While mapping identify ambiguous neural structures, their functional integrity during surgery can be assessed by monitoring techniques only, such as somatosensory evoked potentials (SEPs), transcranial motor evoked potentials (MEPs) from limb muscles and anal sphincters, and the bulbocavernosus reflex (BCR).

Results:

Between 2002 and 2012, we performed 48 surgical procedures in 47 patients with a tethered cord secondary to a variety of spinal dysraphisms. The monitorability rate was 84% for SEPs, 97% for limb muscle MEPs, 74% for the anal sphincter MEPs, and 59% for the BCR. In all patients but one SEP, MEP and BCR remained stable during surgery. Post-operatively two out of 47 patients presented a significant - though transient- neurological worsening. In six patients an unexpected muscle response was evoked by stimulating tissue macroscopically considered as not functional.

Conclusions

Mapping techniques allow to identify and spare functional neural tissue and, vice-versa, to cut non-functional structures that may contribute to cord tethering. Monitoring techniques, MEP and BCR in particular, improve the reliability of intraoperative neurophysiology. IOM minimizes neurological morbidity in tethered cord surgery.
Mirror movements (MM) are unintended movements on one side of the body which are mirror reversals of the contralateral voluntary ones. MM can be seen in healthy children, whereas in adulthood, the persistence or the reappearance of strong and sustained MM is pathological. Persistent congenital MM can be seen in different conditions, ranging from absence of other abnormalities to severe congenital hemiparesis. Congenital MM not associated with other motor abnormalities may be sporadic or familial. The contribution of transcranial magnetic stimulation (TMS) and other non-invasive electrophysiological techniques to characterize the neural mechanisms underlying persistent congenital MM will be summarized. The neurophysiological hallmark of persistent congenital MM is the presence of fast-conducting corticospinal fibers connecting abnormally the hand area of the primary motor cortex (M1) with both sides of the spinal cord. This has been demonstrated by transcranial electric stimulation and TMS studies, showing that stimulation of one M1 elicits bilateral motor evoked potentials of normal latency in the resting hand muscles. Further insight into the origin of the ipsilateral corticospinal projection was provided by task-related modulation of short-interval intracortical inhibition (SICI). In two otherwise normal patients with persistent congenital MM, during intended unimanual contraction, SICI decreased in the “task” hand but was unchanged in the “mirror” hand compared to rest condition. This SICI dissociation strongly suggests that the ipsilateral pathway was not due to branching of crossed corticospinal neurons and supports the existence of a separate uncrossed projection. Moreover, in the same patients, interference with M1 function by focal TMS showed motor output from bilateral M1 during intended unimanual tasks. These data provide a rationale for rehabilitation aiming to reduce MM by favoring activation of crossed corticospinal neurons from the M1 contralateral to the voluntary task and uncrossed corticospinal neurons from the ipsilateral M1. Finally, altered interhemispheric inhibition and abnormal involvement of the supplementary motor area during both unimanual and bimanual movements has been recently found in 7 patients with congenital MM associated with mutations in the RAD51 gene.
Abstracts of Speakers

S42
Functional and effective connectivity in the developing brain

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Question: The EEG response to transcranial magnetic stimulation (TMS) is a new approach to characterize reactivity and connectivity of the brain. However, studies on children’s TMS-EEG responses are yet few.

Method: We used navigated transcranial magnetic stimulation (nTMS) combined with high-density EEG on 30 healthy right-handed subjects (children, n=10, mean 10.5 yrs; adolescents, n=10, mean 16 yrs and adults, n=10, mean 26 yrs). nTMS was targeted to the primary motor cortex (optimal representation site of abductor pollicis brevis muscle) as well as to associative (frontal and parietal) brain regions.

Results: The waveform, amplitude and distribution of TMS-evoked EEG-responses show developmental changes. The oscillatory activity evoked by TMS stimulation changes in strength and duration with development.

Conclusions: nTMS-EEG co-registration suits well for studying developmental changes in brain activation and connectivity.
Functional and effective connectivity in Epilepsy: overview and insight from TMS-EEG studies

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The investigation of brain connectivity in epilepsy from multi-channel EEG, MEG or fMRI has attracted research interest in recent years. As a result of these studies, epilepsy is being increasingly envisaged as a connectivity dysfunction at the network level. Both scalp and intracranial EEG studies explored the dynamics of epileptiform activity primarily in focal epilepsies and revealed distinct changes in the network structure during the evolution of seizures. According to some evidence, synchronizability appears to be decreased during the ictal state but increases prior to seizure termination thereby challenging the traditional view of epilepsy as a purely hypersynchronous state. The advent of the combination of high density EEG with Transcranial Magnetic Stimulation (TMS-EEG) opened up new possibilities by allowing, for the first time in a non-invasive manner, the recording and mapping of neuronal responses induced by TMS at the cortical level (EEG reactivity) as well as the investigation and modulation of functional connectivity between brain areas. Recent studies suggest that TMS can induce short-lasting alterations in brain connectivity in a subset of epileptic patients that can possibly be used for diagnostic or prognostic purposes. In addition, trains of TMS stimuli applied during epileptiform discharges (EDs) appear to terminate them, in a node-specific manner, and restore the altered network structure to pre-ED levels. In conclusion, the conceptualization of epilepsy as a network disorder provides important novel pathophysiological insight. In addition, it may have practical implications by allowing the identification of functionally important network “hubs” the modulation of which by invasive stimulation techniques might exert antiepileptic effects.
Circadian clocks are present in nearly all tissues of an organism, including the brain. The brain is not only the site of the master coordinator of circadian rhythms located in the suprachiasmatic nuclei (SCN), but also contains SCN independent oscillators that regulate various functions such as feeding and mood-related behavior. Understanding how clocks receive and integrate environmental information and in turn control physiology under normal conditions is important because chronic disturbance of circadian rhythmicity can favor the development of health problems. Genetic modifications leading to disruption of normal circadian gene functions have been linked to a variety of psychiatric and metabolic conditions including depression, eating disorders, obesity and cardiovascular disease. It appears that clock genes play an important role in all organs and tissues. I will present evidence for a molecular basis of the circadian clock and discuss how clock disorders may affect health.
Abstracts of Speakers

S45
Circadian rhythms in neurological disease

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Questions

All biological functions are under the control of biological clocks. This includes rhythms in the sleep-wake cycle and in physiological functions of the brain. It is therefore conceivable to understand that regulatory mechanisms of circadian rhythms involved in brain functions may be modified/disturbed/abolished in certain diseases.

Results and Conclusions

Recent studies have evidenced that in various neurodegenerative diseases such as M. Parkinson, M. Alzheimer, Dementia, M. Huntington, fatal familial insomnia as well as during aging biological rhythms in activity/rest, sleep regulation, body temperature, and in the hormone concentrations of cortisol and melatonin are altered and/or abolished. These observations let assume that the biological clock(s) and its timing system on the organism can be affected both by the aging process as well as in disease entities of the CNS. Rhythm disturbances in physiological functions can be used to both in diagnostics of neurological diseases as well as in controlling therapeutic measures. Since light is the most important trigger mechanisms for the biological clocks, this can also be used to alleviate the severity of the disease.
Critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) are common neuromuscular conditions in the Intensive Care Unit (ICU). They are manifestations of sepsis and multiple organ failure (critical illness). They present anytime after the first week in the ICU as difficulty in weaning from the ventilator and limb weakness. Septic encephalopathy often precedes the neuromuscular manifestations. Because of difficulties in clinical assessment neurophysiological studies are a great importance in diagnosis. Motor and sensory nerve conduction studies and needle EMG will identify and characterize these conditions. Muscle biopsy is often helpful. Recovery often occurs in CIP, CIM or when both occur in the same patient but a significant number of patients will have incomplete recovery and some may remain severely weak, and on a ventilator.

It is important to identify these patients so that physiotherapy, rehabilitation procedures and counseling can be instituted. Unfortunately, many of these patients escape detection in the ICU or afterwards. Hence, they may be encountered for the first time undiagosed in various general hospital or outpatient settings.

Neuropathic pain is often related to peripheral pathology of small nerve fibers, the nociceptors. The skin is a window into the peripheral nervous system that helps us analyze nociceptor density and morphology. Although intraepidermal nerve fiber density (IENFD) does not correlate closely with pain intensity, it may help detect small fiber neuropathy, which otherwise remains undiscovered by routine neurophysiology. This lecture will present established and novel methods of analyzing skin innervation. Examples of pain disorders, in which IENFD is altered, will be given.
Abstracts of Speakers

S48
Microneurography - a neurophysiological research method for understanding mechanisms important for neuropathic pain.

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Questions
Neuropathic pain is caused by lesions or diseases affecting the somatosensory system. However, the mechanisms for neuropathic pain are diverse and complex and still partly unknown and it is still a puzzle that the same diseases and lesions in some patients do not cause pain. Most of the research on mechanisms has focused on animal models or experimental models in healthy subjects.

Methods
Microneurography allows us to record directly from nociceptors in awake humans. This research field has previously shown that there are several subtypes of C-nociceptors in healthy subjects and that these subtypes probably have different roles in acute and chronic pain states.

Results
Registrations from patients with neuropathy with and without pain performed by different research groups has revealed several types of pathology including spontaneous activity, multiple spikes and mechanical sensitization in afferent nociceptors (1-4). These mechanisms are thought to be important for the development and maintenance of chronic neuropathic pain. In addition, a large number of probable degenerated fibers has been found (5). However, their role in pain is so far uncertain. Lately, we have also been able to show patterns of activation of C-fibers that might be directly coupled to pathology in sodium channels.

Conclusions
Microneurography recordings in patients with peripheral neuropathic pain has revealed several mechanisms that might be important for the maintenance of neuropathic pain. This could be helpful both in the prevention of but also when searching for better treatment for neuropathic pain.

Since standard electrical nerve stimulation with recording of somatosensory evoked potentials (SEP) only is a test for thickly myelinated Aβ-fibers and the dorsal column pathway, they are not suitable to examine the nociceptive system. As functional test for the nociceptive system, recording of laser-evoked potentials (LEP) has been established and is recommended as diagnostic test in the EFNS guidelines for the assessment of neuropathic pain (Cruccu et al. 2004, 2010). Induced by brief contact-free infrared noxious heat stimuli, LEP reliably indicate lesions - by means of amplitude reduction and/or latency prolongation - of peripheral thinly myelinated fibers like in small fiber neuropathies, spinothalamic tract lesions like in MS, syrinx or trauma, and brain stem lesions like in Wallenberg’s syndrome. This will be demonstrated in clinical case examples. An important aspect will be the relationship of ongoing neuropathic pain and LEP amplitudes, and LEP as a potential predictor for surgery outcome after spinal root decompression. Finally, a brief look at alternative methods to record evoked potentials following stimulation of electrical, mechanical, heat, and cold stimuli will round up this overview on pain-related brain potentials.
Neuropathic pain is one of the most stressful subjective experiences yet with limited biomarkers for objective and quantitative assessments. These features create the difficulties for exploring therapeutic strategies. Various nerve injuries lead to neuropathic pain including diabetic neuropathy, post-herpetic neuralgia, and neuropathies due to chemotherapeutic agents, such as taxol and cisplatin. Neuropathic patients frequently experience heat-induced hyperalgesia, such as burning foot syndrome, tingling, and electric-shock sensations which pose difficulty in quantifying and assessing these symptoms because of their subjective nature. Over the last decade, imaging signatures, especially functional MRI (fMRI) have become essential and integrated approaches to “visualize” neuropathic pain in the brain, in particular task-activated fMRI. This talk will review advances in imaging studies of neuropathic pain, in particular, focusing the “burning” feeling of patients with diabetic neuropathy, the most frequent etiology of neuropathies. We have established a paradigm to record neurophysiological signatures in the brain by applying contact heat stimulation (Diabetes Care 33:2654-2659. 2010). Based on these paradigms, we demonstrated brain activations with unique and shared patterns in different brain regions on innocuous heat vs. noxious heat stimulations. Arming with techniques of contact heat evoked potential (CHEP) and heat-activated fMRI, we document enhanced limbic and striatal activations in diabetic patients with heat hyperalgesia (Hum Brain Mapp 34:2733-2746, 2013). These approaches not only provide imaging signatures for a unique type of neuropathic pain (burning foot syndrome) but also offers new therapeutic targets for neuropathic pain.
Abstracts of Speakers

S51
tDCS: methodological update 2014

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Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation tool suited to introduce plasticity in the human brain. Beyond physiological alterations of cortical excitability, and activity, it has been demonstrated that tDCS is able to modulate plasticity-related cognitive, affective, and motor processes in health and disease. However, knowledge about physiological effects, and optimally suited stimulation protocols to induce respective effects is still limited. This talk will give an overview about recent developments with regard to these topics. It will cover newly obtained knowledge about tDCS physiology, including network alterations, new tDCS protocols which enable strengthening, and prolongation of the effects, and enhanced focality of stimulation. It will also focus on important aspects for tailoring stimulation protocols, like non-linear effects of tDCS, and sources of variability, in the healthy brain, and neuropsychiatric diseases.
Abstracts of Speakers

S52
Overview of VEMPs (vestibular-evoked myogenic potentials).

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The vestibular apparatus is a difficult end organ to assess due to its size and location, with functional assessment being often more useful than imaging. Despite its strong electrophysiological projections to neck and eye muscles, conventional electrophysiological techniques had little role and typical clinical assessment was highly dependent upon the vestibulo-ocular reflex generated by the horizontal canal. In this context, a simple method to measure short latency reflexes evoked by the otolith organs was an important addition to previous practice and probably explains the rapid uptake of VEMPs as an additional diagnostic method, since their description in 1994 (Colebatch et al., 1994).

Since the initial report of cervical VEMPs (cVEMPs - recorded from over the sternocleidomastoid muscles), it has become possible to measure responses evoked in an eye muscle - the inferior oblique (thus oVEMPs: Rosengren et al., 2005). This symposium has been arranged to review advances in knowledge in a number of areas relating to VEMP testing: the induced changes in motor unit firing that underlie the surface responses; the role in diagnosis, best exemplified by the important role of VEMPs in diagnosing superior canal dehiscence (SCD); and upstream, cortical projections.

Areas of controversy remain. Although it appears that high frequency (500 Hz) stimuli mainly activate irregular otolith afferents (Curthoys et al., 2006), it is not clear to what degree the activation of saccule and utricle are altered by the use of either air of bone conducted stimuli and to what extent this is influenced by the choice of target - either ocular or cervical. Lower frequency stimuli - taps and impulsive stimuli, are likely to activate a somewhat different population of vestibular afferents, judging by the different changes seen with ageing (Colebatch et al., 2013).

Finally it has become important to try to standardise the methods used to record VEMPs so that the findings can be compared between laboratories and to maximise the benefit and reduce the risks of testing. Progress has been made for the cVEMP and these recommendations will be presented.

References


Single motor unit firing changes in VEMPs

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Vestibular evoked myogenic potentials (VEMPs) are muscle reflexes evoked by vestibular activation with loud sound, skull vibration or galvanic stimulation. The most common forms are cervical VEMPs (cVEMPs) recorded from the neck muscles and ocular VEMPs (oVEMPs) recorded from the eye muscles. These reflexes are typically recorded using surface electrodes placed over or close to the target muscles. However, surface recordings do not necessarily give an accurate or complete picture of the activity of the underlying muscles. We have therefore investigated the muscle activity producing these reflexes in a series of experiments using single motor unit recordings. We have investigated the cVEMP by comparing the effects of different stimulus types and sites of recording within the sternocleidomastoid muscles. Preliminary data on cVEMPs in the posterior neck muscles will also be presented. We have also recorded the motor unit activity underlying the oVEMP by recording from the inferior oblique and inferior rectus eye muscles. Motor unit activity in human eye muscles during the vestibulo-ocular reflex (VOR) is not well understood, as the associated head and eye movements normally preclude single unit recordings. Application of VEMP stimuli, which elicit only small head and eye movements, has now made this type of recording possible. Synchronous, short-latency bursts or gaps of firing were seen in all of the muscles tested and the timing and polarity of the effects differed according to the stimulus and muscle tested. This research identified the inferior oblique as the eye muscle of origin of the clinical oVEMP, thus validating the physiological basis of this test of otolith function. Single motor unit recordings provide a window into neural activity in humans that is usually only examined using animal models and help identify the pathways of vestibular reflexes.
VEMPs in the diagnosis of superior canal dehiscence (SCD)

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Testing VEMPs has its key clinical significance not only for testing otolith and vestibular nerve function but also for diagnosing superior canal dehiscence (SCD). This syndrome is caused by absence of bone overlying the superior semicircular canal. The diagnosis is based on computerized tomography (CT) images showing a dehiscence of bone separating the labyrinth from the middle cranial fossa. The patients have different auditory/vestibular symptom due to the added “mobile window”, including a vestibular hypersensitivity to sounds. A typical feature for this syndrome is thus, sound induced vertigo and large VEMPs with low thresholds. This specific VEMP finding is important in view of the fact that CT cannot distinguish a dehiscence from thin bone cover. Test of VEMPs do also normalize after corrective surgery and can be used for postsurgical follow-up.

The routine stimulus used in cervical VEMP (cVEMP) testing is high-intensity 500 Hz tone bursts. However, cVEMP is an inhibitory reflex, and cVEMP amplitude to high-intensity stimuli does not consistently distinguish SCD patients. This non-functioning is most likely due to saturation. Consequently, for diagnosing the vestibular hypersensitivity one has to rely on a stimulus with less intensity or on threshold measurements. In contrast, ocular VEMP (oVEMP) is an excitatory reflex and may therefore have a greater potential for indicating a vestibular hypersensitivity to sounds. Several studies have also demonstrated large oVEMP amplitude with a low threshold for SCD patients. In addition, there seems to be other idiosyncrasies in these patients: both the stimulus frequency dependency and the latency of the response are different in SCD patients compared with normals, suggesting a partly different stimulus path.
Abstracts of Speakers

S55
Standardisation of VEMPs

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Background:

Cervical vestibular evoked myogenic potentials (cVEMP) are electromyogram responses evoked by high-level acoustic stimuli recorded from the tonically contracting sternocleidomastoid (SCM) muscle, and have been accepted as a measure of saccular and inferior vestibular nerve function. As more laboratories are publishing cVEMP data, there is a wider range of recording methods and interpretation, which may be confusing and limit comparisons across laboratories.

Objective:

To recommend minimum requirements and guidelines for the recording and interpretation of cVEMPs in the clinic and for diagnostic purposes.

Material and Methods:

We have avoided proposing a single methodology, as clinical use of cVEMPs is evolving and questions still exist about its underlying physiology and its measurement. The development of guidelines by a panel of international experts may provide direction for accurate recording and interpretation.

Results:

cVEMPs can be evoked using air-conducted (AC) sound or bone conducted (BC) vibration. The technical demands of galvanic stimulation have limited its application. For AC stimulation, the most effective frequencies are between 400-800 Hz below safe peak intensity levels (e.g. 140 dB peak SPL). The highpass filter should be between 5-30 Hz, the lowpass filter between 1000-3000 Hz, and the amplifier gain between 2,500-5,000. The number of sweeps averaged should be between 100-250 per run. Raw amplitude correction by the level of background SCM activity narrows the range of normal values. There are few publications in children with consistent results.

Conclusion:

The present recommendations outline basic terminology and standard methods. Because research is ongoing, new methodologies may be included in future guidelines.
Neural signatures of speech localization and recognition in bilateral cochlear implant users

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In normal hearing adults, auditory speech is processed within a postero-dorsal “where” pathway, mediating stimulus localization and an anterior-ventral “what” pathway, mediating stimulus identification. Postlingual deafened adults with bilateral cochlear implants (CIs) often show high speech recognition performance but localization of speech is poor, in particular when discriminating stimuli from the same hemifield. Whether this difficulty relates to the inability to encode the artificial stimuli in specialized auditory cortical pathways or to a possible degradation in these pathways is unknown. In this talk data from an EEG study examining auditory localization and recognition processing in CI users and normal hearing adults will be presented. We examined event-related potentials (ERP) and oscillatory responses to localization and recognition of auditory syllables presented to the right hemifield. We observed larger N1 ERP amplitudes in CI users in the localization compared to the recognition task. Moreover, source localization of oscillatory activity revealed stronger beta-band desynchronization after 200 ms in the postero-dorsal pathway for the localization compared to the recognition task in CI users. This suggests that spatial discrimination processing of auditory syllables in CI users includes similar structures to those previously found in normal-hearing adults. Our finding of seemingly intact auditory cortical pathways implies that the development of signal processing strategies for preserving unambiguous binaural cues, possibly including binaurally coherent jitter, may improve auditory localization abilities of bilateral CI users.
S57
Phonological reorganization of the postlingual deaf and its implication for cochlear implant outcome

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Not having access to one sense profoundly modifies our interactions with the environment, in turn producing changes in brain organization. Deafness and its rehabilitation by cochlear implantation offer a unique model of brain adaptation during sensory deprivation and recovery. Oral communication difficulties induced by post-lingual deafness shape cortical reorganization of brain networks already specialized for processing oral language. Cochlear implants (CI) work well, yet the outcome is not fully accounted by the data routinely available to the clinician. Using fMRI in deaf adults, candidate for a cochlear implantation, and matched normal hearing controls, we explored phonological processing from written material. For easy rhyming tasks, some deaf subjects relied on the ventral lexico-semantic route and right areas, not usually involved in phonological processing. When the tasks were designed to force the use of the dorsal phonological route, some deaf subjects processed phonology faster than hearing controls, without accuracy loss. This paradoxical cognitive gain was mediated by a functional interaction between early visual cortex and the left inferior prefrontal cortex, which by-passed the graphemic and phonological steps usually taking place in left fusiform gyrus and superior temporal cortex. Accelerated phonological processing was accounted for by the recruitment of the right superior temporal sulcus, an area usually involved in paralinguistic processing. In the two experiments, those deaf subjects who showed phonological reorganization of right areas lately became poor CI performers. These data suggest that maintaining active left auditory-based phonology may preserve the possibility to revert to hearing. By contrast optimizing written communication (reading) engaging right areas may compromise future auditory restoration.
S58
Crossmodal plasticity and prognosis of auditory recovery after cochlear implantation in postlingual deaf patients

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Question

The cochlear implant is a neuroprosthesis that allows profoundly postlingual deaf patients to recover speech intelligibility through long-term adaptive processes to build coherent percepts from the coarse information delivered by the implant. Further CI users preserve a striking speech reading ability acquired during the period of deafness while they have reached optimal auditory recovery. Such skill in speechreading is associated to abnormal crossmodal activations regions of the superior temporal cortex normally devoted to processing human voice. These abnormal activity levels diminish with post-implantation time and tend towards the levels observed in normals. However, the temporal evolution of recovery can greatly varies across subject during the first year post-implantation.

Methods

Because the strategy adapted by CI users for speech comprehension is linked to the cortical crossmodal plasticity, we searched for brain regions whom the level activity at time of implantation is correlated with the level of auditory recovery several months later. We used Pet scan brain imaging to analyse the correlation between brain activity at the moment of implantation and auditory word perception scores 6 months later.

Results

Correlations were observed in a set of areas outside the auditory cortex with the highest positive correlation in the right occipital visual cortex. Other correlated areas included the posterior temporal cortex known for audiovisual integration and the left inferior frontal area involved in cognitive functions including speech processing. Thus the initial high activity of the visual cortex provides the best potential to favour auditory recuperation.

Conclusions

Our results suggest the existence of a facilitatory synergy that links both visual and auditory modalities so that a better functional level of one modality leads to the better performance of the other. Such cooperation may be a reflection of the multisensory nature of speech processing.
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S59
Migraine with and without aura

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Few neurophysiological studies have compared migraine with (MA) and without aura (MO), while most of them described abnormalities of spontaneous and specially evoked brain electrical activity in separate groups of migraine patients.

Previous studies employing Steady State Evoked Potentials (SSVEPs) at different contrast and frequency of stimulation showed differences between MA vs MO patients, thus suggesting an involvement of the visual associative cortex in patients reporting aura symptoms (1). Recently different pattern of functional and effective connectivity emerged in EEG of MA vs MO patients under repetitive flash stimulation, probably subtended by increased cortical activation in migraine with aura, and compensatory phenomena of reduced connectivity and functional networks segregation, occurring in patients not experiencing aura symptoms (2). A more recent approach to multichannel EEG under visual stimulation confirmed increased non linear Granger causality in beta band and increased information flow toward frontal regions in 15 MA compared to 15 MO patients, which may outline important pathophysiological difference between migraine phenotypes. An increased capacity in cortical connections and transfer information may subside the perception of aura symptoms, probably favoring the progression of cortical spreading depression.


Figure legend:

Statistical probability maps representing the significant differences between migraine with and without aura in regard to GC information flow across all pairs of electrodes for beta rhythm. The histograms report the amount of information transfer in both directions which are able to differentiate the two groups.

figure 1
Pain direction: exploding or imploding?

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In adult migraineurs, pain direction (exploding or imploding) has been associated with a different response to botulinum toxin treatment. Thus far, there has been no objective evidence in favour of the hypothesis that pain direction depends on different pathophysiological mechanisms.

We conducted some experiments to investigate whether migraine adolescents with pain directed inside (imploding pain) and outside (exploding pain) the head have different mechanisms underlying their migraineous syndrome.

In the first study, concerning the somatosensory system excitability, 20 migraine children were recruited. Ten patients had exploding pain (EP), while 10 patients complained of imploding pain (IP). The recovery cycle of the short-latency somatosensory evoked potentials (SEPs) was measured and compared between both patients' groups. The frontal N30 amplitude recovery cycle was shorter in IP than in EP patients, thus suggesting higher brain excitability in those patients complaining imploding pain (Fig. 1).

Twenty migraine children, 9 with EP and 11 with IP participated to the second study, investigating the psychophysiological mechanisms of spatial attention. The amplitude of the N140 SEP component was measured in a neutral condition (NC), in which patients were asked to disregard the electrical stimulation, and in a spatial attention condition (SAC), in which patients had to count silently brief mechanical targets, made manually by a gauze ball on the tip of the first and the second finger of the hand ipsilateral to electrical stimulation. The N140 amplitude increase during SAC, as compared to the baseline, was higher in IP than in EP patients. This suggests that, as compared with the EP migraineurs, the IP patients had to use a higher amount of attentional resources to accomplish the task.

In conclusion, the present studies suggest that pain directionality represents an important phenotypic element which can be associated with different pathophysiological mechanisms.

Legend

**Figure 1.** Mean SEP amplitudes at different interstimulus intervals (ISIs) in IP (upper) and EP (lower) patients. Black, white, and grey bars correspond to 5 ms, 20 ms, and 40 ms ISIs, respectively. The SEP amplitudes in the double stimulus conditions are expressed as percentage of the corresponding baseline amplitudes, considered as 100%.
Abstracts of Speakers

S61
Spatial characterization of epileptogenic HFOs in intracranial- and scalp EEG

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Epilepsy is one of the most frequent neurological diseases and 30% of patients are refractory to medication. For these patients successful surgical treatment largely depends on the identification of epileptogenic zone. High-frequency oscillations (HFOs) between 80 and 500Hz, which can be recorded with intracranial EEG, may be novel markers of the epileptogenic zone.

This presentation reviews publications which show the link between HFOs and the seizure onset zone. Moreover correlations between the surgical removal of regions generating HFOs and a seizure free post-surgical outcome (for review see Jacobs et al., 2012). The clinical application of HFOs in different types of epilepsies will be discussed (Kerber et al., 2013). Limitations in the clinical application of HFO are still present due to difficulties in identifying HFOs as well as differentiating between physiological and epileptic oscillations. Different methods for improved analysis such as automatic detection, pattern identification and evoking HFOs by electrical stimulation will be discussed (Duempelmann et al., 2012, Melani et al., 2013, van't Klooster et al., ).

A new and very important discovery in the field of HFOs is the identification of HFOs in scalp EEG. Scalp HFOs in the ripple range (80-250Hz) are much less frequent than intra-cranially recorded HFOs. Nevertheless they seem to be more specific for seizure onset areas than spikes and simultaneous scalp and intracranial EEG recordings could show clear cortical correlates of scalp HFOs (Andrade-Valenca et al. 2011, Zelmann et al., 2013). Data from larger patient cohorts are still missing, but if scalp HFOs can be routinely identified, this might widen the yield of HFO analysis to a large group of patients with non-refractory epilepsy.

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The temporal relationship between epileptogenic HFOs and disease activity.

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Rates of high-frequency oscillations (HFOs: ripples: 80-250 Hz; fast ripples: 250-500) vary over time and might be an indicator of disease activity in epilepsy. This could be useful to predict responses to therapy and likelihood of seizure recurrence.

HFOs increase when anti-epileptic medication is reduced, in contrast to spikes. This means that, although HFOs often co-occur with spikes, they behave more like seizures, which increase after medication withdrawal. A similar effect is found when reducing propofol before surgery. Etomidate administration activates seizures, spikes and HFOs. Resection of epileptogenic areas leads to a decrease of spike and HFO rates in brain tissue outside the resected area. Overall HFOs seem to mirror likelihood of seizures. The relation between spikes and seizures and between HFOs and spikes is less consistent.

What is the direct temporal relation between high-frequency oscillations (HFOs), spikes and seizures? Spikes and HFOs often co-occur, but the spikes precede the onset of the co-occurring HFOs. HFOs that co-occur with spikes decrease with medication decrease likewise spikes, in contrast to HFOs that do not co-occur with spikes. Single-pulse stimulation can evoke HFOs, but usually these co-occur with delayed spike-like events. So if there is a relation of cause and effect, it seems that spikes facilitate HFOs rather than HFOs evoke spikes.

HFOs increase before seizures and during seizure onset, while spike rates remain stable or decrease preictally. Seizures are sometimes preceded by a spike. Spike rates increase after seizures, while the rate of HFOs remain stable after seizures. HFOs occur before the first spontaneous seizure in kanaic acid rats and only rats with HFOs ultimately show seizures. The question remains whether HFOs are just epiphenomena that mark a higher seizure susceptibility or actually trigger seizures. HFOs appear as separate events, but might be a sign of non-linearity in the epileptonic areas. The amount of HFOs per area correlate to lower functional connectivity, which diminishes before seizures. The increase in HFO rate preceding seizures might result from network changes.

In conclusion, HFOs are local events that respond to external events in a way that suggests them to be a biomarker that mirror epileptic disease activity. These local events might be a sign of instability and alternative measures could be more specific than event rates.
High frequency oscillations (HFOs) have been studied particularly in the interictal period. Their location appears to be a good indicator of the epileptogenic zone in patients with focal epilepsy. Because of this relationship with epileptogenicity, it is of interest to know if they vary systematically in peri-ictal period, particularly prior to seizures. Experimental work in the pilocarpine model of temporal lobe epilepsy, ripples and fast ripples appear to be specific preictal markers of different seizure types (hypsersynchronous vs. low amplitude fast activity, Levesque et al, 2012). During pre-ictal periods in human patients, there seems to be a non-specific increase in ripples and fast ripples prior to seizure onset and after seizure onset. This is accompanied by a surprising increase in activity of the lower traditional frequency bands (Perucca et al, in press). It appears that there is a discrepancy between experimental and human data, and human seizures are often preceded by an increase in activity in all frequency bands, which may reflect a shift in the state of the brain different from a shift in the level of alertness.


Cortical control of the hand: movement generation and action observation

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The corticospinal tract is derived from multiple regions of the cerebral cortex and through its descending collaterals and terminations makes connections with multiple levels of the sensorimotor system, and exerts a wide degree of influence over different spinal circuits. Although all mammals possess a corticospinal tract, this system actually shows a remarkable degree of variation across species, which probably reflects the relative importance to those species of the different functions to which it can contribute. In primates, the corticospinal projections from the primary motor cortex have long been implicated in the generation of movement, and a large body of work has shown strong relationships between corticospinal discharge and various parameters of movement, such as the force and direction. It has also been possible to show direct causal effects of corticospinal activity on motor output, and to attribute these to direct cortico-motoneuronal (CM) projections to motoneurons of hand muscles. Recently it has been possible to extend these findings to show the involvement of CM projections in skilled tool use. Nevertheless, it is also clear that these direct CM projections do not work in isolation from other descending systems. It is also clear that although these systems can, to some extent, compensate for damage to the corticospinal projections, key features of skilled hand function are permanently lost.

Interestingly, motor cortex can also be active during processes that do not require movement generation *per se*. These include mental rehearsal of motor acts and, intriguingly, observation of the actions of others. Recent work shows that even M1 corticospinal neurons are active during action observation, that is, they behave like ‘mirror neurons’. The study of the discharge of identified corticospinal neurons during action observation and during action execution by the monkey itself provides some clues as to what distinguishes the level of corticospinal activity normally associated with the generation of a voluntary movement. It also reveals the key role of *suppression* of corticospinal neuron activity during certain types of movement, observed and executed.

Funding: The Wellcome Trust, UCL Grand Challenge Scheme
Abstracts of Speakers

S65
Plasticity induced by non-invasive brain stimulation: review of recent progress

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Systematic non-invasive brain stimulation techniques date back to the beginning of the 19th century. The development of the voltaic pile led to first applications of DC stimulation with controlled current intensities in 1801, usually by listing series of treatments of individual patients. Since no controllable “biomarker” for a systematic evaluation of stimulation parameters was available most of these approaches were given up over time. TMS of the motor cortex allows for easy quantification of cortical excitability by measuring the motor evoked potential. Most of our „biomarker data“ on transcranial stimulation effects rely on this technique. In addition MRI, EEG, PET and other techniques provide a conceptual framework which enables hypothesis guided brain stimulation for increasing or decreasing cortical functions and for treatment of patients. This talk will focus on recent progress in transcranial alternating and random noise stimulation techniques.
The combination of pharmacology and transcranial magnetic stimulation (pharmaco-TMS) has considerably improved our understanding of the effects of TMS on the human brain. This presentation will highlight important knowledge and recent advances in the contribution of pharmaco-TMS to the following fields: (1) Characterization of TMS measures of motor excitability (such as motor threshold, motor evoked potential amplitude, cortical silent period duration, paired-pulse measures of cortical inhibition and facilitation) by CNS active drugs with a specific mode of action; (2) characterization of the CNS effects of drugs with unknown modes of action by TMS measures of motor cortical excitability; (3) effects of CNS active drugs on TMS-induced plasticity; (4) TMS-induced changes in endogenous neurotransmitters and neuromodulators; (5) Effects of CNS active drugs on TMS measures of motor cortical excitability in neurological disease.

The content of this lecture is a summary of highlights of a solicited review to be published in Clinical Neurophysiology in 2014.
History will judge the development of magnetic resonance imaging (MRI) as one of the major landmarks in neuroscience, bringing the post mortem neuropathological insights of Charcot and other pioneers to the in vivo routine clinical domain. While MRI retains an important role in the exclusion of alternative pathology in those suspected to have amyotrophic lateral sclerosis (ALS), advanced applications now provide a parallel role as a source of much-needed biomarkers. Neuroimaging more widely continues to provide important clues to pathogenic mechanisms in ALS, which is now firmly established as a multiple system cerebral disorder. With the increasing understanding of brain function in terms of networks, neuroimaging is currently the leading method to study ALS as a motor system, not just neuronal, degeneration. Developments in computational neuroscience and biostatistics mean that combined structural and functional cerebral connectivity can now be studied non-invasively, and this is being extended to the pre-symptomatic period through the study of those carrying genetic mutations linked to ALS. Meanwhile the potential of MRI at routine clinical scanner field strengths, to provide biomarkers sensitive enough in the context of a therapeutic trial is being tested through emerging international collaboration. MRI may ultimately be one part of a multimodal biomarker panel that includes biofluid and neurophysiological measurements.
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S68
Cortical systems underlying the flexible deployment of attention

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Allocation of attentional resources rests on predictions about the likelihood of behaviourally relevant events. There is now accumulating evidence that the inference of stimulus likelihood can plausibly be described by hierarchical Bayesian models that provide a principled prescription of how predictions are updated after new observations. These models can be regarded as variants of predictive coding - in which updates are determined by prediction errors that are weighted by their salience or expected precision. I will present a series of studies employing a novel variant of Posner’s location-cueing paradigm in which the proportion of valid trials (percentage of cue validity) was manipulated across the experiment to create volatile contingencies. The subjects responded with saccadic eye movements to left and right target stimuli preceded by spatial cues (arrows). Computational modelling results of saccadic response speeds as well as functional magnetic resonance imaging (fMRI) data will be presented to shed light on the computational and neural mechanisms underlying flexible attentional control in relation to Bayesian inference. Moreover, data from a psychopharmacological study with the cholinergic agonist galantamine will be shown to illustrate how psychopharmacological agents may affect the computational mechanisms underlying the updating of perceptual beliefs according to Bayesian principles. In sum, the presented findings shall provide further insights into the neural and neurochemical processes of trial-wise inference on the environmental statistics that influence attentional selection.
Abstracts of Speakers

S69
Descending inhibition and facilitation in complex regional pain syndrome (CRPS)

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Dr Lone Knudsen will discuss central mechanisms of pain modulation in complex regional pain syndrome (CRPS). Dr Knudsen’s studies on pain modulation in healthy volunteers and patients with CRPS indicate that, in addition to mechanisms which inhibit pain sensations bilaterally, mechanisms which produce hemilateral effects (facilitatory and inhibitory) on the site of the initiating stimulus exist. She will discuss the potential supraspinal sites underlying these mechanisms. The findings will be discussed in relation to mechanisms of chronic pain and the spread of pain and sensory disturbances that occur in CRPS.
This talk will cover recent attempts to generate known oscillatory signature of mental processes (identified by electroencephalography) through targeted (frequency-tuned) interventions into brain oscillations (controlling of brain rhythms by brain stimulation). This to bias brain oscillations and thereby task performance in specific directions. The talk will focus on the regulation of perception by brain rhythms in terms of “when in time” a stimulus is perceived, “where in space” it is perceived, and “what of the stimulus” is perceived (stimulus content). The results demonstrate rapid cycling of visual perception at frequencies of underlying brain rhythms after their phase reset (by external stimulation), spatial biasing of perception across the visual fields after promotion of parietal alpha signatures through rhythmic transcranial magnetic stimulation (TMS) and biasing of perception towards local or global stimulus features after parietal rhythmic TMS at beta versus theta frequency. Overall, this suggests a causal role of parieto-occipital brain oscillations in the regulation of perception, amenable to controlled interventions by brain stimulation.
Sensory and association areas of the human brain are organized in a distributed manner, requiring an efficient communication mechanism to integrate responses across different cortical regions to guide behavior. How the human brain can achieve this relatively fast and efficient integration of information? A growing amount of studies suggests phase synchronization as a fundamental neural mechanism in cognitive functions requiring large-scale integration of distributed neural activity, supporting both neural communication and plasticity. However, the causality of this communication mechanism for performance is unclear. Here we show that enhancing or diminishing task-related synchronization of oscillations by transcranial alternating current stimulation (tACS) results in antagonistic effects on executive function performance, thereby providing evidence that segregated phase coupling causally contributes to executive functions in humans. These results suggest that phase-dependent timing of neural oscillations can contribute to interregional communication in the service of guiding behavior. More generally, these findings support the idea that oscillatory synchronization in brain networks is indeed functionally important for integrating information that is neurally encoded in a distributed fashion. Last, our study shows that the non-invasive electrical stimulation protocol introduced here can be employed to investigate the causal relevance of interregional oscillatory cortical activity for cognition and behavior. Moreover, the possibility that tACS can successfully be used to artificially induce coupling or decoupling of behaviorally relevant brain rhythms between segregated cortical regions might be of potential relevance for the treatment of neurological diseases, such as Alzheimer’s disease and schizophrenia, where abnormal behavior correlates with “out-of-phase” interregional brain synchronization.
Visual mismatch negativity (vMMN) in clinical studies - a review

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Compared to the clinically oriented auditory mismatch negativity (aMMN) studies, clinical vMMN studies are much fewer in number. Nevertheless, several interesting results were obtained, which support and complement clinical aMMN results, as we will review in this presentation.

A large number of aMMN studies have been conducted in patients with schizophrenia, with the most important results as follows: (1) aMMN deficiency in them reflects the deficient functioning of the NMDA-receptor system and (2) their cognitive/functional deficit, in part due to (1); (3) aMMN deficiency predicts, in clinically high-risk subjects, psychosis onset. vMMN results in schizophrenia patients show an analogous vMMN deficit, with a focus over posterior extra-striate cortical areas (Neuhaus et al. 2013). Previously, Urban et al. (2008) found in these patients a vMMN deficit for direction change of irrelevant peripheral movement. Importantly, in analogy to the frequency-aMMN deficit, the vMMN deficit was not present immediately but only after the illness had lasted for some time (in this case, 3 years). This vMMN deficit was attributed to the dysfunction of the magno-cellular visual pathway which depends on the NMDA-receptor functioning, signifying another interesting similarity with aMMN results.

Some further important clinical vMMN findings are: (a) a normal vMMN in high-functioning autistic young adults, in contrast to their deficits in attentive top-down processing (as indexed by P3 abnormality) (Maekawa et al. 2011); (b) a relationship between the duration of methamphetamine misuse and the vMMN deficit; (c) a vMMN deficit in patients with bipolar disorder (Maekawa et al. 2013), consistent with a part of aMMN studies; (d) vMMN results on aging and Alzheimer´s disease (to be reviewed in separate talk by Andrea Tales).
Visual mismatch negativity to changes in facial expressions in depressed and control participants

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We studied whether visual mismatch negativity (vMMN) can be elicited in an ignore condition when rarely presented “deviant” facial expressions violate regularity formed by repeated “standard” faces, and whether this component is modulated in depression. In the first study, ERPs to neutral, fearful, and happy faces in oddball condition and in equiprobable condition were recorded in healthy participants. Independent component analysis (ICA) applied to the differential response (emotional - neutral) revealed two prominent components within 200 ms latency of which the component peaking at 130 ms post stimulus showed a difference in scalp topography between the oddball and the equiprobable conditions, and might conform to vMMN. In the second study, depressed and control participants were presented with happy and fearful deviants interspersed with neutral standard faces. ICA for vMMN/N170 revealed that both groups showed amplitude differences between responses to standard and deviant faces bilaterally in parietal electrodes, but in depression group the differential response was diminished at right hemisphere. In the third experiment, depressed and control participants were exposed to sad and happy faces among neutral faces (both neutral and emotional faces as standards and deviants). Peak amplitude analysis showed that vMMN/N170 was evident only to the emotional deviants, not to the neutral deviants. Depressed participants showed altered facial processing for both happy and sad faces compared to controls. These results suggest that automatic processing of facial expressions is dysfunctional in depression. They also highlight the need to apply proper control conditions when tracing the group differences to the specific cognitions.
Almost twenty reports have used the visual mismatch negativity (vMMN) to study neurological or neuropsychiatric diseases, to find if perceptual mechanisms responsible for an unintentional prediction of visual temporal events are impaired. The aim of this contribution is to point out important methodical issues limiting the vMMN in current clinical use.

Among published studies very different approaches were used to elicit the vMMN, which results to diverse vMMN components with various localizations in time and space. The amplitude of the vMMN component is usually less than 1 µV, comparable to brainstem auditory potentials, and therefore, high number of single vMMN should be acquired to get a reliable result. As the vMMN represents a difference between responses to the deviant and about five times more frequent standard stimuli, the minimum number of responses is about six times higher compared to the aforementioned brainstem potentials. An attentional component mimicking the vMMN further complicates the examination, thus another visual task has to be incorporated in examination. Beside the attention control the examination design should eliminate a sensory fatigue or refractoriness from the vMMN.

The vMMN seems to be a valuable tool for its very specific neuro-psychological background, however, the concept of the perceptual learning and the attention control requires a high number of responses and puts a distinct load on the patient’s cooperation and attention, which is usually limited. For translation of the vMMN to clinical testing also reproducibility, accuracy and feasibility has to be evaluated.

Supported by the Charles Univ. project PRVOUK - P37/07.
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S75
Safety and ethics of transcranial stimulation 2014

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Non invasive brain stimulation (NIBS) has shown its potential to modulate brain plasticity in human subjects. Transcranial magnetic stimulation (TMS) is a painless procedure that involves a short strong electrical current that is delivered through an insulated coil of wire placed over the scalp (magnetic coil). Depending on the frequency, duration of the stimulation, the shape of the coil, and the strength of the magnetic field, TMS can upregulate or downregulate neural excitability under the stimulating coil. Transcranial direct-current stimulation (tDCS) is a procedure used to polarise brain regions through the application of weak direct currents. tDCS is applied through two surface electrodes placed on the skull and enhances or depresses excitability in the stimulated region depending on the polarity, strength, and duration of stimulation. During the last years we have seen a rapid increase of applications of NIBS in studying cognition, brain-behaviour relations and the pathophysiology of various neurologic and psychiatric disorders. Furthermore, a large number of studies and clinical trials have demonstrated a potential therapeutic application of NIBS, especially for TMS, in psychiatric disorders (i.e. depression, bipolar disorders, obsessions/compulsions, schizophrenia, post-traumatic stress disorder, or drug craving), movement disorders (Parkinson’s disease, dystonia, tics, spasticity, or epilepsy), chronic neurogenic pain and stroke rehabilitation. In 2009 a large panel of Experts have revised and developed a new set of guidelines for the safe administration of TMS. The considerations at the basis of new guidelines include ethical and regulatory aspects, stimulation parameters, physiological and neuropsychological monitoring of subjects, settings in which TMS can be done, composition and expertise of the rTMS team, management of potential adverse effects, and contraindications to TMS. O growing body of attention has been progressively focused by the international scientific community on the uses of NIBS in modulating cortical networks so as to produce “enhancements” of brain functional performances in healthy human subjects, from cognition, to motor and memory functions. Cognitive enhancement can be defined as any augmentation of core information processing systems in the brain, including the mechanisms underlying perception, attention, conceptualization, memory, reasoning and motor performance. To date several studies have reported significant improvements in different tasks involving perceptual, motor, and executive processing following for some time NIBS procedures. According to the WADA (World Anti Doping Agency), Doping is defined as "the occurrence of one or more of the anti-doping rule violations set forth in WADA Code", one of which is "use or attempted use of a prohibited substance or a prohibited method , that has the potential to enhance or enhances human performances or that represent an active or potential health risk". In relation to above, should we consider the eventual enhancement of brain performances in healthy subjects following NIBS procedures as a kind of "neurodoping"? Today ethic guidelines are urgently needed to integrate safety recommendations and to clarify these fundamental issues.
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S76
The diagnostic utility of threshold tracking TMS in amyotrophic lateral sclerosis
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Objective: The diagnosis of amyotrophic lateral sclerosis (ALS) may rely on stringent clinical criteria, resulting in diagnostic delay and inevitable the institution of appropriate therapy. Cortical hyperexcitability, as assessed by the novel threshold tracking transcranial magnetic stimulation (TTTMS) technique, appears as an early feature of ALS. Consequently, the present study assessed the diagnostic utility of threshold tracking TMS and developed algorithms to aid the diagnosis of ALS.

Methods: Prospective studies were undertaken on a cohort of 156 consecutive patients with neuromuscular symptoms (104 ALS and 52 lower motor neuron syndrome, non-ALS syndrome, NALS) and 62 healthy controls.

Results: Short-interval intracortical inhibition (SICI) was significantly reduced in ALS patients (2.4±0.9%) compared to NALS (8.7±0.8%, P<0.0001) and controls (10.6±0.8%, P<0.0001). The MEP amplitude and intracortical facilitation were increased, while the cortical silent period duration was reduced in ALS, all indicative of cortical hyperexcitability. Analysis of receiver operating characteristic curves suggested that threshold tracking TMS distinguished ALS from NALS, with averaged (area under curve 0.76, P<0.0001) and peak SICI 3 ms (area under curve 0.73, P<0.0001) being the most robust diagnostic markers.

Conclusions: The presence of cortical hyperexcitability distinguishes ALS from mimic disorders.

Significance: The threshold tracking TMS techniques may prove useful as a diagnostic investigation for ALS.
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S77
Electrical impedance myography and amyotrophic lateral sclerosis

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Question: Electrical impedance myography (EIM) is a technique for the assessment of neuromuscular disease that is based on the application of a weak, high frequency electrical current to specific muscles and the measurement of the resulting surface voltages. From these voltages, parameters are obtained that provide measures of disease status that can serve as biomarkers in clinical therapeutic trials.

Methods: Multiple studies have been performed using EIM as a biomarker to assess a variety of neuromuscular conditions ranging from sarcopenia to muscular dystrophy to spinal muscular atrophy. Several studies of EIM in ALS have also been pursued. These have included several in human subjects as well as in both mouse and rat G93A models.

Results: This research has demonstrated that EIM is very sensitive to disease status in a variety of conditions and can provide a novel measure of disease progression in ALS. In ALS, these measures outperform ALS functional rating scale-revised, handheld-dynamometry and motor unit number estimation. In animal models, they similarly perform very strongly. EIM data have also been shown to correlate to these other measures. Improved techniques for performing the measurements rapidly and more accurately are also currently in development (see Figure 1); these improvements should simplify the application of the technique in future multicenter clinical trials.

Conclusions: EIM is a promising new technique for the assessment of neuromuscular disease that is particularly sensitive to disease progression in ALS. Its application in future ALS clinical therapeutic trials has the prospect of speeding discovery of effective therapies for this disease.

figure 1
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S78
Beta-band intermuscular coherence: a novel biomarker of upper motor neuron dysfunction in ALS

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We have previously shown that beta-band intermuscular coherence (IMC) is only observed when there is a functioning corticospinal tract and is therefore a potential biomarker of upper motor neuron dysfunction in ALS [1]. We have also shown that beta-band IMC does not change significantly during healthy adult life [2]. More recently we have tested beta-band IMC in 70 unselected patients with possible, probable and definite amyotrophic lateral sclerosis (ALS), according to Awaji criteria, at first presentation to the ALS service at Newcastle Upon Tyne Hospitals.

Lower limb IMC was measured between a calf muscle and an intrinsic foot muscle during an unrestrained ankle dorsiflexion task. Upper limb IMC was similarly estimated between a forearm muscle and an intrinsic hand muscle during performance of an auxotonic precision grip task. Average beta-band IMC was computed for each limb and subject. Control data from 92 normal volunteers (age 22-77) were available from our previous study. The probability distributions of ALS and control data were modelled by variable kernel density estimates, and these estimates used to construct receiver operator characteristic (ROC) curves.

The cumulative probability distribution of beta-band IMC in ALS was similar in shape to that in normal controls but was shifted towards lower IMC values. The area under the ROC curve was approximately 75% for each limb.

Beta-band IMC represents an easily tolerated and inexpensive method for electrophysiological assessment of patients with ALS. Our previous work suggests that the observed abnormalities are explicable in terms of upper motor neuron dysfunction. Upper motor neuron abnormalities have thus far proven difficult to detect in early ALS, and beta-band IMC has potential as a semi-quantitative, clinically applicable biomarker with early sensitivity.

References:


Acknowledgements: Supported by the Wellcome Trust [089893/Z/09/A] & National Institute for Health Research
Ever since the first reports about the P3 component of the event-related EEG potential, in 1965, the meaning of this component has been debated. Hillyard (e.g., Hillyard & Kutas, Ann Rev Psychol 1983) argued that P3b is related to the decision on how to respond to some stimulus ("response set"), different from the decision on how to coarsely classify the stimulus ("stimulus set"). In contrast, the majority view has taken for granted that P3b depends on processing ("evaluation") of stimuli only. Here, akin to Hillyard's view, new evidence is presented in support of P3b's bridging function between stimuli and responses, which may be applied for better understanding of pathological mechanisms as well. The classical "oddball" effect was used: P3b is larger with task-relevant rare than frequent stimuli. Our data show, by means of a double dissociation, that crucial to this effect is not that stimuli are unusual but rather that stimulus-response links are both unusual and automatized: When such links are not readily available, rare stimuli do not evoke P3b (evoking some response-related negativity above the mesial motor cortex instead) and, on the other hand, also frequent stimuli may evoke a large P3b when linked with an infrequent action. Thus, P3b may reflect the uploading of some ready-made stimulus-response link, to replace some alternative, hitherto used stimulus-response link. In this line, we tested whether P3b may reflect the fragility of stimulus-response links in Parkinson's disease, when averaged over trials not only in stimulus-locked manner (as usual) but also in response-locked manner. Indeed, conspicuously, in the patients' response-locked averages, P3b was overlapped by negativity above the mesial motor cortex, similar to our above-noted result in basic research when response selection was made difficult. Thus, conceiving of P3b as an indicator of integrated stimulus-response links will continue to provide good new possibilities for basic and applied research.
S80
The role of the P3 in the formation of perceptual decisions

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How does the brain enable us to make reliable decisions about sensory information that is weak, ambiguous or noisy? In the last twenty years, monkey neurophysiology research has offered important new insights on this process through the identification of neuronal populations that integrate relevant sensory information over time and that trigger action once a threshold quantity has accrued. There has also been a concerted effort to identify analogous signals in the human brain. In fact, since its discovery in 1965, the classic P300 or ‘P3b’ has been strongly linked to the decision making process: it is evoked exclusively by task relevant events requiring decisions; it predicts signal detection on a trial-to-trial basis and its latency varies closely with reaction time under conditions where accuracy is emphasized as well as with factors affecting the duration of stimulus evaluation such as visual ‘noise’. However, a consensus regarding the precise functional role of the P3b has failed to emerge and, in particular, there has been disagreement regarding whether it reflects a process that is triggered before or after the decision has been reached. We have argued that part of this uncertainty arises from the problem of global signal summation in typical discrete ERP paradigms in which functionally discrete signals overlap and therefore cannot be readily disentangled. In our recent work we adopted the simple approach of eliminating sudden intensity transients in a target detection paradigm in order to isolate the neural signatures of decision formation. Analysis of the event-related potential revealed a single, gradually building centro-parietal positivity that exhibited precisely the same integrate-to-threshold dynamics as the ‘decision variable’ signals previously reported in monkeys. A variety of empirical manipulations have confirmed that this decision signal bears many functional similarities to the classic P3b component including polarity, peak coincidence with response execution, topography and contingency on task relevance. Furthermore, we find that the topography and amplitude of the P3b and centro-parietal decision signal are highly correlated across subjects. The current findings call for a novel view of the P3b component as a dynamically evolving decision process.
Abstracts of Speakers

S81
Towards an objective brain measure of pain - Multivariate approaches to electrophysiological data

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The presentation will address multivariate pattern analysis of electro- and magnetoencephalographic data as a tool for pain research. We will show that pain is associated with neuronal responses at different frequencies which partially overlap in time and space. We will present how the different responses provide complementary information about the pain experience and how the multivariate assessment of these responses can be used to predict pain perception from brain activity.
Upper motor neuron (UMN) signs is an essential component of amyotrophic lateral sclerosis (ALS) diagnosis but the one most difficult to show, in particular in very weak and atrophic limbs, as well as in the trunk region. There are no standard operative procedures to test clinical signs for UMN lesion. Although there is consensual agreement that some clinical findings clearly support UMN degeneration, a large grey area is present when dealing with atrophic limbs or less usual clinical signs. In addition, objective neurophysiological methods to detect UMN lesion have been difficult to prove high sensitivity and specificity, good tolerance, easy performance and widespread applicability.

Peripheral nerve and muscle electromyography studies to ascertain UMN change, like as H-reflex and motor unit recruitment, are much influenced by the loss of lower motor neurons (LMN). Conventional measurements from transcranial magnetic stimulation are of limited value; in spite of the high sensitivity of triple stimulation magnetic stimulation this technique is not well tolerated by patients in longitudinal study protocols. More recently, threshold tracking to test cortical excitability has been largely applied by one research group and it could be of high diagnostic yield in early affected patients. Neuroimaging is exciting and a set of different approaches have been explored. So far, no single technique has shown high enough sensitivity and specificity to be applied in routine clinical evaluation of ALS patients. The main advantage is its probable independence from LMN function, but technological sophistication and high costs can limit its use in many centers. The novel concept of intermuscular coherence and its reduction by UMN lesion is a new area being investigated. Its dependence from LMN function and consistency of results in different centers is a major issue not resolved yet.

In the future, it is probable that different techniques will be compared regarding diagnostic properties taking into account clinical findings as the gold standard to identify UMN degeneration in ALS patients. Large multicentric studies are advisable to withstand universal recommendations.
Electrophysiological studies in mouse models of amyotrophic lateral sclerosis (ALS)

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20% of familial ALS cases are caused by mutations in the gene coding for superoxide dismutase 1 (SOD1). Based on this discovery, the best characterized and still most commonly used animal of ALS, the G93A mutant SOD1 mouse model has been generated in 1994.

It has been shown that motor neuron and neuromuscular endplate degeneration in this model starts long before obvious symptoms of motor impairment. Electrophysiological methods such as nerve conduction studies, motor evoked potentials and motor unit number estimation (MUNE) can therefore be used as sensitive markers to monitor disease onset and progression in preclinical trials. Based on the discovery of a large number of novel ALS associated mutations (such as in the TDP-43, FUS and C9ORF72 genes) in recent years, new animal models which will foster new insights into disease mechanisms are currently being generated. Clinical neurophysiological studies will provide a valuable tool to study early preclinical alteration, to evaluate similarities and differences in disease onset and spreading patterns in these new models and thereby help to understand the pathological impact of different mutations.
From a clinical point of view excess of movement and the overflow phenomena are specific features of patients with different types of primary dystonia (generalized, segmental and focal). Several neurophysiological studies have suggested that one important feature in the pathophysiology of dystonia is loss of inhibition. Dystonic patients show prolonged EMG bursts, cocontraction activity and spread of EMG activity to nearby muscles. Loss of inhibition in patients with focal and generalized dystonia has been also demonstrated with studies of spinal cord and brainstem reflexes (blink reflex, reciprocal inhibition and long-latency reflex). Reduced inhibition is also present at the level of the primary motor cortex, as demonstrated by the abnormalities of intracortical inhibition and silent period as tested with TMS technique. Surround inhibition is reduced in patients with dystonia and this may contribute to the defect in focusing motor command. Reduced or loss of inhibition may well cause the abnormalities of cortical plasticity described in dystonia. Whether abnormalities of motor inhibition depend on changes at cortical, brainstem and cerebellum is still unclear.
Deficiency of inhibition in sensory function

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The pathophysiology of primary dystonia is thought to involve dysfunction of the basal ganglia cortico-
striatal-thalamo-cortical motor circuits. In the past, emphasis was placed on the role of the basal ganglia in
controlling movements; in more recent times, however, it has also become clear that they play an important
part in sensory functions. Thus, although the most dramatic symptoms in dystonia seem to be motor in
nature, marked somatosensory perceptual deficits are also present in this disease. Recent behavioral
studies have shown that these sensory functions are compromised in patients with several forms of primary
of primary dystonia. Changes have been found in temporal discrimination and integration of sensory
signals, spatial discrimination of tactile stimuli, perception of the vibration-induced illusion of movement,
and other illusions (the rubber hand and Aristotele’s illusion). The search for abnormalities of sensation was
stimulated by the observation in a primate model of dystonia that showed enlarged and overlapped
receptive fields of the hand in the S1 after stereotypic movements of the hand. Abnormal representation in
S1 of the fingers involved in dystonia characterized by smaller distance between the fingers has been also
observed in patients affected by focal hand dystonia using neuroimaging studies. One possible
pathophysiological mechanisms for these abnormalities could be a loss of inhibition at multiple levels of the
somatosensory system, as documented by somatosensory evoked potentials studies. Consequently,
abnormal processing of the somatosensory input may lead to an inefficient sensorimotor integration, thus
contributing to the generation of dystonic movements.

This talk focuses on sensory function abnormalities described in primary dystonia using different
approaches and techniques and their possible role in the pathophysiology of this syndrome, highlighting
potential implications for innovative therapeutic strategies to aid functional recovery.
Differentiation of Organic and Psychogenic Dystonia

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Psychogenic (functional, medically unexplained) dystonia is said to be the second commonest form of psychogenic movement disorder (after tremor), but it is also acknowledged to be one of the most difficult psychogenic disorders to diagnose with confidence. Historically dystonia as a whole was considered a psychogenic disorder leading to inappropriate treatment for many patients, and hence there is understandable reluctance to make the diagnosis of psychogenic dystonia. However, correct diagnosis is important as treatments for organic and psychogenic dystonia differ markedly, psychogenic dystonia can be treatable, and without treatment irreversible harm can occur. In this talk I will cover the main clinical presentations of psychogenic dystonia, aids for diagnosis (including the use of electrophysiological techniques) and a brief summary of current best practice regarding management.
Introduction: Writer's cramp is a primary task specific dystonia, in individuals with genetic predisposition combined with repetitive performance of a skilled motor act, writing. The motor disturbance, while performing the act causes contractions in muscles not required, with proximal spread with abnormal postures. Neurophysiological studies have shown defects in the neural inhibitory processes, sensorimotor integration and maladaptive plasticity.

Surface EMG is a non invasive technique that would allow objective assessment of the muscles involved in patients with Writer's Cramp. Cocontraction of agonist-antagonist pairs and coactivation of upper limb muscles have been described. However, there have been few studies on the phenomenology of dystonia, tempo-spatial spread of activity and their correlation with functional disability.

Objective: To study the timing, pattern of muscle activation/EMG patterns in subjects with Writer's Cramp using SEMG recordings in distal, intermediate and proximal muscle groups in both upper limbs and to correlate with functional disability and data was compared with normal subjects

Methodology: 16 channel SEMG was obtained during different phases of writing using custom-made hard/software and the timing, activation patterns and spread of muscle contractions in subjects with Writer's cramp and controls

Results: SEMG of 20 subjects with WC was compared with control subjects showed an 'early onset' during motor imagery, agonist-antagonist co contraction and rapid proximal recruitment and mirror activity in the contralateral limb.

Conclusions: Anticipation, delayed relaxation and mirror activation was noted in patients with Writer's Cramp. These findings indicate plausible abnormalities in the circuits involving the basal ganglia, cerebellum, premotor cortex due to maladaptive plasticity, abnormal Sensorimotor Organization and probable defects in the neural inhibitory processes. This study demonstrates the utility of Surface EMG to study the Maladaptive CNS Plasticity in Writer's Cramp

References:

Sivadasan A, Sanjay M, Alexander M, Devasahayam SR, Srinivasa BK. Utility of Multi-channel surface EMG in asseement of focal hand dystonia. Muscle Nerve 2013 September; 48(3) 415-422


In vivo investigation of functional brain networks by CCEPs

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A better understanding of epileptic networks as well as the mechanisms involved in human higher cortical functions requires a detailed knowledge of neuronal connectivity. Little progress, however, has been made until this century in the understanding of neuronal connectivity between functional cortical regions in the living human brain. In the last decade, although limited to patients who underwent chronic subdural electrode implantation for presurgical evaluation of intractable partial epilepsy, an electrical tract tracing method of CCEPs has been established to probe human brain connectivity and epileptogenicity. Cortico-cortical connections are investigated by applying single-pulse electrical stimulation (SPES) to a part of the brain through intracranial electrodes and recording the cortical evoked potentials (cortico-cortical evoked potentials: CCEPs) that emanate from a distant region of the cortex via neuronal projections. In contrast to diffusion tractography that is solely determined by mathematical calculation of water molecules, CCEP provides a unique opportunity to physiologically track in vivo cortico-cortical networks with good spatiotemporal resolution. Since first applied to investigate the cortico-cortical connections involved in the dorsal language stream (Matsumoto et al., 2004), this CCEP method has been applied all over the world to investigate cortico-cortical and cortico-subcortical networks involved in various brain functions by using subdural and depth electrodes. This method provides important connectivity information for functional system mapping in individual patients for presurgical evaluation. Furthermore, by gathering connectivity information from a group of patients, this method provides a rare yet valuable opportunity to generate standardized functional/effective connectivity map that complements other non-invasive connectivity techniques. We review recent SPES/CCEP connectivity studies as well as ongoing clinical application for intraoperative system mapping.
S89
Pathophysiology of the nodal region in axonal Guillain-Barré syndrome

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Acute motor axonal neuropathy (AMAN), an axonal subtype of Guillain-Barré syndrome (GBS), was widely recognized in the 1990’s. Whereas in Europe and North America, acute inflammatory demyelinating polyneuropathy (AIDP) is considered the major subtype of GBS, in East Asia, and Central and South America, AMAN is found for 30–65% of GBS cases. Over the past 20 years, major advances have been made in understanding the immunopathogenesis and pathophysiology of AMAN. Clinically, AMAN is characterized by pure motor involvement, frequent antecedent Campylobacter jejuni enteritis, and serum anti-ganglioside antibodies. Compared with AIDP, AMAN has more rapid progression and earlier nadir, and two patterns of recovery (rapid improvement by resolution of conduction blocks, and slow recovery by axonal degeneration). Electrophysiological studies frequently reveal, as well as axonal degeneration, rapidly reversible nerve conduction block/slowing (resolved within days to a few weeks); the time-course suggests functional or microstructural changes at the nodes of Ranvier, rather than segmental demyelination. It is now established that AMAN is caused by molecular mimicry of human gangliosides by the bacterial lipo-oligosaccharide. An animal model of AMAN immunized by GM1 was developed, and its histological studies show disrupted nodal sodium channel clusters, and paranodal myelin detachment; these changes are likely to account for conduction block in human AMAN. Conventional electrodiagnostic criteria for AMAN were based on assumption of simple axonal loss, and therefore should be reconsidered.
Abstracts of Speakers

S90
Nerve excitability in axonal degeneration and regeneration

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Question: Deriving multiple measures of nerve excitability by “threshold-tracking” techniques emerges as the gold-standard clinical neurophysiologic approach to identify peripheral nervous system pathophysiology. The aim of this presentation is to distinguish excitability changes in the processes of degeneration and regeneration and address their contribution to the excitability measures in peripheral nerve disorders.

Methods: Nerve excitability tests were carried out in cats, humans and mice during peripheral nerve degeneration and regeneration following a mechanical interruption in peripheral nerve continuity and compared with excitability changes in motor neuron disease and demyelinating disorders.

Results: In axonal degeneration/regeneration there is an alteration of fast K+ currents resulting from an altered paranodal myelin compartment. With regeneration/remyelination the internodal length remains short. Assuming a restored voltage-gated Na+ channel (VGSC) density, an increase in number of nodes of Ranvier per unit length would result in an increased Na+ influx per impulse. Accumulating evidence suggests that this would overdrive the energy-dependent Na+ pumping mechanisms leading to membrane hyperpolarization. Furthermore, myelin alterations could also trigger changes in the nodal VGSC isoform expression further altering the excitability as well as increasing the Na+ influx, and subsequently, the energy metabolism stress.

Conclusion: Our data suggest that, apart for changes in passive “cable properties”, changes in voltage-gated ion channel conductances and membrane potentials are reflected by the excitability measures during peripheral nerve degeneration and regeneration. Accounting for the excitability changes due to ongoing axonal degeneration in motor neuron diseases, as well as the altered excitability of shorter internodes in demyelination could advance the understanding of specific pathophysiologic mechanisms in these diseases.
Abstracts of Speakers

S91
Definition, mechanism, manifestations, and importance

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Concussion has become a major public health concern. In the field of sports concussion, the patient population is unique. Under-recognition, under-reporting and downplaying symptoms are all common. It is therefore imperative that we establish reliable, objective tests for concussion. There is no current “gold standard” objective test for concussion, despite the enormous public health impact and widespread media attention to this condition. However, many recent advances in Neurophysiology may dramatically improve our ability to more reliably diagnose and manage concussion.

By the end of this session, attendees will be able to:

1. Discuss the incidence, clinical features, and impact of sports related concussion.

2. Understand the current role of routine EEG, qEEG, EP and MEG in the assessment of concussion

3. Discuss the current role and upcoming techniques of imaging and functional imaging in sports concussion

4. Understand emerging neurophysiological techniques that may show promise in the assessment of concussion, including clinical utility, and novel insights these techniques may provide.
Introoperative Monitoring and Mapping of the Functional Integrity of the Brain Stem

*V. Deletis*

Introduction

Twenty five years ago surgery for the brain stem (tumor, vascular malformation etc.), was mainly performed as a biopsy. Because of lesions localization this surgery, was considered extremely hazardous and would carry very high risk for an extensive postoperative neurologic deficit. Thanks to the development of introoperative neurophysiology (ION), this position is reversed, and many patients finish surgery with minor or no postoperative deficit and consequently with a good quality of life.

Method

Critical review and history of methodologies for introoperative monitoring and mapping of the brainstem, with personal contribution to their development.

Results

The three critical steps in the development of the (ION) of the functional integrity of the brain stem were achieved. The first step was introducing the method of mapping (functional identification) of motor nuclei of the cranial nerves at the floor of fourth ventricle (1,2). Next was the introduction of monitoring corticospinal and corticobulbar (3), motor evoked potentials and finally the introduction of introoperative monitoring of the brainstem reflexes (blink reflex, palato-laryngeal) (4).

Conclusion

Today abundant armamentarium of ION methods is available for the monitoring and mapping of the functional integrity of the brain stem during surgery for its lesion. Their application and interpretation needs certain skills but most of them not complex or complicated. The results of their use showed that surgery within or around the brainstem should not be performed without their use, helping to expand the lesion's removal, while resulting in much better patients' functional outcome.

References:


Abstracts of Speakers

S93
A New Insight to Neurophysiologic Markers of Cortical Motor Speech Areas

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Introduction

The larynx is the final common organ for speech, therefore it receives delicate programming codes for speech execution. After artificially stimulating selective cortical motor speech areas by electric current we try to decode distinctive markers as synchronized time locked electric events from the cricothyroid muscles.

Method

Ten right handed healthy subjects underwent navigated transcranial magnetic stimulation and eighteen patients underwent direct cortical stimulation over the left hemisphere, while recording neurophysiologic markers; short latency response (SLR) and long latency response (LLR) from cricothyroid muscle. Both healthy subjects and patients were engaged in the visual object naming task. In healthy subjects the stimulation was time locked at 10-300 ms after picture presentation while in the patients it was at zero time (Figure 1)

Results

The latency of SLR in healthy subjects was 12.66±1.09 ms and in patients 12.67±1.23 ms. The latency of LLR in healthy subjects was 58.5 ± 5.9 ms, while in patients 54.25±3.69 ms (1). SLR elicited by stimulation of M1 for laryngeal muscles corresponded to induced dysarthria, while LLR elicited by stimulation of the premotor cortex in the caudal opercular part of inferior frontal gyrus, recorded from laryngeal muscle corresponded to speech arrest in patients and speech arrest and/or language disturbances in healthy subjects (2).

Conclusion

SLR elicited by stimulation of M1 for laryngeal muscles corresponded to induced dysarthria, while LLR elicited by stimulation of the premotor cortex in the caudal opercular part of inferior frontal gyrus, recorded from laryngeal muscle corresponded to speech arrest in patients and speech arrest and/or language disturbances in healthy subjects.

References


Upper: Intraoperative mapping during awake craniotomy. The patient and the surgeon are separated with surgical drapes and can communicate with each other. The patient is engaged in visual object naming task. Lower: The results of cortical mapping. Stimulation of the cortical spot marked with red marker 4 elicited SLR, while spot marked with yellow marker 1 elicited LLR in cricothyroid muscle. From the same spot where LLR was elicited, speech arrest was induced for Spanish. (T-tumor location; Blue markers 1 to 7 = somatosensory cortex; Red markers 1 to 3 = primary motor cortex; English, Catalan and Spanish flags = cortical spots for speech arrest for these languages; from these cortical spots LLR was not elicited in the cricothyroid muscle)
Intraoperative Neurophysiology of the Corticospinal Tract (CT)

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In men each CT tract consists of approximately 1 million axons, which originate from a very wide region of the cortex, having diameter from 2 to 20 microns. Phylogenetically, among all species, man has the highest number and the highest percentage of fast conducting heavily myelinated axons. (1). Those fast conducting neurons are an essential element for executions of voluntary movement, therefore maintenance of their functional integrity is of the utmost importance during surgery. Intraoperative methodology for their semi quantitative assessment is the measure of D- wave amplitude, because D wave represent neurogram of the fast conducting neurons of the CT.

There is a lot of evidence that intraoperative monitoring of the motor evoked potentials recorded from the muscle is an inferior method for predicting postoperative motor outcome in contrast with D-wave monitoring. Optimal methodology for monitoring functional integrity of the CT is the combination of both methods ( Fig. 2).

References:


Figures caption

Fig. 1 The D waves recorded from the different species (to the left), with a number of CT axons (to the right).

Fig. 2 (A) Schematic illustration of electrode positions for transcranial electrical stimulation of the motor cortex according to the International 10-20 EEG system. The site labeled “6 cm” is 6 cm anterior to CZ. (B) Illustration of grid electrode overlying the motor and sensory cortices. (C) Schematic diagram of the positions of the catheter electrodes (each with three recording cylinders) placed cranial to the tumor (control electrode) and caudal to the tumor to monitor the descending signal after it passes through the site of surgery (left). In the middle are D and I waves recorded rostral and caudal to the tumor site. On the right is depicted the placement of an epidural electrode through a flavectomy/flavotomy when the spinal cord is not exposed. (D) Recording of muscle motor evoked potentials from the thenar and tibialis anterior muscles after being elicited with multipulse stimuli applied either transcranially or over the exposed motor cortex.

figure 1
Abstracts of Speakers

Figure 2
Mild traumatic brain injury: current neurophysiologic diagnostic techniques

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Questions and Methods: How can clinical neurophysiology and imaging methods contribute to diagnosis of patients with mild traumatic brain injury (MBTI, concussion). Literature was reviewed for studies that assessed clinical utility.

Results and Conclusions: Routine neuroimaging is useful only to exclude MBTI complications. EEG shows suppression, then slowing immediately after concussion.

EEG abnormalities corresponded to amnesia more than to neurologic signs at the ER. Generalized, focal, PDR slowing resolve in weeks to months. EEG changes are non-specific, i.e. are similar to changes seen in many other clinical circumstances. Disadvantages of QEEG outweigh its advantages for clinical diagnosis. The role of BAEP is unclear; it does not correspond to dizziness symptoms. P300 amplitude loss is interesting but not clinically useful.

References:
Abstracts of Speakers

S96
Functional neuroimaging of oculomotor deficits in athletes with mild traumatic brain injury
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Question: There is still controversy in the clinical literature where a single episode of concussion injury resolves spontaneously within few days post-injury or may result in development of post-concussive syndrome.

Method: Based on the increasing evidence that concussion can disrupt multiple brain functional networks, including the oculomotor control network, a series of classic saccadic and smooth pursuit tasks are adopted during functional magnetic resonance imaging (fMRI) scans. Twelve concussed student-athletes diagnosed by medical staff were scanned in acute and sub-acute phases of injury. Twelve age matched athletes without history of concussion were recruited as controls.

Results: Both behavioral/neurological and imaging (fMRI) data revealed differential results between the healthy controls and concussed athletes. Concussed subjects have longer latency time in the saccadic tasks, worse position errors and fewer number of self-paced saccades compared to control subjects. Concussed athletes had additional brain regions and larger activation sites as evidenced by fMRI. Functional connectivity analysis on the default mode network (DMN) deactivation demonstrated failure of complete deactivation in concussed subjects. Additionally, graph theory analysis revealed disrupted whole brain network properties in concussed subjects. On day 30: Most of neurological measures returned to those observed in normal controls. However, fMRI patterns of antisaccade task remained to be abnormal, that appeared to be matched with the relatively worse behavioral results.

Conclusion: It can be concluded that concussed subjects have persistent oculomotor deficits far beyond 7 days post-injury and compromised neural network, even though after they were clinically cleared for return to sport activities. Our findings are consistent with “compensatory” hypothesis that latent brain resources may allow the concussed patients to reach a comparable level performance. That is being said, their behavioral results cannot match those of healthy controls, especially during anti-saccades and self-paced saccades oculomotor tasks. Therefore, collective examination of antisaccades task and brain functional connectivity analyses have potential to be considered as a sensitive assessing tool for assessment of concussion in acute and sub-acute phases of injury.

References:
Abstracts of Speakers

Concurrent fMRI-EEG and the Bereitschafts-BOLD-effect

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The cortical correlates of voluntary actions precede movement by up to 1-2 seconds, as evident in the Bereitschaftspotential. This sustained activity prior to movement is strongly influenced by attention and by arousal levels, showing less activity when actions are relatively unattended and when arousal level is low. While fMRI has revealed key regions that contribute to premovement activity, the relationship between activity in these regions and the Bereitschaftspotential is not well understood. By using concurrent EEG and fMRI measurement and single-trial correlation analysis, we find that the cingulate motor area in the mid cingulate cortex plays a key role in driving sustained activity in the higher motor areas prior to voluntary action. Specifically, we find that trials in which early Bereitschaftspotential activity is large are associated with greater activity in the mid cingulate cortex, and a greater influence of the mid cingulate cortex on sustained activity in the supplementary motor area. This key role of the cingulate motor area in driving sustained activity of the supplementary motor prior to movement can explain how factors such as attention and arousal level also have such a strong influence on early neural activity of the Bereitschaftspotential.
YIA1

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**Question:** Studies of neuromuscular transmission in children are important for the diagnosis of myasthenia. A challenge is that the onset of congenital myasthenic syndrome often occurs when neuromuscular junctions are considered immature (0-4 years of age). Further, there is a shortage of published normal data for pediatric studies of repetitive nerve stimulation (RNS) and single fiber EMG (SFEMG).

**Methods:** We identified all examinations of RNS and/or SFEMG in children, with referring diagnosis of myasthenia, aged 0-18 years from January 2003 until October 2013 at the department of Clinical Neurophysiology, Uppsala University Hospital. A pathological decrement was defined as ≥ 10%.

**Results:** A total of 85 children were identified. Age at examination ranged from 4 days to 18 years (mean: 10.4 ± 6.2 years) and the cohort consisted of 40 girls (47%). A diagnosis of neuromuscular transmission failure was made in 14 children (9 girls; mean age: 6.8 ± 5.7 years), who were significantly younger than the remaining children (p=0.034). RNS was performed in the following muscles: abductor digiti minimi (52%), anconeus (61%), nasalis (52%) and trapezius (57%); a pathological decrement in any muscle was found in only 4 children. SFEMG in extensor digitorum communis (EDC) and/or orbicularis oculi (OO) was pathological in 10 children. Mean MCD in the myasthenic group ranged between 72-106 μs in the EDC and 67-120 μs in the OO. In the group with normal neuromuscular transmission, mean MCD ranged from 21-53 μs in the EDC (N=18) and from 21-53 μs in the OO (N=11). There was an age-dependent correlation of amplitude in all examined muscles, however decrement and jitter values showed no specific age correlation.

**Conclusion:** Although SFEMG was found to be the most sensitive examination for the diagnosis of myasthenia in children, it was performed only in 26% of cases. This large cohort adds important data to the paucity of published normal values for pediatric neuromuscular transmission.
Abstracts of Young Investigator Awardees

YIA2
Different brain network modulation following motor imagery BCI-assisted training after stroke

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Questions
To evaluate the influence of Motor Imagery (MI) training assisted via Brain Computer Interface (BCI) on brain network organization in subacute stroke patients. We analyzed and compared changes of interhemispheric connections estimated before and after two training strategies (with and without BCI support).

Methods
Twenty-eight subacute stroke patients were enrolled and assigned to two groups: 14 patients underwent a one-month motor imagery (MI) training supported by a sensorimotor-based BCI (BCI group) while 14 underwent a similar MI training without BCI support (CTRL group). Before and after training we recorded EEG from 61 positions during 5 minutes of rest. Effective connectivity was computed by means of Partial Directed Coherence. Statistical differences between connectivity patterns were assessed by means of paired sample t-tests (significance was defined by p<.05).

Results
Both trainings led to a different between-group behavior in terms of the overall connection strength with respect to EEG frequency bands: a greater number of interhemispheric connection were significantly (p<.05) increased in strength in beta/gamma and theta/alpha frequency bands for the BCI and CTRL group, respectively.

Conclusions
Overall findings indicate that MI training supported via BCI induces a reinforcement of those interhemispheric connections related to sensorimotor rhythms (higher-band). Differently, a longitudinal training based only on MI (CTRL group) leads to changes in the interhemispheric connections estimated in the lower ranges of frequencies, thus likely reflecting the attentive component of the training. Such different training effect may serve as a base for better understanding of future application of BCI-assisted cognitive training in stroke rehabilitation.

Acknowledgements
This work was partially supported by the European ICT Programme Project FP7-224631 and by the project “Brain Computer Interface-Driven Rehabilitation After Stroke: An Add-On Intervention For Hand Motor Recovery” (RF-2010-2319611) founded by the Italian Ministry of Healthcare.
Consistency over Time of Electroencephalographic Connectivity Measures in Temporal Lobe Epilepsy

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Objective: Connectivity biomarkers of the EEG have been shown to reflect seizure propagation and to indicate the source of abnormal hyperconnectivity. Nevertheless, it is questionable if these patterns are stable over time in different measures of connectivity. Moreover, it would be of interest whether the consistency over time is different in patients with epilepsy.

Methods: To address this topic we examined 9 healthy participants and 13 patients with temporal lobe epilepsy (TLE) on the right (5) and on the left (8) hemisphere. We calculated 14 measures of connectivity from two EEG-recordings separated by two weeks. We correlated these measures for each group and compared the correlations.

Results: We found most consistent results for Geweke’s Granger Causality. For this measure, consistency was found in a different network in healthy participants than in patients. Patients with a focus on the right side showed only a few consistent connections, mostly on the ipsilateral hemisphere, while patients with focus on the left side showed large bilateral consistencies, which was extended frontocentrally over the left hemisphere and parietooccipitally over the right hemisphere.

Conclusion: It is important to note that a higher consistency on the focal side does not indicate that the connectivity is higher in this region. Instead, it suggests that while the brain concert of information flow is generally variable, it may be even more variable in patients with epilepsy, with an exception on the focal region. There, the consistency of connectivity indicates that the pathological changes are a stable pattern in the EEG, being detectable for example with connectivity markers such as Geweke’s Granger Causality.

Legends: GGC consistency for patients with right- (figure 1) and with left-lateralized TLE (figure 2). x-axis: 2-40Hz; y-axis: correlations -1 to +1; green: not significant; red: significant correlations (FDR-corrected p<.00004).
Abstracts of Young Investigator Awardees

YIA4

Bochum ultrasound score versus clinical and electrophysiological parameters in distinguishing acute-onset chronic from acute inflammatory demyelinating polyneuropathy

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Question

We aimed to evaluate prospectively a recently introduced nerve ultrasound score (Bochum ultrasound score - BUS) (1) (Figure 1), clinical and electrophysiological parameters in distinguishing sub-acute chronic (CIDP) from acute inflammatory demyelinating polyneuropathy (AIDP).

Methods

BUS, clinical [sensory symptoms or signs, bulbar palsy, autonomic nerve system (ANS) dysfunction, preceding infections and respiratory muscle involvement] and electrophysiological parameters (A-waves, sural nerve sparing pattern, sensory ratio >1) underwent prospective evaluation in a group of 10 patients (mean age 53.4, SD+/-10.3, 6 women), who referred to our department between January 2012 and May 2013 with clinical presentation of sub-acute poluradiculoneuropathy.

Results

Sensitivity and specificity in distinguishing sub-acute CIDP from AIDP were as follows: BUS: 83.3%, 100%; sensory symptoms: 100%, 75%; lack of ANS dysfunction: 83.3%, 75%; lack of bulbar palsy 83,3 and 50%; lack of preceding infections 66.6% and 50%; lack of respiratory muscle weakness or need for mechanical ventilation 100% and 50%; negative sural sparing pattern: 100%, 50%; lack of sensory ratio >1 100% and 25%; presence of A-waves 33.3% and 25%.

Conclusions

BUS seems to have a comparable high sensitivity and specificity with certain clinical parameters, but a higher sensitivity and specificity compared to electrophysiological parameters, in the distinction of sub-acute CIDP from AIDP.

References


Figure Legends

Figure 1

Ultrasound overview of the anatomic sites of the Bochum Ultrasound score: CSA of the ulnar nerve in a) Guyon’s canal, b) middle upper-arm, c) CSA of the radial nerve in spiral groove, d) CSA of the sural nerve between the two heads of the gastrocnemius muscle (CSA = cross sectional area).
Abstracts of Young Investigator Awardees

figure 1
Abstracts of Young Investigator Awardees

YIA5
Predictor of severity and long distance outcome of patients with critical illness myopathy and polyneuropathy

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Objective: The aim of this study is to investigate predictive value of laboratory findings, clinical parameters on outcome among patients with critical illness Myopathy or Polyneuropathy.

Methods: We retrospectively selected 125 patients with acquired tetraparalysis who underwent mechanical ventilation in the intensive care unit. 110 patients were examined by EMG (electromyography) on suspicion of Critical illness Myopathy (CIM) or Polyneuropathy (CIP). Neurophysiologic tests included motor and sensory nerve conduction studies, F-waves, repetitive nerve stimulation, EMG and direct muscle stimulation. Blood tests, as well as clinical parameters were extracted from the patient’s medical record. Multivariate regression tests were carried out where all clinical and electrophysiological tests were entered as predictors and clinical outcome score and EMG diagnosis was tested as outcome variable.

Results: Of cases, 54.5% had CIM, 15.5 % had both CIM/CIP, and 30% CIP. The remaining 15 patients had central nervous system lesions or Guillain-Barre Syndrome as final diagnosis. Etiology: The most common etiology for acquiring CIM/CIP was abdominal operation (28.4%), pneumonia and respiratory failure (26%), gastrointestinal disease (15%). Clinical status: Muscle strength at the time of the neurophysiological test showed significant linear correlation with clinical outcome, whereas the more severe the muscle weakness the higher the risk for poor outcome (Spearman’s rho 0.406, p=0.001). Electroneurography: Linear correlation was found between compound muscle action potential (CMAP) recorded at abductor digiti quinti muscle and clinical outcome, whereas a decrease in amplitude implied higher mortality (Spearman’s rho 0.280 p=0.002).

Conclusion: Our finding emphasizes the importance of neurophysiological tests in predicting outcome in CIM and CIP. Close clinical and electrodiagnostic testing at an early stage may be useful in preventing irreversible pathological changes.
Question: Tinnitus, the perception of a sound without an external source, is assumed to be a result of reduced inhibition of neurons corresponding to the tinnitus frequency. One possibility to reverse the effects of this maladaptation is to induce inhibition on neurons corresponding to the tinnitus frequency by auditory stimulation. The aim of this study was to investigate the impact of repetitive stimulation with tailor-made notched music on neural activity in temporal and frontal cortical regions of tinnitus patients.

Methods: Ten subjects suffering from chronic tonal tinnitus listened to music passing through a notch-filter centered at the tinnitus frequency (tailor-made notched music) for three hours on each of three consecutive days. Neural activity evoked by either a tone at the tinnitus frequency (tinnitus tone) or by a control tone of 500 Hz was measured by magnetoencephalography (MEG) before and immediately after music exposure. Tinnitus loudness was measured via visual analog scales. A distributed source model was used to investigate the neural activity in auditory as well as in frontal cortical regions in the N1m time window.

Results: Neural activity evoked by the tinnitus tone in the temporal lobe decreased significantly after music exposure, whereas neural activity evoked by the control tone remained unaffected. Additionally, tinnitus loudness was rated significantly lower after music exposure. There was a significant correlation between the reduction of neural activity in the temporal lobe evoked by the tinnitus tone and the tinnitus loudness ratings. Furthermore, there was a significant increase of neural activity evoked by the control tone in the frontal lobe after music exposure, which could not be observed in the neural activity evoked by the tinnitus tone.

Conclusions: Tailor-made notched music evokes neural plasticity in temporal as well as frontal cortical areas of tinnitus patients. Additionally, there is a clear connection between the reduction of tinnitus loudness and the neural reorganization in the temporal cortex. These effects could be demonstrated after a short period of music exposure, indicating a fast neural reorganization and behavioral adaptation.
Abstracts of Young Investigator Awardees

YIA7
Power and Distribution of Slow Wave Component of Spike-Wave Complex toward Seizure Onset in Patients with Focal Cortical Dysplasia

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Question: Slow waves (SW) following spikes are the components to inhibit epileptic activity. To explore the changes of SW activity toward seizure onset, we evaluated power and distribution of SW between the interictal and preictal periods.

Methods: We collected 10 pediatric patients with focal cortical dysplasia who underwent extraoperative electrocortiography. Spike-wave complexes were selected and averaged with spike-triggered averaging during the interictal and preictal periods. More than 100 averaged SW were analyzed in each patient. We quantitatively measured SW powers after spikes, created topographic maps of Z score, and compared SW powers and their distribution between two periods. We compared the number of electrodes showing high Z score (>1.65) between inside the seizure onset zone (SOZ) and outside the SOZ.

Results: Preictal SW powers were higher than interictal SW powers in all patients (P < 0.01, Wilcoxon signed-rank test). The SW power tended to be higher inside the SOZ than outside the SOZ during both periods. From the interictal to preictal period, the number of electrodes with high Z score significantly increased inside the SOZ (21 to 37 electrodes; P < 0.01, Wilcoxon’s signed-rank test) and decreased outside the SOZ (34 to 16 electrodes; P < 0.01, Wilcoxon’s signed-rank test).

Conclusions: Our SW analysis demonstrated SW power increment and confinement to the SOZ toward seizure onset. The SW behaviors represent dynamic inhibition in the SOZ. This analysis will contribute to study of seizure prediction and control.

Figure legends

Figure 1. Z score maps of slow wave powers during interictal and preictal periods in a 3-year-old patient. The region enclosed by the dotted line is SOZ. The maximum Z score in the SOZ was 2.03 during interictal period, and was 3.88 during preictal period. The slow waves with high Z score were more located within the SOZ during preictal than interictal period.

Figure 2. Distribution of slow waves with high power (z > 1.65). From interictal to preictal period, the number of electrodes with high Z score significantly increased inside the SOZ and decreased outside the SOZ (P < 0.01, Wilcoxon’s signed-rank test). The slow wave powers tended to be higher inside the SOZ than outside the SOZ during both periods.

figure 1

figure 2
Abstracts of Young Investigator Awardees

YIA8
Neurophysiological Index Correlates with Disease Severity but not with Duration in Amyotrophic Lateral Sclerosis (ALS)

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Background: Neurophysiological biomarkers to monitor disease course are urgently needed in ALS. The Neurophysiological index (NI) is a recently described parameter that proved useful in cohorts of early stage ALS. Little is known about NI in more advanced disease stages.

Objective: To investigate whether NI correlates with clinical parameters in ALS.

Methods: We recruited 43 consecutive patients with clinically definite and clinically probable ALS (El Escoral Criteria) from Unicamp neuromuscular outpatient clinic between 2011 and 2013. For each subject, disease severity was quantified with the ALS functional rating scale (ALSFRS-R) and the ALS severity scale (ALSSS). NIs of both ulnar nerves were calculated as described previously (de Carvalho et al): (CMAP amplitude / Distal motor latency) x F persistence (%). We employed Spearman correlation coefficient to investigate correlations between NI and clinical data.

Results: There were 25 men and 18 women. Mean age of the patients and disease duration were 53,51 (31-74) and 29,33 (5-96), respectively. Mean ALSFRS-R and ALSSS scores were 28,23 (9-44) and 24,63 (9-37), respectively. Right sided ulnar NIs (n=43) did correlate both with ALSFRS-R and ALSSS scores (r=0.58 and 0.59, respectively). On the left side (n=40), NIs also presented a positive correlation with both scores (r=0.65 and 0.62, respectively). However, NIs on either side were not significantly associated with disease duration.

Conclusion: NI is easy to calculate using routine nerve conduction studies and correlates with disease severity in patients with ALS. It is a promising parameter to monitor disease progression. Longitudinal studies should be performed to confirm these findings.
Abstracts of Young Investigator Awardees

YIA9
The combined effects of anodal tDCS and patterned electrical stimulation on spinal inhibitory interneurons and motor function among patients with incomplete spinal cord injury

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Question: Supraspinal modulation and phase-related sensory input might play an important role for the modulation of spinal reflex and functional recovery of locomotion among patients with incomplete spinal cord injury (SCI). The present study examined the combined effects of anodal transcranial direct current stimulation (tDCS) and patterned electrical stimulation (PES) on the spinal inhibitory interneurons and lower extremity motor function in patients with incomplete SCI.

Methods: Eleven patients with incomplete SCI participated in this single-masked, sham-controlled cross-over study. They randomly participated in the following two sessions: (1) anodal tDCS combined with PES; (2) sham tDCS combined with PES. We applied PES to the common peroneal nerve with a train of 10 pulses at 100 Hz every 2 s for 20 min. Anodal tDCS (1 mA) was simultaneously applied to the primary motor cortex for 20 min. In sham condition, tDCS was delivered for only the first 15 s. We assessed disynaptic reciprocal inhibition (RI) and presynaptic inhibition (D1 and D2) using a soleus H-reflex conditioning-test paradigm. The conditioning-test stimulus interval was set at 2 ms (RI), 20 ms (D1), and 100 ms (D2). The magnitudes of inhibition was assessed before, immediately after, 10 min and 20 min after the stimulation. We measured ankle movement speed before and 20 min after the stimulation.

Results: Simultaneous combination of anodal tDCS and PES persistently increased the magnitude of RI and D2 until 20 min after the stimulation, but the D1 inhibition was not changed at each time point. Sham tDCS and PES increased the magnitude of RI immediately after the stimulation. Anodal tDCS and PES significantly increased the number of ankle movement in 10 s. This improvement was significantly correlated with that of the amount of RI and D2.

Conclusion: Anodal tDCS combined with PES could modulate reciprocal inhibitory interneurons and improve the ankle movement in patients with incomplete SCI.
YIA10

Combining Cutaneous Silent Periods with Quantitative Sudomotor Axon Reflex Testing in the Assessment of Diabetic Small Fiber Neuropathy

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Question: Routine electrophysiological testing is often normal in the evaluation of painful diabetic neuropathy, as it is unable to detect dysfunction of thinly myelinated (Aδ) and unmyelinated (C) small fibers, which may be affected earlier. Although cutaneous silent periods (CSP)¹ and quantitative sudomotor axon reflex testing (QSART)² respectively evaluate these fiber types in the extremities, these two tests have yet to be assessed together. This study aims to compare the function of both fiber types in patients with small fiber neuropathy (SFN) related to glycemic dysregulation.

Methods: 26 patients with SFN and 26 age-matched controls were assessed. Patients with significant large fiber neuropathy were excluded. Nine patients had Type I diabetes, nine had Type II diabetes, and eight had impaired glucose tolerance. The CSP latency and duration were recorded in each extremity (Fig. 1). QSART was performed on the right side (Fig. 2). In addition, sympathetic skin responses (SSR) were recorded, as well as additional autonomic function testing (AFT) including cardiovagal measurements and blood pressure response to head-upright tilt.

Results: 58% (15/26) of patients had abnormal sweat volumes obtained from QSART, while 50% (13/26) of patients had abnormal CSP responses. Combining these two tests increased the sensitivity of testing to 77% (20/26). Only 29% of patients had abnormal SSR, and all of these cases also had a positive QSART result; this statistically significant association (p=0.04, Fisher’s exact test) may reflect common pathways involved in these responses. AFT were abnormal in only 27% of cases, with all but one of these patients demonstrating changes in other tests. Abnormalities were seen equally across all patient groups.

Conclusions: Combining CSP with QSART significantly increases sensitivity of testing when assessing patients with SFN related to diabetes, or prediabetes. This may be because different small fiber types are assessed by each of these tests. Although SSR and other tests of autonomic function have little effect on sensitivity, they can provide additional confirmation of SFN.


figure 1
Abstracts of Young Investigator Awardees

![Graph showing CSP-LR, Rec:Tb Ant 0.3mV/D 30mV/D](image)

**Lower extremity CSP**
Top - Control: normal onset latency and duration
Bottom - Patient: abnormal prolonged onset latency and shortened duration

**Figure 2**

![Graph showing sweat rate over time](image)

**QSART**
Patient: abnormal reduced sweat response from foot site
Abstracts of Oral Presentations

O1
Effects of Quadripulse stimulation over medial frontal cortex on human visuomotor sequence learning.

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Questions

The pre-SMA is reported to play important roles in visuomotor sequence learning. Previous reports suggested that non-invasive brain stimulation such as rTMS or tDCs over learning related areas could modulate human motor learning process. However, the pre-SMA has not been studied in the previous studies. To study whether plastic changes in the preSMA can modulate human visuomotor sequence learning, we studied the effects of quadripulse stimulation (QPS), a new patterned rTMS technique, over preSMA on performance of the visuomotor sequential button-press task (the 2×10 task) reported by Hikosaka et al.

Methods

15 healthy volunteers participated. We applied QPS or sham stimulation over left pre-SMA for 30 minutes. QPS consisted of repeated trains of four monophasic TMS pulses separated by inter-stimulus intervals of 5 ms (QPS-5) or 50 ms (QPS-50) with an inter-train interval of 5 s. QPS-5 was reported to induce LTP in stimulated cortex, and QPS-50 LTD. After QPS, each subject performed the 2×10 task. In this task, participants asked to press 2 illuminated buttons from 16 buttons in the correct order which he must learn by trial-and-error. A total of 10 pairs were presented in a fixed order until completion. As a behavioural outcome, we counted the number of errors to complete 20 successful trials to assess the performance accuracy, and measured the button press reaction time (BP-RT): the time from stimulus onset to the first button press, and the movement time (MT): the time from the first button release to the second button press, to assess the performance speed.

Results

The number of errors was larger in QPS-5 compared to sham stimulation, whereas it did not differ between QPS-50 and sham conditions. Neither MT nor BP-RT differed significantly among any stimulation conditions.

Conclusion

Visuomotor sequence learning could be modulated by QPS over the pre-SMA in human. Our findings suggest that preceding regional LTP over the pre-SMA suppress visuomotor sequence learning. Changes in error number and unchanged performance speed may indicate that the pre-SMA is more associated with the acquisition of sequential procedures than the performance of sequential movements.
Abstracts of Oral Presentations

O2 Detection of Early Neuropathic Abnormalities in Familial Amyloidotic Polyneuropathy by Quantitative Sudomotor Axon Reflex Test (QSART)

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Introduction

Familial Amyloid Polyneuropathy, due to TTR-Val30Met mutation (TTR-FAP), affects small myelinated (Aδ) and unmyelinated (C) fibers. In this group of subjects, the identification of a surrogate marker representing early nerve fiber damage is of utmost importance, taking into account the current possibilities of an early intervention.

Conventional neurophysiological studies are unable to detect early nerve dysfunction in TTR-FAP.

Objective

The main goal of the present study was to evaluate the role of Quantitative Sudomotor Axon Reflex Test (QSART) to identify early neuropathic involvement in TTR-FAP patients.

Methods

Thirty three patients with documented TTR - V30Met mutation and normal conventional nerve conduction studies, were enrolled. Patients were divided in 3 groups: asymptomatic carriers (G1, 9 patients); paucisymptomatic carriers, as defined by suffering from sensory or autonomic symptoms but without sensory or motor deficit on clinical examination (G2, 18 patients); and symptomatic carriers, as defined by abnormal neurological evaluation (G3, 14 patients). Sudomotor curve was assessed in four body regions: forearm (FA), proximal leg (PL), distal leg (DL) and foot (F) on the right side of every patient. Latency, volume, latency and volume ratios between distal (F and DL) and proximal (FA and PL) of the sweat responses were analyzed.

Results

We obtained 41 QSART registers, from 33 Val30Met patients. There were no differences in sex, age and body mass index among the 3 groups.

Statistically significant difference were found; comparing foot sweat latency and proximal/distal sweat latency ratio between G1 and G2 (p=0.008); for distal/proximal sweat volume ratio (p=0.006) and in foot/forearm volume relation (p=0.004) between G2 and G3; and comparing proximal/distal sweat volume ratio between G1 and G3 (p=0.047).

Conclusions

QSART is a sophistically and demanding method to assess small nerve function, which has not been systematically investigated in TTR-FAP before. Sweat foot latency and distal/proximal latency ratio seem to be an effective tool to detect early sympathetic dysfunction in TTR-FAP patients. Future studies comparing this method with other techniques are essential to define its role in diagnosis and measuring disease progression.
O3
Skin conductance activity in newborns: evidences for habituation to pain in an early age

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Habituation to pain is an adaptation process which promotes a reduction in behavioral response to a given pain stimulus over time. This mechanism is not well described in the literature in neonates due to difficulties in characterizing pain in these individuals. The pain in newborns may be evaluated by behavioral and physiological parameters such as COMFORT Behavior Scale and skin conductance activity (SCA), respectively, analyzing the overall score scale and SCA through area under the curve (AUC) and number of peaks per second (NP). The present study analyzed 14 newborns with a mean gestational age of 38 weeks (±2.18), 66% males, birth weight of 3291 g (±922 g) and minute-5APGAR of 9 (±0.3). These subjects underwent five heel pricks for blood glucose curve during a period of 24 hours (0, 3, 6, 12 and 24 hours after birth). The last four events were videotaped and the SCA was measured by Skin Conductance Measure System (SCMS) 15 and 30 seconds after pain events, investigating the effect of time elapsed after the nociceptive stimulus. Data was analyzed by repeated measure analysis over four repeated pain events and showed that there was pain habituation for SCA to the variable AUC at 15 s \(F(1,3) = 36.99, p = .009\) and 30 s intervals \(F(1,3) = 52.04, p = .005\). Also, with good correlation between AUC and COMFORT \(r = 0.98, p = .002\). However, there was no significant habituation effect observed to NP neither to scale response, although decay in the mean values was observed specially to the 4th session, suggesting that there was a process of habituation to pain. Overall, the classic gradual habituation process was not observed to the behavioral dimension, but a pattern of decays and increments with a general tendency to decrease. The newborns scores at pain scale only attended the cut off score of 17 at 1st session, going down and up in the next events. The absence of continuous reduction in the scores for the 3rd session can be explained by the pattern of habituation model presented by Colombo et al. 1. In their model, both functions of sensitization and habituation are considered to generate a third process called aggregated function. Hence, behavioral habituation to pain in neonates is better observed, therefore, by an aggregate function between sensitization and habituation while habituation was clear to the physiological parameter AUC. This observed phenomenon still needs more studies utilizing the psychophysical approach.

Reference

Abstracts of Oral Presentations

O4
FREQUENCY-SPECIFIC INSIGHT INTO MEMORY FOR DIGITS

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Question

The digit span is one of the most widely used memory tests in clinical and experimental neuropsychology. In the forward version, sequences of digits of increasing length have to be reproduced in the order in which they are presented, whereas in the backward version items must be reproduced in the reversed order. The forward task is thought to reflect verbal working memory capacity, and the backward task primarily taxes executive functioning resources. Here, we assessed whether transcranial Alternating Current Stimulation (tACS) can increase healthy individuals’ verbal memory span.

Methods

Online imperceptibly weak electrical currents in the alpha (10 Hz), beta (20 Hz), theta (5 Hz) and gamma (40 Hz) range, as well as a sham stimulation, were randomly delivered over the left lateral posterior parietal cortex, an area which has been previously associated with digit span performance. Each session of stimulation lasted 3-3.5 minutes.

Results

In the forward digit span, stimulation in the beta range significantly increased the number of items recalled, confirming the critical role of beta rhythm in the maintenance and rehearsal of information in working memory. Only minor effects of tACS were observed in the backward task.

Conclusions

These results provide one of the first evidence that tACS can have enhancing effects on memory, even on a relatively stable trait as memory span capacity. Our findings thus pave the way for clinical application of this technique in patients with memory disorders.
Abstracts of Oral Presentations

O5 Cerebro-cerebellar plasticity underlying recovery of body motion perception

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Question

Intact visual perception of body motion is indispensable for motor learning and social cognition. Recent data suggest specific impairment of biological motion processing through lesions to the left lateral cerebellum (Sokolov et al. *Cereb Cortex* 2010), apparently through perturbation of communication with the right superior temporal sulcus, STS (Sokolov et al. *Neuroimage* 2012), a key structure within the action observation network. However, compensatory potential of this circuitry remains unknown.

Methods

To this end, we conducted follow-up assessment of visual sensitivity to point-light biological motion in a patient SL with left cerebellar dysplastic gangliocytoma (WHO grade I), and six healthy matched controls. Functional magnetic resonance imaging (fMRI) and effective connectivity were used to assess underlying brain network plasticity.

Results

Preoperative visual sensitivity to biological motion in patient SL was significantly lower than in healthy matched controls ($\chi^2 = 9.54, p < 0.01$). Sensitivity substantially improved at 8 months ($\chi^2 = 15.12, p < 0.001$) and attained the level of controls at 24 months after neurosurgery ($\chi^2 = 1$, n.s.). As compared to healthy controls, fMRI reveals activation of left cerebellar lobules III and IX ($x = -14, y = -34, z = -22$, and $x = -6, y = -60, z = -56$, respectively; MNI coordinates), representing a midline shift of cerebellar activity. Psychophysiological interaction (PPI) analysis shows that, as in normalcy, the left cerebellum interacts with a region in the right STS ($x = 44, y = -24, z = 0$), but located more anteriorly than in healthy participants.

Conclusions

The outcome indicates a remarkable potential for recovery of biological motion perception after removal of a left cerebellar tumor that appears to be mediated by topographical cerebro-cerebellar network reorganization. The findings open a window for further research on functional compensation and plasticity after cerebellar damage.
Abstracts of Oral Presentations

O6
Comparison of CMAP Duration in CIM and Other Myopathies

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QUESTION

Compound muscle action potential (CMAP) duration has previously been shown to frequently be prolonged in Critical Illness Myopathy (CIM)¹,². Recording prolonged CMAPs in the Intensive Care setting may aid the diagnosis of CIM.² Here, we investigate whether the CMAP duration is prolonged in inflammatory myopathy, and myopathy of other cause (“non-inflammatory”), and compare these to results previously found in CIM².

METHODS

We collected data from EMGs performed in our department since April 2007 on 43 patients with a confirmed diagnosis of myopathy. CMAP duration in the abductor pollicis brevis (APB) and abductor hallucis (AH) muscles were collected. We compared CMAP durations in the “inflammatory” group to the “non-inflammatory group” and to a group of normal controls².

RESULTS

We collected CMAP durations from APB in 33 patients, and from AH in 36 patients.

The mean CMAP duration was significantly longer in the “inflammatory” group than in the controls in APB (6.4 ms (range 5 - 9.5, SD 1.2) v 5.0 ms (range 3.9 - 6.3, SD 0.6) p = 0.0008) and in AH (6.0 ms (range 4 - 9.4, SD 1.3) v 5 ms (range 3.2 - 6.7, SD 0.9) p = 0.020).

The mean CMAP duration was also significantly longer in the “inflammatory” group than in the “non-inflammatorry” group, in APB (p = 0.034) and in AH (p = 0.040).

There was no significant difference in the duration of the CMAPs between the “non-inflammatory” group and the controls in APB (5.46 ms (SD 1.22) v 5.0 ms (SD 0.6) p = 0.88) nor in AH (5.05 ms (SD 1.3) v 5.0 ms (SD 0.9) p = 0.14).

CONCLUSION

The findings suggest that CMAPs can be mildly prolonged in inflammatory myopathies. This may suggest an element of muscle membrane dysfunction in these conditions. This CMAP prolongation is small compared to in CIM, where the mean CMAP duration was 9 ms in APB and 9.4 ms in AH.² Prolongation of the CMAP duration to greater than about 9 ms seems to be fairly specific to CIM. Furthermore, the lack of prolongation of CMAPs in the non-inflammatory myopathies reinforces the potential use of prolongation of CMAPs as a diagnostic tool in CIM.

References


Abstracts of Oral Presentations

O7 
Succesful pilot trial of L-arginine and metformin in Duchenne’s muscular dystrophy”

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Duchenne muscular dystrophy (DMD) is the most common inherited muscle disorder leading to relentless muscle wasting and premature death in affected children. The only currently available symptomatic treatment for DMD consists of corticosteroids, resulting in modest beneficial effects but relevant side-effects. In DMD dystrophin expression is lost disrupting the normal cytoskeletal structure. While most research has focused on the structural consequences, e.g. destabilization of the dystrophin associated glycoprotein complex resulting in muscles fibres that are more sensitive to mechanical damage and thus degenerate. In contrast, we approach the metabolic consequences of dystrophin loss which is associated with a severe reduction of neuronal nitric oxide (NO) synthase (nNOS). NO stimulates the up-regulation of nuclear genes involved in mitochondrial biogenesis and ATP generation. Therefore, NO precursors (as the amino acids L-arginine and L-citrulline) and the biguanide antidiabetic drug metformin (indirect nNOS activator) could serve as treatment for DMD. We were the first using this approach in human DMD patients, and performed an investigator initiated sixteen week pilot study in five ambulant DMD patients with L-arginine and metformin. Biomarker analysis in muscle biopsies of these patients show increased cGMP and nitrotyrosin concentration after treatment and reduced markers of oxidative stress. We observed an improved lipid metabolism using indirect calorimetry, improved functional abilities (motor function measurement (MFM) score), and prolonged walking distances in the 2 min walking distance. MFM scores improved more than the reported mean improvements after onset of (standard) steroid treatment in DMD. Furthermore, quantitative muscle magnet resonance imaging (MRI) indicated that our treatment slows progression of muscle degeneration in DMD. These results must of course be confirmed in a placebo controlled randomized clinical trial (RCT) with a larger group of patients. In case of positive results a more effective and safer symptomatic treatment will be available in DMD and might also lead to the development of even more potent drugs.
O8
Neuronal firing rates in the globus pallidus of children with dystonia

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Question

Previous studies of microelectrode recordings (MER) from adults undergoing deep brain stimulation (DBS) for dystonia have reported no significant difference in globus pallidus interna (GPi) or externa (GPe) firing rate between primary and secondary dystonia1,2. We report MER data from 37 children with dystonia and investigate whether firing rates differ between different types of dystonia.

Methods

MER data were obtained as part of standard surgical procedure to guide electrode position in 37 children (2-18 years, mean 11) undergoing DBS for dystonia: 12 primary, 18 secondary static (e.g. following prematurity) and 7 secondary progressive dystonia due to Neuronal Brain Iron Accumulation (NBIA). Age across groups was not significantly different. Single cell and multiunit extracellular activities were recorded along the microelectrode track in 1 mm steps. Recordings were bandpass filtered (500-5,000Hz) and digitised at 24 KHz. Firing frequencies of individual cells at each level were documented and analysed offline using Wave_Clus spike-sorting software within MATLAB. Electrode placement was confirmed by post-operative stereotactic CT.

Results

Data were available for 155 GPi and 59 GPe cells. Median GPi firing frequencies were 13, 8.5 and 30Hz for the primary, secondary static and NBIA groups respectively. Median GPe firing frequencies were 10, 5 and 11Hz. Kruskal Wallis test revealed a significant effect of dystonia type on GPi (p

Conclusions

GPi firing rate in NBIA is different from that observed in primary or secondary static dystonia. This may explain the absence of differences between primary and secondary dystonias reported previously. Identification of specific firing patterns may help in deciding targets and patient-specific protocols of neuromodulation therapy.

References

Abstracts of Oral Presentations

O9
Motor imagery modulates the spinal reciprocal inhibition among patients with stroke.

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Question

We studied if motor imagery could increase the excitability of motor cortex and spinal motoneuron. Corticospinal projection to the spinal inhibitory interneuron modulates the magnitude of spinal reciprocal inhibition (RI). In patients with upper motor neuron lesions, spinal RI is disturbed. Prior work suggests that decreased RI contributes to spasticity. Restoration of RI is supposed to be important for functional recovery. We hypothesized that motor imagery could modulate the activity of the spinal reciprocal inhibitory interneuron. We assessed whether motor imagery could modulate the paretic forearm RI in patients with chronic hemiparetic stroke.

Methods

Participants were 13 patients with chronic hemiparetic stroke. Their mean age was 48.5 years old and the median time from stroke onset was 17.5 months. RI was assessed with a flexor carpi radialis H reflex conditioning-test paradigm. The conditioning-test stimulus interval was set at 0, 20 and 100ms (RI at 0ms, RI at 20ms and RI at 100ms). Participants were asked to imagine paretic finger extension during assessment of imagery RI.

Results

When compared with the resting RI, motor imagery increased the magnitude of RI at every interstimulus interval (p<0.05)

Conclusions

Motor imagery modulated the RI in patients with chronic stroke. It is supposed that increased motor cortex excitability can modulate the RI. Motor imagery can increase motor cortex excitability and increase the activity of corticospinal projection to the spinal interneuron.
Abstracts of Oral Presentations

O10
Effect size of quantitative muscle imaging in Duchenne muscular dystrophy exceeds the effect size of clinical scores of muscle function

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The aim of this ethics approved one year observational trial was to compare functional abilities and muscle imaging data in 20 patients with genetically confirmed Duchenne muscular dystrophy. Physical assessment was performed using the motor function measurement (MFM) scale. Quantitative magnet resonance imaging (qMRI) of thigh muscles was performed using the two-point Dixon method. One year functional and imaging changes were different according to the age and walking abilities at inclusion (group 1: below the age of seven; group 2: seven years and older and ambulant; group 3: non-ambulant). While patients of the first group still showed improvement of motor abilities, in group 2 the largest effect size (1.2) was found in the D1 subscore (standing and transfer function) of the MFM, and in group 3 the largest effect size was found for the total MFM score (0.66). In contrast, the effect sizes using qMRI was much larger consisting of 1.6 in group 1 (all thigh muscles), 4.1 in group 2 (hamstrings), and 2.3 in group 3 (knee extensors). These data suggest that qMRI has an added value compared to clinical outcome measures when designing therapeutic clinical trials in patients with DMD. Power analysis suggest that there are only a few needed patients to show an effect of a putative novel treatment when using quantitative muscle MRI in DMD.
Abstracts of Oral Presentations

O11
ESTIMATION OF THE MUSCLE FIBER DENSITY FROM THE MOTOR UNIT ACTION POTENTIAL

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Introduction

The aim of this study is the estimation of the muscle fiber density (FD) from the Motor Unit Action Potentials (MUAP) to form a method for monitoring the progress of neuromuscular diseases.

Methods

Data groups representing motor units of neurogenic (n=5), myopathic (n=5) and healthy cases (n=5) were created via EMG Simulator v3.6. MUAPs generated from each data group have been detected through a concentric needle electrode of a scanning EMG system. The spikes of the single fiber action potentials within the MUAPs have been found by computing the second-order derivative of MUAPs to estimate the detected number of fibers. MUAPs from 20 different locations within a Motor Unit Territory (MUT) have been acquired. The fiber density (FD) has been computed by taking the average of these numbers of fibers. True FDs have been computed for each MUT. Mean Square Errors (MSE) have been computed for each data group to determine the sensitivity of the method.

Results

The test statistics of the FDs (Mean±SD) have been found as 4.13±1.31 (Min:2 and Max:8), 2.37±0.98 (Min:1 and Max:5) and, 2.40±0.70 (Min:1 and Max:4) for neurogenic, myopathic and healthy cases respectively. Mean true fiber densities have been 5.66, 2.57 and 1.50 and MSE have been 4.02, 0.15 and, 0.86 for neurogenic, myopathic and healthy cases respectively. These MSE values have been suggested that this method is more selective for myopathic cases compared to neurogenic and healthy cases.

Conclusion

Computation of FD via the second-order derivative of MUAPs can be considered as a beneficial preliminary research. Nevertheless, this method might be extended by taking into account other variables such as maximum amplitude to increase the sensitivity for neurogenic cases.

Keywords

Motor Unit Action Potential, Scanning EMG, Fiber Density, Motor Unit Territory


Abstracts of Oral Presentations

**O12**
Exercise training restores the regenerative potential of injured skeletal muscle via activation of endogenous stem cells.

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**Background**

Skeletal muscle ischemia reperfusion injury (IRI) is a serious clinical problem arising as consequence of vascular thrombosis, limb trauma and is endowed with 10-20% rate of amputation. Satellite cells are myogenic progenitors that offer new source of myonuclei for muscle repair upon injury.

**Objectives**

This study aimed to examine the effect of swimming exercise on the ability of muscle to regenerate via activation of its endogenous stem cells and its impact on muscle performance in model of IRI.

**Methods**

40 rats were divided into 4 groups: I; control, II; IRI with 2 hours ischemia and 2 hours reperfusion, III; IRI and left for 2 weeks recovery, IV; exercise trained groups for 2 months prior to IRI and allowed 2 weeks to recover. Muscle performance was evaluated by measuring [peak twitch tension (Pt), peak tetanic tension (PTT) and fatigue resistance time (FR)]. CD34, marker for satellite cells, was assessed using immunostaining and the area % of CD34 +ve cells was determined using image analysis. Area of alpha smooth muscle actin (αSMA) positive immunoe xpression, indicating activated satellite cells was also detected. Assessment of the area of regenerating fibers was performed in H&E stained sections.

**Results**

IRI induced significant muscle damage that was reflected by subsequent decrease in Pt and PTT and shortening in the FR time. After 2 weeks, few +ve CD34 spindle and oval cells among atypical muscle fibers as well as areas of αSMA were detected and partial improvement in the contractile forces and FR were noticed. In the exercise trained group (IV), multiple +ve spindle cells at the periphery of muscle fibers and more obvious αSMA immunoexpression were detected in typical muscle fibers. There was also marked improvement in the mechanical muscle performance in group IV than in group III. This was further supported by higher significant increase in the area of regenerating fibers in group IV as compared to group III and II.

**Conclusion**

IRI induced significant muscle damage. The process for normal muscle repair for 2 weeks following IRI was not able to restore the normal structure and function in the regenerated muscle. Exercise training activates the satellite cells and enhances the regenerative potential of the injured muscle with almost complete restoration of its mechanical contractile performance.
Abstracts of Oral Presentations

O13
BRAIN’S GAMMA OSCILLATIONS: A NEW STRATEGY TO ANALYZE FUNCTIONAL CORRELATES AND COGNITIVE IMPAIRMENT

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**Question**

The search of functional correlates of oscillatory gamma responses is one of the major themes in cognitive function and cognitive impairment. However, the results often lead to controversies. The present study introduces a new comparative analysis of gamma responses between simple light stimulation and cognitive stimulation by means of P300 oddball paradigm. Responses were determined in multiple sub-gamma bands.

**Methods**

EEGs of 13 healthy subjects were recorded at 32 locations. The spectral analysis of evoked and event related gamma (25-48 Hz) oscillations (EROs) were analyzed in four different time windows (0-150 ms, 200-400 ms, 400-600 and 600-800 ms) by evaluation of inter-trial coherence and event related oscillations in 25-30 Hz, 30-35 Hz and 40-48 Hz frequency bands.

**Results**

Application of ANOVA showed that target stimulation elicited higher gamma phase locking values than simple light in the 200-400 ms (p < 0.003), 400-600 ms (p < 0.003) time windows in frontal locations. The difference between cognitive stimulation and sensory stimulation is seen mostly in the 200-400 ms and 600-800 ms time windows. Parietal EROs showed delays of approx. 100-150 ms in comparison to occipital and frontal locations. Moreover, cognitive signals elicited additive higher frequency responses.

**Conclusions**

The applied strategy allows a better differentiation of functional correlates by reducing controversies. Therefore, analysis of cognitive impairment will attain new dimensions, especially in Alzheimer’s disease.
Non-invasive single-trial EEG detection of human neocortical population spikes

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3Physikalisch-Technische Bundesanstalt, Institute Berlin, Berlin, Germany
4Bernstein Center for Computational Neuroscience Berlin, Berlin, Germany

**Question**
Non-invasively recorded high-frequency (> 400 Hz) components of somatosensory evoked potentials (hf-SEP) are generated by cortical population spikes, as revealed by microelectrode recordings in primates. Until now it was a critical drawback that this approach required averaging hundreds of responses for reliable hf-SEP detection. Here, we establish how to detect human hf-SEP non-invasively in single trials.

**Methods**
Inside a shielded room median nerve hf-SEP were recorded in four subjects spanning the hf-SEP signal-to-noise ratio characteristic for a larger population, utilizing a custom-built 29-channel low-noise EEG amplifier. Features were extracted from band-pass filtered (400-900 Hz) trials by bilinear Common Spatial Patterns (bCSP) to construct both, optimized spatial and temporal filters, and then classified by a weighted Extreme Learning Machine (w-ELM).

**Results**
Human hf-SEP were detected in single trials with a sensitivity of up to 98% and a specificity up to 97% in two subjects, even without any recourse to stimulus timing. Since for the two subjects with lower signal-to-noise ratio these rates dropped to 62-79% sensitivity and 18-28% specificity, optimal recording quality is a critical prerequisite for efficient single-trial detection.

**Conclusions**
Non-invasive low-noise recordings can extract high-frequency EEG components otherwise buried in background noise. Specifically, a refined supervised filter optimization and classification can enable reliable single-trial hf-SEP detection, representing a non-invasive correlate of cortical population spikes. Thus, while low-frequency EEG reflects summed postsynaptic potentials and thereby neuronal input, we suggest that hf-SEP provides non-invasive access to the output of neuronal computation: spiking activity in the responsive neuronal ensemble.
O15
Source localisation of rhythmic ictal activity: a study of diagnostic accuracy following STARD criteria

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²Lund University, Lund, Sweden
³Danish Epilepsy Centre, Department of Clinical Neurophysiology, Dianalund, Denmark
⁴University of Copenhagen, Copenhagen, Denmark

Question

Although precise identification of the seizure onset zone is an essential element of presurgical evaluation, source localisation of ictal EEG signals has received little attention. The aim of our study was to estimate the accuracy of source localisation of rhythmic ictal EEG activity using a distributed source model.

Methods

Source localisation of rhythmic ictal activity was performed in 42 consecutive cases fulfilling inclusion criteria. The study was designed according to recommendations for studies on diagnostic accuracy (STARD). The initial ictal EEG signals were selected using a standardised method, based on frequency analysis and voltage distribution of the ictal activity. A distributed source model - local autoregressive average (LAURA) was used for the source localisation. Sensitivity, specificity and measurement of agreement (kappa) were determined based on the reference standard - the consensus conclusion of the multidisciplinary epilepsy surgery team. Predictive values were calculated from the surgical outcome of the operated patients. To estimate the clinical value of the ictal source analysis, we compared the likelihood ratios of concordant and discordant results. Source localisation was performed blinded to the clinical data, and before the surgical decision.

Results

Reference standard was available for 33 patients. The ictal source localisation had a sensitivity of 70% and a specificity of 76%. The mean measurement of agreement (kappa) was 0.61 corresponding to substantial agreement (95% CI: 0.38-0.84). Twenty patients underwent resective surgery. The positive predictive value for seizure-freedom was 92% and the negative predictive value was 43%. The likelihood ratio was nine times higher for the concordant results, as compared with the discordant ones.

Conclusions

Source localisation of rhythmic ictal activity using a distributed source model (LAURA) for the ictal EEG signals selected with a standardised method is feasible in the clinical practice and has a good diagnostic accuracy. Our findings encourage clinical neurophysiologists assessing ictal EEGs to include this method in their armamentarium.

Figure 1. Flowchart of the study
Figure 2. Ictal source localisation
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figure 1

[Diagram showing the flow of patient cases with details like Eligible patients n=42, Source localisation n=42, Conclusive localisation n=42, Inconclusive localisation n=0, Reference standard n=33, No reference standard n=9, Concordant localisation n=24, Discordant localisation n=9, Operated n=13, Seizure-free n=12, Operated n=7, Seizure-free n=4.]

figure 2

[Images A, B, C, D showing brain scans with color-coded areas and numerical values.]
Detection of Epileptiform Activity Using Multi-Channel Linear Prediction Coefficients and Localization of Epileptic Foci Based on EEG-fMRI Data

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Question

Spatial localization of seizure and interictal epileptiform activity (IEA) onset zones remains a challenge in diagnosis and pre-surgical treatment of drug-resistant epilepsy. We present a novel non-invasive method for semi-automatic detection and localization of IEA based on EEG-fMRI data. The method has 3 stages: automated detection of IEA - IE discharges (IED) and interictal rhythmic activity (IRA); classification of detected activity using cluster analysis; localization of hemodynamic response correlated with IEA.

Methods

Abnormal EEG activity is detected based on the multi-channel auto-regressive model and inverse filter principle. The filter is determined using a reference window representing the normal EEG; the signal passes through the inverse filter, and segments deviating from the reference window are marked as candidate IE activities (CIEA). Cluster analysis of CIEA’s is based on 2 feature extraction methods: Chebyshev polynomial coefficients; multi-channel linear prediction coefficients. Cluster analysis using modified K-means sorts CIEA’s into epileptic activity and other physiological non-epileptic waves or noise. Based on periods of normal vs. IEA, a hemodynamic prediction model is estimated. Blood Oxygen Level Dependent (BOLD) response (fMRI data) is examined, searching for voxels most correlated to the prediction model. 4×2.7×2.7mm voxel size of fMRI data provides high-resolution source localization (SL). SL is also performed with standardized Low Resolution Brain Electromagnetic Tomography (sLORETA). The 2 independent techniques of SL’s are compared to assess consistency of the results. Data from 10 epileptic patients was analyzed.

Results

IED’s and IRA’s were detected with overall True Positive Rate (TPR) of 86% and False Detection Rate (FDR) of 24%. Addition of the clustering stage to the system improved FDR to 5%, with a trade-off of reduction in TPR to 77%. IED’s detected by the system were associated with increased focal BOLD responses in brain areas spatially related to sLORETA localization. In 9 out of the 10 patients the source found was consistent with clinical findings.

Conclusions

Our findings suggest that our semi-automated system may be able to offer both detection and high-resolution spatial localization of pathological interictal brain activity.
A novel method to induce human cortical plasticity using cortical disinhibition

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³Goethe-University, Department of Neurology, Frankfurt am Main, Germany
⁴Fukushima Medical University, Fukushima, Japan
⁵Eberhard- Karls-University, Department of Neurology and Stroke, Hertie Institute for Clinical Brain Research, Tuebingen, Germany

Objective

Cellular studies show that cortical plasticity-inducing stimulation protocols are even more effective when delivered during a state of cortical disinhibition, and we have recently identified a period of late cortical disinhibition (LCD) in human motor cortex. Our aim was therefore to determine whether disinhibition could likewise facilitate plasticity-induction in the human motor cortex. To test this, we used a previously described transcranial magnetic stimulation (TMS) plasticity protocol that targets indirect (I-) wave dynamics (ITMS), and delivered this repeatedly at a timing that either did, or did not, correspond with the temporal course of LCD.

Methods

In 8 healthy participants we recorded motor evoked potentials (MEPs) from the right first dorsal interosseous (FDI) muscle. We delivered TMS doublets (corresponding to individual I-wave facilitation, ISI~1.5ms), with an inter-doublet interval (IDI) optimised to the individual timing of LCD (~200-250ms, ITMS-OPT). Each doublet evoked LCD, and the subsequent doublet was delivered during LCD. Trains of 4 doublets were delivered with an 8 second inter-train interval, and with 6 trains in total (i.e. 48 pulses delivered over ~54 seconds). Control conditions consisted of decreasing (50ms) or increasing (50ms) the IDI, and replacing ITMS with amplitude matched single-pulse (SP) TMS. SP MEPs were recorded pre- and post intervention to investigate effects on cortical excitability.

Results

The IDI corresponding to ITMS-OPT was in the range 220-250ms. SP MEPs were significantly facilitated to ~140% of baseline for at least 30 minutes following ITMS-OPT while the effect of ITMS at other intervals or with SP TMS did not persist beyond 5 minutes.

Conclusion

When paired with disinhibition, 48 ITMS pulses delivered over less than a minute induced a long-lasting (>30min) period of increased corticomotor excitability. There was no effect at intervals not corresponding to disinhibition. We conclude that targeting disinhibition in human motor cortex offers a promising new strategy for increasing the effectiveness of TMS plasticity-inducing protocols.
Abstracts of Oral Presentations

O18 Utility of Revised El Escorial criteria (REEC) versus Awaji Shima criteria (ASC) in diagnosis of Amyotrophic Lateral Sclerosis (ALS): A retrospective study in a tertiary hospital in India.

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The REEC criteria is widely followed for diagnosing ALS but has limitations because of a low sensitivity. The Awaji Shima consensus in 2006 suggested that the electrophysiological evidence of denervation should be taken as equivalent to clinical information.

Aim
To compare in a retrospective study the utility of the Revised El Escorial criteria (REEC) versus the Awaji Shima (ASC) criteria in establishing an accurate diagnosis of ALS in a tertiary hospital.

Methods
The records and electrophysiological data of 70 patients with a suspected diagnosis of ALS evaluated in the period January 2008 to August 2013 were studied. We included patients 18 years or more who had been diagnosed as at least possible ALS as per the REEC. Patients with alternative diagnosis, pure upper or lower motor neuron diseases, familial ALS were excluded from the study. The patients had been investigated with labs, nerve conduction studies, ALS protocol needle EMG and relevant brain or spine MRI. Each patient was assigned the category as per REEC and ASC at the time of presentation. Statistical analysis by cross tabulation and kappa analysis was done.

Results: There were a total of 70 cases in the study. Amongst the 70 patients 25(35.71%) had bulbar onset and limb onset in 45(64.28%). The age of the patients ranged from 22 years to 76 years. As per the REEC there were 7 (10 %) patients in the clinically possible, 12(17.14%) patients in the laboratory supported probable, 31 patients (44.28%) in clinically probable and 20 patients (28.57%) in definite category. As per the ASC 7 patients (10%) were in possible, 28 patients (40.0%) in probable and 35 patients (50.00%) in definite category. In 15 (21.42%) cases the category assigned by the ASC was better than that by REEC. Amongst the 25 bulbar onset cases 9 (36.0%) patients were upgraded from a probable category in REEC criteria to definite in ASC. In 46 (65.71%) cases the categorization in REEC and ASC were concordant.

Conclusions
Our data indicate that using the Awaji Shima criteria made the diagnosis of ALS more likely by at least one category in 21.42% of all cases and 36% of bulbar onset cases and identified at least one additional region of ongoing denervation in 32.85% of cases. Hence Awaji Shima criteria should be used for accurate categorization of ALS at presentation.
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figure 1

<table>
<thead>
<tr>
<th>Table 2: Age profile of patients.</th>
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<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>60-69</td>
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<tr>
<td>70-79</td>
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<tr>
<td>80-89</td>
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<tr>
<td>≥90</td>
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<th>Table 3: Region of nevus present.</th>
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<tbody>
<tr>
<td>Total cases</td>
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<tr>
<td>Nasal septum</td>
</tr>
<tr>
<td>Lower lip</td>
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</tbody>
</table>

<table>
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<th>Table 4: Duration of symptoms and presentation.</th>
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<tbody>
<tr>
<td>Duration of presentation</td>
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<tr>
<td>&lt;1 month</td>
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<tr>
<td>1-3 months</td>
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<tr>
<td>4-6 months</td>
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<tr>
<td>7-9 months</td>
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<tr>
<td>&gt;12 months</td>
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<th>Table 5: Disease classification as per ABCD and ASCD.</th>
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<tr>
<td>Category</td>
</tr>
<tr>
<td>Possible</td>
</tr>
<tr>
<td>Pretable</td>
</tr>
<tr>
<td>Definite</td>
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<table>
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<th>Table 6: Correlation between disease site and classification per ABCD and ASCD.</th>
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<tbody>
<tr>
<td>Disease site</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Lower lip</td>
</tr>
<tr>
<td>Nose</td>
</tr>
<tr>
<td>Oral vestibule</td>
</tr>
<tr>
<td>Oral floor</td>
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<tr>
<td>Oral mucosa</td>
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<tr>
<td>Oral lip</td>
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<th>Table 7: ABCD-ASCD CORRELATION.</th>
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<tr>
<td>Criteria</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>ASD Possible</td>
</tr>
<tr>
<td>ASD Probable</td>
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<tr>
<td>ASD Definite</td>
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<tr>
<td>Total</td>
</tr>
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</table>

Figure 2

Data of patients with updated classification per ABCD as compared to ASCD.
The electrophysiological study of Hirayama disease

*M. li*

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**Objective**

The electrophysiological characteristics of representation of Hirayama diseases were analyzed and summarized for its diagnosis.

**Method**

Electrophysiological testing was performed in eighteen patients who fulfilled the clinical criteria for Hirayama disease. MCV and SCV of median nerve and ulnar nerve and EMG of ADM, APB, EDC, BR, biceps brachii and sternocleidomastoid were detected in all cases; MCV and SCV of peroneal nerve and EMG of AT were examined in one side of lower limbs. MCV and SCV of ulnar nerve and EMG of ADM, APB, EDC, BR were inspected in contralateral sides of eight cases. MCV was done segmentally by stimulating the nerve distally as well as proximally, and determining whether there was nerve conduction block.

**Result**

There was no conduction block in all cases; All the SCV and SNAP normal; All the MCV of peroneal nerve and EMG of AT were normal; The slowing of MCV in upper limbs accounted for 41.3%. The slowing of the amplitude of CMAP in upper limbs accounted for 81.8%. According to EMG of upper limbs, the positive rates of neurogenic damage were 47.0%. The decreasing order of positive rates in different tested muscles was ADM in affected sides, APB in affected sides, EDC in affected sides, ADM in contralateral sides, EDC in contralateral sides, BR in affected sides, biceps brachii in affected sides; there were no neurogenic damage in EMG of BR in contralateral sides and sternocleidomastoid.

**Conclusion**

The electrophysiological features of Hirayama disease were neurogenic damage in unilateral upper limbs, or in bilateral upper limbs one of which had significant neurogenic damage. According to abnormal EMG, spinal anterior horn cells of C7-T1 in affected sides were injured, and C6 and above C6 were rarely involved in. The electrophysiological characteristics of Hirayama disease could provide a clear positioning for the disease diagnosis.
Abstracts of Oral Presentations

O20
High Volitional Load Tasks versus Low Volitional Load Tasks and the Bereitschaftspotential - an sLORETA Brain Mapping Study

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Question

The Bereitschaftspotential, BP or readiness potential is the EEG correlate of volitionally intended movements. Planning and preparation of volitional action starts in the supplementary motor area (SMA [BA 6a and β] and cingulate motor area CMA [BA 24], early BP component, BP1). The SMA/CMA activity is traveling via the basal ganglia (motor loop, cortico-basal ganglio-thalamo-cortical loop) to the primary motor cortex (M1 [BA 4], late BP component, BP2). The final movement execution is carried out by M1, using the program storages of the basal ganglia, especially for well-learned movements that can be performed automatically (subroutines). During BP1 we do not yet consciously perceive our own motor planning, but during BP2 we do. From this observation Libet 1983 inferred that we have no free will in the initiation of the action (BP1) but only in the control of it (BP2). In our opinion free will is involved in both initiation and control, since we expect free will to occur in unconscious brain processes as well (Kornhuber & Deecke, 2012).

Methods

We investigated different volitional loads (high vs. low, by instruction) on the BP by using EEG (28 leads, 10 Ss., 105 sequential flexion tasks [right digits 2-4] per condition) and sLORETA, Low resolution brain electromagnetic tomography.

Results

BP1 with high volitional load starts earlier in SMA/CMA (p < 0.001; 260 ms) and in M1 (252 ms) than it does with low volitional load. Stronger activations we found in the high volitional load tasks in SMA/CMA, M1 and parietally during BP0-100 (p < 0.05; MD in μV: Cz=-1.3, C1=-1.1, Pz=-1.4).

Conclusions

We found earlier onset and stronger activation in high volitional actions, confirming the concept that more willfulness is needed to plan and prepare them. Due to the initiating and controlling role of the SMA/CMA as part of a commanding and supervising pre-motor system, our data indicate a volitional, willful access to movement initiation, consciousness not necessarily being a prerequisite of free will.

References


O21
Neuroprosthetic arm using MEG signals of paralyzed patients
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4Nara Institute of Science and Technology, Kyoto, Japan
5The University of Electro-Communications, Department of Mechanical Engineering and Intelligent Systems, Tokyo, Japan

Abstract

Neuroprosthetic arm control using invasive signals has been shown to afford restoration of motor functions to paralyzed patients. Though, a non-invasive method to test and improve the efficacy of patients using an invasive system remain to be developed. Here, we developed a neuroprosthetic arm controlled by magnetoencephalography (MEG) signals to test and train patients to control the arm by attempting to move their paralyzed limbs.

Methods

A 160-channel Yokogawa MEG system with a real time output port was used. The entrained patients had severe paresis on their upper limbs and gave written informed consent to participate in the study, which was approved by the Ethics Committee of Osaka University Hospital. First, the MEG signals were obtained while the patients attempted to grasp or open their paralyzed hands. The attempted movements were inferred by support vector machine and Gaussian process regression using time-averaged MEG signals. The prosthetic arm was controlled to mimic the inferred movements. For the patient training session, patients controlled the neuroprosthetic arm to grasp and release an object.

Results

The accuracy of inferring the attempted movement type varied among patients from approximately 60 to 80%. Statistical analysis revealed that movement-related signals from around the motor area significantly contributed to the prediction. After the patient training sessions, the accuracy was improved for some patients, suggesting a learning effect.

Conclusions

It was suggested that the developed system is useful to train the patients to control a prosthetic arm and to evaluate the applicability of motor restoration using invasive BMI.
O23
Uncoupling between heart rate and EEG in sepsis

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Question

Healthy organs are thought to behave as coupled oscillators. A correlation between heart rate and power in the alpha band in EEG in healthy subjects has been reported previously. A lower power in heart rate variability in patients with acute brain injury correlates with worse outcome. In this study, we aimed to assess the variability of heart rate and EEG and their relationship in patients with sepsis.

Methods

Fifty-two septic patients not receiving any sedative drug at the time of monitoring were prospectively identified and divided into a comatose (Glasgow Coma Scale [GCS]≤8; N=30) and non-comatose group (GCS>8). Thirteen subjects with no history of neurological or cardiac disorder and a normal EEG were retrospectively included as controls. A 30-minute artifact and seizure-free EEG and EKG recording was collected between 6am and 10am. Heart rate variability, variability of the power in the alpha frequency band, and the relationship between them were quantified using linear (least-square periodogram and magnitude square coherence) and nonlinear (Shannon entropy and mutual information) methods. These measures were compared between the three groups and correlated to outcome as measured by the Glasgow outcome scale.

Results

Low and very low frequency (<0.015Hz) variations of the EEG alpha power and the heart rate were significantly lower in patients with sepsis compared to controls. Coherence and mutual information between heart rate and EEG alpha power were also lower in patients with sepsis, in particular in comatose patients. Greater variation of the alpha power around 0.02Hz was correlated with better outcome.

Conclusion

Heart rate and EEG alpha power vary in a coupled way in healthy individuals. Sepsis was associated with lower variability and decreased coupling. Greater variation of EEG alpha power in specific frequency bands, and to a lesser extent greater coupling, were associated with better outcome.
Abstracts of Oral Presentations

O24 An EEG and fMRI investigation into the therapeutic mechanism of Deep Brain Stimulation in Psychiatric Disorders.

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Obsessive-Compulsive Disorder (OCD) is a psychiatric disorder characterized by obsessions - involuntary thoughts - and compulsions. OCD is associated with excessive activity and connectivity within the frontostriatal brain network. Electrically stimulating the frontostriatal network using Deep Brain Stimulation (DBS) has been effective in alleviating the symptoms in treatment-resistant OCD. However, the working mechanisms of DBS remain unknown. The objective of this study has been to elucidate the mechanism underlying therapeutic DBS in psychiatric disorders. We carried out this endeavor by examining how DBS influences the oscillatory activity in the EEG as well as the BOLD signal both during rest and symptom provocation in EEG.

Using a DBS ON/OFF design, we show that DBS normalizes the activity and connectivity between the frontostriatal network. Using resting-state EEG we showed that frontal theta phase-stability is reduced by DBS. Since brain areas communicate by increasing phase-synchrony, decreases in phase-stability reduce the capacity for brain regions to phase-synchronize. Notably, we also found that frontal theta power in response to symptom-provoking stimuli — a potential biomarker for OCD — is normalized to comparable levels of frontal theta power elicited by neutral stimuli, while leaving frontal theta power in response to neutral stimuli intact.

Taken together, our results suggest that DBS normalizes the excessive connectivity of the frontostriatal system in OCD patients by reducing the ability of a brain area to receive and send signals to brain areas at optimal times.

Figure 1 Schematic illustration of phase-stability. C Reduction of phase-stability during DBS ON in absence of power differences.

Figure 2 A Schematic illustration of symptom provocation task. B & C Time-Frequency representation of Power and statistics.


Electrophysiological signatures of plasticity in the visual and auditory cortex after cochlear implantation

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Question

Previous studies have suggested that sensory deprivation as well as cochlear implantation can induce cortical plasticity (Pantev et al., 2006; Sandmann et al., 2012). In our study we assessed the question how the deprivation-induced cortical reorganization affects the adaptation of the auditory cortex to the cochlear implant (CI) signal.

Methods

We conducted a prospective longitudinal study which used electroencephalography (EEG) to examine post-lingually deafened CI users (N=10; mean age: 59 years) before as well as after implantation. A group of matched normal-hearing listeners (N=12; mean age: 60 years) served as control. The two groups performed a discrimination task with different frequency-modulated tones (auditory condition) and patterns of coherent motion (visual condition).

Results

The results revealed an enhancement of auditory discrimination ability over the period of one year following cochlear implantation. At the same time, CI users showed an increase of the N1 event-related potential (ERP) for the auditory condition, and a decrease of the P1 ERP for the visual condition. Importantly, the amplitude of the visual ERP was inversely related to the speech recognition ability with a CI.

Conclusions

Our results demonstrate a rapid adaptation of the auditory cortex in elderly CI recipients and indicate associations between changes in the visual and auditory modality during CI rehabilitation.

References


O26
Non-invasive alternating current stimulation to improve visual impairment after post-chiasmatic lesions

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Non-invasive brain stimulation using alternating current stimulation (ACS) has recently been shown to improve vision after optic nerve damage. It is assumed that transorbital ACS induces neuronal networks to propagate synchronous firing probably activating partially damaged areas surviving the injury.

The aim of the 'Restoration of Vision after Stroke' (REVIS) ERA-Net is to determine if transorbital ACS may also have a positive impact on vision restoration in patients with post-chiasmatic visual pathway lesions. In particular, the potential of non-invasive ACS in ameliorating vision impairment following stroke (hemianopia) is the key issue addressed by the REVIS study group.

This contribution presents results of a first randomized, controlled, blinded clinical trial including patients with post-chiasmatic lesions. 10 days of either ACS (n=15) or sham-stimulation (n=14) were applied. During the treatment course a progressive improvement of perimetric thresholds within areas of residual vision was observed only in the ACS-group. After intervention performance in central 5° visual field was improved and defect depths in 30°-threshold perimetry was significantly reduced only after ACS. An increase in subjectively perceived visual functioning/vision-related quality of life (composite score of National Eye Institute Visual Function Questionnaire 39) was reported by rtACS-treated patients while there was no significant change in the sham-group. Health-related quality of life (Short Form Health Survey SF-12) did not change significantly after treatment in either group.

Non-invasive rtACS did not improve absolutely impaired areas of the visual field defect. Therefore, careful selection of patients according to presence of residual vision is crucial since absolute hemianopic defects are unlikely to improve by brain stimulation techniques. Together with changes of EEG coherence measures this finding indicates that residual vision activation is associated with plastic alterations in neuronal networks and that rtACS is a promising approach to partially restore vision loss in unilateral stroke. Understanding how to modulate the balance between synchronized and desynchronized states within cortical networks in the human brain may enable tACS to become a potential therapy in the treatment of stroke-related vision deficits.
Abstracts of Oral Presentations

O27
Measuring Neural Excitability using Deep Brain Electrical Stimulation and Sensing

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Aim

This paper introduces a new method for estimating the excitability of brain networks. The motivation for this research was to develop a system that can track pathological changes in excitability, in diseases such as epilepsy. The ability to track excitability may provide a method for anticipating seizures and intervening therapeutically.

Method

Four normally healthy canines were implanted with the Medtronic Activia PC+S deep brain stimulation and sensing system. The devices were used to probe the circuit of Papez, with electrical stimulation in the anterior nucleus of the thalamus to measure evoked potentials in the hippocampus. The canines were given three different dosage levels of anti-convulsant medication in an attempt to manipulate the excitability of the network.

Results

The results showed changes in the morphology of the evoked potentials, following a circadian profile and reflecting times of drug delivery.

Conclusion

The results demonstrated that we were able to measure and manipulate neural excitability in the circuit of Papez of canines. Under the assumption that neural hyper-excitability is a precursor to epileptic seizures, this new method will provide a systematic way to titrate therapies for effective seizure prevention.
O28
Comparison of the language lateralizations suggested by magnetoencephalography and navigated transcranial magnetic stimulation in healthy subjects using a picture naming task

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Question

Magnetoencephalography (MEG) and navigated transcranial magnetic stimulation (nTMS) are promising non-invasive tools in the examination of language organization as part of presurgical studies before epilepsy or tumor surgery. This study aims to compare the language lateralization by these two techniques using a picture naming task in healthy subjects.

Methods

Nineteen healthy subjects (age range 21-55 years) were studied with a picture naming task in MEG and nTMS. Results of five subjects are presented here. In MEG, sequential single equivalent current dipole source estimates were calculated separately over left and right temporal regions from 200 to 600 ms after the picture presentation. Laterality index (LI) was calculated by comparing the average source strength (dipole moment) on each hemisphere (LI=(left-right)/(left+right)).

In nTMS, the same picture naming task was used and 1-s trains of five TMS stimuli (5Hz, starting at 300 ms after picture onset) were applied to interfere with the naming task performance. The number of naming errors on each hemisphere was used to calculate the laterality index in a similar manner as in MEG.

Results

Both MEG and nTMS suggested left hemisphere language dominance (defined as LI>0.1) in four out of five subjects. In one subject, nTMS suggested right dominance (LI<-0.1) whereas MEG indicated bilateral language presentation (LI=0.07).

Conclusions

Based on our preliminary analysis, language lateralization seems to be fairly consistent between MEG and nTMS as estimated from responses to a picture naming task in healthy subjects. More extensive analysis of our data in healthy subjects and comparison to invasive studies (Wada procedure) in patients are needed to investigate these promising new techniques in language lateralization.
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O29
Beyond skeletomotor function of human basal ganglia: oculomotor, visual and affective neurons

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Deep brain stimulation (DBS) is an effective treatment of motor dysfunction in Parkinson’s disease and primary dystonia. However this treatment may be accompanied by unwanted side effects such as changes of mood, motivation, body weight or visual dysfunction. To confirm the neurophysiological nature of non-motor complications we searched for any neurons in the subthalamic nucleus (STN), substantia nigra pars reticulata (SNr) and globus pallidus (GP) involved in processing visually presented emotional scenes.

Nineteen Parkinson’s disease patients, which underwent implantation of DBS electrodes to the STN or GP, were investigated with simultaneous intraoperative microelectrode recordings and single channel electrooculography during a visual emotional task containing a series of photographs varying in emotional valence and arousal. In 4 patients, a visually guided saccade task was additionally performed.

Out of 183 neurons that were detected, 130 were found in the STN, 30 in the SNr and 23 in the GP. Twenty percent of the neurons in each of these structures showed eye movement-related activity. The neurons in the STN were located mostly in its ventral part and were related to visual scanning and not to visually guided saccades. In the STN, we observed 35 neurons whose firing rate changed significantly within first 500 ms after the presentation of the photograph suggesting their participation in visual or attention mechanisms. The activity of 14 STN neurons showed significant changes during a 500-1500 ms interval in the alpha band of the instantaneous firing rate relating to the emotional content of the presented photographs. The activity of 8 of neurons was related to arousal while the activity of another 6 neurons changed in relation to emotional valence.

Our results showed that the basal ganglia contains a relatively high share of oculomotor neurons suggesting their critical role in eye-movement control. In addition, the STN neurons involved in visual processing and in transmission of emotional information provide evidence of separate management of the affective dimensions of valence and arousal. Therefore, it is not surprising that DBS may have various non-motor consequences.

Supported by grants: IGA MZ ČR NT12282-5/2011; research projects: MŠM 0021620849, MŠM 6840770012 and PRVOUK-P26/LF1/4
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O30
Non-invasive monitoring of intracranial pressure in human: validity, repeatability and responsiveness

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Background

We validated and tested a hand-held device to non-invasively monitor changes in intracranial pressure (ICP), that is based on evoked otoacoustic emissions (EOAEs) in a clinical setting.

Methods

We validated ICP shifts, assessed with non-invasive EOAE-based measurements against invasive ICP measurement in n=17 patients undergoing diagnostic lumbar puncture or continuous ICP monitoring. Additionally, n=42 healthy subjects were included in three different studies. To assess repeatability (intra- and inter-rater reliability), in duplo supine and upright measurements (n=15 subjects) were compared. To assess responsiveness, subjects were measured supine and upright in the morning and afternoon (day-time responsiveness; n=11), and on two consecutive days (day-to-day responsiveness; n=10). Intraclass-correlation coefficients (ICCs) were used to compare measurements. Posture-changed variability was assessed in 33 subjects by comparing tilting-induced ICP changes to findings from literature.

Results

EOAE-based non-invasive ICP shift measurements correlated well with invasive ICP measurements (r=0.69; p=0.029). Intra-rater measurement-to-measurement and Inter-rater-reliability repeatability were high (ICC=0.99). Morning-to-afternoon and day-to-day measurements had ICCs of 0.96 and 0.97 (for upright) and 0.90 and 0.96 (for supine), respectively. Body-posture changes induced ICP changes of 8.7 cm H20 (95%CI 5.0-12.4; upright-supine) and 18.7 cm H20 (95%CI 11.0-25.9; supine to -30˚ tilted head-down), which is consistent with findings from literature.

Conclusion

This EOAE-based hand-held device offers an easy, non-invasive, yet valid, reliable, and reproducible method for monitoring ICP changes.
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O31
EEG monitoring for early outcome prediction in patients with postanoxic coma treated with mild therapeutic hypothermia

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Question

What is the value of continuous EEG for prediction of outcome of comatose patients after cardiac arrest treated with mild therapeutic hypothermia (MTH)?

Methods

In a prospective cohort study, we included subsequent patients with postanoxic encephalopathy after cardiac arrest, all treated with MTH. Continuous EEG was recorded during the first five days of ICU admission. Visual classification of EEG patterns was performed in 5 minute epochs at 12 and 24 hours after cardiac arrest by two observers independently, blinded for patients’ conditions and outcomes. Patterns were classified as iso-electric, low-voltage, epileptiform, burst-suppression, diffusely slowed, or normal. Burst-suppression was subdivided into patterns with and without identical bursts. Primary outcome measure was the neurological outcome based on each patient’s best achieved Cerebral Performance Category (CPC) score within 6 months after inclusion.

Results

One-hundred-forty-eight patients were included, initial results of the first 56 patients were recently published [1]. 68 (46%) had favourable outcome (CPC 1-2). In patients with favourable outcome, EEG patterns improved within 24 hours after cardiac arrest, mostly towards diffusely slowed or normal. At 24 hours after cardiac arrest, the combined group of iso-electric, low voltage, and “burst-suppression with identical bursts” was invariably associated with poor outcome (sensitivity 48%, specificity 100%, positive predictive value (PPV) 100%, negative predictive value (NPV) 66%). At 12 hours, normal or diffusely slowed EEG patterns were strongly associated with good outcome (sensitivity 56%, specificity 96%, PPV 93%, NPV 67%).

Conclusions

EEG monitoring allows reliable prediction of both good and poor neurological outcome of postanoxic encephalopathy in patients treated with MTH within 24 hours after cardiac arrest.

References


Figure 1
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EEG patterns at 12 and 24 hours after cardiac arrest for patients with good and poor neurological outcome. (CPC=Cerebral performance category, BS non identical=burst-suppression without identical burst, BS identical=burst-suppression with identical bursts.)

figure 1
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O32
Magno-cellular streams involvement in Alzheimer’s disease: an evidence of a network diseases

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Question

Alzheimer’s Disease (AD) impairs visual function early and functional losses are correlated with cognitive level impairment. Recently a primary involvement of the visual magnocellular visual subsystem as cause of AD has been put forward. To test this hypothesis we evaluated electrophysiologically visual subsystem (magno and parvo) in a group of AD patients, using equiluminant chromatic Pattern Electroretinograms (ChPERGs) and Pattern Visual Evoked Potentials (ChVEPs) in attempt to detect a magnocellular deficit.

Methods

Data were obtained from 10 AD pts (mean age+ 1SD 78.7 ± 4.83 yrs) not yet undergoing any treatment, and from 10 age- and sex-matched healthy controls (mean age+ 1SD 71.3 ± 7.2). ChPERGs were recorded monocularly in response to equiluminant red-green (R-G) and blue-yellow (B-Y) stimuli, known to emphasize the contribution of parvo- and konio-cellular streams respectively, and achromatic luminance (Lum) yellow-black horizontal square gratings of 0.3 c/deg and 90% contrast (K), reversed at 1Hz, displayed on a monitor at a viewing distance of 24 cm (59.2*59 deg field). ChVEPs were recorded to onset (300 ms) and offset (700ms) equiluminant chromatic sinusoidal gratings of different K (90 and 25%). Diagnosis was clinically and neuro-radiologically established, after having excluded other possible causes of dementia.

Results

Our data showed evident abnormalities both in latency and amplitude of Lum PERGs in AD patients compared with controls (p<0.01), while no significant differences were found in ChPERGs between the two groups. VEPs and RCT analysis did not revealed a retinocalcarine pathway involvement associated with AD.

Conclusions

The abnormalities of responses arising from the magnocellular streams of visual processing could indicate a primary dysfunction of the M-pathways in AD, providing further evidence that cognitive decline might represent a network disease.
Down syndrome (DS) is the most common genetic disorder associated with mental retardation. In the Ts65Dn model mice present altered interneurons inhibition that can be rescued by pharmacologically blocking all GABA<sub>A</sub> receptors.

Several protocols of transcranial magnetic stimulation (TMS) have been designed to study cortical excitability (CE) and both intracortical inhibition and facilitation (ICI-ICF), the latter also through coupled suprathreshold stimuli (I-wave).

Patients with a GABA<sub>A</sub> receptor mutation linked to inherited generalized epilepsy showed reduced intracortical inhibition and an increased facilitation. Conversely the administration of GABAergic drugs reduce both ICF and I-wave peaks. At present few studies have considered these variables interesting for drug trial design and DS patient follow-up.

We studied 10 DS, non epileptic patients (5 females and 5 males, mean age 24.5) and compared them with 10 age and sex-matched healthy individuals. In each individual we recorded resting motor threshold (RMT) of the APB as a measure of CE; ICI-ICF at 3, 5, 10 and 15 ms of interstimulus interval; and I-wave from 1.0 to 3.4 ms of interstimulus interval with increases of 0.2 ms.

There were no significant differences in CE between the two groups. DS patients showed a statistically significant increase of facilitation in the ICI-ICF protocol both at 10 and 15 ms interval (Figure 1). Concordantly they also showed a statistically significant increase of I-wave peaks almost at all intervals.

Our results show that patients with DS present an increased intracortical facilitation that may be due either to the lack of inhibition through the GABAergic system, and/or to an incremented Glutamatergic interneuronal output. Unexpectedly these results point at a very different conclusion than that attained by animal models.

Our study might suggest a malfunction of the GABAergic system since our results are similar to those reported in patients with a GABA<sub>A</sub> receptor mutation. Nonetheless further investigation is needed to solve this issue.

This is the first study addressing interneuronal function dynamics in young DS patients. The TMS analysis is easy to perform either with or without navigation systems coupled with the stimulator, and it might be extremely valuable for drug testing and cognitive follow-up.
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O34
Short latency inputs from ventral premotor cortex to the primary motor cortex in healthy humans

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Question
The ventral premotor cortex (PMv) has an important role in the motor control. In animals, strong connections have been revealed between PMv and M1 at latencies shorter than 1ms. However, such short latency PMv-M1 connection has not been shown in humans. Here, we aimed to show some short latency PMv-M1 connection using paired transcranial magnetic stimulation (TMS).

Methods
In 10 healthy volunteers, the conditioning stimulus (CS) over PMv (3cm anterior and 2.5cm lateral to the hand motor area) set an intensity of 90%active motor threshold for M1 was applied 0.5ms to 3.5ms [inter-stimulus intervals(ISIs) = 0.5 ~3.5ms] prior to the test stimulus(TS) over M1 during slightly voluntary contraction. The TS was set to produce posterior-anterior directed induced currents (PA) eliciting I1-waves.

Results
Single CS over PMv suppressed motor evoked potential (MEP) at an ISI of 1.5ms. Double or quadruple CS pulses separated by2ms enhanced MEPs at an ISI of 0.5ms. Multiple CS did not induce any M1 suppression. Post-stimulus time histogram confirmed the PMv stimulation enhancement of a single peak evoked by M1 stimulation (I1-wave).

Conclusions
Our results first reveal that PMv inputs directly project the cortico-spinal (CTS) neurons in M1 at a short latency in humans. We consider that the PMv stimulation produces EPSP at the M1 cortico-spinal neurons about 2.0ms after the stimulation, which is followed by IPSP in humans. Repetitive PMv stimulation at 2ms interval may temporally summate EPSPs at the CSTNs.
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O35
How transcranial magnetic stimulation impacts on the human brain’s resting state networks?

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Question

Transcranial magnetic stimulation (TMS) is known as a noninvasive clinical tool that is used for treatment of various disorders of the central nervous system. Repetitive TMS (rTMS) is a type of TMS which is used for activation or inhibition of cortical areas. The neurobiological mechanisms underlying efficacy of rTMS remain unclear. Resting state networks (RSNs) represent coherently fluctuating brain regions observed in the resting human brain. The visualisation of RSNs was first obtained by the functional magnetic resonance imaging (fMRI). Later the correlation between fluctuations of the RSNs and the dynamics of electroencephalography (EEG) spectral amplitudes was established. The aim of the study was to investigate changes of the activity of RSNs detected by EEG before and after rTMS.

Methods

5 healthy persons (all male, the mean age 23.6±2.7 years) were enrolled. The 60-channel EEG with resting eye-closed state was recorded during 15 minutes. Then acquired data were splitted to the epochs each of 2 seconds long. RSNs were localised using independent component analysis (ICA). Neuronavigation system NBS eXimia Nexstim was used for cortical mapping and locating the point of the stimulation. rTMS (1 Hz, 100% motor threshold, 400 stimuli) was performed over the areas with the high activity (hotspots), which were presented in the biggest number of RSNs among all subjects. The EEG was repeated again after rTMS session. Covariance maps of RSNs activity were created in MATLAB (EEGLAB v.12.0.2.5b).

Results

Among 20 independent components (ICs) we chose the most similar to described RSNs in previous studies. The hotspots were located near Brodman areas 7 and 39. Mean intensity of the stimulated hotspots after low-frequency rTMS decreased from 21.6±1.7 down to 13.4±1.9 pu (p<0.05) - fig 1. We also found changes in other points of selected RSNs.

Conclusions

Currently we found that the activity of RSNs significantly changed after low-frequency rTMS over their most active areas. The collected data could be useful in comparing with changes in RSNs in unhealthy persons, especially in those which diseases are suspected to be related to RSN abnormalities. We suppose that in some disorders we can possibly impact on the functional activity of the RSNs by rTMS and therefore alter the disease progression.

figure 1

[Fig. 1. Example of spectral EEG activity distribution at a spatial map. a) Red area is the most active point before}
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O36
Sleep spindle scoring: Performance of humans versus machines

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Question
What is the agreement in spindle scoring within, between and among experts? How does spindle scoring by humans compare to automated spindle scoring algorithms?

Methods
We crowd-sourced the collection of spindle scorings from 24 experts in a large and varied dataset of EEG (C3-M2) from 110 middle-aged sleeping subjects. Epochs were scored by an average of 5.3 unique experts. Two experts scored parts of the dataset multiple times. We developed a simple method to build a large gold standard by establishing group consensus among expert scorers. We tested the performance of six previously published automated spindle detectors against the gold standard and refined methods of performance analysis for event detection.

Results
We found an interrater agreement (F1-score) of 61±6 % (Cohen’s Kappa (κ): 0.52±0.07) averaged over 24 expert pairs and an intrarater agreement of 72±7 % (κ: 0.66±0.07) averaged over two experts. We tested the performance of individual experts to a gold standard compiled from all the expert scorers and found average agreement of 75±6 % (κ: 0.68) over the 24 experts. We recompiled the gold standard and excluded the single expert whose performance was being assessed, and found an average agreement of 67±7 % (κ: 0.59). Overall, we found the performance of human experts to be significantly better than the automated sleep spindle detectors we tested (maximum F1-score of detectors: 52 %).

Conclusions
Sleep spindle characteristics between subjects are very diverse which makes the scoring task difficult. The low interrater reliability suggests using more than one expert when scoring a dataset.
Clinical features of sleep-related eating disorder induced by hypnotics

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Question

Sleep-related eating disorder (SRED) is categorized in parasomnia in the revised edition of the International Classification of Sleep Disorders, showing recurrent episodes of eating and drinking during main sleep episode. It has been reported that the onset of SRED is sometimes associated with hypnotics. However, the features of SRED induced by hypnotics are not clear yet.

Methods

There were 10 patients whose SRED episodes occurred after taking hypnotics, and SRED episodes disappeared after reducing or discontinuation of the responsible drugs (secondary SRED induced by hypnotics), and 32 patients who was diagnosed SRED without specific cause, i.e. the other sleep disorders such as sleep apnea syndrome, restless legs syndrome; use of certain hypnotics (primary SRED). We compared clinical features between two groups.

Results

Eight patients took two kinds of medication and the other two patients took three kinds of medication out of ten patients with secondary SRED induced by hypnotics. The most used medication was flunitrazepam (n=5), followed by zolpidem (n=3), and triazolam (n=3).

There was a significant difference in age at self-reported onset of SRED between two groups (primary SRED: 25.7y vs secondary SRED induced by hypnotics: 39.6y). The ratio of patients who reported they had comorbidity of nocturnal eating syndrome (NES), and history of sleepwalking during childhood were significantly higher in primary SRED than in secondary SRED induced by hypnotics. The ratio of patients with total amnesia about episodes was significantly higher in secondary SRED induced by hypnotics than in primary SRED.

Conclusions

The features of secondary SRED induced by hypnotics are different from those of primary SRED. This study suggests that SRED might be divided into some subtypes, i.e. pure parasomnia, and confusional awakening from sleep due to hypnotics.
Abstracts of Oral Presentations

O38
Subcortical mapping and intraoperative diffusion tensor tractography 3.0T of the corticospinal tract in supratentorial intrinsic tumor surgery. Reliability study.

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Introduction

The course of the corticospinal tract (CST) can be identified using subcortical mapping (scMEP). The threshold technique (scMEP-trsh) is considered to be reliable in setting the safe zone. Intraoperative DTT and scMEP-trsh correlation is thought to be more precise because of brainshift elimination.

Question

Is intraoperative DTT 3.0T reliable enough comparing to CST mapping in nonselected patient series?

Methods

25 patients were enrolled consecutively and prospectively from 7/2010 to 7/2012. Inclusion criteria: solitary supratentorial intracerebral lesion compressing or infiltrating the CST. scMEP was performed by monopolar (cathodal) stimulation (500Hz, 400μs, 5 pulses) with navigated probe. CST DTT was made both at preoperative and intraoperative 3.0T MRI. scMEP-trsh current and probe-CST distance were recorded at 155 points before iMRI (preoperative scans), and at 103 points after iMRI (intraoperative scans). Current-distance correlations were performed both for pre-iMRI and for post-iMRI data separately.

Results

scMEP-trsh before iMRI ranged from 1.0-30.0mA (mean 12.6 ± 6.6), after iMRI 0.5-24.0mA (mean 10.0 ± 5.25). The correlation coefficient pre-iMRI was R = 0.470 (p < 0.001), post-iMRI was R = 0.338 (p < 0.001). MRI radical resection was achieved in 17 (68%), subtotal in 5 (24%) and partial in 3 (12%). The lowest scMEP-trsh was >10.0mA in 6 (24%), 5.1-10.0mA in 9 (36%), ≤ 5.0 mA in 10 (40%). Postoperative motor deficit developed in 8 (32%), permanent remained in one case (4%) - scMEP-trsh ≤ 5.0mA. Intraoperative DTT was unreliable because of image distortion in 9 (36%). No technical failure was recorded in neurophysiological mapping.

Conclusion

The linear current-distance correlation was found both in pre-iMRI and in post-iMRI data. Correlation of post-iMRI data was weaker than pre-iMRI. Intraoperative DTT was unreliable in 36%. Subcortical CST mapping remains superior to intraoperative DTT. Mapping provides true and direct intraoperative information about position of CST under wall of resection cavity, with minimal technical failure.

Supported by IGAMZCR12253-5.
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O39
Intraoperative neurophysiological monitoring in patients with spinal cord injuries. Experimental study.

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Question

Intraoperative monitoring (IOM) is usually not performed in patients with acute traumatic spinal cord injuries. It would be necessary in those patients who need immediate surgery to treat the vertebral fractures which caused the injury. However, we feel that it is important to assess the functional state of the spinal cord during these surgeries. Is IOM feasible in these cases?

Methods

In five experimental pigs the thoracic spinal cord was exposed in three segments via bilateral laminectomies. Four sublaminar epidural catheters were placed at T3, T6, T11 and L1. The spinal cord was severed at the T8 level. At the T12-T13 and at the T4-T5 level, progressive compression of the spinal cord was performed with a precise compression device using a pair of parallel sticks sequentially shortening their distances 0.5 mm every 2 minutes. Cord-to-cord evoked potentials (EP), D-wave and epidural somatosensory evoked potentials (SEPs) were obtained with each mean of compression.

Results

In all the cases cord-to-cord EPs were obtained, in both cranial and caudal segments. Spinal cord compression causes the loss of the cord-to-cord EP with a 5mm compression cranial to the lesion, and with a3 mm compression caudal to the lesion. D-wave was capable of detecting injuries above the acute lesion, while epidural SEPs detected the injuries below the lesion.

Conclusion

It is possible to perform IOM using appropriate electrophysiologic techniques in patients with acute spinal cord injuries, both above and below the lesion. The spinal cord segments caudal to the lesion are more sensitive to new injuries than those cranial to the lesion.
O40

Inter- and intrahemispheric inhibition and their role in mirror movements pathophysiology.

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Question

Mirror movements (MM) are unintended and unaware movements of the limb, which remains at rest, during performing intentional movements with the contralateral one. The fibers running through corpus callosum play an important role in inhibition of contralateral hemisphere during performing unilateral motor tasks. MM occur with higher frequency in patients with pathology of corpus callosum. The aim of this study was to determinate the role of corpus callosum in MM’s generation in patients with central nervous system disorders with involment of pyramidal tract.

Methods

Clinical evaluation of MM was performed in patients with motor neuron disease (n=36), multiple sclerosis (n=25), acute ischemic stroke (n=17) and control group (n=31). Then all the studied groups were subjected to transcranial magnetic stimulation (TMS) in order to assess the excitatory and inhibitory functions of motor cortex.

Results

The frequency of MM was higher in patients with multiple sclerosis, patients with motor neuron disease and in stroke patients (in limbs without paresis), compared to control group. The duration of ipsilateral silent period (iSP), which reflects the function of corpus callosum, was significantly shorter in patients with motor neuron disease and in damaged hemisphere in stroke patients compared to control group. The lack of iSP in one hemisphere in all patient groups occurred in conjunction with shorter duration of contralateral silent period (cSP), which reflects the intrahemispheric inhibition.

Conclusion

The fibers of corpus callosum play an important, but probably not exclusive role in MM’s pathophysiology. An additional shortening of intrahemispheric inhibition contralateral to pathological interhemispheric inhibition may facilitate MM occurrence.
O41
Mirror Movements in Multiple Sclerosis

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Question

Demyelination and loss of midline crossing fibers at callosal and brainstem level is a feature of patients with multiple sclerosis (MS). One of the functions of these fibers is inhibition of unwanted mirror activity when performing a unilateral task. We examined whether the presence of mirror electromyographic activity (mEMG) correlated with corpus callosum or brainstem volumes in MS patients.

Methods

In 13 adult controls and 20 mildly disabled relapsing-remitting MS patients, we studied unilateral reaction time. They had to perform ballistic wrist-extension movements at perception of an electrical low intensity imperative stimulus (IS), given to either ipsilateral or contralateral index fingers (baseline trials). In 20% of trials at random, we activated brainstem motor pathways by a startling auditory stimulus simultaneously with IS (StartReact trials). Brainstem (bsVol) and corpus callosum (ccVol) volumes were measured by MRI employing free computer-assisted softwares (FreeSurfer&FSL).

Results

Bursts of mEMG were observed in 15.4% of ipsilateral baseline trials in healthy subjects. This percentage did not increase with StartReact trials (11.5%). Patients had significantly more mEMG in StartReact trials (35.0%, p=0.03) but not in baseline (12.5%). There were no differences between patients and control subjects in contralateral trials. The StartReact effect was significantly reduced in patients and more so in contralateral than ipsilateral trials. Patients with mEMG (60%) had significantly lower bsVol than those without mEMG (p=0.049), but no differences were found in ccVol (p=0.813).

Conclusions

Patients with MS have an abnormal inhibitory motor control during unilateral ballistic movements which is associated with brainstem atrophy but not with corpus callosum atrophy.
Abstracts of Oral Presentations

O42
The functional connectivity in motor execution and imagery in NIRS(Near Infra-red Spectroscopy) data based on joint recurrence plot.

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Question

In recent years, it is reported that brain activity is not originated from the region by itself, but originated from several regions. In this study, we examined the functional connectivity among the three regions in both hemispheres, (1) pre-motor area and supplementary motor area, (2) primary motor area and (3) primary sensory area on performing motor execution or imagery.

Methods

NIRS refers Near Infra-red spectroscopy, with which the brain activity can be measured non-invasively and low-restrictedly. Using a few wavelengths of near infra-red light, the relative hemoglobin concentration changes evoked by the brain activity can be measured. Recently, many studies have been reported in clinical cases such as rehabilitation or psychic medicine.

In this research, we detect the functional connectivity in NIRS data using joint recurrence plot (Marwon, 2007). Recurrence plot is one of the useful method in time series analysis, which visualize the inner structure of a time series. Moreover, joint recurrence plot detects the relationships between two time series by a statistical method (Iwayama, 2012).

Eleven normal subjects (age: 23-36 years) participated in the examination. All of them were judged as the right-handed with Edinburgh handedness inventory. With pacing visual stimuli, subjects are instructed to execute grasping or to image grasping hands during task periods. A session consists of pre-task (20s), task (20s) and post-task (20s). Session was repeated five times in each measurement.

All experiment were performed according to the tenets of the Declaration of Helsinki and under the approval of the Ethics Committee of the Tokyo Denki University. Written informed consent was obtained from all the subjects after the explanation of the natural and possible consequences of the study.

Results and Conclusions

In motor imagery task, the functional connectivity are significantly larger in the premotor cortex and the supplementary cortex between both hemispheres. On the other hand, no significant difference in functional connectivity is found in motor execution. Our study shows that joint recurrence plot can be a useful tool for detecting functional connectivity on-line, therefore, it could contribute the rehabilitation or the brain machine interface.
Morphology and Histology of the Biological Clock

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**Question**
In all living organisms endogenous clocks enable the temporal organization of vital functions and social contacts. Also in man, body and brain underlie biological rhythms, which control the sleep-wake cycle, physical and mental performance, mood and health, and rhythmic changes of metabolic and hormonal systems. What is the "hardware" of these endogenous clocks?

**Methods**
Interdisciplinary studies by means of neurobiological, immunochemical, genetic and molecular methods have revealed basic features of biological clocks and many of the underlying mechanisms potentially applicable in the biomedical field.

**Results**
We show structural details of the biological clocks, which are basically multioscillator systems: the self-sustained rhythm generators (pacemakers), the Zeitgeber receptors, which convert external periodicities into time cues for the synchronization of internal and external rhythms; and the signals and signaling pathways for the information processing between the component parts of the clock system. The functional histology of the mammalian suprachiasmatic nucleus (SCN), the master pacemaker of the circadian multioscillator system, shows various distinct compartments and target areas of afferent and efferent information signals. Besides this rather well understood central pacemaker, pilot results reveal peripheral clocks, e.g., a food-entrainable oscillator and a pacemaker of seasonal rhythms. We demonstrate that the isolated perspective of a reduced methodological approach may hinder the understanding of the complexity of biological clocks.

**Conclusion**
The detailed knowledge of structure and histology of the clock components, as well as the ontogenetic and rhythmic variability of their functional appearance are essential for better understanding e.g., the effects of microsurgery, and of genetic or pharmacological manipulations.
O45
Lateral inhibition in somatosensory cortex of migraine without aura patients between attacks

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Question

Here, we investigated lateral inhibition and habituation within the somatosensory cortex in a group of migraine without aura (MO) patients compared to healthy volunteers (HVs) by stimulating two peripheral nerves simultaneously, while recording somatosensory evoked potentials (SEPs).

Methods

SEPs were elicited by electrical stimulation of the right median and ulnar nerve at the right wrist separately and simultaneously (300 sweeps per condition), in 25 MO patients between attacks and in 20 HVs. We measured parietal N20-P25 amplitudes and we evaluated cortical lateral inhibition (CLI) as the ratio = MU/(M+U)*100, where MU is the SSEP amplitude obtained simultaneously stimulating both median and ulnar nerves (MU), and M+U is the sum of amplitudes obtained by stimulating each nerve separately (M+U). CLI was calculated on the 1st and the 3rd block of 100 averaged sweeps, as well as on grand average of 300 sweeps. Habituation was calculated as the slope of the linear regression between the 1st and the 3rd block of 100 averaged sweeps.

Results

SSEP N20-P25 amplitudes lack of habituation in MO patients (p=0.02). CLI was close to statistical significance (p=0.058) and significantly different (p=0.039) respectively on both 3rd block and grand-average. On Pearson’s test, there was a positive correlation between the habituation slope and grand average CLI (r=0.488, p=0.02) in HV, not so in MO (r=0.320, p=0.119). However, when data of HV and MO patients were combined the habituation slope was positively correlated with CLI (r=0.432, p<0.01).

Conclusions

These results suggest that lateral inhibitory mechanisms within somatosensory cortex may be malfunctioning in migraine between attacks and contribute to induce lack of habituation of N20-P25 SSEPs amplitude during stimulus repetitions.
Abstracts of Oral Presentations

O46
Ripples and Waves in absence epilepsy: High Frequency Oscillations (HFOs) in scalp EEG

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Introduction

High frequency Oscillations (HFOs) have provided better understanding of ictogenesis. There are no studies of HFOs in scalp EEGs in patients with absence epilepsy.

Aim

To study the occurrence of HFOs (80 - 250 Hz) in scalp EEGs among patients with absence epilepsy.

Methods

Seven patients with absence epilepsy (CAE-6, JAE-1; M:F=3:4; age=9.7±4.6 years; age at onset: 7±3.2 years) were evaluated with scalp EEG (sampling rate: 2048 Hz) in the GalileoNT® system using standard procedures. The finite impulse response (F.I.R) filter on the longitudinal bipolar montage was adjusted to a band pass of 80 - 250Hz using the E-emagine software® and the sensitivity and paper speed were modified to study the HFOs. Five hundred and two HFOs noted in 911 artifact free generalized seizure discharges were analyzed. Ictal discharges were associated with clinical absences and lasted >9.48 seconds.

Results

The HFOs were associated with inter-ictal generalized spike-wave discharges (IIGSWDs-76/288), ictal GSWDs (IcGSWD-382/530), sporadic GSWDs (sGSWDs-44/83). HFOs were not associated with occipital intermittent rhythmic delta activity (OIRDA). IcGSWDs had more HFOs when compared to IIGSWD (χ² = 156, d.o.f. =1, OR=7.2, 95% CI: 5.2-9.9, p<0.0001). The onset of HFOs was temporally related to the spike component and not to slow waves. Spherical head dipole modelling of the HFOs associated with IIGSWDs and IcGSWDs were located in fronto-centro-parietal regions.

Conclusion

This study on HFOs in absence epilepsy enhances the spectra of electrophysiological changes. Future study especially with simultaneous EEG-fMRI might improve the understanding of the centrencephalic vs. neocortical origin of generalized seizures.
Abstracts of Oral Presentations

O47
The mechanism of recovery of upper extremity motor function among patients with chronic stroke; Modulation of cortical and spinal interneuron induced with hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy.

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Question

Functional recovery from stroke has been shown to occur even in chronic and moderate to severe hemiparesis. It is supposed to be based on cortical and spinal plastic changes. However, few studies assess the cortical and spinal plastic change simultaneously and investigate the relationships between these cortical and spinal circuit changes and clinical improvement. The purpose of this study is to investigate the relationships of functional recovery with intracortical inhibition and reciprocal inhibition.

Methods

Participants were 61 patients with chronic hemiparetic stroke. The participants used non-invasive EMG controlled neuromuscular electrical stimulation and wrist hand orthosis for 8 hours a day during 3 weeks (Hybrid assistive neuromuscular dynamic stimulation therapy; HANDS therapy). Fugl-Meyer test upper extremity motor score (FM), modified Ashworth scale (MAS) and Motor activity log amount of use score (MAL) were assessed before, post and 3 months after the end of HANDS therapy. Paired pulse TMS paradigm was applied to assess the short intracortical inhibition (SICI). Reciprocal inhibition (RI) was assessed with a flexor carpi radialis H reflex conditioning-test paradigm. The conditioning-test stimulus interval was set at 0, 20, 100ms (RI at 0ms, RI at 20ms, RI at 100ms).

Results

FM, MAL and MAS improved with HANDS therapy (P<0.01) and these improvements lasted for 3 months (p<0.01). We found significant disinhibition of affected SICI, and strengthened RI at 20ms and 100ms with HANDS therapy. The change of FM from before to 3 months after HANDS therapy was correlated with the change of the affected SICI from before to post HANDS therapy (P<0.01). The change of wrist MAS from before to post HANDS therapy was correlated with the change of RI at 100ms (P<0.05).

Conclusions

In chronic stroke patients with moderate or severe hemiparesis, functional improvement of upper extremity motor function and spasticity was based on the disinhibition of affected hemisphere and modulation of reciprocal inhibition.
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O48
The use of repetitive transcranial magnetic stimulation to enhance stroke recovery

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Background

Despite the intense efforts devoted to prevent and abort cerebral ischemia, some individuals will continue to have completed infarctions. Failure of prevention or intervention does not, however, preclude therapeutic approaches to enhance recovery. The stroke-affected hemisphere can be doubly disabled, by the stroke itself and by an increased inhibition from the non-stroke hemisphere. Thus rTMS interventions are designed to increased activity in the affected hemisphere and/or suppress activity in the non-stroke hemisphere. In this review I try to answer the following questions through our previous studies: 1) Is excitatory stimulation to stroke hemisphere better than inhibitory stimulation to non-stroke hemisphere? 2) Is there a best frequency for stimulation of the stroke hemisphere? 3) For dysphagia: whether rTMS excitatory stimulation to the non-stroke hemisphere or stroke hemisphere have long term effect on dysphagia and whether rTMS is helpful in brainstem lesions where there is no direct damage to cortex? 4) Finally For Aphasia: is the dual magnetic pulse stimulations enhance post-stroke aphasia?

Figure 1

Changes in mean different rating scores of dysphagia (A), Barthel index (B), NIHSS (C), and hand grip strength (D) at the four assessment points for the patients with LMI. Data are expressed as mean ±SE.

References


figure 1
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O50
The spatial context of retrieved memories is reflected by neural Activity in Human Hippocampal Formation

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Spatial navigation is supported by a network of “place cells” that exhibit increased firing whenever an animal is in a certain region of an environment. We here addressed the question as to whether this neural representation of location form part of the spatiotemporal context into which episodic memories are encoded. Based on recordings of neurons in the human medial temporal lobe neuronal activity, analyses were performed on a hybrid spatial and episodic memory task. Place-responsive cells active during virtual navigation showed activation during the subsequent recall of navigation-related memories without actual navigation. Place-responsive cell activity was reinstated during episodic memory retrieval. Neuronal firing during the retrieval of each memory was similar to the activity that represented the locations in the environment where the memory was initially encoded.
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O51
Behavioural and electrophysiological effects of static magnetic field stimulation over the occipital cortex

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Question

We previously reported that continuous application of Transcranial Static Magnetic Field Stimulation (tSMS) over the motor cortex induces a reduction of cortical excitability lasting several minutes after the end of tSMS. In the present study, we further explore static magnetic field effects on EEG oscillations in the visual cortex and during visual attentional performance in healthy humans. We specifically test a hypothesis that our previous tSMS effects in motor cortex could be related to an increase of alpha band activity, and therefore, associated with an “inhibitory” effect.

Methods

Thus, we investigated the effects of tSMS (real or sham) placed over visual cortex in two studies: a first experiment, in which tSMS was simultaneous applied during ten minutes eyes-open resting EEG recording; a second experiment, in which visual attention was measured in the context of tSMS during performance of a visual search paradigm. In both experiments, EEG and behavioural measurements were made during, and 10 minutes following, tSMS application.

Results

As predicted, the application of real, but not sham, tSMS over the visual cortex resulted in a significant increase in alpha band power. In the visual search task, real and sham tSMS groups displayed a similar behavioural profile, with reaction times (RTs) increasing with increasing task demands. Critically, however, a significant slowing of RTs emerged on trials with the highest difficulty levels during real in comparison to sham tSMS.

Conclusions

Our results therefore suggest that tSMS has a profound influence on oscillatory alpha activity, which we suggest reflects a modulation of visual cortical excitability. Secondly, our behavioural results indicate that tSMS over the occiput alters visual search performance, slowing responses to stimulus detection. Importantly, this was not a general task impairment, but a tSMS-induced slowing of visual search specific to high attentional load levels. We speculate that this slowing is secondary to a decrease in underlying alpha oscillations. Further studies using tSMS are required to extend the knowledge of the functional significance of brain oscillations changes induced by the application of small magnets over the scalp.
O52
Influence of slow oscillatory transcranial direct current stimulation (so-tDCS) during waking on EEG and sleep-related parameters

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Question
Slow oscillatory tDCS (so-tDCS) was shown to have an impact on EEG and cognitive functions (Kirov et al. 2009). The goal of the present study was to reproduce EEG findings of so-tDCS during daytime in awake subjects and to measure effects on sleep-related parameters. In addition stimulation at 5.5Hz was applied in order to investigate whether similar findings as with so-tDCS can be obtained.

Methods
A randomized, sham-controlled, single-blind crossover trial with 20 healthy individuals was performed. Subjects were divided in 2 groups differing in stimulation frequency. Stimulation took place in the morning on 2 days. One stimulation session consisted of 5 blocks (5x5min) followed by stimulation free intervals of 1min after each block. Tests (PVT, DSST, KSS) were performed before and after stimulation. Resting EEG was recorded before, during and after stimulation. Stimulation parameters: group A: f=0.75Hz, group B: f=5.5Hz, waveform: sinus, current: 550μA, DC offset: 275μA, current density: 17.3μA/cm², electrode positions: (F3)/(F4)-mastoids.

Results
There were no significant differences between sham and active stimulation regarding PVT, DSST, KSS and EEG for both groups. A tendency of increased theta activity could be observed following active stimulation at 5.5Hz compared to sham stimulation.

Conclusions
Differences between the present and former studies (lower current density, stimulation during quiet wakefulness) may be the reason for the non-significant findings for stimulation at 0.75Hz. Theta activity might be increased by stimulation at 5.5Hz. The small sample size may be the reason why the observed increase did not reach a significant level.

References
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O53
Electrical impedance myography for the evaluation of the tongue musculature in amyotrophic lateral sclerosis.

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Question

The majority of individuals diagnosed with ALS show signs of bulbar impairment at the onset of disease or as disease progresses. A measure that is sensitive to disease onset and progression would be of significant clinical importance, assisting with early diagnosis and serving as a biomarker of bulbar health in clinical trials. The recently developed technique of EIM provides quantitative data on muscle health by measuring localized tissue impedance. EIM has been evaluated as a biomarker of muscle abnormalities in limb musculature in ALS, showing a reduction in phase as disease progresses. However, EIM of the tongue has not been studied in patients with ALS. Thus, our objectives are:

1. Compare tongue electrical impedance myography (EIM) 50 kHz phase values in patients with amyotrophic lateral sclerosis (ALS) to those of age-matched healthy controls;
2. Correlate these values with measures of bulbar function.

Methods

Nineteen subjects with ALS and 16 healthy age-matched controls participated. All participants with ALS showed signs of bulbar impairment (e.g., tongue fasciculations, atrophy, weakness). EIM of tongue was performed using a novel tongue depressor electrode array (see Figure). Severity of disease (e.g., ALS Functional Rating Scale-R, bulbar subscore, speaking rate during a reading task) and tongue function (maximum strength and endurance) were correlated with EIM values.

Results

Independent-samples t-tests revealed significantly smaller phase values (p < 0.001) (mean±standard deviation) for ALS participants (10.7±3.7°) than for controls (16.4±1.8°). Correlations between EIM values and most measures of bulbar function were non-significant; however, a correlation between phase and tongue endurance was identified in participants with ALS (r = 0.48, p=0.045).

Conclusions

EIM of the tongue can distinguish patients with ALS from healthy controls and correlates with one measure of tongue function. Further refinement, validation and study of this biomarker for the evaluation of bulbar dysfunction is warranted.

Figure 1 Legend

Tongue depressor electrode array attached to commercial impedance measuring device.

figure 1
Abstracts of Oral Presentations

O54
Diagnostic utility of cortical hyperexcitability in Amyotrophic Lateral Sclerosis

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Question

The diagnosis of amyotrophic lateral sclerosis (ALS) relies on identification of a combination of upper (UMN) and lower motor neuron (LMN) clinical features. Such clinical criteria have resulted in significant diagnostic delays, perhaps beyond the therapeutic window period. In order to improve the sensitivity of diagnostic criteria, recently the Awaji criteria have been developed whereby neurophysiological evidence of LMN dysfunction was equated with clinical features of LMN dysfunction. While these criteria appeared to increase the diagnostic sensitivity for ALS, the involvement of UMNs was not objectively assessed by the Awaji criteria. Given that cortical hyperexcitability, as reflected by the threshold tracking transcranial magnetic stimulation (TTTMS) technique, was an early feature in ALS, the present study assessed the diagnostic utility of TTTMS, when compared to Awaji criteria, in establishing of an earlier diagnosis of ALS.

Methods

Prospective cortical excitability studies were undertaken on a cohort of 82 patients classified as either "possible" or "probable/definite" ALS based on the Awaji criteria.

Results

Short-interval intracortical inhibition (SICI) was significantly reduced in ALS patients (1.3 ± 1.1%) when compared to controls. Importantly on subgroup analysis, there was a comparable reduction of the averaged SICI in the ALS cohorts compared to controls (SICI
POSSIBLE 1.3 ± 1.3%, P<0.0001 SICI
PROBABLE/DEFINITE 1.4 ± 1.7%, P<0.0001). In addition the cortical silent period (CSP) duration was significantly reduced in the ALS patients and the Awaji subgroups when compared to controls (CSP
ALS 178.1 ± 5.1, P <0.00001; CSP
CONTROLS 214.9 ± 3.6; CSP
POSSIBLE 169.2 ± 6.5, P<0.0001; CSP
PROBABLE/DEFINITE 188.0 ± 8.3, P<0.05). Of further relevance, the diagnostic accuracy of the TTTMS technique was 77% compared to 40% for the Awaji criteria in the present ALS cohort.

Conclusions

Cortical hyperexcitability appears to be an early diagnostic biomarker for ALS. The TTTMS technique may prove useful as a diagnostic aid for establishing an earlier diagnosis of ALS.
Abstracts of Oral Presentations

O55
Towards truly mobile EEG and brain-computer interfaces

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Question

Conventional EEG recording technology requires that individuals avoid gross movement during data acquisition. This strongly limits the possibility of monitoring human brain function during everyday life behavior. Aiming to overcome this limitation, a small, wireless and head-mounted 14-channel EEG system was developed. Several studies will be presented evaluating the quality of single-trial EEG and event-related P300 potentials (ERP) recorded while individuals went for a walk outside of the laboratory and performed an auditory selective attention task, and while they performed a 6 x 6 matrix P300 speller task.

Methods

In a first study two-class auditory oddball data were recorded from 16 participants sitting indoors in an office and walking outdoors [1]. In a second study three-class auditory oddball data were collected from 20 participants while sitting and walking outdoors [2]. In addition, the quality of the mobile EEG system was compared to an established laboratory EEG system. 13 participants performed an online P300 copy-speller task with both systems [3].

Results

Our results show that good-quality ERPs can be obtained in daily-life situations such as walking outdoors. In addition, single-trial analysis by means of linear discriminant analysis confirmed that single-trial P300 responses could be reliably obtained. Finally, the amplifier comparison study revealed that the mobile EEG system performed as good as a traditional, wired laboratory EEG amplifier in the online P300 copy-spelling task. Very similar classification accuracies were obtained.

Conclusions

The studies demonstrate the potential of the light, miniaturized, head-mounted and wireless EEG system, which tolerates gross movement to a large extent. In the future it will be possible to monitor the neural correlates of cognitive functions in daily life situations.

References


Abstracts of Oral Presentations

O56
Event-related potentials (P300) in patients with cerebrovascular diseases combined with the metabolic syndrome.

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**Question**

Metabolic syndrome (MS) raises the risk of cerebrovascular diseases (CVD). Cognitive decline is one of the MS complications. Neurophysiologic method that can estimate the cognitive dysfunction is event-related potentials (P300). The aim of our study was to investigate the features of the P300 in patients with CVD caused by the MS and compare these results with clinical data.

**Methods**

We examined 52 patients with a CVD and the MS, mean age 65±7, 14 men and 38 women. 31 patients suffered from chronic brain ischemia and 21 patients had stroke in anamnesis. All patients were divided into two groups: the MS combined with diabetes mellitus type 2 (DM 2) 28 persons and without it - 24 persons. Control group consisted healthy subjects, n=21. Patients were tested by Montreal cognitive assessment (MoCA). P300 were enrolled with hearing and counting the rare (target) tones and next pressing the button on the rare tones.

**Results**

Most of patients from the both groups complained on a memory loss. The mean MoCA score in group of patients without DM 2 was 24.6 and in group with DM 2 was 22.8.

P300 responses in both groups of patients were not consistent, the counting were inaccurate, there were lower percentage of the right pressing the button, and prolonged reaction time (RT) on the button pressing, especially in patients with DM 2. Also, latency of the P3 was more prolonged and amplitude of the N2/P3 was lower in patients from both groups in comparison with control group (p<0.005). The significant differences of P300 indices among groups of patients were revealed in latency of the P3 and the RT (p<0.05) (tab.).
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<table>
<thead>
<tr>
<th>Groups</th>
<th>Counting the rare tone, latency of the P3, msec.</th>
<th>Inaccurate counting, percentage, %</th>
<th>The button pressings, latency of the P3, msec.</th>
<th>The right button pressings, percentage, %</th>
<th>The average reaction time (RT), msec.</th>
<th>Amplitude of the N2/P3, mcV.</th>
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<tr>
<td>MS without DM 2, n=24</td>
<td>423±36</td>
<td>14%</td>
<td>417±35</td>
<td>77±8</td>
<td>334±32</td>
<td>9.5±4</td>
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<td>MS with DM 2, n=28</td>
<td>451±47</td>
<td>43%</td>
<td>436±30</td>
<td>68±23</td>
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<td>Control group, n=21</td>
<td>348±17</td>
<td>0</td>
<td>334±29</td>
<td>91±9</td>
<td>294±27</td>
<td>11.5±4</td>
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</tbody>
</table>

## Conclusion

Patients from both groups with CVD combined with the MS had cognitive decline, especially in group with DM type 2 that was confirmed by P300 data. P300 is important in diagnostic of cognitive decline in patients with CD caused by MS, especially at an early stage of the disease because DM 2 leads to more severe cognitive impairment.
O57
The effect of direct or mirror vision of the hand on the processing of nociceptive and non-nociceptive somatosensory inputs: an ERP study

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Question

Previous studies have shown that the illusion of looking at the hand through a mirror reduces the perception [1-3] and the magnitude of the brain responses elicited by nociceptive stimuli delivered onto the hand. This observation, referred to as the analgesic effect of viewing the hands, contrasts with the results of other studies showing that direct vision of the hand onto which non-nociceptive somatosensory stimuli are applied enhances the amplitude of non-nociceptive somatosensory event-related potentials (ERPs) [4]. These contradicting observations could result from many factors, in particular, the fact that direct vs. mirror vision of the hand may induce distinct effects. In this study, we compared directly the effect of direct and mirror vision of the hands on the perception and ERPs elicited by non-nociceptive and nociceptive stimuli.

Methods

Thirteen participants received nociceptive laser stimuli and non-nociceptive electrical stimuli on the right hand. In different blocks, we compared (i) the effect of direct vision through a glass window of the right hand or an object placed on top of the right hand and (ii) the effect of mirror vision of the hand or object (participants looked at the reflection of their left hand or object through a mirror, creating the illusion of looking at the right hand or object). We measured the intensity of perception and magnitude of non-nociceptive and nociceptive ERPs.

Results

Contrary to previous reports, we did not observe significant differences in the perception. The magnitude of nociceptive ERPs was reduced with direct vision of the hand. The magnitude of non-nociceptive ERPs was enhanced when viewing both the hand and the object through the mirror.

Conclusion

Our data suggest that direct vs. mirror vision of the hand do not exert the same effect on the processing of nociceptive and non-nociceptive somatosensory stimuli delivered to the viewed hand.


O58
Dual effects with EMG-controlled functional electrical stimulation (FES) and transcranial direct current stimulation (t-DCS) on the brain cortical perfusion among strokes

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The aim of this study was to investigate the dual effects with a EMG-controlled functional electrical stimulation (EMG-FES) and transcranial direct current stimulation (t-DCS) on upper extremity function and brain perfusion among stroke patients. The sides to which hemisphere anodal or cathodal t-DCS can directly modify corticomotor excitability or prime the effects of motor function were examined. The subjects were 10 chronic stroke patients with moderate impaired hemiparesis. They had anodal or cathodal t-DCS to C3 or C4 in international 10-20 system for 20 minutes. Because cathodal t-DCS to unaffected hemisphere resulted in the immediate upper extremity dysfunction in three moderate impaired hemiparetic patients, cathodal t-DCS experiment was no more adopted for others. The sides to which hemisphere anodal t-DCS can directly modify corticomotor excitability or prime the effects of motor function were examined. Clinical functional evaluation and Near Infrared Spectroscopy (NIRS) were examined and they had upper extremity FES followed with t-DCS. Immediate functional improvement showed in five patients after anodal t-DCS to unaffected hemisphere and in three patients with mild hemiparesis after anodal t-DCS to affected hemisphere. Anodal t-DCS and EMG-controlled FES induced the functional improvement and increase of the affected side brain perfusion in NIRS in all patients. The extent of functional improvement and laterality of sensory motor cortex (SMC) perfusion in NIRS, however, revealed the variability among individual stroke patients. It was hypothesized that there should be functional effect variability of the adequate side of t-DCS among moderate impaired hemiparetic patients. The sensory motor integration due to FES and global brain activation of t-DCS might facilitate the perfusion of SMC and resulted in more functional improvement of hemiparetic upper extremity in some stroke patients.
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O59
Association between Rectus abdominis denervation and ventilation dysfunction in patients with amyotrophic lateral sclerosis

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Objective

Neurogenic changes of EMG of rectus abdominis muscles were regarded as an evidence of lesion in lower motor neuron involved in thoracic cord in amyotrophic lateral sclerosis (ALS). Denervation of rectus abdominis muscles was examined to detect association with ventilation dysfunction in ALS.

Methods

We collected the clinical data including ALSFRS and Forced vital capacity (FVC) of 116 patients with sporadic ALS in Department of Neurology of Peking University Third Hospital from 2009 to 2013. Standard needle EMG was recorded from at least three limbs, at sternocleidomastoid and rectus abdominis muscles. Only spontaneous activity (fibrillation potentials (fib) and positive sharp waves (psw)) and pattern of recruitment were studied in rectus abdominis muscles. The differences of EMG changes between rectus abdominis muscles and FVC were analyzed. Of the total, there were 30 patients with an ALSFRS score less than 4 in the respiratory subset. The relationship of fib-psw of rectus abdominis muscles and dyspnea was also observed.

Results

The mean FVC in the 116 ALS patients was 83.6% (range 45%-131%, SD 17.1) of predicted. FVC > 80% accounted for 73 patients (mean ALSFRS score 33.9, SD 4.2) and FVC < 80% 43 (mean ALSFRS score 30.9, SD 5.3). Compared with patients with normal FVC (60/73, 82.2%), Fib-psw in rectus abdominis muscles showed significantly difference for FVC < 80% (42/43, 97.7%). Moreover, there were more spontaneous potentials in patients with symptom of dyspnea (30/30, 100%) than those without (72/86, 83.7%).

Conclusions

Spontaneous potentials of rectus abdominis muscles were associated with ventilation dysfunction as well as dyspnea. The hypothesis was supported that diaphragm and rectus abdominis muscles were involved concomitantly in ALS. Respiratory function, such as FVC, should be performed in patients when fib-psw of rectus abdominis muscles were detected.
Can single pulse stimulation help to distinguish between pathological and physiological high frequency oscillations?

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Rationale

High Frequency Oscillations (HFOs; Ripples (R) 80-250 Hz and Fast Ripples (FR) 250-500 Hz) are new EEG biomarkers that predict the seizure onset zone (SOZ) in patients undergoing epilepsy surgery. Removal of FR correlates with seizure freedom. FR are considered pathological. Spontaneous R can be a mixture of physiological and pathological events. HFOs can be evoked with Single Pulse Electrical Stimulation (SPES) during chronic electrocorticography (ECoG)
¹. Evoked HFOs are specific for the SOZ. We hypothesize that SPES elicits selectively pathological HFOs.

Methods

Data of 6 patients who underwent chronic ECoG and SPES before surgery. SPES (10 monophasic pulses of 1ms, 4-8mA, 0.2Hz, on pairs of adjacent electrodes) was performed in a set of 64 electrodes sampled at 2048Hz. Time Frequency analysis of delayed SPES responses was done¹. Averaged responses per stimulation and per electrode were classified as evoked R or FR. In 1 min epochs, before or >1h after SPES, spontaneous HFOs were automatically detected² and visually checked (FIR high pass R>80Hz at 5μV, FR>250Hz at 1 μV, 0.4s/page, AVR). SOZ electrodes were marked. We compared the percentage spontaneous vs. evoked HFOs in the SOZ. At electrode level, we calculated sensitivity and specificity for spontaneous vs. evoked HFOs for the SOZ. Significance was assessed with Mann Whitney U (p<0.05).

Results

We found spontaneous and evoked HFOs in all patients. The percentage of R in the SOZ was higher for evoked than for spontaneous R (25 vs 42% p=0.08). For FR no difference was found (51 vs 52%). At electrode level, evoked FR showed a higher sensitivity than spontaneous FR (61 vs 32% p=0.16) for the SOZ.

Conclusion

Evoked R tend to arise more often in the SOZ than spontaneous R. As expected we found no significant differences for FR. SPES seem to selectively elicit pathological HFOs, demonstrating the advantage of stimulus locked HFOs. SPES is a helpful clinical tool to delineate the epileptic focus.


Fig 1: Percentage spontaneous vs. evoked HFOs in the SOZ.

Fig 2: Density of HFOs at electrode level for spontaneous vs. evoked R (A&B) and FR (C&D).
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figure 1

% Spontaneous vs. evoked HFOs in the SOZ

figure 2
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EARLY ABNORMAL SPONTANEOUS ACTIVITY FINDINGS IN AXONAL VARIANT OF GUILLAIN BARRE SYNDROME: Is this a new variant of Guillain Barre Syndrome.

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Objective

To evaluate the earliest denervation potentials in axonal variant of GBS.

Background

Guillain Barre Syndrome (GBS) is one of the most important acute neurologological emergency. Denervation potentials on needle EMG is the hallmark of axonal damage. Usually this is a time dependent phenomenon. The degeneration of axon depends upon length of axon to be degenerated. Studies claim variable time duration for denervation potentials from two weeks to three weeks.

Material/Methods

This is a cross-sectional survey of patients admitted and referred for neurophysiologic assessment. Clinical and neurophysiologic data of GBS patients over a period of three years and three months and ten days was collected. NCS/EMG performed by a qualified neurophysiologist. Diagnosed cases of GBS with available data of NCS/EMG were included. Patients with history of Diabetes Mellitus, previous history of any sort of neuropathy and demyelinating variants after diagnosis were excluded as well. Clinical and Neurophysiologic data were collected on Performa for analysis.

Result

Total forty three patients were diagnosed as GBS and those with axonal variants were finally included. Out of forty three, eighteen had axonal variant of GBS and rest of them demyelinating variants. Twelve patients of axonal variant (31%) showed fibrillation potentials, positive Sharp Waves and increased insertional activity within 4-12 days of symptoms onset and six (69%) beyond that period. Total twelve patients were finally included. Active denervation in the form of fibrillation potentials and positive sharp waves were noted frequently and decreased interference pattern in almost all patients. NCS were performed before EMG examination.

Conclusion

Fibrillation Potentials, Positive Sharp Waves and decreased interference pattern were noted in early course of disease in GBS patients interestingly before two weeks of symptoms onset. This study raises the query for a possible new Hyperacute or Fulminant variant of GBS. These findings need further histopathology and etiologic correlation as well as further prognostic importance.

Key words

GBS Guillain Barre Syndrome, NCS Nerve Conduction Study, EMG Electromyography.
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O63

Proprioceptive and Sympathetic nerve fibers affection in Guillain-Barré Syndrome

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Question

Could Proprioceptive and sympathetic fibers be affected in patients with Guillain Barre Syndrome (GBS)?

Method

The proprioceptive Ia afferent fibers conduction velocity using electrically induced reflex activity (R1), and Sympathetic skin response (SSR) were studied in upper and lower limbs of 20 patients fulfilling the criteria of GBS and 20 Healthy volunteers.

Results

Median nerve Proprioceptive Ia afferent fibres CV sowed significant slowing in patients: 29.5±17.4 m/s compared to control subjects: 68.1±16.8 m/s. Posterior tibial nerve Proprioceptive Ia afferent fibres CV sowed significant slowing in patients: 30.3±19.1m/s compared to control subjects: 57.4±16.1 m/s. Nine patients (45%) showed absent SSR in the hand, while 12 patients (60%) showed absent SSR in the foot.
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Hand SSR showed significant delay: 1.26±0.3 sec and decrease of amplitude: 54.2 ±43.8 μV in patients compared to control: 1.08±0.2 sec, 99.4±64.4 μV. Foot SSR showed significant delay: 1.8±0.6 sec and decrease of amplitude: 16.5 ±6.2 μV in patients compared to control: 1.6±0.2 sec, 36.5±23.8 μV.

Conclusions

The study of electrically induced reflex activity revealed significant involvement of proprioceptive Ia afferent fibers in patients with GBS and was correlated significantly with the severity of neuropathy. SSR study showed significant involvement of sympathetic fibers in patients with GBS but not correlated with the severity of neuropathy.
P1
Brain Plasticity for Rajyoga Meditation: An Resting State EEG-fMRI Study

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Background and Purpose

Understanding the role of brain in bringing about awareness and consciousness has always been a challenging area of neuroscience and an impressive debate on effect of meditation in various aspects. Our study aims at understanding the effect of Rajyoga Meditation. We hypothesized that effect of Rajyoga Meditation may be visualized using simultaneous EEG-fMRI as changes in neurohemodynamic correlates.

Methods

We studied twenty male long term (more than 10 years) Rajyoga Meditators (RMs) and twenty healthy control (HCs) with the mean age of 30 (SD 10) year using EEG-fMRI. We used functional magnetic resonance imaging (fMRI) for examining the default mode network (DMN) and Electroencephalography (EEG) derived quasi-stable states known as EEG-microstates to examining the brain stability over the time. The EEG-microstates were convolved with resting fMRI to understand the changes in meditators compared with healthy controls.

Results

Significant spatial differences with the DMN in RMs, compared with HCs. We noted that the long term meditators have lower intensity with lesser number of voxel in medial prefrontal cortex (MPFC), posterior cingulate cortex (PCC) as compared to healthy people at rest and this activity was further reduced during meditation where as increased in medial temporal cortex (MTC). The average duration of EEG microstate corresponding to DMN, in healthy control was 80ms (30ms to 240ms) and mediators was 90ms (50ms to 310ms)(P value).This significantly increased to 120ms (70ms to 370ms during meditation.

Conclusion

EEG-fMRI is a valuable technique in understanding the effects of meditation. Decrease DMN and Increase in the duration of EEG-microstates could suggest increased brain stability, less ruminative thought in meditators. Increased MTC in DMN network is indicative of a better cognitive process.

Key Words

Rajyoga Meditation, simultaneous EEG-fMRI, DMN, EEG-Microstate
When task-irrelevant salient stimuli are added to perceptual discrimination tasks, these stimuli are typically found to elicit a prominent frontal P3a component in the event-related potential (ERP) of healthy participants. Recently, comparable P3a-like waveforms have been detected in tasks tapping more sophisticated cognitive functions including mental set shifting and probabilistic decision making. By analyzing the common and divergent features of P3a-like activity across these paradigms, the present study aimed at elucidating its functional role in executive processing. Sixteen young and healthy participants completed both auditory and visual variants of the three-stimulus oddball paradigm, a task-switching paradigm closely modeled to the Wisconsin Card Sorting Test and a decision-making task requiring the integration of probabilistic information. We found frontal P3a-like amplitudes to be enhanced by novel stimuli, feedback stimuli informing about changes in task contingencies and probabilistic cues informing about states. P3a components were isolated by means of principal component analysis and compared across experimental paradigms. Results suggest the P3a to be an electrophysiological indicator of the brain’s orienting response. Our findings are discussed with regard to deficient novelty detection and executive processing in basal-ganglia movement disorders and the role of fronto-striatal networks in resolving uncertainty.
P3
A longitudinal study of auditory evoked field and language development in young children.

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The relationships between the remarkable language development in young childhood and maturation of brain functions related to the human voice are still not well understood. Our previous study showed that the significant relationship between auditory evoked field (AEF) and language performance in 2- to-5-year old children (Yoshimura et al.,2012). In this study, we investigated the relationship between the voice evoked field and language development in young human children using magnetoencephalography (MEG) with a longitudinal design. Twenty typical developing children were recruited (aged 36-75 months old when they participated in the first measurement). These same children were re-investigated 11-25 months after the first measurement. To investigate developmental changes in each participant’s neural brain response to voice stimuli, an AEF component (i.e., P1m) was examined. In addition, we examined relationships between brain responses and the language performance. P1m peak intensity to the voice stimuli showed a significant increase in both hemispheres in the second measurement compared with the first measurement (Figure1). However, no significant differences were observed in P1m latency. Interestingly, our results reveal that children who showed a greater increase in P1m intensity in the left hemisphere showed higher linguistic performance(Figure2). Hence, our results indicate that the P1m component evoked by voice stimuli is a neurophysiological marker for the language development for young children. In addition, MEG is a technique that can be used to investigate maturation of the auditory cortex based upon auditory evoked fields in young children. Ours is the study to demonstrate a significant relationship between the development of the auditory processing system and the development of language abilities in young children.


Figure 1. Source modeling of P1m component evoked by auditory stimuli in one subject.

Figure 2. The correlation between the percent change in the standardized score of the language conceptual inference task in K-ABC and change in the P1m amplitude in the left hemisphere (a) and right hemisphere (b).
**Objective**

Patients with attention deficits after traumatic brain injury (TBI) have difficulties filtering out irrelevant stimuli and are easily distracted, but the mechanisms and neural basis of these impairments in active inhibition are unclear. The purpose of this study was to examine active inhibition of irrelevant stimuli and evaluate its neural basis using functional near infrared spectroscopy in patients with attention deficits after TBI.

**Method**

Ten TBI patients and 10 healthy control subjects participated in this study. The Paced Auditory Serial Addition Test (PASAT) was performed with (distracting PASAT) and without (PASAT) distracting Japanese kana phonetic characters presented between each number.

**Results**

Healthy controls performed better than TBI patients on both the PASAT and the distracting PASAT. When performing the PASAT, healthy controls showed significant activity in every region of interest except the right lateral prefrontal cortex (PFC), but TBI patients showed significant activity only in the left anterior PFC and left lateral PFC. When performing the distracting PASAT, the right lateral PFC was active in healthy controls, but not in TBI patients.

**Discussion**

These results confirm that patients with moderate-to-severe TBI were affected by distractors that influenced order processing. We suggest that the working memory of TBI patients was affected by distracting stimuli, whereas that of healthy individuals was not.
P5
Dopamine enhances the introspection of visual illusion

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Question

Visual illusion is the internally constructed reality against the physical one. The introspection to the illusion, therefore, is a window to our subjective experience shaped in the brain. The current study aimed to identify the default states of molecular and neural systems that generate the introspection of visual illusion.

Methods

Participants completed a ponzo illusion task that required a perceptual response followed by an estimate of confidence in their decision. We objectively quantified variability in metacognitive sensitivity, the ability to discriminate correct from incorrect illusory perception, between individuals and then related these interindividual differences to dopamine transporter (DAT) availability using [¹⁸F]FE-PE2I PET and those to activity in resting-state brain networks measured by functional MRI.

Results

Metacognitive sensitivity was negatively correlated with striatal DAT availability. Moreover, resting-state activity that correlated with interindividual variations in metacognitive sensitivity and striatal DAT availability was overlapped in the dorsolateral prefrontal cortex, a region associated with metacognitive ability in literature.

Conclusions

Reduced DAT availability, which indicates the decreased dopamine turnover, was associated with the enhanced introspection of visual illusion. Our finding points to an interrelationship between dopaminergic neurotransmission and resting-state activity for the introspection of illusory perception, or subjective reality.
P6
Hemodynamic Evaluation of Cognitive Shifting in Children with Autism Spectrum Disorder

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Question

The restrictive, stereotyped behavior in children with autism spectrum disorder (ASD) is considered to be related to deficits in executive function. In particular, cognitive shifting in executive function is deeply associated with stereotyped behavior in ASD. Previous investigations using fMRI have clarified that the lateral prefrontal cortex is involved in cognitive shifting when flexible changes in attention were needed. However, a few studies have revealed a direct association between cognitive shifting tasks and lateral prefrontal cortex activity in children with ASD.

Methods

We examined cognitive shifting in 7- to 12-year-old children with ASD (n=14) and typically developing children (TDC, n=20) using the dimensional change card sort (DCCS) task. Two groups were matched age and intelligence quotient. In addition, using near-infrared spectroscopy (NIRS), we examined prefrontal brain activity in conjunction with cognitive shifting.

Results

ASD children provided fewer correct answers (p < 0.001) and slower reaction times (p < 0.05) in the task than TDC in DCCS task. Furthermore, the children with ASD displayed a decline in right lateral prefrontal cortex activity during the task compared with TDC (p < 0.05). In addition, a negative correlation was observed between the severity of autism and brain activity during the task (infant; r = -0.55, p < 0.05, present; r = -0.71, p < 0.01).

Conclusions

These results suggest that the activity and physiological indices used in this study might be useful for identifying the symptoms of ASD and discriminating ASD from other disabilities.
P7
Expectancy and saliency contributions to the Stimulus Preceding Negativity

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Abstract

Question

The Stimulus Preceding Negativity (SPN) is a slow negative non-motor potential elicited by temporally predictable stimuli that has been related with anticipation processing for the upcoming stimulus. The SPN has been interpreted as a subcomponent of the late Contingent Negative Variation (CNV) even if its identification is difficult with a classical CNV paradigm.

Our aim was to investigate if a non-motor triplet paradigm that provides salient unpleasant stimuli could be able to elicit an anticipatory expectancy or, in neurophysiological terms, the SPN.

Methods

We deliver trains of three stimuli (triplets S1-S2-S3): S1 and S2 always belong to the same sensory modality (auditory or electric) whereas S3 can belong either to in the same sensory modality (triplet “same” session, A1A2A3/E1E2E3) or to the alternative modality (triplet “different” session, A1A2E3/E1E2A3). In each of the 30 healthy subject, we evaluated the presence of the SPN in the interval time preceding S1, S2 and S3.

We did not provide any task instructions to the subjects and motor responses were not required.

Results

We did not find any negative slow potential in the interval time that preceds S1. In triplets “different” session, we could identify a SPN preceding S3 in triplets A1-A2-E3 and preceding S2 in triplets E1-E2-A3. In triplet “same” session, we could observe a SPN preceding both S2 and S3 but only in the electric modality (triplets E1-E2-E3).

Conclusions

In our paradigm only those stimuli learnt to be both predictable and salient are able to elicit a slow negative potential interpreted as SPN. Our findings show that the SPN could be easily elicited with this non-motor triplet paradigm where it electively anticipates the presentation of salient unpleasant stimuli.
The dimensionality of chaotic attractors reveals specific functional dynamics of brain sensory information processing

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Dimensional complexity of brain neuronal networks is frequently estimated with the correlation dimension which provides information about the degrees of freedom of a dynamic system. It has been applied to EEG or MEG for studying the cortical dynamics underlying cognitive processing but up to now the relationship between complexity and specific cognitive neural correlates is far from clear. With original real time brain information processing analysis method, changes in dimensionality are found to be correlated with specific somatosensory information processing related ERPs and fronto-parietal gamma synchronizations. Our results are suggesting that the correlation dimension enables to reveal changes in neuronal attractors parameters related to brain sensory information processing and to dissociate functional dynamics of similar EEG patterns which have dramatic opposite effects in terms on consequences for the behavior.
P9
Psychomotor performance and heart rate variability in healthy young adults: gender differences and clinical implication

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Psychomotor performance plays an important role in the medical practice, especially surgery one. Heart rate variability (HRV) may reflect the value of adaptation in the daily life. We hypothesized that there is the link between motor test results and HRV in healthy young adults.

92 six-year medical students 22-24 yrs (25 men and 67 women) underwent complex computerized psychomotor testing and 5-min. ECG recording done in the same day in the morning during spring 2013. HRV was accessed in the time and frequency domains.

Gender differences were seen only in 3 tests: finger tapping rate over 5 consecutive 4-sec. periods was greater in men, they have done interference motor test more accurately and had lesser simple visual-motor reaction time (SVM RT, 232.7+/-7.8 ms vs 284.3+/-12.0 ms; p=0.0002). Women had greater heart rate, but lesser sympatho-vagal balance (LF/HF), lower relative power of low frequency (LF%, vasomotor modulation) and greater - of high frequency (HF%, parasympathetic drive) band.

In men significant positive correlations exist between interference RT and parameters characterizing HRV: SDNN, total spectral power (TP, mc2), power of very low frequency (VLF, ms2; r=0.70; p<0.01) and relative power of VLF (VLF, %, r=0.50, p<0.05) band corresponding thermoregulation and activity of hypothalamic-pituitary-adrenal axis. Interreactive variation in the flicker fusion test was related negatively, but SVM RT - positively with HRV (TP, VLF, HF).

In women static and dynamic tremor rate positively correlated with relative power of VLF waves. RT on the moving object in the middle of testing was negatively related with HRV, but interference RT - positively (HF).

In conclusion, motor performance in healthy young adults is tightly related with heart rate variability. This fact gives the opportunity to consult the graduated medical students preferring medical specialty on the physiological base for their health maintaining.
P10
Electrophysiological signatures of probabilities in a Bayesian oddball paradigm

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Against the background of the increasing popularity of the Bayesian-brain hypothesis and the associated assumption of distinct neural representations of prior and likelihood probabilities in the human brain, we examined whether (a) ERPs can be demonstrated to be sensitive to variations in Bayesian probabilities, and (b) two neural processes are dissociable on the level of ERPs, with one being sensitive to changes in prior probability and the other being sensitive to changes in likelihood probability. Participants’ (N = 16) behavioral and electrophysiological responses to the first of a sample of four balls drawn in an urn paradigm were analyzed as a function of prior probability (represented by the frequency of a particular urn type) and likelihood (represented by the frequency of a particular ball type in this urn). Participants were instructed to indicate which of two ball stimulus types (frequent vs. rare) had been presented, and to decide which of two possible urn types (frequent vs. rare) the respective ball sample had been drawn from. Independent manipulation of prior probabilities (.7 vs. .9) and likelihood probabilities (.7 vs. .9) yielded a 2 × 2 within-subject design. Bayesian model selection was applied to clarify associations between amplitude variations in ERP and the experimental manipulations. Results suggest distinct neural representations of prior and likelihood probabilities, with prior probability being associated with components similar to the classic P3a component, and likelihood probability being associated with components similar to the classic P3b component.
We investigated the relationship between reaction time (RT) and response variability and somatosensory Go/No-go potentials. Event-related potentials (ERPs) following electrical stimulation of the second (Go stimulus) or fifth (No-go stimulus) digit of the left hand were recorded from sixteen subjects, and Go and No-go stimuli were presented at an even probability. The subjects were instructed to respond to the Go stimuli by pushing a button with their right thumb. We analyzed the correlation between RT and the somatosensory N140 and P300 components, and between the standard deviation (SD) of RT and the N140 and P300. Neither the amplitude nor latency of the No-go-N140 (N140 evoked by No-go stimuli) or the Go-N140 (N140 evoked by Go stimuli) related significantly with RT and the SD of RT. There was a significant negative correlation between RT and the amplitude of the No-go-P300 (P300 evoked by No-go stimuli) at Fz and C3, indicating that subjects with a shorter RT had a No-go-P300 of larger amplitude. The latency of the Go-P300 (P300 evoked by Go stimuli) at Pz and C3 showed a significant correlation with RT. The SD of RT was significantly correlated with the amplitudes of the No-go-P300 at C3 and Go-P300 at Pz and C4, and the latency of the No-go-P300 at Cz and Go-P300 at Fz, Cz, Pz, C3, and C4. These results suggest that response speed and variability for the Go stimulus in Go/No-go paradigms affect No-go-related neural activity for the No-go stimulus. In addition, judging from the difference of results in the relationship between RT and the N140 and P300 components, and between the SD of RT and the N140 and P300, No-go-N140 and No-go-P300 would reflect different neural activities and characteristics during response inhibitory processing.
P13
Analysis of cortical sources with words in Spanish in preschool Mexican children

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Question

What is the location of the cortical sources of two auditory stimulus: /ajos/ (garlic) and /ojos/ (eyes), extracted from an oddball paradigm in preschool Mexican children with and without language problems?

Methods

To determine the presence of language problems, we consider articulation difficulties in the soft neurological signs of Assessment Child Neurology (ENI: Evaluacion Neurologica Infantil). We perform an electroencephalogram (EEG) recorded with Neuroscan System using a 64-channel electrode cap with Ag/AgCl electrodes. During EEG recording, participants were exposed to auditory stimulation of an oddball paradigm with 400 stimuli, with /ajos/ as standard stimuli (80%), and /ojos/ as deviant stimuli (20%). We extracted signal corresponding to each word and analyzed separately.

Results

Participants were 10 male children with mean age of 5 years 7 months, 5 with language problems and 5 controls. In two cases with language problems, source cortical for both words wasn’t identified and in the other three cases, cortical sources of positive activity were located in the frontal areas. In control cases, we identified response for the two stimulus words with cortical sources in areas right fronto-central and posterior areas for the word /ajos/ and fronto-central for the word /ojos/.

Conclusions

Sources cortical of auditory stimulus depend to the characteristics of each stimulus and its processing. Children with appropriate language had more defined and specific localization of cortical sources.
P14
The effect of mastication on Go/No-go decisional processing: An event-related potential study

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The purpose of the present study was to clarify the effect of mastication on Go/No-go decisional processing using event-related potentials (ERPs). The two experiments consisted of two conditions, Mastication and Control. The eleven normal subjects performed seven sessions of a somatosensory Go/No-go paradigm for approximately four minutes, Pre (before Mastication), Post 1, 2, 3, 4, 5, and 6 (after Mastication). After one session, the subjects were asked to chew gum for five minutes at a relaxed self-pace. In total, there were six gum-chewing intervals. For Mastication, a special gum base that was odorless and tasteless was prepared, and the gum was removed from the mouth during the ERP recording periods. The Control condition included the same seven sessions, but the subjects were instructed to relax without chewing gum in each interval. Somatosensory stimuli were delivered to the second (Go stimuli) or fifth digit (No-go stimuli) of the left hand, and the subjects had to respond by pushing a button with their right thumb as quickly as possible after the Go stimulus. Reaction time (RT) and the standard deviation (SD) were recorded, and the peak amplitude and latency of the somatosensory N140 and P300 components were analyzed.

In Mastication, RT was significantly shorter in Post 1, 3, and 6 than Pre. By contrast, the RT in Control did not differ between Pre and the other sessions. The peak amplitude of the Go-N140 in Mastication was significantly larger in Pre than Post 6, but that in Control was significantly larger in Pre than Post 2, 3, 5, and 6. The peak latency of the Go-P300 in Mastication did not change with repeated sessions, but that in Control was significantly longer in Post 4 and 5 than Pre. No effects of Mastication on the peak amplitude and latency of the N140 and P300 were found in the No-go trials.

These results suggest that mastication affected ERP waveforms elicited by the ‘target’ stimulus, rather than ‘non-target’ stimulus. In other words, the effect of mastication would be found on response execution processing in Go trials, rather than inhibitory processing in No-go trials. Since the present study prepared a special gum base that was odorless and tasteless, factors of odor and taste could be ruled out. This is the first study to investigate the effect of mastication on Go/No-go decisional processing.
P15
Functional properties of the human brain network underlying attentional control

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Previous studies have demonstrated task-related changes in brain activation and inter-regional connectivity but the temporal dynamics of functional properties of the brain network during task execution is still unclear. In the present study, we investigated task-related changes in functional properties of the human brain network underlying attentional control by applying graph-theoretical analysis to magnetoencephalography (MEG). Subjects performed a cue-target attention task in which a visual cue informed them of the direction of focus for incoming auditory or tactile target stimuli, but not the sensory modality. We analyzed the MEG signal in the cue-target interval to examine neuronal oscillations and network properties during attentional control. In the cue-target interval, beta activity was desynchronized in the sensori-motor region including premotor and posterior parietal regions in the hemisphere contralateral to the attended side. In beta frequency, global hubs were found around the sensori-motor and prefrontal regions, and functional segregation over the entire network was decreased during attentional control compared to the baseline. Thus, network measures revealed task-related temporal changes in functional properties of the human brain network, leading to the understanding of how the brain dynamically responds to task execution as a network.
P16
Developmental changes in face perception during childhood: An event-related potential study

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We investigated the development of brain activity related to face perception was investigated in 8- to 13-year-old children by event-related potentials (ERP). We used three stimuli: (1) Upright face, (2) Inverted face, and (3) Eyes. A negative component (N170) was evoked by all conditions in the bilateral occipito-temporal areas of 8- to 13-year-old children. N170 to the Eyes stimulus was significantly larger than that to other stimuli, which indicated that children were more afraid of eyes than adults. The latency of N170 significantly decreased with age in all conditions. The amplitude and latency of N170 was larger and longer, respectively, to the Inverted face stimulus in 10- to 13-year-old children, and double peaks for N170 were also observed in many of these subjects. The latencies of the first and second peaks that were recorded in younger children and adults, respectively, indicating that 10 years old is a critical period between children and adults. N170 in 13-year-old children was similar to that in adults. These results demonstrated that brain activity related to face perception begins to mature from 10 years old, and almost reaches the adult pattern by 13 years old.
Neurophysiological markers of disrupted anticipatory expectancy in the adult ADHD pathology

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Question

The assessment of the Attention Deficit/Hyperactivity Disorder (ADHD) in adults is often challenging particularly due to the absence of specific diagnostic criteria and the frequent comorbidities.

We applied a recently developed non-motor triplet protocol in a adult ADHD population to study both the short-term habituation (STH) both the anticipatory attention (as reflected by the stimulus preceding negativity, SPN).

Methods

We recorded 26 adult ADHD patients and 26 age-matched control subjects that did not receive any instructions about the task. The triplet protocol provides for the delivery of trains of 3 stimuli (triplets S1-S2-S3) where S1 and S2 always belong to the same sensory modality (auditory or electric) whereas S3 can belong either to the same sensory modality or to the alternative modality. Amplitudes of N1-P2 evoked potentials were measured and then compared to assess the STH entity. We also evaluated the presence of the SPN in the S1-S2 and S2-S3 interval time.

Results

Compared to controls, the ADHD group showed a significant N1-P2 amplitude reduction in response to S1 across different sensory modalities and also a significant attenuation of the SPN that precedes electric unpleasant stimuli. STH modulation profile was not impaired.

Conclusions

We hypothesize that a reduced attentional elemental processing to the sensory environment combined to a blunted responsiveness to unpleasant stimuli may impair the anticipatory expectancy to the upcoming salient stimuli.

Since these findings reflect an atypical anticipatory processing, the SPN evaluation may represent a potentially useful tool in the diagnostic assessment of the adult ADHD pathology.
P18
Functional Mapping of Expressive Language Area with ECoG and ECS

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Question

Patients suffering from intractable epilepsy, who are candidates for surgical treatment, have to undergo several functional mapping procedures to make precise diagnosis for epileptogenic foci and eloquent brain regions. In this work we investigated the sensitivity and specificity of an ECoG based real-time functional mapping system cortiQ (g.tec, Austria) compared to the standard clinical ECS mapping.

Methods

Based on task-related gamma-band oscillations, the system identifies large cortex areas within minutes. More precisely, the frequency band of interest covers 60 to 170 Hz, excluding power-line and its higher level harmonics. In order to extract only the task-related activation, the band-power during the active phase is referred to a baseline interval of the same time. The study included ECS and cortiQ mapping with an epileptic patient having 236 subdural electrodes implanted. The dominant left hemisphere was covered by high-density grids with inter-electrode distance of 5 mm. A picture naming task was performed to identify the language areas with cortiQ and ECS, respectively.

Results

The cortiQ mapping consistently showed activation over inferior frontal gyrus in two independent runs. A next-neighbor comparison led to a sensitivity of 77.80 % and a specificity of 88.75 % with respect to the ECS mapping.

Conclusions

The modalities show a good overlap, which is even more convincing due to the high number of tested electrodes in the area of interest, caused by the high-density grid. The cortiQ mapping is a powerful supportive tool, as it provides very fast information to reduce the number tested electrodes during ECS mapping.

figure 1
P19
Proactive control of interference in working memory - a combined TMS-EEG study

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Question

Cognitive control can be reactive or proactive in nature. Late-acting reactive control aims to reduce consequences of cognitive conflict, early-acting proactive control attempts to anticipate or minimize cognitive conflicts. Earlier functional brain imaging studies demonstrated an activation of the left inferior frontal gyrus (IIFG) in reactive as well as in proactive control of interference in working memory (WM). This study intended to prove the causal role of the IIFG in proactive control of interference in WM.

Methods

12 subjects (mean age 25 years) performed a modified recent-negative task. A different frequency of conflicts during experimental blocks of trials preferentially induced reactive or proactive control (Burgess & Braver, 2010). EEG was recorded while navigated Transcranial Magnetic Stimulation (NTMS) of the IIFG was applied before probe presentation. Analyses included behavioral data as well as amplitudes of an event-related potential supposed to reflect interference control in WM, called N450 (Tays et al., 2008).

Results

NTMS of the IIFG before probe presentation impaired proactive control of interference in WM (p < 0.001). Proactive control was accompanied by larger amplitudes of the N450 (p < 0.01). A positive correlation was found between amplitudes of the N450 and proactive control (Spearman-Rho: 0.58, p < 0.03).

Conclusions

Our results confirm a causal role of the IIFG in proactive control of interference in WM. The N450 is a correlate of proactive rather than reactive control in WM.
P20
Gamma-band synchronization during eye gaze perception between directly facing individuals
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Perception of facial expression and eye gaze direction of others is a key ability in typical social interaction which requires not only recognition of the local pattern around eyes but the global processing such as evaluating relationship between the outline of the face, and other parts of the face. Recent neuroimaging studies on the perception of facial expression have elucidated that the changes in eye gaze directed to the observer evoke specific neural responses in the posterior inferior temporal and posterior superior-temporal regions. However, it is still unclear how the changes in the eye gaze direction between the directly facing subjects changes the spontaneous brain activities in the both subjects.

We used simultaneous recordings of the neuromagnetic (MEG), EEG on a pair of directly facing subjects, i.e., the sender and the observer of the eye gaze, to measure changes in the spontaneous brain activities while the observer perceives changes in eye gaze direction of the sender. The MEG signals were analyzed in the time-frequency domain to evaluate event-related changes in the spontaneous brain activities induced by the onset of eye movements. Significant increase in the gamma-band power was observed in the eye-contact condition compared to the averting condition in the right superior parietal, bilateral posterior superior-temporal, and the frontal areas of the observer. Together with the preliminary results from the frequency-domain Granger- Geweke causality analysis, the current results indicate that the connectivity between (a) the bilateral frontal areas, and (b) the right frontal and parietal areas might be crucial for the perception of eye gaze of the directly facing person. The increase in gamma-band activities in these regions might reflect the integration of information processed individually in these regions for eye gaze perception.

figure 1
P21
Activation and Deactivation Patterns during Visual Working Memory Task: A Simultaneous EEG-fMRI Study

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Introduction

Working memory is a crucial cognitive function. We aimed to examine brain deactivation (negative) and activation (positive) Patterns during visual working memory task using simultaneous EEG-fMRI.

Methodology

Twenty right handed healthy volunteers in the mean age of 23.67±4.53 years and no of years of education was 16.58±2.8 years were recruited. EEG signal was recorded using 32 channel MR compatible system. fMRI with BOLD-EPI sequence (TR: 4000, 85 dynamics). We investigate the brain region activation and deactivation for visual working memory task in both EEG and BOLD signal. Further, as per fMRI activation brain connectivity was analyzed using region of interest based (ROI) in posterior cingulate cortex (PCC) seed.

Result

We found negative BOLD signal correlations with lower frequency (theta) band of EEG in the medial prefrontal cortex (MPFC) and PCC. In the other hand positive correlations found in BOLD signal with high frequency (alpha and beta) band of EEG in dorsolateral prefrontal cortex (DLPFC), inferior frontal cortex (IFC) supramarginal and medial temporal lobe. Also we noted that PCC seed was connected with many regions especially negative correlation of posterior cingulate region and MPFC region which associate with default mode network (DMN) and dorso-lateral prefrontal region (DLPFR), inferior frontal cortex (IFC) and supramarginal gyrus as positive correlation.

Conclusions

These findings demonstrate that the brain as a complex dynamic unit with positively and negatively correlated networks in perfect coherence during cognitive process such as working memory. As per the default mode hypothesis that certain brain areas show task induced deactivations across a wide range of cognitive tasks with harmony of positive correlation of which could associate with memory process.

Key words

Visual Working Memory, simultaneous EEG-fMRI, positive and negative correlations

Reference

P22
Cortical kinematic processing of executed and observed goal-directed hand actions

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Question

How is neural activity modulated in a time-sensitive manner by the kinematics of executed and observed goal-directed hand actions.

Methods

We recorded whole-scalp magnetoencephalography (Elekta Oy) from 11 right-handed subjects (6 F, 5 M; mean age 31.1 years) during two 5-min conditions (Self, Other). During Self, subjects pinched with their right hand green foam-made pieces mixed in a heap with pieces of other colors placed on a table in front of them, and put them in a plastic pot on the right side of the heap. During Other, subjects watched an actor, hidden by a screen but the right hand visible, to perform the same task 1.5 m in front of them. Subjects’ and actor’s forefinger movements were monitored with an accelerometer. Electromyograms (EMG) were recorded from upper limb muscles bilaterally. Coherence between accelerometer signals and (1) MEG signals (CohMEG), (2) alpha-band envelope (Cohα), and (3) beta-band envelope (Cohβ) were separately assessed. Sources of coherent brain activity were then identified using Dynamic Imaging of Coherent Sources.

Results

During Self and Other, CohMEG occurred at movement frequency (F0) or its first harmonic (F1) in the right posterior superior temporal gyrus, and bilaterally in the superior parietal lobule and the primary sensorimotor hand area (SM1ha) (Figure 1). Furthermore, Cohα occurred at F0 in SM1ha bilaterally (Figure 2). No EMG activity was observed during Other.

Conclusions

This study demonstrates that observing others’ hand actions engages the viewer’s brain in a similar kinematics-related manner than during own actions. The results bring novel insights into how brain activity covaries with essential features of others’ movement.

figure 1
Abstracts of Poster Presentations – Poster Session 1 – Assessment of cognitive function

Figure 2
P23
EEG response reflects that contribution of cognitive processes on perception is variable

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Question

The creation of conscious and meaningful perceptions from sensory information should be fast and action-guiding. This requires fast integration of stimulus-driven activity with endogenous processes, such as prior experiences and intentions. A flexible mechanism may increase the impact of endogenous processes when the quality of the sensory information is poor or inconclusive. Visual illusions, such as visual ambiguity, provide a tool to investigate the brain response when the sensory information available is largely inconclusive for the generation of a meaningful percept.

Methods

The EEG response during ambiguous and unambiguous perception was measured in twelve participants. Artefact-free epochs were extracted and the oscillatory theta response was extracted for all epochs using a single Morlet wavelet of six cycles and a centre frequency of 5.5 Hz (approximate frequency range: 4 to 7 Hz).

Results

The EEG theta response was larger at frontal than at occipital regions in all of our twelve participants when the stimulus was ambiguous. This pattern was not found during unambiguous perception. Perceptual switches lead to an overall increase of theta activity.

Conclusions

This outcome indicates that the contribution of endogenous processes on perception is variable. Anterior theta activity is specifically important for coherent perception when sensory information is ambiguous or inconclusive. Flexibility of endogenous processes may be a general phenomenon adjusting neural communication strategies on task demands (see also Mathes et al., 2012, Psychophysiology).
Aging effects on EEG alpha activity during internal and external motor sequence generation

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Question

Generation of action may rely on external guidance or be motivated internally, engaging partially distinct cerebral networks (Passingham 1987, Ciba Foundation Symposium 132, 151-164). Neuroimaging studies have shown a general age-related increase in processing resources related to motor control and sensory processing (Vallesi et al. 2011, J Cogn Neurosci 23, 801-815), accompanied by a reduced differentiation between the two networks of action generation (Heuninckx et al. 2010, Neurobiol Aging 31, 301-314). In an attempt to explore the electrophysiological correlates of motor generation modes, the present study examines the age effects on alpha activity related to the execution of externally- and internally guided finger sequences.

Methods

Thirty elderly (60-84 years) and 30 young (19-29 years) participants with normal cognition underwent 2 visuomotor tasks requiring sequential button-presses with the right index (1), middle (2) and fourth (3) fingers. In the externally-generated condition (Cued), the finger sequence was instructed by visuospatial cueing. In the internally-generated condition (Fixed), a fixed finger sequence (1-2-3) was generated following neutral visual cueing. Alpha power, individually determined between 7 and 13 Hz, was analyzed within 2-sec contiguous time segments in 6 regions of interest (ROIs) using an analysis of covariance, with Task and ROI as within- and age group as between-subject factors, while controlling for response speed.

Results

Reaction time was slower in older than younger subjects, and in the cued than in the fixed condition. Older made more errors than younger subjects in the fixed condition. Independently of condition and response speed, posterior alpha activation was larger in older than younger subjects. In contrast with the younger subjects showing larger alpha activation for cued than fixed finger sequences, the older subjects displayed similar activation for both types of sequences.

Conclusions

The present study brings electrophysiological evidence for an age-related increase in processing resources during finger sequence generation, and shows that the networks for generating externally- and internally-guided finger sequences become less differentiated with aging.
Neural correlates within spatial and non-spatial attention using electrocorticographic signals in humans

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Previous studies have revealed that right parietal cortex might play a key role in maintaining attention especially regarding spatial information. However, relatively little is known about the cortical areas involved in non-spatial feature attention and about brain frequency oscillations underlying neural mechanisms for spatial and non-spatial attention. We investigated the cortical areas and frequency oscillation involving during spatial and nonspatial attention task. Electrocorticographic (ECoG) signals were recorded while ten epileptic patients performed spatial and non-spatial attention tasks. Spatial attention led to reduced low frequency oscillations over right parietal, when non-spatial attention also had low frequency oscillations suppressed in both parietal, more on the right side, but other regions (frontal, temporal). In contrast, spatial attention showed increased high frequency oscillation in right parietal lobe, but nonspatial attention showed increased high frequency oscillation in both parietal, temporal and frontal area.

These findings implicate that both spatial and non-spatial attention affect right parietal cortex. However, spatial attention mainly depends on the right parietal cortex whereas non-spatial attention conducts on the several regions including right parietal, left parietal, right frontal, and right temporal regions.
P24
Aberrant connectivity of the inferior frontal cortex in anorexia nervosa
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Question
Neuroimaging studies, investigating the neural profile of anorexia nervosa (AN), have revealed a predominant imbalance between the reward and inhibition system of the brain. However, no study thus far has examined, in currently ill AN patients, whether these changes can also be determined independent of task condition using resting-state functional magnetic resonance imaging.

Methods
We investigate resting-state functional connectivity using degree centrality and then granger causality to analyze effective connectivity, to understand directional aspects of potential alterations, in AN patients compared to healthy controls.

Results
We were able to show that the bilateral inferior frontal gyrus (IFG) is a major hub in AN patients revealing reduced functional connectivity (Fig.1). Furthermore, we found decreased effective connectivity from the right IFG to the mid cingulum and increased effective connectivity from the bilateral orbitofrontal gyrus to the right IFG. For the left IFG, we only observed increased effective connectivity from the bilateral insula to the left IFG. Of note, scores reflecting physical activity correlated with connectivity patterns of the right IFG. Moreover, aberrant effective connectivity from and to the IFG was additionally related to behavioral inhibition.

Conclusions
These results suggest that AN patients have a reduced connectivity within the cognitive control system of the brain and increased connectivity within regions important for salience processing. We speculate that an exaggerated processing of salient stimuli places an increased demand on the inhibitory system, which could be a potential risk factor for hyperactivity in AN.

Figure legend
Figure 1. Decreased functional connectivity in the inferior frontal gyrus measured by degree centrality in anorexia nervosa patients compared to healthy controls (p<0.05, FWE corrected) (AN: anorexia nervosa; HC: healthy non-athlete controls; HCA healthy athlete controls).
P25
Coherences during motor imagery as a possibility to distinguish patients with disorders of consciousness.

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Question

Distinguishing between different states of consciousness such as minimally conscious state (MCS) and vegetative state (VS) with high accuracy is still a challenge. In order to improve accuracy of diagnoses, objective markers for consciousness are being investigated. The study at hand investigated changes in coherences calculated from EEG recordings during motor imagery.

Methods

EEG was recorded in 11 VS and 13 MCS patients. Coherences covering frequencies from 1 to 28Hz between 17 electrodes for a resting condition and a motor imagery condition were computed. The difference between rest and motor imagery was taken for each patient. These differences were compared between the two groups of patients.

Results

No significant difference between the two patients groups was found. Even when the p-values were not corrected for multiple comparisons, the results were ambiguous and therefore impossible to interpret in an obvious way. Across several frequencies the differences between coherences during motor imagery and rest were either higher in the UWS group or in the MCS group.

Conclusions

The results yielded no evidence for a difference between the two patient groups during the performance of motor imagery. The results imply that both groups of patients were not able to perform motor imagery in a sufficient way that would be detectable by coherence analysis. The explored trends are likely to reflect normal fluctuations in the EEG of these different patient groups, showing once again the difficulties of group statistics in such comparisons.
P26
Multiple frequency functional connectivity in the hand somatosensory network: An EEG study

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Question
We aimed at investigating the dynamics of communication among nodes of the primary somatosensory neuronal network.

Methods
Multichannel EEG responses evoked by median nerve stimulation were recorded from six healthy participants. We investigated the directional connectivity of the evoked responses by assessing the Partial Directed Coherence (PDC) among five neuronal nodes (brainstem, thalamus and three in the primary sensorimotor cortex), which had been identified by using the Functional Source Separation (FSS) algorithm. We analyzed directional connectivity separately in the low (1-200 Hz, LF) and high (450-750 Hz, HF) frequency ranges.

Results
LF forward connectivity showed peaks at 16, 20, 30 and 50 ms post-stimulus. An estimate of the strength of connectivity was modulated by feedback involving cortical and subcortical nodes. In HF, forward connectivity showed peaks at 20, 30 and 50 ms, with no apparent feedback-related strength changes.

Conclusions
In this first non-invasive study in humans, we documented directional connectivity across subcortical and cortical somatosensory pathway, discriminating transmission properties within LF and HF ranges. The combined use of FSS and PDC in a simple protocol such as median nerve stimulation sheds light on how high and low frequency components of the somatosensory evoked response are functionally interrelated in sustaining somatosensory perception in healthy individuals. Thus, these components may potentially be explored as biomarkers of pathological conditions.

Fig. 1 - Dynamics of effective connectivity among LF recruited neuronal pools
Up PDC among subcortical and cortical sources integrated in the [1-200] Hz frequency range shown in the 0-80 ms interval. In blue forward propagation direction and in red the backward. Main PDC components appear at 16, 20, 30 and 50ms. Network connectivity at these latencies is shown in the Bottom part of the Figure, coding the connection strength by the connector thickness.

Fig. 2- Dynamics of effective connectivity among HF recruited neuronal pools
The same scheme as Figure 1, showing PDC behaviour integrated in the [450-750] Hz.

References
Abstracts of Poster Presentations – Poster Session 2 – Connectivity

P27
Reverberant cortico-cortical interactions in early phases of movement inhibition

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Living in dynamic environment continuously requires the rapid generation of motor responses when necessary but also the promptly inhibition of actions when they would be unsuitable. In the last years many studies have investigated the role of various cortical and subcortical brain regions in inhibitory control and converging evidence suggest a crucial role of the right Inferior Frontal Gyrus (rIFG) and of the pre-Supplementary Motor Area (pre-SMA). However the precise role and the exact timing of the contribution of these areas remain unclear. The aim of the present study was to investigate the role of rIFG and pre-SMA in motor inhibition by establishing the specific time course and the causal interactions of these regions in relation to the left primary motor area (LM1).

In a sample of 10 healthy subjects paired transcranial magnetic stimulation (TMS) was delivered over the rIFG-LM1 and over pre-SMA-LM1 before and 50, 75, 100, 125, 150, 175 and 200 ms after the presentation of visual stimuli in a simple GO/NOGO task. For each interval, Motor Evoked Potentials (MEPs) and Reaction Times (RTs) were collected. To further gain information about rIFG/pre-SMA control over M1 an EEG/TMS study was also performed. When the conditioning stimulus was applied over the rIFG, MEPs were markedly and selectively increased for the NOGO trials at 50 (p=0.003), 100 (p=0.002) and 150 ms (p=0.001) after the stimulus onset. No differences were found at 75, 125, 175 and 200 ms after cue presentation for the NOGO trials and at any delay for the GO trials. A similar temporal profile of cortico-cortical activation was found for the pre-SMA-LM1 connectivity for the NOGO trials peaking at 50, 100 and 150 ms after the cue onset. RTs were slowed down at 100 (p=0.004) and 150 (p=0.013) ms after the stimulus presentation in all experimental conditions. EEG/TMS session revealed that magnetic pulse over the rIFG and, to a lesser extent over SMA, evoked an increase in the beta activity over M1 (p=0.03). The temporal profile of MEPs modulation, peaking every 50 ms and the beta increase over M1 indicated by the EEG/TMS session, strongly suggest a common monitoring action of rIFG and pre-SMA in stop processing mediated by reverberant oscillation in the beta rhythms.
P28
Effects of Ginkgo biloba Extract EGb 761® on Dopamine-Mediated Executive Functions and their Neurophysiological Correlates: An Exploratory Study in Patients with Mild Cognitive Dysfunction

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Question
The study was performed to explore whether Ginkgo biloba extract EGb 761®, which increased dopamine levels in the prefrontal cortex in animal studies, modulates dopamine-dependent executive functions and their neurophysiological correlates in the human brain.

Methods
Twenty volunteers, aged 45 to 65, with mild cognitive impairment were enrolled in an open-label trial. Before and after 8-week treatment with EGb 761® (240 mg per day) tests investigating error monitoring (flanker-stop task) and reward processing (gambling task) were administered. Neurophysiological correlates of error monitoring (error-related negativity, ERN; lateralized readiness potential, LRP) and reward processing (feedback-related negativity, FRN) were recorded. Tests for attention and verbal fluency as well as rating scales for attention and depression were administered.

Results
In the error monitoring experiment, participants had shorter reaction times and a tendency towards increased error rates, along with a decrease in the ERN and in the LRP latency for incongruent stimuli. This can be interpreted in terms of a shift towards faster but less accurate reactions on the speed-accuracy trade-off curve. In the reward processing paradigm, a number of effects were seen in the ERP: a stronger positivity to the feedback stimuli post-intervention and an increase of difference between gain and loss ERPs. In the attention tests, reaction times were significantly shorter after treatment and ratings of attention and mood improved significantly.

Conclusions
The results of our experiments are compatible with the hypothesis that EGb 761® enhances dopamine-dependent cognitive processes.
Autism spectrum disorder (ASD) is characterized by impaired development of social interaction and communication skills and a restricted repertoire of activities and interests. Although the neurodevelopmental and genetic underpinnings of ASD have been extensively investigated, the etiology of the disorder has remained elusive, and clinical diagnosis continues to rely on symptom-based criteria. Functional magnetic resonance imaging (fMRI) of the brain is a powerful tool for exploring biomarkers of psychiatric and developmental disorders. In the present study, resting state (rs-) fMRI and a neural network algorithm were used to classify a large sample of patients with ASD and control subjects (n = 640, mean age = 13.0 years). Image data from 312 subjects with ASD (age range: 7-19 years; male/female: 273/39) and 328 subjects with typical development (age range: 6-19 years; male/female: 267/61) was downloaded from the multi-center research project (Autism Brain Image Data Exchange, ABIDE). Only subjects under 20 years of age were included in the analyses. The subject's brain activity was measured during resting condition by using 3 Tesla MRI scanner for six minutes. Correlation matrices of 90 distinct regions computed from rs-fMRI time-series data were entered into a probabilistic neural network (PNN) for classification. The PNN classified the two groups with approximately 90% accuracy (sensitivity = 92%, specificity = 87%). The accuracy of classification did not differ between the institutes where the original data were collected, or with experimental and imaging conditions, sex, handedness, or intellectual level. Medication status and degree of head movement did not affect accuracy values. The present study indicates that an intrinsic connectivity matrix produced from resting state fMRI data could yield a possible biomarker of ASD. These results also support the view that altered network connectivity within the brain contributes to the neurobiological underpinnings of this disorder.
**P30**

**Test-retest reliability and inter-subject variability of the Phase Lag Index (PLI), a measure of functional connectivity in EEG analysis.**

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**Question**

Peak frequency (pkF) and relative band power (rPw) are stable EEG features in healthy adults. PLI is a measure of functional connectivity not relevantly influenced by volume conduction (Stam 2007). Is PLI test-retest-reliability (TRT) comparable to pkF and rPw? Does epoch length matter?

**Methods**

34 healthy subjects (mean age: 36.6y; female: 82%) had 256-channel EEG at baseline, year 1 and 2. Signal space, eyes-closed resting state data were preprocessed and segmented (E12= 12 epochs of 4.1 sec; E04= 4 epochs of 12.3 sec). Regional PLI (5 inter-hemispheric, 2x10 intra-hemispheric, 10 intra-regional connections) was calculated by averaging over respective electrode pairs (frontal, central, temporal, occipital, parietal; BrainWave 0.9.98, Stam) in theta-, alpha1-, alpha2- and beta-band. Corresponding pkF and regional rPw was calculated. Intraclass correlation coefficients (ICC) over time and coefficients of variation (CoV) between subjects were determined. Effects of number of epochs and frequency bands were analyzed (paired t-test, ANOVA).

**Results**

Table gives grand means over regions and time points. PLI_E12 was higher compared to PLI_E04 with lower CoV and higher ICC; beta-band ICC was lowest. rPw had higher ICC but also higher CoV compared to PLI_E12. PkF had high ICC (=.84) and low CoV (=.1).

<table>
<thead>
<tr>
<th></th>
<th>mean PLI</th>
<th>mean CoV</th>
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<td>E12</td>
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<tr>
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<td>0.25*</td>
<td>0.40</td>
<td>0.25*</td>
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<td>0.28*</td>
<td>0.69</td>
<td>0.70</td>
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<tr>
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<td>0.20</td>
<td>0.31*</td>
<td>0.44</td>
<td>0.31*</td>
<td>0.61</td>
<td>0.68$</td>
</tr>
<tr>
<td>beta</td>
<td>0.07</td>
<td>0.18*</td>
<td>0.28</td>
<td>0.18*</td>
<td>0.46</td>
<td>0.48o</td>
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* p<.001 for E12 vs. E04; ° p<.001 beta vs. other bands; § p<.001 for E12 vs. rPw

**Conclusion**

TRT and inter-subject variability of PLI are better using short rather than long epochs of identical total duration. Short-epochs-PLI show good but lower TRT compared to pkF and rPw; however, PLI inter-subject variability is lower than in rPw. PLI is sufficiently reliable to be used as an EEG measure of functional connectivity.
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P31
Enhanced network efficiency during eyes-open state compared to eyes-closed resting state: An MEG study

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Question
A question to be addressed is how different are the eyes-closed (EC) and eyes-open (EO) states across frequency bands in terms of efficiency and centrality of the resting state brain functional network.

Methods
We investigated both the global and nodal efficiency and betweenness centrality during the EC and EO resting states in 39 volunteers. Mutual information was used to obtain the functional connectivity for each of the 4 frequency bands (theta, alpha, beta, and gamma), and efficiency and centrality measures to assess functional network characteristics were calculated.

Results
We demonstrated that the cortical hubs with high centrality were maintained in the EC and EO resting states, but in terms of the efficiency of the brain functional networks, these two resting states can be differentiated from each other. Enhanced Eglob values were found in the (t₃₈ =-4.877, p<0.001), alpha (t₃₈ = -3.994, p<0.001) and beta (t₃₈ = -2.306, p<0.05) bands in the EO state compared to those in the EC state. Moreover, it turned out that in the EO state, the functional network was reorganized to enhance Enodal at the nodes related to both the default mode and the dorsal attention networks and sensory-related resting state networks.

Conclusions
This result suggests that in the EO state, the brain functional network was efficiently reorganized facilitating the adaptation of the brain network to the change in state, which could help in understanding brain disorders that have a disturbance in communication with external environments by using the adaptation ability of brain functional networks.
Modulation of the human SMA-M1 motor network by active-passive bilateral movement priming

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Bilateral priming is a promising new adjuvant therapy to promote motor recovery in stroke patients (Stinear et al. [2008] Brain 131: 1381). However, the neurophysiological basis of bilateral priming is not completely understood. Here, we studied the effect of active-passive bilateral movement priming (APBP) on excitability and connectivity in the supplementary motor area (SMA) - primary motor cortex (M1) network. Healthy human subjects completed 20 minutes of APBP, involving active left wrist extension/flexion at 1Hz coupled with passive right wrist motion in a mirror-symmetric (MIR) or alternating (ALT) pattern. M1 excitability and SMA-to-M1 connectivity for right extensor carpi radialis muscle was probed by single- and paired-pulse TMS in three conditions: at rest, prior to right hand extension, and prior to left hand extension. Results showed task-dependent modulation of M1 excitability and SMA-to-M1 connectivity at baseline. M1 excitability at rest increased after both MIR- and ALT-APBP. There was no APBP-induced change in M1 excitability during preparation of a right hand extension. However, during preparation of a left hand extension there was a significant Pattern x Time effect: after MIR-APBP M1 excitability increased more in the late vs. early preparatory phase, whereas after ALT-APBP M1 excitability increased more in the early vs. late preparatory phase. SMA-to-M1 connectivity decreased after ALT-APBP at rest, but did not change in any of the other conditions. Findings show both task- and pattern-dependent modulation of M1 excitability and SMA-to-M1 connectivity following APBP and suggest an inhibitory role for SMA in controlling the non-active M1 during voluntary movement generation.
P33
EEG FUNCTIONAL CONNECTIVITY MODIFICATIONS OF CYCLIC ALTERNATING PATTERN IN NOCTURNAL FRONTAL LOBE EPILEPSY

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PURPOSE

Cyclic Alternating Pattern (CAP) is the marker of sleep instability and is known to modulate some types of sleep epileptiform activity. In this study we employed a non-linear measurement of EEG functional connectivity, the Synchronization Likelihood (SL), in order to test the hypothesis that modifications of EEG synchronization occur in the A1 subtypes of CAP in patients affected by Nocturnal Frontal Lobe Epilepsy (NFLE), compared to controls.

MATERIALS AND METHODS

19-channels sleep EEG recordings of 5 non-lesional NFLE patients and 7 good sleepers were acquired. A total amount of 923 4-sec epochs, containing artifact-free and manually scored A1 CAP subtypes, were extracted from light and slow wave NREM sleep stages. For each epoch, SL was computed between all pairs of channels in the standard frequency domains (delta 0.5-4 Hz, theta 4-8 Hz, alpha 8-13 Hz, sigma 12-15 Hz, beta 13-30 Hz, gamma 30-48 Hz). The corresponding connectivity matrix for each epoch, sleep stage and subject was averaged over channels in order to achieve a global estimation. Two-way ANOVA, using group as between subjects factor and sleep stage as within subjects factor, was used to test significant SL modifications.

RESULTS AND DISCUSSION

The mean global SL, computed on the A1-containing epochs, was significantly higher for the gamma band in NFLE patients compared to controls (P=0.002), without sleep stage effects. No significant differences were observed for the other bands. This finding indicates gamma hyper-synchronization as a key phenomenon of interictal epileptiform EEG activity, interwoven in the dynamic framework of sleep instability underlying CAP.


P34

Age-related decline in functional connectivity of the vestibular cortical network

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Question

In the elderly, major complaints concern dizziness and increasing number of falls [1], which may be related to altered central processing of vestibular sensory input [2]. Here we used galvanic vestibular stimulation (GVS) during functional imaging (e.g., [3]) to study the effect of healthy aging on central vestibular processing.

To better characterise the effects of healthy aging on brain function we assessed its signatures beyond the mere BOLD-signal amplitude, such as functional connectivity or temporal BOLD-signal variability [4-6].

Methods

Functional and structural MRI were performed at 3T (GE Signa Hdx). The data from 39 subjects (right handed, age 20-70 years) was preprocessed and analysed regarding the following characteristics: significant age-dependent changes in BOLD-signal amplitude, in voxel-based morphometry, in functional connectivity assessed by tensor independent component analysis, in structural connectivity expressed as fractional anisotropy, and in temporal BOLD-signal variability using partial-least-squares analysis.

Results

Age-correlated decreases of functional connectivity and increases of temporal BOLD-signal variability were associated with multisensory vestibular networks. In contrast, no age-related functional connectivity changes were detected in somatosensory networks or during a motor paradigm used as control. The functional connectivity decrease was not due to structural changes but to a decrease in response amplitude undetected by SPM analysis.

Conclusions

Our data suggest the possibility that both the age-dependent functional connectivity decrease and the variability increase are connected to deteriorating reciprocal cortico-cortical inhibition with age, related to vestibular multimodal integration of sensory inputs.

Acknowledgements: The authors are grateful for support by Bundesministerium fuer Bildung und Forschung (Grant Number BMBF - FKZ 01 E0 0901) and Deutsche Stiftung Neurologie.

References

Dominant change in intra-hemispheric information flow in fronto-parietal network in the gamma band during propofol-induced loss of consciousness

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Question

A question to be addressed is whether inter- and intra-hemispheric information flow in fronto-parietal (FP) network in the gamma band in various conscious states (awake and propofol-induced loss of consciousness) are different or not.

Methods

We investigated net information flow in the gamma (25~40Hz) frequency band using time-delayed mutual information. EEG signals at frontal (F3, F4) and parietal (P3, P4) channels were obtained from 10 subjects under general anesthesia. Propofol was used for general anesthesia and concentration was changed from 5 μg/ml to 3 μg/ml. Kruskal-Wallis test was performed to assess the change in net information flow.

Results

We found the change in intra-hemispheric FP information flow in the gamma band according to the conscious state ($\chi^2=10.55$, d.f.=3, p=0.014), whereas there was no significant change in inter-hemispheric FP information flow.

Conclusions

Reduction in inter-hemispheric connectivity in disease of consciousness (DoC) (Oradia-Caro et al., 2012) was reported, which implies the relevance of inter- or intra-hemispheric information flow to conscious state. Since the important role of gamma band cortico-cortical connectivity in FP network during propofol-induced loss of consciousness was found (Boly et al., 2012), we focused on inter- and intra-hemispheric information flow in FP network in the gamma band. From our results, we conclude that the loss of consciousness induced by propofol is more associated with intra-hemispheric information flow in FP network, unlike propofol-induced loss of consciousness in DoC in terms of information flow.

References


figure 1
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P36
The maturation of mismatch negativity networks in late normal adolescence

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Question
Mismatch negativity (MMN) is an electroencephalographic (EEG) response related to attention control. The goal of this study is to investigate the development of the cortical network generating the MMN from adolescence to early adulthood.

Methods
MMN and dynamic causal modelling is used to study the cortical network generating MMN in healthy young adults and adolescents. An auditory odd-ball paradigm is used to elicit MMN in two groups of healthy subjects with mean age 14 (n=52) and 26 (n=26). Networks with different hierarchical complexity with up to five cortical nodes (right and left primary auditory cortex (rA1 & lA1), right and left superior temporal gyrus (rSTG & lSTG), and right inferior frontal gyrus (rIFG)) were analysed using dynamic causal modelling.

Results
Bayesian model comparison showed that the five node model with modulation of all extrinsic and intrinsic connectivity between and within the cortical nodes was the most likely of all models. Model inversion showed that adolescents had reduced backward connection from rIFG to rSTG (p<0.04) together with increased excitatory activity at rSTG (p<0.02) with reduced modulation of intrinsic modulation at rSTG (p<0.02) and reduced forward connectivity from lA1 cortex to lSTG (p<0.03).

Conclusion
The cortical network generating the MMN continues to develop in adolescents as they reach adulthood. Cortical regions in the temporal and frontal lobes important for auditory processing mature with increasing interconnectivity together with increased sensitivity of the temporal regions for changes in sound stimuli i.e. increased modulation of activity in the temporal regions on stimulus switch.

Figure 1. Effect of age on MMN. ERP for standard tone, deviant tone, and MMN-waveform. Grand average for the two populations (blue - adults, red - adolescents) over the vertex, Cz, with mastoid reference.

Figure 2. Schematic model of cortical network generating MMN consisting of 5 cortical regions (lA1, rA1, lSTG, rSTG and rIFG) with interconnections and intrinsic connectivity. We found reduced connectivity from rIFG to rSTG and lA1 to lSTG (blue arrows). There was increased activity at rSTG (shown in red). Moreover, there was reduced modulation of activity at rSTG on stimulus switch (blue feedback arrow).
P37
Human brain networks in physiological and pathological aging: a graph theoretical analysis of cortical connectivity from EEG data

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Question
Can the mathematical approach of graph theory describe the brain networks' organization in physiological and pathological aging?

Methods
The physiological aging was evaluated with a database of 113 EEG, divided in three groups: Young (18-45 years), Adult (50-70 years) and Elderly (>70 years). The pathological aging was evaluated with a database of 378 EEG, divided in Alzheimer disease (AD), mild cognitive impaired (MCI) and normal elderly subjects. Graph theory functions were applied to the undirected and weighted networks obtained by the lagged linear coherence evaluated by eLORETA in delta, theta, alpha1, alpha2, beta1, beta2 and gamma bands.

Results
In the physiological aging, normalized Characteristic Path Length (λ) presented the pattern Young>Adult>Elderly in the higher alpha band, Elderly also showing an increase in delta and theta bands respect to Young. Normalized Clustering coefficient (γ) and small-world network modeling (σ) showed non-significant age-modulation.

In the pathological aging, λ presented differences between normal cognition and dementia in theta band (MCI subjects similar to healthy subjects), while γ showed a significant increment for AD group in delta, theta and alpha1 bands; finally, σ presented significant interaction between AD and MCI groups showing a theta increase in MCI.

Conclusion
The present EEG study suggests that graph theory can disclose functional connectivity networks, allowing to evaluate functional integration and segregation of the brain. The present results showed that the functional integration was prejudiced in both physiological and pathological aging, while the functional segregation of brain networks is more evident only in the pathological aging.
Effects of hyperventilation on brain connectivity

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**Question**

Hyperventilation is a widely used EEG activation method, that modify plasma CO2 provoking diffuse EEG slowing. Aim of the study was to evaluate the modifications in brain connectivity due to hyperventilation in normal subjects and in a group of patients with cryptogenic focal epilepsy.

**Methods**

We analyzed ordinary EEG recordings in 17 normal subjects and 22 patients with focal cryptogenic epilepsy. Exclusion criteria were: migraine, cerebrovascular disease, sleep disorders, MRI abnormalities and use of drugs, apart from Antiepileptic drugs in epilepsy group. We used 19 scalp electrodes positioned according to the International 10-20 system; sampling rate was 128 Hz; bandpass filter was 0-64 Hz. We performed visual artifact rejection and selected segments before hyperventilation (PRE), during the activation technique (HYPER) and five minutes after return to normal breathing (POST). In order to analyze the neural generators we used low resolution electromagnetic tomography (sLORETA software). We analyzed EEG lagged coherence between 19 ROIs for the following bands: delta (1-4 Hz), theta (5-7 Hz), alpha (8-13 Hz), beta (14-30 Hz) and gamma (31-60 Hz). We also performed intergroup analysis of mean lagged coherence. Statistical comparisons were performed by means of non parametric tests.

**Results**

In both groups we found that hyperventilation significantly increases EEG power in theta, alpha, beta and gamma bands (p<0.001). However functional connectivity was increased by hyperventilation in delta, theta, alpha and beta bands. (p<0.001) These modifications revert toward PRE condition in POST. Intergroup analysis of mean lagged coherence shows significant differences between normal and epileptic subjects in every considered band for HYPER condition (p<0.001); in Alpha band we found significant difference for PRE (p<0.001), HYPER (p=0.002) and POST (p<0.001) conditions; finally, in Gamma band we found significant difference for PRE (p=0.001) and HYPER (p<0.001) condition.

**Conclusions**

Hyperventilation modifies brain connectivity, both in normal and focal cryptogenic epileptic patients. The significant differences between the two groups permit to hypothesize that this activation method led to different brain connectivity patterns in normal subjects when compared to epileptic patients.
Hypothalamic functional connectivity networks

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Question

To achieve homeostatic control, specific hypothalamic sub-regions integrate peripheral and central signals influencing different aspects of eating behavior. Hereby especially the ventromedial and lateral hypothalamus nuclei play a prominent role. In humans, neuronal networks connected to different hypothalamic sub-regions remain elusive.

Methods

We used ‘resting-state’ functional magnetic resonance imaging to identify the neural circuitry projected from the ventromedial (VMH) and lateral hypothalamus (LH), respectively. In 78 normal-weight subjects, a seed-based functional connectivity analyses was applied. To further elucidate the influence of different physiological states, the effect of subjective feeling of hunger (n=78) and postprandial changes after glucose (n=23) and fat ingestion (n=10) were analyzed in normal-weight and obese subjects.

Results

The ventromedial hypothalamus associated network revealed its strongest functional connections to the nucleus accumbens, the orbitofrontal cortex and fusiform gyrus; by contrast the lateral hypothalamus network included the dorsal striatum, thalamus, midbrain, insula, cingulate and prefrontal cortex (Fig. 1). Both networks showed increased FC based on subjective feeling of hunger. Normal-weight and obese subjects revealed changes in FC in both networks after glucose and fat ingestion dependent on eating behavior and insulin levels. Especially glucose ingestion revealed major changes in these networks leading to increased FC between the lateral hypothalamus, thalamus and prefrontal cortex and between the ventromedial hypothalamus and fusiform gyrus.

Conclusions

We hypothesize that the ventromedial hypothalamus network is associated with the hedonic impact, while the lateral hypothalamus network with the motivational side of food reward. These networks can provide new targets for treating obesity and related diseases.

Figure legend

Figure 1. Topography of intrinsic functional connectivity for the (A) lateral and ventromedial (B) hypothalamus overlaid on inflated t1 template (p<0.05, FWE-corrected for multiple comparisons).
Visuomotor functional connectivity: a TMS study

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Objective

The interaction between visual inputs and motor system is of crucial importance in movement control and in human disease like photosensitive epilepsies. Thus, we wanted to study the functional connectivity between visual and motor cortex. We used the paired transcranial magnetic stimulation (TMS) technique, a reliable tool to investigate time related changes in functional connectivity.

Materials and Methods

Sixteen healthy volunteers (7 women, 21-51 yrs) participated in this study. First, we measured the resting motor threshold (RMT) of the left hand motor area and the phosphene threshold (PT). The paradigm consisted in a conditioning stimulus (CS) delivered over the phosphene hotspot of the visual cortex at different intensities (80 and 90% of the PT) and followed at random interstimulus intervals (ISIs) (12, 15, 18, 21, 24, 27, 30, 35 and 40 ms) by a test stimulus (TS) over the left motor cortex to evoke a motor evoked potential (MEP) of ~ 1 mV from the right FDI. The conditioned-MEP was expressed as a percentage of the unconditioned-MEP amplitude. One-way ANOVAs analyzed the effects of the CS with “ISIs” as main factor and followed by post hoc t-test with LSD correction. A p value <0.05 was significant.

Results

One-way ANOVA showed a main effect of ISI when the CS intensity was 80% PT (F (9,90)=3.410, p=0.001) and 90% PT (F(9, 99)=3.081, p=0.003). Post hoc analysis with LSD correction confirmed that the size of the conditioned-MEP compared to the test MEP was significantly reduced at 18, 21, 24 and 40 ms (all p<0.05) and almost significant at 35 ms (p=0.054) when the intensity was 80% PT, and significantly reduced at 18, 21, 27, 30, 35, 40 ms (all p<0.02) when the intensity 90% PT was considered. No effect was detected with a control CS delivered over the parietal cortex using the same paradigm.

Discussion

The present data show that in subjects at rest, conditioning stimuli over the visual cortex produce significant inhibitory changes on the corticospinal excitability with a time course between 18 and 40 ms. The inferior occipitofrontal fasciculus might be the direct efferent pathway from the occipital extrastriate cortex that is rapidly transmitting the visual information to the premotor areas.

Conclusions

The present results demonstrate the existence of functional inhibitory occipitomotor connections that may be activated by means of TMS. This may be a useful method to study the pathophysiology of photosensitive epilepsies.
Nigroputaminal Connectivity Employing Probabilistic Tractography with Emphasis on Anatomical Plausibility

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Question

Nigroputaminal connectivity is difficult to determine with diffusion tractography (Massey and Yousry 2010). Therefore, anatomical plausibility needs to be validated as prerequisite for meaningful quantifications of connectivity. Among other factors, the local model of diffusion and parameters of the tracking algorithm are sources that impact anatomical plausibility of tractography results. Here, we analyzed nigroputaminal interconnections with emphasis on anatomical plausibility in a cohort of young healthy subjects.

Methods

We acquired 3T high resolution structural and diffusion weighted images of 60 right-handed young healthy subjects (♂: 30; age: 24.6 ±1.9). Two methods to model the local diffusion signal (Ball-and-stick (bedpostx); Constrained Spherical Deconvolution (CSD)) were applied. Probabilistic tractography was tested for optimized parameters to reconstruct the nigroputaminal pathway. "Normalized relative connectivity" was determined to account for different size of seeds and targets. Connection probability maps of probabilistic tractography results (Fig. 1) were examined visually to estimate anatomical plausibility. "Plausibility Tracking" was used to create averaged streamlines of probabilistic tractography results and to further analyze the underlying diffusion signal.

Results

Reconstruction of nigroputaminal interconnection was significantly affected by tracking parameters and choice of local diffusion model. CSD covered the localization of fibre entries into the putamen as well as the localization of pathways more completely (Fig. 1) and two streamline bundles could be distinguished by mapping local diffusion characteristics onto resulting streamlines. Preliminary results (n=10) showed significantly higher left versus right nigroputaminal "normalized relative connectivity" with lower variability in CSD results.

Conclusions

An anatomically plausible analysis of nigroputaminal interconnections can be obtained by tractography methods if tracking parameters are carefully validated with respect to anatomical plausibility and a sufficient model of local diffusion is chosen. We aim to statistically evaluate resulting connectivity values to estimate normative variance of nigroputaminal connectivity as a reference for future studies.

figure 1
Mild hypoxia affects synaptic connectivity

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4University Twente, Clinical Neurophysiology, Enschede, Netherlands

**Question**

80% of patients with chronic mild cerebral ischemia/hypoxia have cognitive impairment. Structural neuronal damage is lacking and the cause of neuronal dysfunction is unclear. As half of the cerebral energy consumption is used for synaptic transmission, and synaptic failure is the first consequence of acute complete anoxia, synaptic dysfunction is a candidate mechanism.

**Methods**

Because measurement of synaptic functioning in patients is problematic, we use cultured networks of rat cortical neurons on a multi-electrode array as a model system. These were exposed to hypoxia (partial oxygen pressure lowered from 150 to 40-50 Torr) during three (n=14) or six (n=8) hours. Synaptic functioning was assessed before, during, and after hypoxia by spontaneous network activity, functional connectivity, and synaptically driven network responses to electrical stimulation. Action potential heights and shapes and non-synaptic stimulus responses were measures of individual neuronal integrity.

**Results**

During hypoxia of three and six hours, there was a 60-80%, statistically significant, decrease of all measures of synaptic functioning (Figure 1), whereas direct responses and action potentials remained unchanged (Figure 2). These changes were largely reversible.

**Conclusions**

Our results indicate that in cultured neuronal networks, partial hypoxia during three or six hours causes isolated disturbances of synaptic connectivity. We speculate that in chronic mild cerebral ischemia, synaptic failure plays a role in the emergence of cognitive impairment.

**Reference**

1Hofmeijer Stroke 2012

Figure 1. Statistically significant decrease of functional connectivity during hypoxia in cultured neurons

Figure 2. No changes of action potential height and shape during hypoxia in cultured neurons
Abstracts of Poster Presentations – Poster Session 2 – Connectivity

Figure 1

Figure 2
P44
Functional connectivity network breakdown and restoration in blindness

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Question

Loss of vision after brain damage is thought to be caused mainly by the primary tissue loss. Little is known how the damage affects interactions in widely distributed brain networks and how this, in turn, contributes to vision loss. We now studied functional connectivity in the brain of partially blind subjects to delineate the role of wide range neuronal networks in blindness.

Methods

Resting state eyes-closed EEG activity was recorded in patients with partial optic nerve damage (n=15) and uninjured controls (n=13). Power density and functional connectivity (coherence, Granger Causality) were analyzed, the latter as (i) between-areal coupling strength and (ii) individually thresholded binary graphs. Functional connectivity was then modulated by non-invasive repetitive transorbital alternating current stimulation for 10-days (rtACS for 40 min daily; n=7; sham, n=8) to studied how this would affect connectivity networks and perception.

Results

Blind patients had lower EEG spectral power (p=0.005) and decreased short- (p=0.015) and long-range (p=0.033) coherence in the high-alpha EEG band (11-14Hz) and less densely clustered coherence networks (p=0.025). rtACS strengthened short- and long-range coherence again which correlated with recovery of detection ability (r=0.57, p=0.035) and processing speed (r=0.56, p=0.049).

Conclusions

Peripheral damage to the visual system permanently hampers spontaneous cortical synchronization and functional networks topology. Synchronization breakdown accompanies loss of perceptual abilities, therefore we argue that cortical activity might either hamper or facilitate perception in patients. Based on these findings cortical functional connectivity emerges as a therapeutic target in vision restoration.

Figure 1

Coherence networks topology. The first two columns show coherence networks graphs with black dots representing standard EEG electrode positions. All graphs contain the same number of edges (connections). The difference graphs (3rd column) display edges present in controls but missing in patients (blue) and edges missing in controls but present in patients (red). The most pronounced between groups differences occur in the alpha II band.
Abstracts of Poster Presentations – Poster Session 2 – Connectivity

P45
Event related desynchronisation/synchronisation (ERD/ERS) in the actual and imagined reaching movements

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Question

Despite growing number of published papers, the ERD/ERS potentials, which give real time information on the ongoing neural activity, is still poorly understood when comparing actual vs. imagined reaching movements.

Methods

Eleven subjects were reaching and imagining reaching with right hand toward the target in the right upper quadrant of touch screen. Reaction and movement times were measured for actual reaching. EEG was recorded by 64 electrodes. After off-line artefact rejection, ERD/ERS for each subject were measured in alpha and beta frequency bands for frontal, central, centro-parietal and occipital electrodes. Differences between both tasks were compared using boothstrap method.

Results

Reaction and movement times were 369±65 ms and 383±78 ms respectively. In actual reaching, alpha ERD and beta ERD were significantly stronger 0.5 s and 2.5 s, respectively, before target onset. In imagined reaching, ERD was stronger in all electrodes around reaction time. Thereafter differences in alpha ERD become non significant for 0.5 s to 0.7 s in left frontal and central to parietal electrodes respectively. On the right side, we found significant ERD differences approximately 0.2 s after actual reaching onset. ERS rebound was stronger in both bands approximately between 1 and 2 s after actual reaching onset.

Conclusion

Actual and imagined reaching activated similar cortical areas including the primary motor cortex. Stronger alpha and beta ERD across the entire bands in imagined reaching around movement onset may be due to undetermined strategy or the need to refrain the actual movement. Longer ERD during reaching and stronger ERS rebound after it may reflect muscle activation and proprioceptive feedback.
P46
Ipsilateral connectivity between posterior parietal and primary motor cortex at high temporal resolution with dual-site TMS

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Introduction

Studies on primates have provided evidence for direct connections from ipsilateral parietal cortical areas to primary motor cortex (M1). Little is known about these intrahemispheric parietal-to-motor networks in humans. Here we used high-focal dual-site TMS to tap into effective connectivity between posterior parietal (PPC) and M1 in the intact human brain. Diffusion tensor imaging (DTI) was used to examine whether effective premotor-to-motor connectivity correlates with the macrostructure of white matter underlying the stimulated areas.

Methods

13 handed healthy subjects (mean 25, range 22 - 29) were included in this study. Using two highly focal minicolls, TMS was given to the left M1 and PPC. The paired-pulse paradigm consisted of a first suprathreshold (S1) to M1 and a second subthreshold (S2) to PPC stimulus which was given at interstimulus intervals (ISIs) ranging from 0.8- to 4.8- in 0.4-ms steps. Two S2 intensities of 90- and 70% RMT were applied. Subjects underwent whole-brain DTI at 3 T (3 acquisitions of 32 directions: b=1000 and five b₀ images). The data was pre-processed and analysed using FSL and TBSS. GLM and randomise were used to test for a relationship between individual changes in effective parietal-motor connectivity and regional fractional anisotropy (FA).

Results

Dual-site TMS revealed an ISI and S2 dependent modulation of parietal-to-motor facilitation as indexed by a change in motor evoked potential (MEP). The ANOVA for the S2 of 90% RMT was significant for the main effect of ISI [F(11, 132)=1.98, P<0.05]. The post hoc tests revealed a significant increase of mean MEP amplitude at ISI of 1.2-, 2.4 and 4.8 ms in comparison to test pulses alone or conditioned MEP at 0.8 ms. There was no valid modulation of M1 at the S2 of 70%. The analysis of the DTI data showed that individual differences in effective connectivity show highly specific correlations with FA in white matter underlying the stimulated areas.

Conclusions

Dual-site TMS demonstrates a dynamic modulation of M1 excitability through ipsilateral PPC-to-M1 inputs in an I-wave specific matter. This innovative brain mapping approach can be used to non-invasively probe effective connectivity of short latency, fast ipsilateral PPC-to-M1 connections. Intra-individual differences in effective connectivity (as indexed by dual-site connectivity) is correlated with the microstructure of the input fibres to M1.
LP3
Weighted time-varying network differences between cognitively intact and impaired MS patients using correlation as connectivity measure

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Question
Multiple Sclerosis is the most frequently encountered neurodegenerative disease in young adults (Inglese, 2006). Although approximately half of the MS patients suffer deteriorated cognitive abilities, the underpinnings this cognitive deterioration are poorly understood and no sufficient biomarkers have yet been developed (Schoonheim et al., 2013).

Methods
We have included 305 MS patients, 162 of which were denoted as cognitively impaired based on extensive neuropsychological testing. All patients underwent an EEG oddball experiment. Based on the averaged response to target stimuli, we constructed weighted networks using correlation as connectivity measure.

Results
For most edges, weights were significantly different between both patient groups, with the most significant edges in centro-parietal region. Next, we applied a sliding time window approach to track the origins of these differences to a particular time window of the cognitive process. We found two time windows with significantly different edge weights, one on the rising and one on the decreasing flank of the P300.

Conclusion
A simulation showed that the observed differences can partially be explained by the range of amplitudes included in the time window. Bearing this information in mind, we carefully interpreted the results and showed that correlations can be used to extract more information from the data than a mere amplitude analysis.

Figure 1
Differences obtained using a sliding time-window approach. Selected time-frames: (A) 212-312 ms, (B) 284-384 ms and (C) 328-428 ms. The -log10 of the p-values are denoted in the color bar. On the left-hand side one sees the signal used to construct the networks for each patient. Red = mean curve of CP patients, Blue = mean curve of CI patients.

References

figure 1
Predictor of severity and long distance outcome of patients with critical illness myopathy and polyneuropathy

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Objective

The aim of this study is to investigate predictive value of laboratory findings, clinical parameters on outcome among patients with critical illness Myopathy or Polyneuropathy.

Methods

We retrospectively selected 125 patients with acquired tetraparalysis who underwent mechanical ventilation in the intensive care unit. 110 patients were examined by EMG (electromyography) on suspicion of Critical illness Myopathy (CIM) or Polyneuropathy (CIP). Neurophysiologic tests included motor and sensory nerve conduction studies, F-waves, repetitive nerve stimulation, EMG and direct muscle stimulation. Blood tests, as well as clinical parameters were extracted from the patient’s medical record. Multivariate regression tests were carried out where all clinical and electrophysiological tests were entered as predictors and clinical outcome score and EMG diagnosis was tested as outcome variable.

Results

Of cases, 54.5% had CIM, 15.5 % had both CIM/CIP, and 30% CIP. The remaining 15 patients had central nervous system lesions or Guillain-Barre Syndrome as final diagnosis. Etiology: The most common etiology for acquiring CIM/CIP was abdominal operation (28.4%), pneumonia and respiratory failure (26%), gastrointestinal disease (15%). Clinical status: Muscle strength at the time of the neurophysiological test showed significant linear correlation with clinical outcome, whereas the more severe the muscle weakness the higher the the risk for poor outcome (Spearman’s rho 0.406, p=0.001). Electroneurography: Linear correlation was found between compound muscle action potential (CMAP) recorded at abductor digiti quinti muscle and clinical outcome, whereas a decrease in amplitude implied higher mortality (Spearman’s rho 0.280 p=0.002).

Conclusion

Our finding emphasizes the importance of neurophysiological tests in predicting outcome in CIM and CIP. Close clinical and electrodiagnostic testing at an early stage may be useful in preventing irreversible pathological changes.
Brain function in iNOS knock out or iNOS inhibited (l-NIL) mice under septic shock.

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Introduction

Occurrence of microcirculatory dysfunction due to an excessive nitric oxide production by the inducible nitric oxide synthase (iNOS) is often seen as a motor of sepsis related organ dysfunction. Blocking the iNOS may improve organ function. In an endotoxic shock model we investigated neuronal functional integrity in iNOS knock out (−/−) or l-NIL treated wild type (wt) animals.

Methods

Four groups of each 10 male mice (28-32g) were studied: wt, wt+LPS (5mg/kg body weight i.v.), iNOS (−/−)+LPS, wt+LPS+l-NIL (5mg/kg body weight i.p. 30 min before LPS). Electric forepaw stimulation was performed before LPS/vehicle and then at fixed time points repeatedly up to 4.5 h. N1-P1 potential amplitudes as well as P1-latencies were calculated from monopolar EEG recordings. Additionally, cerebral blood flow was registered with laser Doppler. Blood gas parameters, mean arterial blood pressure, glucose and lactate levels were obtained at beginning and end of experiments. From plasma IL-6, IL-10, CxCl-5, ICAM-1, NSE, nitrate/nitrite levels were determined.

Results

The typical decline in blood pressure, occurrence of cerebral hyperemia, acidosis and increase in lactate levels was prevented in both iNOS blocked groups. Also, SEP amplitudes were stabilized, remaining in the range of controls. Effects were related to a blocked nitrate/nitrite level increase since inflammation markers were similar in all sepsis groups. Due to the chosen time window NSE levels as well as P1-latencies remained in the normal range.

Conclusions

Stabilizing the macro- as well as microcirculation iNOS blocking showed neuroprotective. Our data support modern sepsis guidelines recommending an early prevention of microcirculatory failure.
P49
CLINICAL UTILITY OF BEDSIDE ELECTROMYOGRAPHY IN CRITICAL ILL WITH SUSPECTED NEUROMUSCULAR DISEASES

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Introduction

EMG is performed commonly in EMG laboratory. The reports about bedside EMG in diagnosis of patients with critical illness is limited. The objective is to investigate the utility of bedside EMG in diagnosis and management of critical illness patients with suspected neuromuscular diseases.

Methods

Bedside EMG was performed in 34 critical illness patients with weakness and respiratory involvement, including segmental motor nerve conduction studies, sensory nerve conduction studies, F waves, concentric needle EMG and repetitive nerve stimulation. The manifestation and clinical utility of bedside EMG in critical illness patients with suspected neuromuscular diseases were analyzed.

Results

Amplitude of CMAP and motor conduction velocity was normal in 5 patients with paralysis, including 3 with serious weakness which support the lesion located in central nervous system. Motor nerve conduction block, slow conduction velocity and decreased amplitude was detected in 6 patients with serious weakness, which support the diagnosis of demyelinating neuropathy. 19 patients had decreased amplitude of CMAP with normal motor nerve conduction velocity. F-wave persistence was0 in 55% patients. Amplitude of sensory nerve action potential decreased in 28.6% patients. Low-frequency repetitive nerve stimulation showed decrement response of compound muscle action potential (CMAP) in 4 patients. Bedside EMG can help to confirm or exclude diagnoses and guide the management in 82.4% patients, confirmed the diagnoses of peripheral neuropathy but have no effect on management in 11.8% patients, were inconclusive in 2 patients.

Conclusions

Bedside EMG is useful for the diagnosis and management of critical ill with suspected neuromuscular diseases, motor nerve conduction studies and repetitive nerve stimulation is more valuable. Individualized protocol for EMG studies should be made on the basis of clinical problem.
Abstracts of Poster Presentations – Poster Session 3 – Critical illness and sepsis

P50
Muscle ultrasound for early assessment of critical illness neuromyopathy in severe sepsis

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Introduction

ICU acquired weakness often is clinically difficult to be assessed in the acute phase of sepsis, as most patients are mechanically ventilated and/or sedated. Muscle ultrasound is emerging as a promising tool in the diagnosis of neuromuscular diseases.

Method

Prospective observational study in a single academic medical center of 21 patients with septic shock, 7 patients with severe sepsis, and 26 healthy controls. Patients underwent clinical neurological examinations, muscle ultrasound, and nerve conduction studies on days 4 and 14 after onset of septic shock or severe sepsis, respectively. Healthy controls of similar age underwent clinical neurological evaluation and muscle ultrasound only. DRKS00000642

Results

Nerve conduction studies showed typical measurements for CIP. Ultrasonic echo intensity of muscles was graded semiquantitatively in 4 grades. In muscles of proximal and distal upper and lower extremities the detection of fasciculations was evaluated. 75% of patients showed a mean echotexture greater than 1.5, which was the maximal value found in the control group. A significant difference in mean muscle echotexture between patients and controls were found at day 4 and day 14 (both p<0.001). In addition, from day 4 to day 14 the mean grades of muscle echotexture increased in the patient group (p=0.085). Healthy controls revealed the lowest number of fasciculations (in 7 to 10% in proximal and distal arms and proximal leg, 38% in the distal leg). Patients revealed more muscular regions in which fasciculations were detected in comparison to controls (p= 0.08 at day 4 and p=0.002 at day 14).

Conclusion

Muscle ultrasound is an easily applicable, non-invasive diagnostic tool to evaluate muscle and nerve impairment in patients with severe sepsis in the intensive care unit and could be an additive tool to gold standard, but more invasive techniques such as electromyography and/or muscle biopsy.
P51
The additional information of median nerve SSEP in anoxic brain injury compared to EEG findings

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The lack of somatosensory evoked potentials (SSEP) of the median nerve is used in the prognostic evaluation of patients with diffuse cerebral anoxia. Bilateral lack of cortical SSEP indicates poor outcome and death.

In a retrospective study the prevalence of missing SSEP in patients with diffuse cerebral anoxia was studied and compared to the electroencephalographic (EEG) findings in order to determine predictive EEG-changes.

From 2004-2011, 110 patients (75 men; 35 women, median age 69 years) with anoxic brain injury were investigated with EEG and SSEP. Two to five days after anoxia routine EEG and bilateral SSEP of the median nerve was performed. Six months after 102 patients had died.

In 107 patients the SSEP could be evaluated. Forty-four patients lacked cortical responses bilaterally and all died. Sixty-three patients showed cortical responses and 55 of these died. The sensitivity of predicting death by the lack of cortical SSEP was 44%, the specificity 100% and the positive predictive value 100%.

The EEG findings were abnormal in all patients. The characteristic EEG findings were diffuse low frequency.

In these patients median nerve SSEP did not add any valuable information while SSEP in patients with low frequency changes gave additional prognostic information.
Fatigue and amygdala shrinkage following acute systemic inflammation in rats.

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Question

Severe systemic inflammatory disorders commonly cause a prolonged fatigue syndrome. Various neuro-immuno-endocrine interactions come into consideration to mediate maladaptations of cognitive performance and emotional behaviour, but the etiology remains unknown so far. To identify vulnerable areas, we screened the brain for macro-structural alterations over time.

Methods

T2-weighted brain magnetic resonance images were acquired longitudinally at baseline as well as 1, 2, 4, 8 and 12 weeks following peritoneal application of lipopolysaccharide (LPS; 3 months old rats) and processed by deformation-based morphometry. Sickness was scored during the first week and long-term behavioural abnormalities were investigated by the open field and the accelerated RotaRod test. Changes in neuronal activity and microglia activation were examined by immunohistochemistry (Arc, Iba).

Results

LPS induced severe sickness in the animals for about 4 days. Following recovery from this acute illness, rats showed reduced endurance to sustain motor performance and an anxious/depressive phenotype for at least 4 weeks. In addition to an acute whole brain volume loss of about -1 %, area-restricted gray matter shrinkage evolved bilaterally in the basolateral amygdala (-11%) and the auditory cortex (-5%), persisted for up to 2 weeks and then normalized during the remaining period of observation. The shrinkage was associated with activation of microglia and reduced neuronal activity.

Conclusions

Severe systemic inflammation is associated with long-lasting and reversible reduction of neuronal activity and shrinkage in the amygdala - the central regulator of vigilance, mood and emotions. Understanding of the underlying pathomechanisms and effects on the processing in connected networks, e.g. the auditory system, may help to improve the treatment of infection-related cognitive impairments.
Blink Reflex: differentiating between Alzheimer disease and vascular dementia

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Question

There is no definite electrophysiological test to discriminate between Alzheimer disease and vascular dementia. The pathophysiology of vascular dementia is different from Alzheimer disease and vascular events in patients with vascular dementia may alter blink reflex parameters; as a result, we hypothesized that this test could differentiate between 2 forms of dementia.

Methods

The patients suffering from dementia were enrolled from 2 University hospitals of Tehran University of Medical Sciences. In each group, 20 patients (>50 years) with Alzheimer, vascular dementia, and mixed dementia were recruited. Alzheimer patients were diagnosed according to DSM IV criteria and the patients with vascular and mixed dementia were recruited based on Hachinski criteria, history, and brain MRI. Blink reflex parameters including R1, R2, and R2c latencies were compared between the 3 groups of dementia. For analysis, the latencies between 2 sides were averaged.

Results

The mean (±SD) age of patients in Alzheimer, vascular, and mixed forms was 72.21±8.35, 65.75±11.46, and 73.63±10.72, respectively (p>0.05); and in similar order, the mean (±SD) mini-mental status examination scores of patients were 17.02±3.98, 17.64±4.13, and 17.47±3.96 (p>0.05).

According to one-way ANOVA results, there was only a statistically significant difference in mean R2c scores for the 3 dementia subtypes: F=4.69, p=0.01; however, the difference for mean R1 and R2 latencies was not significant between 3 groups. Post-hoc comparisons for R2c indicated that the mean score for Alzheimer group was significantly different from vascular and mixed forms. The mean R2c (±SD) in 3 groups was 38.95±6.21, 46.69±10.49, and 41.90±6.61 (in above order). Vascular group did not differ significantly from mixed group.

According to the best performance point on the ROC curve, cutoff value for R2c differentiating Alzheimer from other 2 types was 44 milliseconds (sensitivity = 0.64, specificity = 0.92); in addition, the area under ROC curve was 0.81.

Conclusions

It seems that the dysfunction of brainstem reticular pathways is present in dementias with vascular component (vascular and mixed) due to vascular events in brain stem, so that blink reflex may help in differentiating between Alzheimer disease and those with vascular components.
CSF levels of tau protein are related to detrimental SLAI and LTP-like cortical plasticity in AD patients.

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In animal models of Alzheimer’s disease (AD), Beta-amyloid and tau proteins interfere with synaptic transmission. Recently, we showed that AD patients are characterized by an impairment of Long Term Potentiation (LTP)-like cortical plasticity. Furthermore AD patients have a weakened Short Latency Afferent Inhibition (SLAI) that is a neurophysiological measure known to be under cholinergic control, reflecting the cholinergic dysfunction occurring in the pathology. Cerebrospinal Fluid (CSF) sampling is an useful tool in clinical practice in detecting AD biological markers and predicting disease progression. Low levels of Beta-amyloid are typically found in AD patients. Moreover, it has been proposed that high levels of t-tau in AD patients CSF are related to a faster cognitive decline and more malignant form of dementia. Aim of this study is to investigate the relation between CSF values of Beta-amyloid, T-tau and p-tau and cortical plasticity in a sample of AD patients. All patients underwent lumbar puncture for CSF sampling for clinical testing. By means of repetitive transcranial magnetic stimulation we tested in 55 AD patients the LTP/LTD-like effects induced by the intermittent TBS (iTBS) and continuous TBS (cTBS) protocols applied over the primary motor cortex, and the efficacy of SLAI circuits. Each patient was evaluated for iTBS and cTBS plasticity induction in two different sessions. In each session twenty motor evoked potentials were collected at baseline and over the same hot-spot at 1-5, 6-10, 11-15, 16-20 and 21-25 minutes after TBS protocols. K-means cluster analysis including the 3 CSF biomarkers was carried out.

The three resulting clusters differed by the value of T-tau: cluster 1 (low levels of T-tau=250); cluster 2 (intermediate levels of T-tau=750); cluster 3 (high levels of T-tau= 1150). There was no difference between clusters regarding age, gender, years of education, baseline neuropsychological global measurements, or APOE genotype. We found that cluster 2 showed more impaired LTP-like cortical plasticity and SLAI efficiency, while cluster 1 and cluster 3 have surprisingly the same pathological trend for both measures.

Our results shed light on the role of tau protein in the physiopathology of AD, showing a similar U shaped-curve related to the level of LTP impairment and SLAI deficiency.
P55
VISUAL SENSORY AND VISUAL COGNITIVE NETWORKS RESPOND DIFFERENTIALLY IN BRAIN OSCILLATORY RESPONSES OF MILD COGNITIVE IMPAIRMENT

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Background
Mild cognitive impairment (MCI) is mostly a pre-dementia phase of Alzheimer’s disease. We investigated sensory evoked oscillatory responses (SEO) and target event-related oscillatory responses (VERO) of visual modality in order to understand underlying changes in dynamics of sensory and cognitive networks in MCI.

Methods
A total of 43 consecutive patients with MCI (mean age= 74.0 year) and 41 age-, education-matched normal elderly controls (mean age=71.1 year) were participated to the study. Classical visual oddball was used for VERO and simple flashlight for SEO. Oscillatory responses at delta frequency range (0.5-3 Hz) was examined. Repeated measures of ANOVA was performed for 4 x anteriorposterior, 3 x coronal, 2 x paradigms (VERO and SEO).

Results
Across all subjects, topography and size of amplitudes differed between SEO and VERO responses, being highest over occipital in SEO, whereas over frontal in VERO. Moreover, VERO peak-to-peak amplitudes reached to almost double values of SEO (Fig. 1). The ANOVA on amplitude of delta oscillatory responses revealed that there were no direct group differences. However significant results were observed for groupXparadigm [F (1.81)=5.046, p< 0.03]. Post-hoc analysis indicated that the difference between groups were significant for delta VERO responses, but not in visual SEO.

Conclusions
Target delta VERO are decreased in MCI whereas not in visual SEO. Based on notion that visual sensory networks are reflected by SEO and cognitive networks by VERO, our findings indicate that differential circuits are available for sensory and cognitive functions. MCI subjects seem to have impairment in cognitive network, but not in sensory network of visual modality. Brain oscillatory responses bear a potential to be searched as a biomarker and are helpful in investigating and understanding the brain dynamics in cognitive dysfunctions such as MCI.

Acknowledgements: This study was supported by TUBITAK 112S459 grant.
Abstracts of Poster Presentations – Poster Session 4 – Dementia

P56
Human brain cortical effective connectivity and excitability in Alzheimer’s disease: a combined EEG-TMS study

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Purpose

Applying the “graph theory” to the human brain, is possible to consider the central nervous system as a set of structural/functional neuronal aggregates (nodes) and connections (edges) (Sporns et al. 2005). In this view Alzheimer's disease (AD) is emerging as a possible chronic brain disconnection syndrome (He et al. 2008). In fact in AD, connectivity from one to other brain areas is markedly reduced. Electroencephalography (EEG) and transcranial magnetic stimulation (TMS) co-registration allows the recording of specific responses, considered a reflection of cortico-cortical connectivity and functional state (Ferreri et al. 2011). The aim of the present study is to assess the potential of navigated TMS-evoked EEG responses in studying motor cortex reactivity and cortical connectivity in AD.

Methods

Supra-threshold single TMS of the left primary motor cortex was carried out during a multi-channel EEG recording on 13 patients with mild Alzheimer’s disease without motor deficits and 13 healthy age-matched volunteers. Motor evoked potentials (MEPs) from the opposite hand were simultaneously recorded.

Results

Single pulse TMS induced EEG responses characterized by the well know sequence of negative deflections peaking at approximately 8, 18, 44, and 100 ms alternated with positive peaks at approximately 12, 30, 60 and 180 ms post-TMS. AD patients showed at specific latencies clear amplitude change in the recruited sensorimotor network as well as in MEPs amplitude.

Interpretation

EEG-TMS is a promising tool to better characterize changes in functional cortical connectivity and reactivity in the AD patients.

Essential bibliography


Potential Cognitive Decline Links to Angiotensin-Converting Enzyme Gene but not Hypertension: Evidence from Cognitive Event-Related Potentials

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Questions

In aged population, control of hypertension has been linked to beneficial effects in terms of cognition in cross-sectional and prospective follow-up studies, but such results remain controversial. The interaction between environmental and genetic vascular factors probably explains these findings. The aims of the present study are to investigate the effect of hypertension and angiotensin-converting enzyme (ACE) genotypes on cognitive event-related potentials (ERPs) and whether the impact of ACE genotypes on P300 ERPs is related to the influence of hypertension.

Methods

Using Cognitive Abilities Screening Instrument (CASI), we recruited 97 mentally healthy middle-aged and older adults. Medical history was collected and blood pressure, ACE insertion/deletion and Apolipoprotein E polymorphism, and auditory ERPs were measured for all participants.

Results

When the participants were stratified according to the presence or absence of hypertension, there was no difference in scores of CASI, the percentage of ACE genotypes and measurement of ERPs (Table 1). The subjects with D/D homozygote displayed significantly decreased amplitude and delayed latency of P300 ERPs, although the score of CASI and the percentage of hypertension showed no difference (Table 2).

Conclusions

The subjects with the D/D genotype tend to have a low amplitude and long latency of P300 ERPs which reflected subtle cognitive impairment. There was no association between hypertension, CASI scores and measures of P300 ERPs. Using ERPs, potential cognitive decline was linked to ACE genotypes, independent of the effect of hypertension.
Latencies of Vagus somatosensory evoked potentials are prolonged in Mild cognitive impairment

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Question

In a pilot study, Vagus somatosensory evoked potentials (VSEP) were shown to be prolonged in Mild cognitive impairment (MCI). We now aimed at reappraising this finding in a cohort of 200 randomly selected subjects aged between 70 and 75 years.

Methods

VSEP were performed by stimulating the auricular branch of the vagus nerve (electrical square impulses, 0.1msec duration, interstimulus interval 2sec, 8mA). Recording of evoked potentials was done ipsilateral at electrode positions C3-F3, C4-F4, Fz-F3 and Fz-F4 (band-pass 0.1Hz-1kHz, analysis time 10msec, averaging of 100 artifact-free epochs). Five ANOVAs for repeated measurements were done separately for each of the VSEP latencies (P1, N1, P2) and amplitudes (P1N1, N1P2) with the inner subject factors stimulation/recording side and electrode position and the between subject factor diagnosis. VSEP raters were blinded for the diagnosis.

Results

In 8 subjects, no clear potentials could be detected. In the remaining 14 subjects with MCI (10 male; age 75.1 +/- 1.1 years; MMSE 27.1 +/- 3.0, DemTect 10.3 +/- 2.0) and 178 cognitively unimpaired subjects (91 male; age 74.7 +/- 1.5 years; MMSE 29.1 +/- 1.2; DemTect 16.3 +/- 1.8), statistical analysis revealed a significant main effect for the between subject factor diagnosis for the latencies N1 (F=7.442, df=1, p=0.007) and P2 (F=8.432; df=1, p=0.004).

Conclusions

The main conclusion of the here presented confirmation of prolonged VSEP latencies in MCI is that the concept of VSEP is reliable. VSEP has the potential for an easy applicable screening tool in the diagnostic repertoire of Alzheimer’s disease.
P59
Event Related Potential (ERP) and SPECT patterns in subtypes of Mild Cognitive Impairment (MCI) as early functional markers of cognitive decline

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Question
To study the P300 and N400 ERPs and SPECT perfusion in MCI; to correlate ERP and SPECT patterns with neuropsychological (NP) profile. To test functional early markers of cognitive decline in MCI patients and specifically in Subjective (SCI), amnestic (aMCI) and multidomain (mMCI) subtypes.

Methods
Forty-three MCI patients (aged 66.4±7.6 yrs; 12 women, 31 men) were assessed by a broad NP battery test. ERP recordings: visual and auditory oddball P300; N400 by semantically congruous and incongruous adjective-pair paradigm. Brain SPECT by 99 mTc HMPAO with analysis of Brodmann areas (BAs). Statistical analysis: Fisher’s exact test for group differences and Spearman’s rank correlation coefficient for correlations.

Results
NP testing identified 8 SCI (normal profile), 17 aMCI and 18 mMCI patients. These last two groups scored slightly lower on short-term verbal and episodic memory tests, significantly poorer in mMCI group. As a whole, P300s and N400 were altered in 44.2% and 86% of patients, respectively. The frequency of ERP abnormalities was similar in SCI and aMCI groups (P300: 25% and 23.5%; N400: 87.5% and 70.6%, respectively) whereas it was significantly higher in mMCI (P300 72.2% and N400 100% of patients). All patients showed perfusion defects in both limbic lobes (BA 36) and a significantly lower perfusion in left prefrontal, frontal and temporal lobes compared to the right ones. Significant differences of hypoperfusion emerged between SCI and mMCI groups for left frontal (BA45) and temporal (BA21) areas. P300s correlated significantly with short-term memory in mMCI patients. Poor correlations emerged between ERP and SPECT findings.

Conclusions
ERP and SPECT findings revealed a high detection sensitivity of functional impairment in MCI subtypes, including SCI individuals who have a normal NP profile. This suggests that functional alterations precede clinical onset of memory complaint providing pathophysiological information before clinical/structural evidence. The N400 appears particularly sensitive for early detection of semantic memory abnormalities in MCI patients. These methods may assist clinicians in earlier diagnosis of MCI and are potentially useful as screening instruments for assessing MCI, detecting preclinical dementia and monitoring the staging of conversion from MCI to dementia.
Abstracts of Poster Presentations – Poster Session 4 – Dementia

P60
NEUROPSYCHOLOGICAL ASSESSMENT IN GERIATRICS AND ITS ROLE ON DIFFERENTIAL DIAGNOSIS

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Background

Mild Cognitive Impairment (MCI) is suggested as the prodromal stage of Alzheimer’s Dementia (AD). Depression (DP) in the elderly may cause cognitive impairment similar to AD. The neuropsychological (NPS) assessment is indicated as a gold-standard examination towards differential diagnosis. We aimed to investigate NPS pattern to find different specific performances in the nosological categories cited.

Methods

170 (100 women) older adults, mean age 73.5 and educational level 4.24 were divided into MCI (67), DP (31) and AD (76) . One-way ANOVA, with Sidak post hoc, were used, and effect sizes were measured with \( \eta^2 \) and Cohen’s “d” in the following tasks: MMSE (Global Cognition), Rey’s Auditory Verbal Learning Test (Memory), Frontal Assessment Battery (Executive Functions), Token Test (Language), Lawton Scale (Activities of Daily Living) and Geriatric Depression Scale (depressive symptoms).

Results

No differences in age and educational level was found, but the groups differed in Global Cognition (\( \eta^2=0,1 \)), functional level (\( \eta^2=0,23 \)), depressive symptoms (\( \eta^2=0,35 \)), Executive Functions (\( \eta^2=0,18 \)), Language (\( \eta^2=0,15 \)), immediate (\( \eta^2=0,12 \)) and delayed (\( \eta^2=0,12 \)) recall and recognition (\( \eta^2=0,13 \)) components of episodic memory. Post hoc analyses (figure 1) suggest that specific differences occurred:

1) between MCI and AD: Global Cognition, functional level, depressive symptoms, Executive Functions, Language, immediate and delayed recall;

2) between DP and AD: Global Cognition, functional level, depressive symptoms, Executive Functions, Language, immediate and delayed recall and recognition;

3) between MCI and DP: depressive symptoms, immediate recall, delayed recall and recognition from episodic memory.

Conclusions

Our results show evidences of important contributions of the NPS assessment to differential diagnosis between AD, DP and MCI. Special emphasis is given to measures of depressive symptoms, functional level and recognition from episodic memory.

References


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Figure 1: Significant differences and effect sizes (d) between groups

![Figure 1](image-url)

- Functional Level
- Depressive Symptoms
- Global Cognition
- Immediate Recall
- Delayed Recall
- Recognition
- Executive Functions
- Language

**p < 0.05**
Higher level but not lower level parallel visual pathways are functionally altered in patients with mild cognitive impairment

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Objective

Spatial vision and object recognition are processed in parallel by the dorsal (D) and ventral (V) streams. Such visual information is behaviorally impaired in Alzheimer’s disease (AD). We studied how V and D streams are functionally altered in patients with mild cognitive impairment (MCI) who turned out to be AD.

Methods

The functions of the D- and V-streams at lower (L) and higher (H) levels were separately evaluated in MCI patients, healthy old and young adults with a 128-ch EEG machine. Each group consisted of 15 subjects. Visual stimuli were optimized to stimulate each stream separately. At L-level, red-green isochromatic gratings were used for V while achromatic gratings for D. At H-level, words [Kanji (ideogram) for V; Kana (phonogram) for D], faces for V, and coherent radial optic flow (OF) motion for D were employed.

Results

In all groups, occipital N1 for chromatic stimuli and steady-state responses for achromatic stimuli were major components of VEPs at L-level. In ERPs, occipito-temporal N170 were obtained in both words and faces, and occipito-temporal N170 and parietal P200 were elicited by OF. In comparison between MCI and old adults, there were no significant differences in VEPs for chromatic and achromatic stimuli between the two groups. In contrast, a significant prolongation of N170 latencies for faces and Kana but not Kanji was observed in MCI. N170 and P200 latencies for OF were also significantly prolonged in MCI. N170 amplitude and P200 latency for OF was closely related with the Mini-Mental State Examination score. Similarly, the latency and amplitude of P200 for OF and N170 latency for Kana were most closely correlated with the Wechsler Memory Scale-Revised Logical Memory (delayed recall).

Conclusions

These findings suggest that the activities of V and D streams at H-level are impaired with preserved L-level function in MCI patients. Since the high correlation between H-D related ERP and neuropsychological tests was obtained, H-D related ERP can be the most sensitive biomarkers for early detection of MCI.
Occipital sources of resting state alpha rhythms are related to local gray matter density in subjects with amnesic mild cognitive impairment and Alzheimer’s disease

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Objective

Occipital sources of resting state alpha rhythms are abnormal in patients with amnesic mild cognitive impairment (MCI) and Alzheimer’s disease (AD). Here we hypothesized whether the activity of these sources is related to neurodegeneration in occipital lobe as measured by magnetic resonance imaging (MRI).

Methods

Resting-state eyes-closed EEG rhythms were recorded in 30 healthy elderly (Nold), 37 MCI, and 40 AD subjects. Neurodegeneration of the occipital lobe was indexed by weighted averages of gray matter density (GMD). EEG rhythms of interest were alpha 1 (8-10.5 Hz) and alpha 2 (10.5-13 Hz). EEG cortical sources were estimated by LORETA.

Results

Results showed a positive correlation between GMD in the occipital lobe and the magnitude of occipital alpha sources in the MCI and AD subjects. Furthermore, there was a positive correlation between the magnitude of alpha sources and the cognitive status as revealed by Mini Mental State Evaluation score all subjects.

Conclusion

These results suggest that in amnesic MCI and AD subjects, occipital sources of resting state alpha rhythms reflect AD neurodegeneration in the occipital lobe.

Significance

Cortical sources of resting state EEG rhythms in AD patients are promising for preliminary screening of elderly subjects at risk for AD.
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P63
D2 agonist administration restores altered cortical plasticity in Alzheimer’s disease patients.

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In animal models of Alzheimer's disease (AD), amyloid beta fragments interfere with mechanisms of cortical plasticity such as long-term potentiation (LTP) and long-term depression (LTD). Accordingly, recent evidence showed that in AD patients LTP-like cortical plasticity is impaired, while LTD seems to be preserved. Despite its major role in synaptic plasticity mechanisms, the involvement of dopamine (DA) in controlling cortical plasticity mechanisms in AD is still debated. A crucial role dopaminergic networks in cognitive and motor processes has been well established but largely unexplored in AD. Here we aimed at investigating whether administration of a D2 agonist could modulate cortical plasticity in AD patients, as measured by standard theta burst stimulation (TBS) protocols applied over the primary motor cortex (M1). Three groups of mild AD patients were tested before and after four weeks of treatment with rotigotine, rivastigmine or placebo. Each patient was evaluated for plasticity induction of LTP/LTD-like effects using respectively intermittent TBS (iTBS) or continuous TBS (cTBS). Central cholinergic activity was also evaluated by means of the short latency afferent inhibition (SLAI) protocol. Neuropsychological evaluations were performed to assess memory, executive functions and visuo-spatial abilities. At baseline AD patients showed the previously described pattern of impaired LTP-like cortical plasticity as assessed by iTBS. After two weeks of D2 agonist administration we observed a remarkable change in the iTBS protocol effects, revealing that LTP-like plasticity was strikingly enhanced. No effects were seen in the rivastigmine and in the placebo group. LTD-like cortical plasticity induced by cTBS was not modulated in any condition. Cholinergic activity was slightly increased by both rotigotine and rivastigmine groups. Neuropsychological testing showed that increased levels of LTP-like cortical plasticity in the rotigotine groups was paralleled by an improvement in the MMSE and in executive functions. Our findings highlight a role for dopamine in the pathophysiology of AD suggesting that a dysfunction of D2-like receptors is involved in mechanisms of altered cortical plasticity and providing novel implications for new therapies based on dopaminergic stimulation.
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P64
Disturbed directions in white matter hyperintensity based vascular dementia: An EEG connectivity study

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Objective

In white matter hyperintensity-based vascular dementia (WMH-VaD) long distance white matter tracts are primarily involved. We aimed to investigate which functional changes are related to these lesions.

Methods

Resting-state electroencephalography (EEG) studies of 17 WMH-VaD patients and 17 age- and gender matched non-demented controls were analyzed in the delta, theta, alpha1 and 2, and beta frequency bands. Undirected functional connectivity between electrodes was established with the Phase Lag Index (PLI) and directed functional connectivity with the directed phase lag index (dPLI).PLI and dPLI were related to performance on cognitive testing.

Results

Mean PLI did not differ between patients and controls. In the control group, dPLI showed anterior to posterior phase gradients in all except the delta band. In the VaD patient group however, this pattern was significantly different without a clear directional pattern. No relationship between the directed and undirected functional connectivity with cognition was found.

Conclusions

This study shows a clear front-to-back direction of connectivity in cognitively intact individuals. In VaD patients with extensive WMH, this pattern is lost.

Significance

Structural damage at the regions of long distance white matter tracts may induce changes in the direction of phase relationships of distinct brain regions.

figure 1
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figure 2
Spectral quantitative EEG analysis on patients with vascular dementia and Alzheimer disease

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Alzheimer disease (AD) and vascular dementia (VD) are neuro-degenerative diseases that lead to cognitive decline. Although both diseases present with similar clinical symptoms, the underlying biological mechanisms are different. One of the most common diagnostic examinations of such diseases is the electroencephalogram (EEG). So far, clinical EEG assessment is mainly done through expert visual inspection, searching for relatively few clearly visible signs of pathology, while usually not considering other quantifiable measures, hence potentially discarding important features that are not immediately visible. In this study we focused on the comparison of quantitative EEG analysis of patients with Alzheimer disease (n=114), vascular dementia (n=114) and healthy elderly controls (n=114). The spectral analyses of 342 EEGs, recorded under awake resting eyes closed and open conditions, were compared using curve fitting with a combination of a power loss and gaussian function estimating six coefficients. Significant differences between the three groups were found in several of those coefficients that are intrinsically related with delta (1-4Hz), theta (4-8Hz), alpha (8-13Hz) and beta (13-30Hz). Results: both AD and VD groups show increased amplitude in delta band when compared with controls, in particular VD patients. The same trend happens for the alpha amplitude, however for occipital and temporal regions the AD patients have lower alpha amplitude than controls. The AD and VD groups show lower alpha peak frequency, however that decrease is more pronounced in the VD group. Moreover, the dispersion of alpha frequency is wider for both AD and VD groups, especially for the AD group.

figure 1
Neurophysiological Index Correlates with Disease Severity but not with Duration in Amyotrophic Lateral Sclerosis (ALS)

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Background

Neurophysiological biomarkers to monitor disease course are urgently needed in ALS. The Neurophysiological index (NI) is a recently described parameter that proved useful in cohorts of early stage ALS. Little is known about NI in more advanced disease stages.

Objective

To investigate whether NI correlates with clinical parameters in ALS.

Methods

We recruited 43 consecutive patients with clinically definite and clinically probable ALS (El Escoral Criteria) from Unicamp neuromuscular outpatient clinic between 2011 and 2013. For each subject, disease severity was quantified with the ALS functional rating scale (ALSFRS-R) and the ALS severity scale (ALSSS). NIs of both ulnar nerves were calculated as described previously (de Carvalho et al): (CMAP amplitude / Distal motor latency) x F persistence (%). We employed Spearman correlation coefficient to investigate correlations between NI and clinical data.

Results

There were 25 men and 18 women. Mean age of the patients and disease duration were 53,51 (31-74) and 29,33 (5-96), respectively. Mean ALSFRS-R and ALSSS scores were 28,23 (9-44) and 24,63 (9-37), respectively. Right sided ulnar NIs (n=43) did correlate both with ALSFRS-R and ALSSS scores (r=0.58 and 0.59, respectively). On the left side (n=40), NIs also presented a positive correlation with both scores (r=0.65 and 0.62, respectively). However, NIs on either side were not significantly associated with disease duration.

Conclusion

NI is easy to calculate using routine nerve conduction studies and correlates with disease severity in patients with ALS. It is a promising parameter to monitor disease progression. Longitudinal studies should be performed to confirm these findings.
P66
Quantitative electromyography of the external anal sphincter in Chinese healthy volunteers.

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Objective

Quantitative electromyography of external anal sphincter has been widely used in neurological, urological and obstetrics departments. Studies on reference values of external anal sphincter electromyography were limited and the results were various. The aim of the study was to explore the normative data in Chinese healthy volunteers and established a practical reference range in clinical use.

Method

Sixty-two healthy volunteers (aged 20-62 years) attended the study. Motor unit potentials (MUP) were obtained from the EAS of the subjects using multi-MUP analysis. The MUP parameters (Amplitude, Duration, Area, Turns and Phases) were statistically caculated. The possible factors that has influence on the parameters of MUP was also analysed.

Results

All subjects completed the examination. The mean MUPs amplitude of all subjects was 533.41 ± 87.41 μ V (95%CI 511.21-555.61), the mean duration was 9.92 ± 1.31ms (95%CI 9.59-10.26), the mean area was 474.17 ±122.92μ V *ms(95%CI 442.96-505.39),the mean turns was 3.72 ± 0.49 (95%CI 3.60-3.84) and the mean number of phases was 3.85 ± 0.39 (95%CI 3.75-3.95). Further analysis revealed transvaginal delivery history, sex, and age have correlations with the parameters of MUPs.

Conclusion

The reference range of external anal sphincter quantitative electromyography was established in Chinese. The sex, age and history of transvaginal delivery have close relationship with external anal sphincter electromyography parameters.
P67
Value of neurophysiological examination in diagnosis of hereditary neuropathy with liability to pressure palsies

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Objective

Explore the value of neurophysiological testing in diagnosis of hereditary neuropathy with liability to pressure palsies (HNPP).

Methods

Two HNPP probands from different pedigrees and 7 HNPP patients from the two pedigrees were analysed with neurophysiological testing.

Results

Two HNPP probands with symptoms of single peripheral neuropathy were tested 15 nerves, including median nerves, ulnar nerves, superficial radial nerves, peroneal nerves, tibial nerves and sural nerves. Sensory conduction velocity (SCV) of these nerves totally decreased. Motor conduction velocity (MCV): the conduction of median nerves and tibial nerves in one case was normal, but the other decreased; ulnar nerves of elbow and peroneal nerves of fibular head both decreased. There were local conduction blocks in inching potentials of ulnar nerves and peroneal nerves in the two probands. 7 HNPP patients from the two pedigrees with or without symptoms of peripheral neuropathy were tested MCV of 48 nerves: there were 5 median nerves with prolonged distal latency in 9, and the abnormal ratio was 55.6%; there were 3 ulnar nerves with prolonged distal latency in 9, and 8 with decreased conduction in elbow in average 36.2 m/s, and the abnormal ratio was 88.9%; there were 4 peroneal nerves with prolonged distal latency in 7, and 5 with decreased conduction in fibular head in average 36.7 m/s, and the abnormal ratio was 71.4%; there were 4 tibial nerves with prolonged distal latency in 7, and 4 with decreased conduction in average 38.2 m/s, and the abnormal ratio was 57.1%. 7 HNPP patients were also tested SCV of 49 nerves: there were 9 median nerves with decreased conduction in 9, and the abnormal ratio was 100%; there were 8 ulnar nerves with decreased conduction in 9, and the abnormal ratio was 88.9%; there were 7 superficial radial nerves with decreased conduction in 9, and the abnormal ratio was 77.8%; there were 5 peroneal nerves with decreased conduction in 7, and the abnormal ratio was 71.4%; there were 5 tibial nerves with decreased conduction in 7, and the abnormal ratio was 71.4%; there were 6 sural nerves with decreased conduction in 7, and the abnormal ratio was 85.7%.

Conclusions

It is an objective evidence for neurophysiological examination in the diagnosis of patients with HNPP. There can be found abnormal nerve conduction in asymptomatic nerves and family members, especially in the more vulnerable entrapment. So neurophysiological examination is crucial for diagnosis and early interventions of patients with HNPP.
The possibilities of combined application of electroneuromyography, transcranial and segmentary magnetic stimulation in complicated spinal cord injuries.

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Background

The TMS method have been used for diagnostic reasons in the case of traumatic spinal cord since 1992-1998 (Dvorac, Tegenthoff, McKay, Cheliout-Heraut). Nowadays, the neurophysiologic criteria for verification of spinal shock final, neurophysiologic evaluation of rehabilitation potential in early stage of SCI are still incomplete.

We aimed to develop the standard of complex neurophysiologic examination for SCI patients. 20 patients (12 male, 8 female; aged from 21 to 54 years) with traumatic spinal cord in anamnesis were examined for the period of 2 years.

The duration of the disease was from several days to 9 years. 19 cases of SCI were caused by trauma (diving, road accident, fall from heights) and 1 patient had a bullet wound of the neck. The traumatic process was located on the neck (the 1st group), thoracic level (the 2nd group) and cauda equina level (the 3d group).

Methods

For the patients of the 1st group (n=8) we applied the methods of stimulative electroneuromyography of upper and lower extremities, transcranial and segmentary magnetic stimulation: cervical and lumbar level.

Stimulative electroneumyography of lower extremities combined with TMS and magnetic stimulation of lumber level were applied in the 2nd group patients (n=9). Stimulative and needle electromyography measurements were performed for 2 patients of the 3d group.

Results

The neurophysiologic evaluation of the 1st and the 2nd patients' groups revealed:

1. The absence of F-wave in early posttraumatic period. The supposed, that the time of F-wave appearance coincides with the finish of spinal shock.

2. The probe with human motor cortex facilitation induced by repetitive transcranial magnetic stimulation permit to reveal bigger than assumed rehabilitation potential in the case of strong chances of the motor evoked potential.

3. For the patients with cervical level injury we recommend to perform segmentary magnetic stimulation of lumbar level.
Objective

To study prospectively electrophysiological subtypes of Guillain-Barre syndrome (GBS) and the clinical characteristics of different subtypes in central and southern China, and to screen out the clinically related factors which predict that the disease severity, so as to guide the early intervention.

Methods

Seventy-one consecutive GBS patients between Jan 2008 and Dec 2011 were enrolled, who were hospitalized and fulfilled the criteria for the clinical diagnosis of GBS. Demographic information and clinical manifestations were registered, disease severity was assessed by Hughes GBS disability score (H-GBS-DS); based on the electrophysiological findings in the patients, the subtypes were classified, and the clinical, electrophysiological features and their correlations were analyzed. Taking the grade of H-GBS-DS (whether > or = 3 or not) as a dependent variable, using logistic regression model to predict the clinical relevant factors.

Results

(1) There were 32 cases classified as AIDP subtype (45.1%, 95% confidence interval [CI] 34~58%); 9 AMAN (12.7%, 6~23%); 10 AMSAN (14.1%, 7~25%); 1 inexcitable (1.4%, 0~8%); 19 equivocal (26.8%, 15~34%). (2) Among the three main subtypes of AIDP, AMAN and AMSAN, those with age over 30 years accounted for 37.5%, 33.3%, and 90%, respectively ($\chi^2 = 9.256, P = 0.008$); those with respiratory tract infection within 4 weeks before onset of symptoms accounted for 50%, 22.22% and 10%, respectively ($\chi^2 = 6.272, P = 0.044$); those who had their neurologic deficits reaching a peak within 1 week accounted for 62.5%, 100% and 40%, respectively ($\chi^2 = 7.892, P = 0.011$). (3) In the patients with H-GBS-DS > or = 3, the odds ratio was 0.113 (95% CI 0.027~0.476, $P = 0.003$) for initial involvement of cranial nerve(s), 9.614 (2.496~37.024, $P = 0.001$) for initial involvement of limb(s) and 4.281 (1.003~18.265, $P = 0.049$) for autonomic dysfunction, respectively.

Conclusions

AIDP was the main GBS subtype in central and southern China, in which infection of respiratory tract was the main prodromic event. AIDP and AMAN were the predominant subtypes in younger persons, and the patient with AMAN had a more rapid progression. As the predicting factor of disease severity, those with initial involvement of cranial nerve had a lesser extent of disability, whereas those with initial involvement of limb and complicated with autonomic dysfunction had more severe degree of disability, therefore more attention should be paid and additional treatment should be administered clinically.
Hemifacial spasm complicated with auricular symptoms: Treatment with onabotulinumtoxinA and electrophysiological evaluation

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Question

The patients of hemifacial spasm (HFS) may complicate with auricular symptoms. The aims of this study are to determine the effect of onabotulinumtoxinA (BTX-A) injection into posterior auricular muscle (PAM) and to compare the clinical and electrophysiological changes between regular sites and additional PAM injection of BTX-A.

Methods

Sixty-three consecutive HFS patients complicated with auricular symptoms such as tinnitus or murmur, “ticking” or a “clicking” sound and discomfort on the same side, referred to our department, were enrolled. The patients were largely randomized into two groups of BTX-A treatment according to the order of referral, one was regular group including 33 cases whose injection sites were routinely; another was PAM group including 30 cases, in which 4 units of was additionally injected to PAM. Before injection, the test of blink reflex was performed and lateral spread of blink reflex to orbicularis oris (OO) and PAM, i.e. abnormal muscle response (AMR), were recorded, and the peak-peak amplitude of AMR was measured. The patients were followed-up clinically and electrophysiologically at least 4 weeks (29.47 ± 2.53 days) later. Results: 1) The patients reported that their auricular symptoms subsided after injection in both groups, the remission rate was 45.5% (15/33) in the regular group and 76.7% (23/30) in the PAM group, respectively, with higher rate in the PAM group (χ² = 6.40, P = 0.011). 2) In both groups the AMR amplitude decreased significantly after injection. In the regular group, the OO amplitudes (μV) before and after injection were 304.00 ± 30.34 and 129.33 ± 9.59 (t = 5.820, P = 0.000), and PAM amplitudes, 298.00 ± 33.28 and 184.67 ± 20.21 (t = 2.818, P = 0.014), respectively; in the PAM group, OO amplitudes were 405.33 ± 66.71 and 116.00 ± 9.99 (t = 4.214, P = 0.001), PAM amplitudes, 390.00 ± 53.58 and 72.00 ± 9.67 (t = 6.011, P = 0.000), respectively. 3) PAM amplitudes in the PAM group decreased more significantly compared with those in the regular group (t = 4.237, P = 0.001).

Conclusion

In the patients of HFS complicated with auricular symptoms, the electrophysiological studies are helpful for the guidance of treatment; and the auricular symptoms could be better improved after BTX-A injection into PAM in addition to those regular injection sites.
The Relationship between Hyperhomocysteinemia and Sympathetic Nerve Lesions in Type 2 Diabetic Mellitus Patients

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Objective

To study the effect of hyperhomocysteinemia (Hhcy) on type 2 diabetic mellitus (DM) sympathetic nerve function by skin sympathetic reflection (SSR) technology to explore the relationship between Hhcy and diabetic automatic neuropathy (DAN).

Method

According to total homocysteine (tHcy) level, patients of type 2 DM were divided into two groups: 52 cases with Hhcy, 50 cases without Hhcy as a control group. Fasting blood glucose (FBG), glycated hemoglobin (HbA1c), total cholesterol (TC), triglyceride (TG), serum creatinine (Scr), blood folic acid and VitB₁₂ level were measured in all patients. SSR in all the four limbs were performed in all patients with a Danmark Keypoint.net electromyography device. The mean latencies and amplitudes of SSR, the abnormality rate of SSR, upper limb/lower limb latency ratio and amplitude ratio of SSR were recorded.

Results

The general clinical and biochemical data were compared: blood folic acid, VitB₁₂ level in Hhcy group [respectively for (2.83±1.28) ng/ml, (187.73±82.73) pg/ml] were obviously lower than that of NHhcy group [respectively for (3.64±1.52 ng/ml, (271.24±104.25) pg/ml](P < 0.05); and there were no significant difference in other indexes of the 2 groups (P > 0.05). Hhcy group had higher abnormality rate of SSR than NHhcy group (86.54% vs 70.00%, P < 0.05). Lower limbs SSR of Hhcy group had longer mean latencies than that of NHhcy group [respectively for (2742.71±318.29) ms, (2507.15±307.46) ms](P < 0.01), lower mean amplitudes than that of NHhcy group [respectively for (0.30±0.13) mV, (0.34±0.15) mV](P < 0.05), and there were no statistical differences between between the two groups in upper limbs SSR. (P > 0.05). Furthermore, SSR latency ratios of upper limb/lower limb in Hhcy group was lower than that of NHhcy group (0.55±0.13, 0.60±0.08)(P < 0.01); SSR amplitude ratios of upper limb/lower limb had not statistical differences between the two groups (P > 0.05). Using spearman related analysis found that abnormal SSR had positive correlation with tHcy (rₜₐₓ = 0.947), and negative correlation with blood folic acid, VitB₁₂ level (rₛ = -0.881, rₛ = -0.851)(all P < 0.01).

Conclusion

The tHcy level has positive correlation with sympathetic nerve lesions in type 2 DM patients. Hhcy increases the incidence of sympathetic nerve lesions and meanly damage lower limbs small fiber nerve. SSR technology is a simple and feasible method to detect DAN. Meanwhile, Blood folic acid and VitB₁₂ level in patients of type 2 DM with Hhcy are reduced significantly.
P72
Selective paralysis of Long thoracic nerve with concomitant involvement of the lateral cutaneous nerve of the forearm. An unusual form of Parsonage-Turner syndrome

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¹GNA G.GENNIMATAS, NEUROLOGY, ATHENS, Greece

Case report

Male patient, age 32, presented to the neurophysiology department of our clinic complaining of having difficulty raising his right arm up straight. His symptoms started 2 months ago with severe pain in the right shoulder and arm, followed by weakness in raising his arm. He had no recent history of trauma, infection, shoulder injury, vaccination or vigorous exercise. His family and personal medical history was free of connective tissue disorders, polyneuropathies and lung cancer. On physical examination there was limitation of shoulder elevation, scapular winging with rotation of the inferior angle toward the midline, and prominence of the vertebral border, due to paresis of the right serratus anterior muscle. He also complained of mild hypesthesia at the lateral surface of his right forearm. The rest clinical examination including tendon reflexes was normal. The EMG examination showed positive sharp waves and fibrillations on the right serratus anterior muscle with reduced recruitment of motor units. The ENG examination showed an absent SNAP of the right lateral cutaneous nerve of the forearm. MRI of the cervical spine and the brachial plexus was normal.

Discussion

Parsonage-Turner syndrome typically concerns two or more nerves. Long thoracic nerve is affected in almost 50% of male patients and the lateral cutaneous nerve of the forearm is one of the sensory nerves usually affected. We report a rare case where only the long thoracic nerve and the lateral cutaneous nerve of the forearm are involved. No other nerve was affected.
P73
Median nerve inching: an electrophysiological normative study to diagnose carpal tunnel syndrome

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Question
This study was aimed to obtain preliminary normative data of median sensory nerve inching in our setup and population as it is useful for electrodiagnosis of carpal tunnel syndrome.

Methods
Orthodromic inching technique of the median nerve stimulating the second digit was performed on 42 wrists of 14 males and 7 females. The mean ages of males and females were 28.1±1.68 yrs and 26.4±3.6 yrs respectively. The sensory nerve action potential (SNAP) latency and amplitude were measured in segments 3 cm proximal to the distal wrist crease and 4 cm distal to it.

Results
The mean SNAP latency and amplitude in males was 1.93±0.31ms and 30.53±10.65µV respectively. In females, the mean SNAP latency was 1.75±0.2ms and amplitude, 32.8±10.41 µV. The mean conduction delay per centimeter (CD/cm) was 0.19ms in both genders. The maximal CD/cm was 0.3ms in males and 0.35ms in females in the segment 1cm distal to the distal wrist crease. The abnormal cut-off value, calculated as the maximal CD/cm + 2SD was 0.63/0.57ms in males and females respectively.

Conclusion
Since, these nerve conduction study parameters vary with the laboratory conditions, demographic profile and anthropometric measurements of the population; this median sensory nerve inching study provides preliminary normative data that will aid in electrodiagnosis of carpal tunnel syndrome.

Keywords
carpal tunnel, conduction delay, inching, sensory
Clinical Utility of the Inpatient EMG

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OBJECTIVE

To evaluate the diagnostic and clinical value of inpatient electromyography (EMG), identify technical limitations and review the neurological conditions diagnosed by inpatient EMG.

METHODS

Inpatient EMGs performed at our institution between October 2011 and November 2013 were retrospectively reviewed. Pre and post-test diagnoses, clinical management, safety, technical limitations, indication and demographics were analyzed. EMG was considered of significant value in cases where the study a) identified or excluded treatable disease; b) guided diagnostic studies; c) prevented additional evaluation; d) assessed treatment efficacy; e) aided prognostication; f) localized disease given complex or limited clinical examination.

RESULTS

102 studies were reviewed. The most common indication for EMG was weakness (77) and most were referred by the neurology service (84). A neurological etiology was found in 84 patients. Pre- and post-EMG diagnoses differed in 45 patients. Common diagnoses included chronic axonal neuropathy (21), critical illness myopathy/neuropathy (20), radiculopathy (12), inflammatory/necrotizing myopathy (8), motor neuron disease (7) and acute inflammatory demyelinating polyradiculoneuropathy (6). Common mononeuropathies were median (7) and peroneal (5). EMG detected upper motor neuron disease in 5 patients. 73 studies were thought to have significantly impacted management. 19 allowed for localization in patients with severe encephalopathy compromising clinical examination. 22 EMG-confirmed diagnoses led to aggressive immune therapy. 11 prompted inpatient muscle or nerve biopsy. Significant electrical artifact was present in 5 studies and 4 had slow conduction velocities from cool limb temperature. Other challenges included patients with significant encephalopathy (3), pain (2) or very acute disease (4). 5 studies were limited or non-diagnostic. No post-procedure complications were reported.

CONCLUSION

Inpatient EMG studies are safe, can be performed with minimal limitation, and often provide diagnostic clarity through precise localization. Electrodiagnostic studies frequently differ from pre-test clinical impression, often change management, and provide greater diagnostic certainty in hospitalized patients. A prospective study is underway.
P75
Analysis of clinical and neurophysiological features in patients with eosinophilic fasciitis

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Objective

Investigate clinical and neurophysiological features in patients with eosinophilic fasciitis in order to further enhance awareness of the disease.

Method

Two cases diagnosed as eosinophilic fasciitis were tested by neurophysiology, and retrospectively analyzed their clinical features and neurophysiological findings.

Results

Peripheral blood eosinophils were increased in 2 cases with hardening of skin and subcutaneous tissues, flexion contracture of hands, movement disorder of fingers and squat difficulties. One male patient, 10 years old, could not bounce, and toe joints of another 51-year-old male patient were buckling. Neurophysiological findings: Needle EMG showed that the insert potentials of muscles extended, and there were fibrillation potentials and positive sharp waves when resting and short-time, low-voltage potentials with increasing polyphase potentials in light contraction, and pathologic disturbances phase whose amplitude was lower than 2mv appeared in heavy contraction. Proximal muscles changed much more evident than the distal muscles. Nerve conduction velocity showed that motor and sensory nerve conduction velocities were normal in 10-year-old male patient, while the amplitude of compound muscle action potentials of lower limbs decreased in 51-year-old male patient, but the conduction was normal, as well as motor and sensory nerve conduction velocities of upper extremities. There were no obvious abnormalities in F waves.

Conclusions

Eosinophilic fasciitis mainly involves the distal joints without obvious weakness and Raynaud's phenomenon. The disease can affect the tendon sheath, which can lead to collagen and fibrosis, so that sometimes the tendons are obviously hard cords. There can be pain, tendon swelling and tenderness of joints. Neurophysiological changes are mainly myogenic damage, and sensory nerves are generally not involved.
Increased antagonist muscular activations in cervical SCI participants: Evidence of altered reciprocal inhibition during voluntary elbow contractions

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Voluntary contractions imply simultaneous activation of agonist and antagonist muscles necessary for both joint stability and for high movement precision. After a cervical Spinal Cord Injury (cSCI), studies have shown increased activation of antagonist muscles during voluntary or evoked contractions. It was hypothesized that this alteration could be the result of the muscular atrophy occurring after a cSCI, but studies on evoked contractions suggested it could be explained by reduced cortical control of reciprocal inhibition mechanism controlling activation of antagonist muscles. This study investigates to which extent the modulation of antagonist muscular activations in cSCI participants could be the result of altered reciprocal inhibition by analyzing the modulation of muscle activations during actual elbow flexion and extension, i.e. contractions that are intact or altered by the cSCI. We compared the net joint torque measured with a dynamometer and normalized agonist and antagonist muscle activations calculated from EMG of representative elbow extensors and flexors in 8 cSCI and 10 healthy participants performing actual isometric elbow flexion and extension contractions at 3 force levels. In flexion, the net torque was equivalent between groups and elbow extensors activation only was higher for the cSCI group. Increased extensors activation, acting as agonists, could be caused by both altered reciprocal inhibition and muscular atrophy occurring after cSCI. In extension, the net torque was lower and elbow extensors activation was higher for the cSCI group. When comparing muscle activations at similar net torque in extension, extensors and flexors activations were higher for the cSCI group. While increased extensors activation, acting as agonists, could still be explained by the muscular atrophy occurring after a cSCI, this is not the case for flexors muscles, which preserve its integrity despite the injury. The increased flexors activation, acting as antagonists, suggests that the alteration of the cortical control of the reciprocal inhibition mechanism is noticeable only when the sensory afferent feedbacks are equivalent. Overall, these results suppose that the reciprocal inhibition mechanism is more sensitive to the net torque actually produced rather than to the attempted force level.
Pelvic floor electrophysiology patterns associated with faecal incontinence

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Introduction

Pelvic floor electrophysiological tests are essential for assessment of patients with faecal incontinence.

Aim

The present study was conducted to determine the patterns of pelvic floor electrophysiology that are associated with faecal incontinence.

Subjects

The present study included 40 patients with faecal incontinence and 20 apparently healthy subjects as a control group.

Methods

All patients were subjected to history taking, clinical examination, proctosigmoidoscopy, anal manometry and electrophysiological studies. Electrophysiological studies included pudendal nerve motor conduction study, pudendo-anal reflex, needle electromyography of the external anal sphincter and puborectalis muscles, pudendal somatosensory evoked potential and tibial somatosensory evoked potential. The control group was subjected to electrophysiological studies which include pudendal nerve motor conduction study, pudendo anal reflex, pudendal somatosensory evoked potential and tibial somatosensory evoked potential.

Results

The most common pelvic floor electrodagnostic pattern characteristic of faecal incontinence was pudendal neuropathy, abnormal pudendo-anal reflex, denervation of the external anal
P78
The effect of new insole to decrease the spasticity for stroke patient by evaluating reciprocal inhibition from ankle dorsiflexion to ankle plantar flexors

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We develop a new insole to decrease the spasticity of lower extremities for stroke patients. The purpose of this study is to evaluate the effect of this insole.

8 stroke patient took part in this study. Control is age matched 6 cases.

Electromyography was used to measure a muscle activity during standing position with and without a new insole. Reciprocal inhibition from tibialis anterior (TA) to ankle flexors was measured. Subject performed a voluntary plantar flexion contraction. Effect of common peroneal nerve stimulation on the rectified and averaged stimulus-triggered soleus EMG was recorded. The short-latency reciprocal inhibition was seen at a latency of 40 msec after the stimulus. The amount of inhibition was expressed as percentage of inhibition.

The result showed that there was not significant difference between the short-latency reciprocal inhibition with(61.4±18.1%) and without(60.1±16.4%) insole for control subject. On the contrary, for stroke patients, the short-latency reciprocal inhibition with insole (69.0±4.1%) was significantly bigger compared with that without insole (83.7±4.9%).

These results suggest that this insole must reduce the spasticity for patients with stroke by recruiting reciprocal inhibition system.

figure 1

The amount of background of soleus EMG was measured as the average in a time window from 50 to 10ms before the stimulus. The short-latency reciprocal inhibition is seen at a latency of 40ms.
Fig. 2. Result of reciprocal inhibition without and with insole on soleus

4 times trial: without → with → without → with insole

without

with

The short-latency reciprocal inhibition with insole on soleus muscle is much bigger compared with that without insole.
Role of Electrodiagnosis in the management of chronic constipation due to pelvic outlet obstruction

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**Background**

The two major mechanisms of organic constipation are colonic slow transit and outlet obstruction. Anismus (spastic sphincter muscles) is one of the principal causes of outlet obstruction.

**Objective**

1) to evaluate the role of sphincter electromyography (EMG) and pudendal nerve terminal motor latencies (PNTMLs) in clarifying the pathogenesis of pelvic outlet obstruction; and 2) to assess the role of sphincter muscle botulinum toxin injection in treatment of anismus.

**Methodology**

47 adult patients and ten matched control volunteers were included in the study. Patients presented with chronic constipation due to pelvic outlet obstruction, selected according to Rome II criteria. The diagnosis was confirmed by proctosigmoidoscopy, defecography and anal manometry. Sphincter EMG of external anal sphincter (EAS), puborectalis (PR) and levator ani muscles were assessed during rest, squeezing and straining. Increased resting tone and failure of muscle relaxation during strain were considered as evidence of anismus. PNTMLs were measured using St Mark’s electrode.

30 patients were treated by a variety of surgical options according to the diagnosis. EMG guided local injection of botulinum toxin into spastic sphincter muscles were performed in 10 patients suffering from anismus. Disposable long hypodermic EMG monopolar needle electrode was used. The dose was adjusted for each muscle (50-100 units) according to the degree of muscle spasticity detected by EMG.

Patients were clinically followed up for 6 months; in addition EMG reassessment for injected patients was performed 4 weeks following injection.

**Results**

Rectal prolapse was the diagnosis in 16 patients (3 of them had EAS neuropathic changes), rectocele in 16 and anismus in 16 (table 1).

PNTMLs are significantly delayed in patients with anismus. There was a statistically significance clinical (figure 1) and EMG improvement after botulinum toxin injection in 8 patients. Improvement lasted for 12-20 weeks. No adverse systemic or local effects were recorded.

**Conclusion**

electrodiagnostic tests are greatly helpful in the diagnosis of anismus, and in detecting sphincter muscle weakness which helps guiding surgeons to the type of operation. Local botulinum toxin injection represents a useful safe addition to the few available therapeutic options for anismus.
Abstracts of Poster Presentations – Poster Session 5 – EMG 1

figure 1

<table>
<thead>
<tr>
<th>Item</th>
<th>Patients Mean ± SD</th>
<th>Controls Mean ± SD</th>
<th>t</th>
<th>p</th>
<th>Sig.</th>
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<td>*Resting activity (ms/4)</td>
<td>26.4 ± 14.6</td>
<td>8 ± 2.02</td>
<td>2.71</td>
<td>0.02</td>
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<tr>
<td>A/T (uV)</td>
<td>265 ± 30.66</td>
<td>166 ± 7.42</td>
<td>2.53</td>
<td>0.02</td>
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<td>T/A</td>
<td>178.4 ± 33.71</td>
<td>85.8 ± 22.05</td>
<td>2.42</td>
<td>0.03</td>
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<tr>
<td>*Squeezing activity (ms/4)</td>
<td>433.6 ± 188.65</td>
<td>363.6 ± 5.63</td>
<td>0.63</td>
<td>0.54</td>
<td>NS</td>
</tr>
<tr>
<td>A/T (uV)</td>
<td>618 ± 293.68</td>
<td>528 ± 87.07</td>
<td>0.81</td>
<td>0.41</td>
<td>NS</td>
</tr>
<tr>
<td>T/A</td>
<td>425.6 ± 188.67</td>
<td>390.6 ± 6.7</td>
<td>1.03</td>
<td>0.33</td>
<td>NS</td>
</tr>
<tr>
<td>*Exerting activity (ms/4)</td>
<td>16.8 ± 36.44</td>
<td>10 ± 2.02</td>
<td>2.33</td>
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<tr>
<td>A/T (uV)</td>
<td>279 ± 72.83</td>
<td>261 ± 18.29</td>
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<td>0.78</td>
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<td>T/A</td>
<td>215.9 ± 108.06</td>
<td>140 ± 7.94</td>
<td>2.33</td>
<td>0.04</td>
<td>S</td>
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</table>

Table 1: EMG data of the FPR muscle in patients (with spastic FPR) and controls

figure 2

Figure 1: Comparison of clinical data before and after injection of botulinum toxin.
P80
Comparison of classical time analysis, wavelet and "cloud" methods in neurogenic and myogenic conditions

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The subject of intensive study over the past few years has been the search for new diagnostic methods that would enable a more accurate analysis of electromyographic signal, which would lead to proper classification of motor unit action potential (MUAP). As a result of this pursuit a new diagnostic parameter called wavelet index (WI) was defined. The aim of the study was to:

- estimate the muscle function in health and in various neurogenic and myogenic conditions by means of QEMG, wavelet analysis and automated interference pattern analysis modified by Stalberg (turns and amplitude analysis - so called cloud);

- compare the sensitivity and specificity of wavelet index with parameters used so far for motor action potential classification as well as with the diagnosis based on cloud analysis in order to estimate the muscle pathology in various diseases.

Methods 372 subjects, both outpatients and inpatients, were examined in order to establish the reference values. After the norms for individual muscles had been established, 50 healthy subjects from the test group were tested as a screen for potential diseases. The next step was to examine 22 patients with primary muscular disorders and 38 patients with muscle dysfunction of neurogenic origin. On the basis of the aforementioned tests the sensitivity and specificity of wavelet index was estimated as follows:

Results - for brachial biceps muscle - in myogenic cases: sensitivity 0,5, specificity 0,95; in neurogenic cases: sensitivity 0,84, specificity 1,0;

- for the first dorsal interosseus muscle - in myogenic cases: sensitivity 0,5, specificity 1,0; in neurogenic cases: sensitivity 1,0, specificity 1,0;

- for lateral vastus muscle - in myogenic cases: sensitivity 0,43, specificity 1,0; in neurogenic cases: sensitivity 0,94, specificity 0,87;

- for anterior tibial muscle - in myogenic cases: sensitivity 0,57, specificity 0,95; in neurogenic cases: sensitivity 0,97, specificity 0,79.
P81
Critical illness polyneuropathy with demyelination caused by central nervous system infection

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Question

Critical illness polyneuropathy (CIP) is manifested mainly as damage to axons of nerve fibers, and the myelin sheath usually is not involved.

Methods

Herein we describe one case of CIP with demyelinating disease caused by central nervous system (CNS) infection and present the findings of electromyography and neuromuscular biopsies.

Results

This CIP case exhibited damaged peripheral nerve axons and demyelination of peripheral nerves. Electromyography revealed decreased amplitudes of compound muscle action potential (CMAP) of the upper and lower extremities; the motor conduction velocity of the tibial nerves and common peroneal nerves of the lower extremities was lowered; the F waves of the median and ulnar nerves were undetectable. Sensory nerve examination revealed no abnormalities. Needle electrode examination showed a large number of fibrillation potentials and positive sharp waves. A biopsy of the tibialis anterior muscle showed small angular fibers, insignificant muscle fiber necrosis or regeneration, and inflammatory infiltration. Sural nerve biopsy showed that the number of myelinated nerve fibers was reduced and that some nerve fibers had segmental demyelination and axon degeneration. Electromyography repeated two weeks later revealed that the median and ulnar nerve F waves had an occurrence rate of 100%, with a significantly prolonged latency.

Conclusion

Further research of CIP patients together with systematic electrophysiological studies on nerves and neuromuscular pathological studies will be of great significance in determining the presence of demyelination of peripheral nerves in CIP and in understanding the pathogenesis of CIP.
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P82
The relation between fiber density and macro EMG amplitude in reinnervation

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Objective

To elucidate the relation between the Macro EMG parameters fiber density (FD) and the Macro amplitude in reinnervation in the purpose to use the FD parameter as a surrogate marker for reinnervation instead of the Macro amplitude.

Methods

Macro EMG were performed in old polio patients which showed a broad range of reinnervation measured as increase in age matched FD and Macro amplitude. The Biceps Brachii and the Tibialis anterior muscles were investigated.

Results

FD and Macro MUP amplitude showed a non-linear correlation for both muscles. Also a great spread of various FD for a given Macro amplitude level was present. FD was more sensitive for changes but showed lesser degree of pathology than the Macro amplitude.

Conclusion

There is a non-linear relation between the FD and the Macro MUP amplitude in the Macro EMG recordings regarding reinnervation in old polio. This non-linear relationship was due to technical reasons and may also be an effect from muscle hypertrophy, the later may also cause the great spread of the parameters.

Significance

The FD parameter has a relation to Macro MUP amplitude but cannot alone be used as a quantitative marker of reinnervation.
P83
PROPOSAL FOR REVISION OF AN OLD CONCEPT IN CONDUCTION STUDIES.

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Introduction

Changes of physiological parameters are expected to occur with aging [1, 2]. Usually latencies are referred as prolonged, amplitudes smaller and velocities slower than in adults under 60 years. Our present data disagree with this old concept.

Objective

To describe normal values of the conduction nerve studies (CNS) in patients over 70 years old.

Methods

Retrospective study of patients over 70 years old that underwent CNS for routine diagnosis of upper and/or lower limbs common diseases. For upper limbs disorders, normal values of the lower limbs were obtained and for lower limbs disorders, normal values of the upper limbs were used. Ulnar, median, superficial peroneal and deep peroneal nerves were studied. Sensory and motor latencies, amplitudes and velocities were evaluated.

Results

The age ranged from 74 to 94 years old. Sixty four nerves were studied, 14 were from upper limbs. The sensory amplitude of the ulnar ranged from 16 to 42 µV, of the median from 18 to 50 µV. On upper limbs velocities varied from 51 to 62 m/s. On lower limbs, velocities varied from 40 to 57 m/s. Latencies, amplitudes and velocities for the deep peroneal ranged from 2.9 to 5.0 ms, 1.7 to 9.6 mV and from 40 to 51 m/s, respectively.

Discussion

Old and modern text books and papers about conduction studies reported that latencies are prolonged, amplitudes are lower and velocities are slower in elderly than in young people [3, 4]. We propose revision of this old concept and would like to request assistance of other neurophysiologists for this purpose.

References


Legends
Abstracts of Poster Presentations – Poster Session 5 – EMG 1

Table 1 - Sensory CNS on the upper and lower limbs from old age patients.

Table 2 - Motor CNS on the lower limbs from old age patients.

**figure 1**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (years)</th>
<th>Velocity (m/s)</th>
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Surround inhibition phenomenon tested by the method of cutaneous silent period

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Purpose

Surround inhibition (SI) is a physiological mechanism that simply provides the quality of sensory input and motor output of the nervous system. SI was previously tested by somatosensory evoked potential (SEP). We have aimed to apply SI phenomenon with the cutaneous silent period (CSP) which is a cutaneomuscular spinal inhibitory reflex mediated by A delta fibers.

Methods

Eleven healthy subjects (35-47 years), were evaluated in this study. Nociceptive stimulation was applied to digit II (Median nerve-M) and V (Ulnar nerve-U) as individually and two nerve stimulation at the same time. Four CSP responses were recorded in APB and ADM muscles of right hand. Cortical SEP(N20) responses were recorded following M and U stimulation as individually and together as well.

Results

CSP and SEP were elicited in all subjects. Latency and duration of the SP on the M-APB, U-APB and M+U-APB were respectively (81.6+14.4/38+12.6), (78.3+6.9/39.9+6.7) and (60.8+11.5/44.9+12.5). N20 SEP latencies and amplitudes were found as (20.5+1.1/1.5+0.6), (20.8+1.5/1+0.2) and (21+0.9/1.7+0.7) by the same manner.

Discussion

Amplitudes of N20, obtained by stimulation (M+U), were smaller than the arithmetic sum of the values obtained by the stimulation each of M and U, which was also demonstrated in previous studies. Durations of CSP intervals, with stimulation of (M+U) nerves, are shorter than the arithmetic sum of the values obtained by individual stimulations of M and U nerves. These results lead to a suggestion that CSP may be an alternative method for the demonstration of SI phenomenon.

Keywords

Cutaneous silent period (CSP), Surround inhibition (SI)
P85
Electrophysiological Study in MELAS Patients

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QUESTION
To investigate the electrophysiological features of patients with MELAS.

METHODS
Needle electromyography (EMG) and nerve conduction study (NCS) were performed in 21 patients who were diagnosed with MELAS according to the published diagnostic criteria in 1996 during the last decade.

RESULTS
Needle EMG showed myopathic change in 9 (42.86%) patients, with 6 (66.67%) of them exhibiting muscle weakness. Only 1 (4.76%) of the 9 patients demonstrated neurogenic damage by needle EMG. Less fibrillation potentials and positive sharp waves were found in two of the nine cases. NCS were abnormal in 3 (14.29%) patients without clinical evidence of neuropathy. Among which, demyelinating change was found in two and axonal damage in one.

CONCLUSIONS
In our MELAS patients, needle EMG revealed myopathic change in 42.86% and neurogenic damage in 4.76%, and literature reported in mitochondrial encephalomyopathies were myopathic change in 40%-60% cases and neurogenic damage in 9%-40% cases. Less fibrillation potentials and positive sharp waves were detected in two of the nine cases with myopathic change. Needle EMG showed myopathic change in 3 cases without clinical muscle weakness, which indicates needle EMG can detect subclinical mild muscle fiber damage. Nerve conduction study may verify subclinical nerve fiber damage, either demyelinating or axonal, in MELAS patients without clinical evidence of neuropathy.
Abstracts of Poster Presentations – Poster Session 5 – EMG 1

P86
EMG Guided Botox Therapy in the External Anal Sphincter during 2000-2010

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Introduction

This retrospective study comprises 106 adult persons, referred from the Department of Surgery at our hospital for treatment trial with botulinum toxin in the external anal sphincter during the years 2000-2010. The majority of the patients suffered from chronic anal fissure (n=85; 80.2 %), and had tried several pharmacological treatments before the referral. The remaining diagnoses were anal spasm and pain in 16 subjects (15.1%) and severe constipation of different origin in five (4.7%).

The material consisted of 59 females (mean and median ages 39.6 and 42 years respectively; range 17-73) and 47 males (mean and median ages 48.4 and 48 years respectively; range 20-82).

Method

EMG guided insertions in the external anal sphincter (EAS) were made with a concentric needle electrode which were adjusted for injection purpose. Each side of EAS was investigated as to activity and appearance of motor unit potentials, and with the needle in optimal position botulinum toxin A was injected. Number of units injected depended on the size of the subject and the degree of symptoms. Most subjects were given a starting dose of 10 or 15 units in each side of EAS, hence a total dose of 20 or 30 units. If further treatment was indicated at follow-up by the referring physician, the dose was adjusted if necessary.

Results

Of all subjects 57 (53.8%) got sufficient relief after one treatment, and needed no further botox therapy. One treatment was sufficient to the same degree in females (31/59, 52.2%) and males (26/47, 55.3%). Two treatments were given to 28 subjects (26.4%; 15 females and 13 males). Hence, 80.2% of patients were helped by one or two treatment sessions with botox. However, there were subjects who needed further treatment sessions; two females and two males needed longterm treatment with at the most 12 treatments. In many patients life-styles changes were pointed out and added to the pharmacological therapy. No patient had adverse effects of the botox therapy.

Conclusion

Botox therapy is one of the treatment options for chronic anal fissure, anal spasm and pain and severe outlet obstruction. In this material covering a period of 11 years with EMG guided botox therapy to 106 patients, of whom the large majority had chronic anal fissure, botox treatment in EAS proved to be an effective and safe treatment.
AMPLITUDES OF POSITIVE SHARP WAVES AND FIBRILLATION POTENTIALS: DO THEY HAVE CLINICAL IMPORTANCE?

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Introduction

Fibrillation potentials and positive sharp waves are spontaneous potentials originate from individual muscle fibers in case of loss of axonal connection. They have unique morphologies and sounds. In daily routine practice, density of spontaneous potentials is assessed by a semiquantitative method. Here, we aimed to test importance of amplitudes of spontaneous denervation potentials and their relation with clinical features.

Patients and Method

This is a cross-sectional study conducted among patients who were referred for electrophysiological investigation due to development of motor deficit and/or pain and able to declare the exact time of that motor deficit and/or pain. Patients with weakness attributed to muscle or neuromuscular junction disorder were excluded. Age, disease duration, muscle groups and level of lesion were recorded.

Results

A total of 66 patients and 113 muscles were included in the study. Mean age was 45.9±17.4 years and there were 44 male patients (66.7%). Amplitudes of fibrillation and positive sharp waves were higher in males (p_{fib}=0.011, p_{psw}=0.016), in patients with disease duration of less than two months (p_{fib}=0.001, p_{psw}=0.005) and plexus/radicular lesions (p_{fib}=0.034, p_{psw}=0.002). Amplitudes of positive waves were also higher in muscles with larger sizes (p=0.015). Regression analyses showed that amplitudes of both fibrillation potentials and positive sharp waves were related to gender (p_{fib}=0.016 and p_{psw}=0.014) and disease duration (p_{fib}=0.005 and p_{psw}=0.021).

Conclusions

Direct relationship between spontaneous potential amplitude and muscle fiber size has been known. Besides, amplitudes were thought to be inversely related to the distance from recording electrode and disease duration. Muscle fibers that were denervated for a long time without reinnervation would undergo atrophy and hence generate low-amplitude fibrillation potential and positive sharp waves. Therefore measuring the spontaneous potential amplitude which is simple, convenient, inexpensive, fast, and repeatable procedure was suggested to determine evolution of atrophy and clinical outcome. Amplitudes of spontaneous denervation potentials could be used as a confidential parameter to reflect chronicity. Still, parameters like gender and patient age should be kept in mind while interpreting the amplitude of denervation potentials in regard to predict chronicity and thereby prognosis.
E-Norms: A novel technique to extrapolate normal values from a patient population data

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Question

Normal ranges of many biomedical values are unavailable for some subpopulations—such as infants and children—due to extra burden the measurement may inflict on these cohorts. Since these values are unlikely to be obtained through epidemiologic studies, innovations in estimating normal ranges from other sources may serve to provide some insight. We present a scenario to derive a hypothetical reference range using a technique we developed and refer to as extrapolated norms or e-norms.

Methods

To derive reference values from a patient population, the data are collected, sorted by ascending order and compiled into a line graph with values plotted against the ranks of the order. This results in an inverted S-shaped curve that has three distinguishable parts: a relatively steep line at the lower left, transitioning into a relatively flat portion resembling a beam at the middle, and ascending into another steep portion at the upper right. We theorize that the beam of the curve contains data that approximates reference values derived from individuals whose study results do not reveal the condition they were referred for. We consider that the two steep lines represent values that lie outside this reference range. Using second derivative, followed by conservatively selecting the highest 50% of the data points as the constituents of the beam, we pool the data that lie within this defined beam and use them to derive mean and standard deviation to calculate an e-norm of these reference values.

Results

Simulations followed by visual confirmations showed that the 50% threshold could isolate the beam of a curve in distributions that are normal and mildly skewed. Our method was tried with various sets of laboratory data, including nerve conductions and SFEMG data, and revealed findings that closely correlated with reference data collected from healthy subjects.

Conclusion

The method we describe to derive e-norms from a patient population data appears to be robust against extreme values and can be useful in recovering normal ranges from a less-than-normal cohort. While there is a great potential in using the e-norms method, more validations in different biomedical markers as well as clinical validation are needed to confirm our hypothesis.
P89
Do higher proximal ulnar nerve compound muscle action potentials result from higher conduction velocities of axons mediating the second of its two negative peaks?

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Introduction

Compound muscle action potentials (CMAP) in the belly-tendon (BT-CMAP) montage typically has two distinct negative peaks. The first one, detected by the belly electrode (B-CMAP), represents mainly the near-field potentials of the hypothenar muscles while the second one corresponds to the far-field potentials generated by the interossei and other deep ulnar nerve motor branch-innervated muscles as detected by the tendon electrode (T-CMAP). Some people have bigger CMAPs after elbow and not wrist ulnar nerve stimulation. We hypothesised that in this case the axons innervating muscles on the radial side of the hand conduct faster compared to those innervating hypothenar muscles.

Methods

Sixty-eight ulnar nerves of 34 healthy subjects (18 females) were studied. BT-CMAP, B-CMAP and T-CMAP were simultaneously recorded to wrist and elbow ulnar nerve stimulations. Conduction velocities were calculated for each of the two negative peaks of the BT-CMAPs (CV1 and 2), for the negative peak of the B-CMAP (CV3), and for the positive peak of the T-CMAP (CV4).

Results

Bigger proximal BT-CMAP amplitudes were associated with higher CV4 compared to CV3 and vice versa (p = 0.012) while the distal to proximal peak 1 to peak 2 BT-CMAP latency differences negatively correlated with CV1-CV2 (p = 0.0001) and CV3-CV4 (p = 0.0013).

Conclusion

Higher conduction velocities of the second BT-CMAP peak compared to the first one can result in bigger elbow than wrist CMAP amplitudes.
Electromyographic findings in statin induced myopathy and neuropathy

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Question

Statins are frequently used lipid-lowering agents and rhabdomyolysis is a rare but well documented complication. Literature reviewing also showed development of neuropathy in chronic statin users. Will neuropathy developed in the acute stage of statin induced rhabdomyolysis?

Methods

We compare and discuss serial electromyographic and muscle biopsy findings in two cases of statin induced rhabdomyolysis.

Results

Both patients were aged 60 to 70, with multiple metabolic diseases. Proximal weakness, impaired respiratory function, and high creatine kinase level were presented at acute stage. At first electromyographic findings showed reduced motor conduction velocities and lower amplitudes, marked fibrillations, myotonic discharges, increased polyphasias and small motor unit potentials, and mixed with some large motor unit potentials. The first impression was severe active axonal neuropathy with possible myopathy. In the recovering stage, the marked fibrillations persisted, but the motor conductions and amplitudes returned to normal. The fibrillations disappeared and more large motor units presented in the later follow-up studies. The muscle biopsy at acute stage revealed diffuse infiltration of inflammatory cells around muscle fibers, but the nerve endings were intact.

Conclusions

Giving the severe fibrillations and slower conduction, the electromyographic findings may be confusing in acute stage of statin induced rhabdomyolysis. The active neuropathy picture disappeared subsequently and a chronic neuropathy picture developed in the follow-up studies. Because muscle biopsy findings showed severe myopathy without evidence of neuropathy, the marked fibrillations were explained by acute reversible membrane irritation in myopathic disorder. The chronic reinnervating change in the follow-up electromyographic studies may be due to metabolic disorders or aging effects.
**P91**

The most appropriate window width for the “Clustering index method”.

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⁵Fukushima Medical University, Neurology, Fukushima, Japan
⁶Sapporo Azabu Neurosurgical Hospital, Neurosurgery, Sapporo, Japan

**Question**

Clustering index (CI) method is a noninvasive and quantitative analysis method of single channel surface EMG (SEMG) for diagnosing neurogenic and myopathic changes. This index aims to evaluate how the total area of the SEMG signals is clustered into large single motor unit potentials (MUPs). For this purpose, unitary windows with an appropriate width need to be set out. In the first study applying this method to the tibialis anterior (TA) muscle, the window width was determined as 15 ms, so that the window would cover large single MUPs observed in this muscle. In the second study done in the abductor digiti minimi (ADM) muscle, the window width was determined as 7.5 ms so that it would achieve the best discrimination between normal and neurogenic signals. The latter approach has not been attempted for the TA muscle and there may be a more appropriate window width. In this study, we aimed to find out the most appropriate window width for the CI method at the TA muscle.

**Methods**

Signals collected in the previous study and some newly-collected materials were reanalyzed. Re-evaluated subjects were 65 normal volunteers, 13 patients with neurogenic disorders, and 20 patients with myopathic disorders. The CI values were calculated using different window widths from 5 to 27.5 ms at the interval of 2.5 ms. The Z-score of the mean residual values after linear regression for the normative data was calculated for each subject. Because we expected that this method is sensitive for both neurogenic and myopathic subjects, the sum of mean absolute values of Z-scores for neurogenic and myopathic subjects were used as a primary indicator.

**Results**

The sum of mean absolute Z-score values was highest when the window width was set at 17.5 ms (7.65; 4.31±1.34 for neurogenic subjects and -3.33±1.84 for myopathic subjects). Using this window width, the sensitivities for neurogenic and myopathic patients were 100% and 65%, respectively. The specificity for control subjects was 97%.

**Conclusion**

The most appropriate window width in the CI method for the TA muscle seems to be 17.5 ms.
**P92**  
The impact of double stimulation on F-wave for evaluation of upper motor neuron dysfunction.

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**Question**

Whether F-wave elicited by double stimulation is useful to evaluate spinal excitability in spastic patients?

**Methods**

1) To remind the F-wave change in supra-maximal double stimulation in median nerve, inter-stimulus interval (ISI) of 10 to 500ms were given in 9 healthy controls. 2) To clarify whether the sensory conditioning affects F-wave in ulnar nerve, sub-motor threshold conditioning stimulation to the fifth digit and supra-maximal test stimulation were done in 8 healthy controls. 3) To investigate the effects of supra-maximal double stimulation on F-wave in spastic patients, supra-maximal double shocks of 50ms ISI in median nerve was delivered in 9 cervical myelopathy (CM), 6 spastic quadriplegia (SQ) including primary lateral sclerosis and 22 healthy controls. One hundred consecutive double stimuli were given in all examination and F-wave frequency was calculated.

**Results**

1) F-wave frequency with supra-maximal double stimulation was clearly reduced at 20-70ms ISI (p<0.01) in controls. 2) There was no significant difference for F-wave frequency when sub-motor threshold conditioning was given. 3) F-wave frequency at 50ms ISI in CM and SQ were significantly higher (p<0.01) than in healthy controls.

**Conclusions**

The reduction of frequency with double stimulation at 20-70ms ISI including 50ms ISI was occurred only with motor conditioning input to the spinal cord in healthy controls. This means only preceding Ia input can affect spinal excitability via inhibitory interneuron in central nervous system. The release of frequency reduction at 50ms ISI in spastic patients indicates that this method has an impact to detect upper motor neuron dysfunction by F-wave study.
P93
Dysphagia and Autonomic Functions in Alzheimer's Disease

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Question
The purpose of this study was to investigate oropharyngeal swallowing parameters in Alzheimer’s disease (AD) using electrophysiological methods in correlation with autonomic functions.

Method
Forty AD patients, 20 age-matched normal controls (NC) and 20 young NC were included in the study. Dysphagia limit (DL) and sequential water swallowing (SWS) tests were used for evaluation. Cardiac rhythm, respiration and sympathetic skin responses (SSR) were synchronously recorded.

Results
Dysphagia was found in 30/40 (75%) of AD patients and mean DL was 16.5±1.01mL in AD group where it was >25mL in control subjects. Cardiac rhythm was found to be accelerated during swallowing apnea in all groups. Mean swallowing times were 8.41s, 6.22s and 5.50s, and swallowing apnea times were 8.82s, 6.3s, and 5.57s, in AD, old NC and young NC, respectively (p<0.05). During swallowing, triggered SSR occurred in 95% of subjects in both of NC groups, and only in 55% of AD patients.

Conclusions
Although without any complaint about swallowing, AD patients were found have dysphagia in electrophysiological studies. In the elderly, some electrophysiological changes were found to occur during swallowing when compared to young people. Swallowing time was found to be prolonged in elderly but much more prolonged in AD. Swallowing triggered SSR was also found to be disturbed in almost half of AD patients.
P431
Sympathetic Skin Response Latency Difference Between Multiple Sclerosis Patients and Normal Controls During Sequential Water Swallowing

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Question

Sympathetic skin responses (SSRs) are recorded in response to electrical shocks to major peripheral nerves and also be evoked by other types of stimuli. During sequential water swallowing (SWS), an arousal SSR can be produced. The interval between first swallow and SSR was found important related with central demyelination. This interval in Multiple Sclerosis patients was compared with normal control subjects during SWS.

Methods

Thirty-one RRMS patients (mean age 32.3), 20 MS attack patients (31.9) and 20 normal controls (31.2) were included in the study. Attack patients were reevaluated after attack was resolved. Dysphagia limit (DL) and SWS studies were done. DL and SSR latencies during SWS of all groups were recorded and statistical analysis was done by using SPSS.

Results

Mean DL was 19 ml in attack patients, 19.5 ml after the attack, 17 ml in other MS patients. During SWS, SSR latency in normals was 1.18 sec, in patients without attack was 2.07 sec, it was 1.72 sec during attack, 1.92 sec after the attack. All MS patients groups had longer latecies when compared with normals and this was statistically significant (p<0.05). Also, there was a statistically significant difference between two MS groups (after attack group and without attack group).

Conclusions

Probably because of central demyelination SSR latencies were found to be longer than normals. But it was interesting that without attack group had the longest latency time. Without attack group’s disease duration was longer than attack group. Progress in the disease may cause SSR latency difference. Central mechanism of this pathology needs discussion.
validity of the 50% rule for the nerve conduction study of the lower-limb

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Questions: For nerve conduction studies (NCSs), the 50% rule in the interside variation of the amplitude has been widely used for judging abnormality. However, there have been few reports that actually investigated this issue for individual nerves. In our preceding study, we demonstrated that 50% rule is not always applicable for the lateral antebrachial cutaneous nerve. The aim of this study is to test the validity of the 50% rule in lower-limb nerves.

Methods: Subjects were 30 healthy volunteers (17 men and 13 women, 25–93 years). Motor NCS was examined at the tibial nerve and the fibular nerve recorded at the extensor digitorum brevis (EDB) muscle and at the tibialis anterior (TA) muscle. Sensory NCS was examined at the sural nerve (antidromic and orthodromic methods), superficial fibular nerve, and the medial planter nerve. Both sides were examined for each nerve. The peak-to-peak amplitude of the compound muscle action potential (CMAP) or the sensory nerve action potential (SNAP) was measured and was compared between both sides.

Results: The amplitude difference between both sides was less than 50% for all subjects only for the CMAP of the tibial nerve (maximal difference: 35%) and the fibular nerve recorded at TA (max 32%). The amplitude difference exceeded 50% in 23% of subjects for the CMAP of the fibular nerve recorded at EDB (max 95%), in 7% of subjects for the antidromic SNAP of the sural nerve (max 69%), in 3% of subjects for the orthodromic SNAP of the sural nerve (73%), and in 20% of subjects for the SNAP of the superficial fibular nerve (max 83% and unrecordable at one side for 1 subject). For the SNAP of the medial planter nerve, side difference exceeded 50% in 3% of subjects (69%) and both sides were unrecordable in 7% of subjects.

Conclusions: The 50% rule should be applied with caution for most of the lower-limb nerves.
P94

Jaw jerks and a brief brain “twinkle” while reading

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Keywords

Reflex epilepsy, Reading epilepsy, EEG

Case report

At the age of 17, a Caucasian woman firstly experienced repetitive episodes of jaw jerks reproducible by reading for about one minute. She was diagnosed as a case of anxiety-disorder and was treated psychotherapeutically over a period of 9 years. However, no improvement was achieved, but the patient developed anxiety towards reading of all forms of text. She was able to control symptoms only when she immediately disrupted reading for a few seconds. Nevertheless, sometimes she felt a slight alteration of consciousness what she called a short brain “twinkle”. The disorder led to significant social and educational problems.

Whilst reading at night the patient developed a first generalized seizure at the age of 26 and was admitted to our emergency unit. She presented with a bilateral ocular hematoma, whereas the neurological status was intact. Laboratory examination was normal except for moderately elevated creatine kinase levels. The patients’ medical history revealed no vascular risk factors, drug abuse or major illness.

Investigation included cranial MRI, standard EEG, sleep-deprived EEG, and reading-provoked EEG. After 3, 5 and 7 minutes of reading jaw jerks occurred and corresponding generalized transient 3-4/sec spike wave complexes followed by generalized rhythm-deceleration were detected. Thus, the present disorder was regarded as a reading epilepsy.

Conclusions

Bickford and colleagues first described reading epilepsy in 1954. Meanwhile, only some more than 100 cases have been published. A primary and a secondary type of reading epilepsy have been distinguished. This presented case was classified as a primary form and highlights the importance of early diagnosis and treatment in order to prevent patients from negative social and educational impact.

References

How benign are the "Benign" Partial Epilepsies? The role of electroencephalography in determining the outcome of children with Benign Partial Epileptic syndromes

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Question

The childhood benign focal epilepsies are a group of genetically determined epileptic syndromes, mainly consisting in Benign Epilepsy with Centrotemporal Spikes (BECTS) and Benign Occipital Epilepsy. Tipically, these syndromes are associated with an overall good outcome with remission of seizures before 14 to 18 years, normal imaging studies, as well as a normal psychosocial development of the child. This is the reason why they have been classified as „benign” occurrences at an early age, with remission in a few years, leaving no sequelae. However, as links between electrical status epilepticus in sleep (ESES) patterns and the activation of epileptiform discharges with sleep in these syndromes are being drawn, we consider it important to determine what is the impact of the interictal epileptiform activity, mainly in the form of sleep - induced activity, on the mental performances of these children and their psychoemotional development, over time.

Methods

We have analyzed the cases of ten children with BECTS and two children with benign occipital epilepsy, by determining the frequency of their seizures, the types of seizures encountered, the electroencephalographic recordings during sleep and by evaluating their cognitive and psychoemotional status.

Results

The types of seizures encountered were polymorphic, with a large variability within the same syndrome and atypical clinical manifestations for the form of epilepsy in question. A part of the children displayed an important pattern of activation of epileptiform discharges during sleep, which was correlated to periods of emotional and behavioral abnormalities and some degree of cognitive decline manifesting with lowering of school performance.

Conclusions

Clasically, syndromes classified as „benign” were thought to have no impact on the child’s development and little emphasis was put on the electroencephalographic recording, as long as the clinical evolution was favorable. However, lately, as activation of epileptiform discharges with sleep in these syndromes are possibly progressing towards ESES, more attention needs to be paid to the child’s cognitive abilities and the possible decline in this area over time, also taking into account and weighing the benefits and risks of antiepileptic medication.
P96
Age-specific characteristics of seizures, ictal encephalographic (EEG) pattern and postictal
generalized EEG suppression in Dravet syndrome

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Question

How do seizures of Dravet syndrome (DS) change with age in their electroencephalographic (EEG) features and phenotype?

Methods

Review of electroclinical features of 63 seizures in 23 patients with DS using 24-hour video-EEG in three
different age groups: group 1 (0 - 5 years old); group 2 (6 - 10 years old); and group 3 (11 or above).

Results

Included 7, 11 and 5 patients in groups 1, 2, and 3 respectively. Younger children were more likely to have
provoked seizures (p = 0.05) while awake (p = 0.005), seizures preceded by myoclonus (p = 0.04) and
focal seizure semiology (p = 0.02) with long seizure duration (> 3 min., p = 0.0004). Older children were
more likely to have seizures from sleep (p = 0.004), generalized seizure semiology (p = 0.01) and short
seizure duration (< 1 min., p = 0.0007). A generalized discharge was the most commonly observed ictal
EEG pattern (15/23, 65%), and was more frequently found in older children (p = 0.01). Overall, 44% of
patients (10/23) showed unclassifiable seizures or seizures with discordant EEG findings. Postictal EEG
suppression was found in 11 (48%) patients.

Conclusions

Three main points emerged. Seizures changed with age in their phenotype, duration, and EEG features.
Seizures often defied characterization as focal or generalized, as presentation was mixed. The convulsions
seldom qualified as simple generalized tonic-clonic. Nearly half of our patients had generalized convulsive
seizures followed by postictal EEG suppression, a possible biomarker for sudden unexpected death in
epilepsy.
P97
Frontal lobe epilepsy versus NREM sleep parasomnia: Clinical and EEG characteristics

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Background
Nocturnal paroxysmal events may be characterized clinically, and by video EEG and video polysomnographic recordings, but even when applied rigorously it is often difficult to distinguish between frontal lobe epilepsy (FLE) and NREM parasomnia (NREM-P).

Aim of study
To assess the value of high frequency EEG synchronization during pre-ictal state in order to differentiate between FLE and NREM-P.

Methods
We analyzed the clinical features as well as macroscopic EEG and polysomnographic recordings of 12 patients with frontal lobe epilepsy and 12 patients with NREM parasomnia. Short time Fast Fourier Transformation (FFT), spectral data analysis as well as spectral coherences were evaluated among all electrodes at 1-10 seconds prior to the nocturnal episode in both patient groups.

Results
Evaluation of clinical features of frontal lobe seizures and NREM parasomnia events showed significant differences between the two groups. FLE seizures had shorter duration (<2 min), higher frequency per night (mean 9.75+3.9) as well as per month (mean 22.75+8) as compared to NREM-P events (mean 4.33+3.9 and 15.6+12.6 respectively). The semiology of FLE seizures were more stereotyped (p<0.0001) than NREM-P attacks with higher incidence of dystonic or tonic posturing and abrupt offset with recollection (p=0.011) of the event. In comparison, the semiology of NREM-P events was heterogenous, with a more gradual offset and with the patient often going back to sleep and having only a vague or no recollection of the event. Our results were consistent with a higher positive FLEP scale in FLE (mean 5.42+2.3) as compared to NREM-P (mean -2.65+3.6). No abnormal rhythmic activity was observed in the macroscopic EEG recordings of most patients (FLE 58% n=7, NREM-P 92% n=11). In contrast, FFT analysis of the EEG signal showed remarkable increases of phase coherence in the high frequency beta and gamma range, mainly occurring around the frontal areas in patients with FLE prior to seizures. This was not observed in patients with NREM sleep parasomnia patients.

Conclusion
The clinical features of FLE and NREM sleep parasomnia differ importantly. In addition EEG signal analysis with focus on the high-frequency EEG bands is a useful tool in distinguishing between nocturnal events.

Glossary
FLE - frontal lobe epilepsy
REM - rapid eye movement, NREM - non-REM
Methionine-enriched diet increases susceptibility of rats to epilepsy: the role of sodium - potassium pump

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**Question**

Methionine is a sulfur-containing essential amino acid. Its metabolism is closely related with those of homocysteine, common risk factor for variety of disorders. Its involvement in regulation of hyperexcitability has been recently recognized, but not completely understood. The aim of this study was to examine the effects of methionine nutritional overload on susceptibility of rats to homocysteine-thiolactone-induced epileptic activity in rats and contribution of brain Na\(^+\)/K\(^-\)-ATPase (sodium pump) activity in these effects.

**Methods**

Male Wistar rats were randomly divided into control and experimental group, fed from 30\(^{th}\) to 60\(^{th}\) postnatal day with standard or methionine-enriched diet (double content comparing to standard, 7.7 g/kg), respectively. A single subconvulsive dose of D, L homocysteine-thiolactone (HCT, 5.5 mmol/kg, i.p) was used to challenge epileptic activity in these rats. Convulsive behavior was assessed by seizure incidence, latency time to first seizure, number and intensity of seizure episodes during 90 min post injection. Sodium pump activity was determined in synaptic plasma membranes isolated from the whole brain.

**Results**

Rats from experimental groups developed seizures upon single subconvulsive dose of HCT with significantly higher incidence comparing to those from control group. Seizure latency was significantly decreased, and number of seizure episodes per rat significantly increased in experimental group fed with methionine-enriched diet comparing to control group. No significant difference in intensity of seizures was observed between these groups. Sodium pump activity was significantly decreased in experimental comparing to control group of rats.

**Conclusions**

It could be concluded that methionine nutritional overload increases susceptibility of rats to seizure development. This effect could be, at least in part, attributed to observed decrease of brain sodium pump activity.
P99
Sleep K-complex triggered paroxysmal activities in extra-frontal epilepsies.

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Introduction

K-complex may occur spontaneously or be elicited by auditory stimulations. Two studies already reported the occurrence of Sleep K-complex triggered seizures in nocturnal frontal lobe epilepsy. We herein investigated whether paroxysmal activities triggered by K-complex could occur in other types of epilepsy.

Methods

A one year review of sleep recordings in our center provided two cases (0.42%) where K-complex triggered paroxysmal discharges.

Results

Case 1: 3 year-old boy with epileptic encephalopathy and microcephaly with cerebellar hypoplasia of unknown origin. Interictal EEG activity: slowed background activity, left temporal spikes, bifrontal high amplitude spikes, and diffuse tonic discharges. Sleep: poorly organised with few spindles and spontaneous K-complex. All the 23 K-complex recorded, were elicited by auditory stimulations: four followed by isolated spikes and five by diffuse “tonic-clonic” discharges, all asymptomatic. Case 2: 38 year-old woman, with left temporal epilepsy since age of 18. Interictal EEG activity: spontaneous left temporal spikes. Sleep: among the 31 K-complexes recorded, 8 spontaneous and 15 elicited by auditory stimulations were followed by left temporal paroxysmal discharges. In both cases, a progressive building up of triggered discharges was observed, since the repetition of K-complex was associated with a prolongation of the discharges, while latencies remained stable. In few cases, a refractory period was transiently observed, during which new stimulations failed to evoke K-complex.

Conclusions

Pathophysiology of K-complex triggered seizures or paroxysmal discharge remains unknown, but this link could be more common than previously observed and not confined to nocturnal frontal epilepsy.
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P100
MAGNETIC RESONANCE IMAGING OF SYMPTOMATIC EPILEPSY IN CHILDREN AFTER MENINGOENCEPHALITIS

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Background

Epilepsy is one of the most complex medical and social problem at present time. The high prevalence of the disease in paediatric population of Uzbekistan (10 per 1,000) determines the importance to develop effective measures for early diagnosis, new approaches to correction of treatment and prevention of complications of epilepsy.

Objective

To identify MRI findings of symptomatic epilepsy in children with inflammatory etiology such as meningoencephalitis.

Materials and Methods

MRI studies were conducted with 35 children with the diagnosis of symptomatic epilepsy after meningoencephalitis. Children ages ranged from 1 year to 14 years.

Results

In our study the main symptoms of epilepsy after meningoencephalitis were multiple lesions of white and gray matter, their predominant bilaterality and symmetry, a clear demarcation from the surrounding tissues. In the study of 35 children who recovered from meningoencephalitis following MRI signs were found, in 5 (14.3%) cases it was midline shift of the brain, in 12 (34.3%) cases it was asymmetry of the lateral ventricles. Subarachnoid perivascular space expansion was found in 22 (62.9%) cases, which often revealed in the fronto-temporal region of the brain. Expansion of the subarachnoid space was revealed in 19 (54.3%) cases, mainly due to atrophy of the brain.

Conclusion

Magnetic resonance imaging has an important role in the clinical diagnostics of epilepsy, the use of which in the study of symptomatic epilepsy is one of the important conditions of adequate diagnosis, treatment and prognosis of the disease.
P101
Defining the role of imaging methods in diagnostics symptomatic epilepsy in children.

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Purpose/Introduction

Defining the role of MRI and CT in the comprehensive assessment of the state of the central nervous system (CNS) in children with symptomatic epilepsy

Subjects and Methods

The object of the study were 28 patients with symptomatic epilepsy aged from 1 to 14 years. Debut of seizures observed in a wide range of ages from 1 month to 10 years (mean 6.3 ± 4.9). All patients underwent EEG (electroencephalography) studies, magnetic resonance imaging and computed tomography.

Results

Structural changes of brain were found in 45.6% of all examined patients in MRI and CT. Pathological changes in the EEG were found in 77.2% of patients. Regional epileptiform activity, represented by a complex-acute or slow waves recorded in 51.9% of cases. Changes on MRI were detected in 44.6% of patients. CT allowed us to determine the state of the ventricular system and subarachnoid spaces. the following MRI signs were found, in 5 (14.3%) cases it was midline shift of the brain, in 12 (34.3%) cases it was asymmetry of the lateral ventricles. Subarachnoid perivascular space expansion was found in 22 (62.9%) cases, which often revealed in the fronto-temporal region of the brain. Expansion of the subarachnoid space was revealed in 19 (54.3%) cases, mainly due to atrophy of the brain.

Discussion/Conclusion

Thus, at present, CT and MRI are the main methods of neuroimaging in the diagnostics of symptomatic epilepsy in children. However, it should be noted that only the focused research, knowledge-based clinics, medical history, EEG findings, MRI and CT scans in total identifies epileptogenic focus.
NEUROLOGICAL STATUS OF CHILDREN WITH EPILEPTIC ENCEPHALOPATHY

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Relevance

Epileptic encephalopathy - is a condition where abnormal electogenesis of brain is the cause of disorders of the brain functions. In this condition the epileptic process itself leads to progressive brain damages. The difficulties of correct diagnosis of neurological status of these patients lies in the fact, that at the moment there is no specific complaints of seizures, although in some cases the survey can reveal seizures in patients history. So these patients often come to the observation of psychiatrists or defectologists.

The purpose of the study

To study the features of neurological status in children with epileptic encephalopathy.

Materials and Methods

We studied 119 children aged from 3 to 14 years, 69 of them were diagnosed with epileptic encephalopathy and 50 with symptomatic epilepsy. The debut of seizures was observed in a wide age ranges from 1 month to 10 years (mean 7,4 ± 0,44). In this study we used clinical, neurological and instrumental methods of investigation (EEG electroencephalography).

The results of the study

The study of neurological patients with epileptic encephalopathy revealed the prevalence of cognitive impairment, decreased intelligence, memory and thinking. In neurological status of patients with symptomatic epilepsy it is often revealed the predominance of focal neurological symptoms.

In the study of cognitive functions of children with epileptic encephalopathy type I and symptomatic epilepsy more severe intellectual disabilities was observed compared to children with epileptic encephalopathy type II.

Conclusion

Thus, a detailed clinical and neurological analysis of patients correlated with EEG data allowed to exclude the incorrect diagnostics of epileptic encephalopathy in children.
P103

Stereoelectroencephalographic 3-D mapping of epileptogenicity using responses to single-pulse electrical stimulation

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Rationale

We aim at delineating the seizure onset zone (SOZ) using cortico-cortical evoked potentials (CCEP) as a result of single-pulse electrical stimulation (SPES) on stereotactically implanted depth electrodes for presurgical evaluation of patients with drug-resistant epilepsy. We illustrate the activation maps in a neuroimaging framework that combines the intracranial electrode stereotactic coordinates with the MRI, providing an exact spatial representation of the brain activation.

Methods

Three patients with focal temporal and frontal epilepsy and one with multi-focal rolandic epilepsy were investigated using stereoelectroencephalographic (SEEG) method. We have applied single pulse bipolar stimulation on different contacts pairs and recorded the responses on other 62 contacts. Constant current biphasic pulses having variable amplitude in the range 1 to 5 mA from pulse to pulse were applied in a pseudo-random sequence using a programmable stimulator (Guideline LP+, FHC Inc, Bowdoin, ME). We mapped the propagation of the stimulus through the epileptogenic network by analyzing CCEPs. We looked for specific evoked responses that are known to represent a biomarker of the epileptogenicity, like high-frequency oscillations (HFO) and delayed responses (DR). 3D maps of the responses have been created and exported as DICOM series and loaded in the surgical planning software to be visualized along with patient’s anatomy, as seen on the standard MRI scans.

Results

3D activation maps were created for the qualitative (HFO, DR) responses. The activation thresholds based on the fast responses stimulus-response curves and the additional information provided by stimulation-evoked DRs and HFOs contributed to a more accurate localization of the SOZ. HFOs showed 53.8% SOZ specificity based on response location (RL)(Figure 1), and 57.2% SOZ specificity SOZ based on stimulation location (SL). DRs showed 40.8% SOZ specificity based on RL (Figure 2) and 59.9% SOZ specificity based on SL. Results were retrospectively analyzed and were correlated with the standard method that uses spontaneous activity for delineating the SOZ.

Conclusions

3D maps in stereotactic coordinates of the responses to single pulse stimulation can provide valuable information to delineate SOZ and the epileptogenic networks.
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P104
ESES spectrum - what lies underneath, treatment options and the importance of EEG monitoring

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**Question**

ESES (Electrical status epilepticus during slow sleep) is thought to be a rare phenomenon representing a non-convulsive status epilepticus, which characterizes the epilepsy syndromes BECTS (Benign Partial Epilepsy of Childhood with Centro-temporal Spikes ), CSWS (continuous spikes and waves during slow sleep ) and Landau Kleffner Syndrome. The brain can look normal at MR scan or can show various abnormalities. We propose to study the anatomic background and efficacy of treatment for diagnosis and monitoring in these cases.

**Methods**

We have studied retrospectively and prospectively 5 children over a period of three years. Three children had normal brain MRI and received different medication Sulthiam, Dexametasone and ACTH; two patients with unprogressive structural brain damage were on double therapy, ACTH with Ethosuximide and Dexametason and Levetiracetam. EEG was performed in the awake state, drowsiness and slow sleep at the beginning of treatment, after a week, a month and then every three months.

**Results**

Correlating clinical picture, EEG pattern and evolution, two patients were diagnosed with BECTS, one with Landau-Kleffner Syndrome, one with hypoxic-ischaemic encephalopathy, one with schizencephaly. The quickest response on EEG was obtained in the most clinically affected patient with Dexamethasone and Levetiracetam. A fragmentation of EEG pattern was seen after a week when we treated with Dexamethasone and Ethosuximide. All five patients displayed at one month of treatment improved EEG models and resolution of ESES.

**Conclusions**

In all our cases the anatomical findings did not influenced the therapeutic response. We emphasize the importance of EEG monitoring with awake, drowsiness and sleep recordings, even in the absence of clinical seizures. Sleep EEG represents the most important tool in diagnosis and treatment.

**Key words**

ESES, EEG, anatomic background
P105
DELAYED RECOGNITION OF SEIZURE REFRACTORINESS IN TEMPORAL LOBE EPILEPSY WITH MESIAL TEMPORAL SCLEROSIS

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Introduction

Temporal lobe epilepsy (TLE) with mesial temporal sclerosis (MTS) constitutes the most frequent indication of epilepsy surgery in adults. Surgery is often delayed, due to several factors: initial benign presentation, with periods of remission; delay in the recognition of refractoriness; and access to epilepsy surgery programs. Delay in surgical treatment is of particular importance in developing countries, where access to surgical treatment is often very difficult.

Objectives

To study a population of patients with TLE-MTS who underwent surgical treatment in an epilepsy surgery program in Brazil, and to assess the occurrence of remission periods prior to surgery and time until refractoriness.

Patients and methods

We included 120 patients (67 female) with unilateral TLE-MTS submitted to surgical treatment - 44 right anterior temporal lobectomy (ATL), 76 left ATL; 1 patient was submitted to left selective amygdalo-hippocampectomy (ASH). All patient underwent a comprehensive pre-surgical evaluation, including EEG, prolonged video-EEG monitoring, high-resolution MRI, as well as neuropsychological, psychiatric and social evaluations. Remission period prior to surgery was defined as a period of at least one year free of all seizures, after onset of habitual seizures. Time until refractoriness was defined as the time from epilepsy onset until poor seizure control was observed.

Results

Thirty-four patients (28.3%) had at least one remission period, which ranged from 1 to 17 years (mean 3.8 years; median 2 years). Time until refractoriness ranged from 1 to 21 years (mean 5.46 years, median 4 years). Epilepsy duration ranged from 10 to 57 years (mean 26.3 years).

Discussion

Good seizure control and quality of life improvement are the goals of epilepsy surgery. Delayed recognition of refractoriness due to several factors, including the occurrence of remission periods, may postpone surgical treatment and lead to additional morbidity in TLE-MTS patients. Efforts must be made in order to identify potential candidates.
P106
Fronto-parietal coherence in the assessment of short-term memory loss in patients with partial epilepsy.

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Background

Recently, examines the role of the fronto-parietal synchronization in memory processes. There is evidence of changes in resting state cortical EEG theta rhythm in patients with mild cognitive impairment and Alzheimer’s disease. Memory impairment is fairly common symptom of epilepsy and it seems interesting to study the fronto-parietal coherence in epilepsy.

Patients and Methods

We examined 34 people with partial epilepsy, the mean age was 32.9 years, and 17 healthy control group, the mean age was 30.5 years. For EEG recording, we used the 19-channel EEG (10-20% ) and mathematical processing package "Neuron-Spectrum" (Russia). Recording took place in a resting state, was used for the analysis of the record for 20 seconds without artifacts. Estimation of the spectral coherence of the theta rhythm was conducted in the following leads: F3-P3, F4-P4, F3-F4, P3-P4. Subjects performed a test for short-term memory «Digit Span».

Results

Memory deficits were found in 58% (20) of patients, in the control group of memory impairment has not been. Fronto-parietal coherence in patients with memory decline differed significantly (p = .001) from healthy and patients without memory impairment. Fronto-parietal coherence level in the group with memory impairment decreased depending on the amount of digits in the test (p=.005).

Conclusion

We assume that the fronto-parietal scalp EEG coherence may play a role in the assessment of cognitive impairment in patients with epilepsy.
ELECTROCORTICOGRAPHIC EVIDENCE AND SURGICAL IMPLICATIONS OF DIFFERENT PATHOPHYSIOLOGIC SUBTYPES OF TEMPORAL LOBE EPILEPSY

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QUESTION
Mesial temporal lobe epilepsy (MTLE) might have a focal or a network pathophysiology. We hypothesize that changes in the interictal spiking activity during electrocorticography (ECoG) reflect changes occurring in the epileptic network. The elimination of mesial interictal spikes is tightly linked with the epileptogenic zone (EZ) resection.

METHODS
25 patients diagnosed with MTLE were intraoperatively evaluated by ECoG with a 4 x 5 grid over the lateral temporal cortex and an 8-electrode mesial strip. Total Spiking Activity (TSA), defined as the mean spikes/min for all mesial channels, was computed before and after lateral cortectomy (LC). Based on the TSA after LC, a tailored anterior medial temporal resection (AMTR) was carried out.

RESULTS
At the last follow-up (19.1 ± 1.4 months), patients were characterized as Engel's class I: 84%, II: 8%, or III: 8%. During LC, TSA recorded from the mesial strip did not change in 14 patients, increased in 3 patients and decreased in 8 patients. In 20% of patients, the mesial activity completely disappeared following the LC, and mesial structures were spared. All of these patients were Engel's class IA. The TSA in the mesial strip during the basal recording was located in the occipital region (80%) and did not change after LC.

CONCLUSIONS
Our results strongly suggest the existence of pathophysiologic differences within subtypes of MTLE. The identification of these subtypes is fundamental for an individualized surgical approach.

figure 1
figure 2

During Lateral Cortectomy

After Lateral Cortectomy
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P108
Long-term Clinical and EEG Consequences of Idiopathic Partial Epilepsies

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This study includes 61 consecutive patients followed by ourselves in a private office. All patients were diagnosed as having idiopathic partial epilepsy (IPE) and followed by for 3-18 years, mean 8 years. According to syndromic classification of epilepsies and epileptic syndromes, patients were gathered into diagnostic groups as 1: Benign Rolandic Epilepsy (BRE), 2: Panayiotopoulos Syndrome (PS), 3: Childhood Epilepsy with Occipital Paroxysms (Gastaut-type), 4: Atypical Benign Partial Epilepsy (ABPE) and 5: Cases with intermediate characteristics.

Main parameters evaluated in the study were age at onset of epilepsy, seizure characteristics as type, frequency, duration, relation with sleep-wake cycle, patient and family history for paroxysmal disorders and clinical course of the seizures. Distribution of interictal spike-wave in the EEGs were analyzed and their localizations were questioned in relation to age of the patient at the time of recording.

Number of patients with typical BRE was 17, PS 9, Childhood Epilepsy with Occipital Paroxysms (Gastaut-type) 8 and ABPE 1. Remaining patients exhibited either characteristics common for more than one syndrome, or, some features within the borderlines of IPEs.

Ratio of patients with idiopathic epilepsy in at least one family member was % 38 and with parental consanguinity was % 8

Spike distribution in the EEGs was not only related to the syndromic characteristics of the patients but also to the age at the EEG recording.

Results are discussed in view of the related literature.
Effects of low-frequency rTMS on EEG nonlinear parameters and the expression of synaptophysin in epileptic rats

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Objective

To investigate the changes of several EEG nonlinear dynamic parameters and expression of synaptophysin in rat hippocampus, and explore the underlying anti-epileptic mechanism of rTMS.

Methods

Epilepsy rat model was made by using lithium-pilocarpine, and the rats were divided into non-stimulus group and stimulus group, the control group was set up at the same time. The stimulus group rats were treated with rTMS at 0.5Hz, 40%MT, 100 plus/train, 5 train/day, interval of train is 30 seconds, for 7 consecutive days.(1) The EEG nonlinear parameters were obtained from the rats for analysis on 7th, 14th, and 28th day post-stimulus, respectively, including approximate entropy(ApEn), correlation dimension(D2), point wise correlation dimension(PD2), lyapunov exponent(LE), kolmogorov entropy (KE) and complexity(Cx).(2) The brain tissue were taken on 7th, 14th, and 28th day after the stimulation in each group, and immunohistochemical staining was used to detect the expression of SYN in the rat hoppocampus.

Results

(1) The mean values of D2, PD2, LE and KE for non-stimulus and stimulus rats were significantly lower than those of healthy rats(P<0.05), whereas the values of Cx and ApEn were not significantly different from those of healthy rats(P>0.05). The mean values of D2 and KE for stimulus rats were significantly lower than those of non-stimulus rats(P<0.05), whereas the values of LE, PD2, Cx and ApEn were not significantly different from those of non-stimulus rats(P>0.05).(2) Compared with the control group, Expression of SYN in the non-stimulus group was significantly higher (p<0.05) .Compared with the non-stimulus group, expression of SYN in the stimulus group had no significant change in 7 days after the stimulation (p>0.05) ; but showed significant change in 14 days and 28 days after the stimulation (p<0.05) .

Conclusion

(1) Complexity of epilepsy rat's brain electrical physiological activities is simpler than that in the normal rats. The low frequency rTMS has an inhibitory effect on epilepsy rats.
P110
ELECTROMAGNETIC FIELDS EMITTED BY MOBILE PHONES AND EEG SPIKING FREQUENCY IN PATIENTS WITH FOCAL EPILEPSY

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Despite the increase in mobile telephone technology use and possible related adverse health effects, no studies have investigated the impact of GSM like signal on the ongoing spiking activity in human epileptic patients.

To this extent, following a double-blind, crossover, counterbalanced design, the brain electrical activity of twelve epileptic patients has been recorded under both Real and Sham exposure. Each of them was recorded before the exposure (pre-exposure/baseline session), during the Real or Sham exposure (during-exposure session), and after the exposure (post-exposure session), each session lasting 45 minutes. As dependent variables both spiking activity (spikes count) and EEG quantitative indices (spectral power and coherence data) have been considered.

Spiking activity tended to be lower under Real than under Sham exposure. EEG spectral content analysis indicated a significant increase of Gamma band under Real exposure, mainly evident in Parieto-occipital and Temporal areas. Connectivity data indicated increased interhemispheric (left temporal to right frontal ROIs) instantaneous coherence, in the Beta frequency band, in the ‘during-exposure’ condition compared to the ‘baseline session’. No significant modification of lagged coherence was measured in any condition.

Results indicated that GSM exposure in epileptic patients slightly influence EEG rhythms and spiking. These modest effects do not indicate an increased risk for these patients as a consequence of using mobile phones.
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DACRYSTIC STATUS EPILEPTICUS: A CASE REPORT

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QUESTION

To describe the clinical and electrographic features of a patient who presented a status epilepticus of persistent crying.

METHODS

Twelve year-old girl who was admitted in our hospital for headache, nausea, left upper limb paresis and dysarthria without fever that progressively evolved to a mental state alteration with persistent unmotivated crying. She received a cord blood transplantation for the treatment of a chronic myeloid leukemia six months ago. Cerebrospinal fluid analysis was negative for the most frequent viral and bacterial infectious agents. Cranial MRI revealed only a decreased diameter of M2-M3 segments of right median cerebral artery. Serial EEG recordings were performed.

RESULTS

EEG initially showed a focal slow activity in right fronto-temporal regions. 24 hours after we found profuse interictal epileptiform activity localized in temporal and frontal left hemisphere regions and in frontal right hemisphere region with a slowed background activity. A consecutive EEG performed 2 days after showed bifrontal rhythmic 2.5 Hz delta waves preceded by sharp waves that disappeared with the administration of endovenous midazolam bolus (5 mg.); after that it persisted some interictal abnormalities in the recording; mental state improved and crying was no more present. An antiepileptic treatment was instaured (levetiracetam and lacosamide) producing a resolution of clinical manifestations and a normalisation of EEG recordings.

CONCLUSION

Dacrystic seizures are a very infrequent ictal manifestation. They usually have a focal origin, mostly in fronto-temporal non-dominant hemisphere regions. We present a unique case of dacrystic status epilepticus without an elucidated etiology.
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P112

Perspectives of neurosurgical treatment of epilepsy patients in resource poor countries - study in Georgia

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Question

Focal brain abnormalities are major risk factors for pharmacoresistant epilepsy (PRE) and surgical treatment of these patients is the most effective way. In resource limited countries epilepsy surgery is not largely accessible because of restricted availability of intracranial EEG monitoring and functional brain imaging, that leads to complete stagnation of development of epilepsy surgery. However, not all patients require further diagnostic procedures, if there is unequivocal concordance in seizure semiology, localization of brain lesion on MRI and epileptiform activity on EEG.

Aim

To estimate the rate of concordance between seizure semiology, EEG and MRI data in people with PRE.

Methods

Patients with uncontrolled seizures were recruited at Institute of Neurology and Neuropsychology, admitted between 2009-2012 years. All of them were clinically reexamined, underwent standard 20-minute interictal EEG and a high-resolution MRI (3T) according to epilepsy protocol.

Pharmacoresistance was defined according to Kwan, et al. 2010. Epileptiform EEG abnormalities were defined as focal epileptiform discharges: spikes, spike-wave complexes, and sharp waves.

Results

82 persons were investigated (mean age 26 years, SD 12). Fifty five (67%) were female. MRI revealed: mesial sclerosis - 15 case (18%), focal cortical dysplasia (FCD) - 5, tuberous sclerosis - 2 and brain tumour 3 cases. No lesion was found in 24 (29%) cases. In remaining 38 patients various brain abnormalities were detected. Localization of possibly epileptogenic lesions on MRI was in concordance with seizure semiology and EEG findings in 15 (18%) cases (mesial sclerosis - 11, FCD - 2, polymicrogiria - 1, hypothalamic hamartoma - 1). In 22 (27%) cases ambiguous data were obtained. In remaining 21 (26%) people multifocal or diffuse abnormalities were detected that were irrelevant for epilepsy surgery.

Conclusion

According to our study, in up to one-fifth of patients could be considered as good candidates for epilepsy surgery without needs of further high technological pre-operative assessment procedures. However, most patients in our cohort require more deep investigations for proper localisation of epileptogenic focus.

Acknowledgement: The study was funded from Shota Rustaveli National Science Foundation grant.
Correlation of Neuropsychological and Electrophysiological findings in patients with epilepsy

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Question

The goal of the study was to investigate the correlations of neuropsychological and electrophysiological data in adult patients admitted at Epilepsy Centre for diagnosis of epilepsy.

Methods

Standard EEG and Neuropsychological findings of persons with age range of 18-79 years, admitted at the Epilepsy Centre (01.01.2011 - 31.12.2012) of the Institute of Neurology and Neuropsychology (INN) for diagnosis of epilepsy were analyzed. Brief Neuropsychological Test for adults was compiled from A. Luria’s neuropsychological tests and A. Benton Visual Memory Retention Test. Luria’s syndrome analysis approach was used for neuropsychological conclusion and probable localization of brain dysfunction. EEG criteria for identification of prevalent localization of pathological area were mainly sharp waves, pick-waves, poly-pick waves and pick and slow waves. Statistical procedures for categorical data, non-parametric statistics: phi correlation, Pearson\(\chi^2\) coefficient were used.

Results

After multidisciplinary investigations of 585 people, 255 male/ 320 female, 101 persons were diagnosed as having non-epileptic seizures, 113 - with Generalized Epilepsy, 371 - with Focal Epilepsy.

From total group 548 (93.7\%) had pathological indicators on EEG and out of them the normal neuropsychological functioning has only 55(10\%); in remaining 37 persons with normal EEG normal neuropsychological functioning were reviled in 22 cases (61\%). Comparing Generalized, Focal and non-epilepsy seizures, there was a moderate to severe neuropsychological dysfunction in the group of focal epilepsies and no or mild dysfunction in persons with non-epileptic seizures (\(\chi^2=77,395, p<0.005\)).

High concordance revealed between EEG and Neuropsychological data in case of frontal, frontal-temporal, frontal-temporal-parietal localizations (PC=0.693, \(p<0.024\), Cramer’s V=0.231, \(p<0.05\), CC=0.569, \(p<0.05\)). No compatibility was in cases of occipital localization.

Conclusions

There is a high correlation of EEG and neuropsychological findings especially in frontal and fronto-temporal epilepsies. Neuropsychological assessment could easily capture temporal lobes dysfunction in combination with other brain regions, then pure temporal area’s dysfunction. Failure in occipital localization coincidence can be explained by the weakness of neuropsychological test in identification of occipital lobes dysfunction.
P117
Quantitative EEG alterations in alcohol-dependent patients with epileptic seizures - pilot study.
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Question
The aim of study was to analyze features of quantitative electroencephalography (qEEG) in alcohol-dependent subjects with epileptic seizures.

Methods
The study comprised 24 alcohol-dependent patients (19 men, 5 women, aged 40 - 54; mean: 49 years), admitted to the Neurological Department after generalized seizures, and 28 healthy controls (21 men, 7 women, aged 30-45 ;mean 37,5 years). All the subjects underwent EEG with further spectral analysis including absolute power of the five frequency bands: delta, theta, alfa, beta1 and beta2.

Results
The patients in comparisons with the controls were characterized by significantly higher power of all five analysed bands (P<0,0001) in the majority of channels, except for alfa band in parietal regions, beta2 band in the left temporal region and delta band in right temporal region.

Conclusion
The increased absolute power within all analysed frequency bands in alcoholic patients with recent epileptic seizures may suggest the state of the general cortical hyperexcitability. The influence of chronic alcohol abuse and epileptic seizures upon bioelectrical activity of the brain requires further investigations.
P118
Difference in sleep architecture between left and right temporal lobe epilepsy

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Question

Sleep disturbance is common in patients with epilepsy. The abnormal sleep architecture is characterized by frequent shifts in sleep stages with numerous awakenings and longer duration of light sleep following sleep onset, especially in patients with temporal lobe epilepsy (TLE). However, any relationship between seizure lateralization and sleep macrostructure in patients with any type of epilepsy remains unknown. The present study compared sleep architectures in patients with left and right TLE (LTLE and RTLE).

Methods

This study included 17 patients with TLE (7 men and 10 women aged 17 to 50 years) who underwent simultaneous polysomnography and long-term video EEG monitoring. Ten and seven patients were diagnosed with LTLE and RTLE, respectively. Sleep stages were scored based on the American Academy of Sleep Medicine criteria. Total sleep time, sleep latency, REM latency, sleep efficiency, time and percentage of each sleep stage, and apnea-hypopnea index were compared between LTLE and RTLE.

Results

Percentage REM stage was significantly (p = 0.021) lower in patients with LTLE (10.1±5.9%) than in those with RTLE (16.3±2.9%). Other parameters showed no significant difference between the two groups.

Conclusions

Epileptic dysfunction of the left temporal lobe was associated with reduction of REM sleep. The present result contradicts a previous report that left hemispheric cerebral infarction was associated with higher percentage REM stage.
Feature pre-processing for neonatal seizure detection

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On Neonatal Intensive Care Units (NICU) many vital parameters are recorded. Automatic Electroencephalography analysis could enhance the application of NICU brain monitoring. Recently, a new seizure detection method was introduced using Support Vector Machines (SVM).

Objective

Aim of our project is to further optimize SVM classification accuracy.

Methods

First, a Kalman filter (KF) was used to remove noise from both feature and classifier output time series in order to reduce short false detections. Second, EEG baseline feature correction (BC) was introduced to reduce inter patient variability in feature distributions. The performance of the detection methods is evaluated on 56 single channel routine EEG recordings from 39 both term and pre-term newborns. The area under the receiver operating characteristics curve (AUC) is used to evaluate the performance of the classification method.

Results

SVM without any of the proposed pre-processing steps achieves an AUC of 0.759. The highest AUC of 0.877 is achieved on baseline corrected features with a Kalman smoother used for training data pre-processing and a fixed-lag KF used to filter the classifier output.

Conclusions

Both BC and KF significantly improve neonatal epileptic seizure detection.

Significance

This paper introduces significant improvements for the state of the art neonatal epileptic seizure detection algorithm.

figure 1
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figure 2
P120
EEG changes in patients with epilepsy and comorbid diseases

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Question
Comorbidity refers to the coexistence of two or more diseases in the same person. Epilepsy and the comorbid disorders can occur and exist without causality or interconnection between them.

Methods
Our research is clinical and epidemiological, retrospective, and covers patients with epilepsy who were treated in the Clinic for Paroxysmal diseases at the Multiprofile Hospital for Active Treatment in Neurology and Psychiatry “St. Naum” -Sofia, for the period between January, 2003 and December, 2012. There are 1, 624 patients with epilepsy and a specific type of comorbid disease: 849 women and 775 men. The age range of the included patients is 18 - 93 years of age. The medium age for women is 45,9 (SD±16,2) years and for men it is 45,4 (SD±16,9) years. The data used is part of hospital documentation and EEG examinations.

Results
Out of all examined patients with epilepsy and a specific comorbid disease, 916 (56,4%) patients have diffuse changes in the background activity, 32 (2%) patients have generalized paroxysmal activity, 157 (9,6%) patients have disorganized background activity with generalized paroxysmal activity, 591 (32%) of the patients have focal activity. There is a dependency between the EEG changes of some most often encountered somatic and neurological diseases.

Conclusions
The presence of comorbid diseases relates to a higher risk for aggravating the condition of the patient, increasing the EEG changes, a presence of interdependence between the separate diseases, as well as between their treatment.
P121
Investigation of low complexity seizure detection algorithm for closed loop devices in epilepsy treatment
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Question

Intelligent novel devices for treatment of epilepsy for closed loop applications as developed in the cluster of excellence BrainLinks BrainTools at the University of Freiburg need algorithms for early online seizure detection with low computational costs. This study investigates the question, whether simple time domain features allow accurate seizure detection at an early seizure stage.

Methods

3633 hours of continuous invasive EEG recordings from 18 patients as given by the EPILEPSIAE database were the basis of the study. Recordings were performed with either subdural grid and strip or stereotactic depth electrodes. The recordings contain 298 seizures with eight different seizure patterns. 93% percent of the seizures can be assigned to either one of the following patterns: Rhythmic beta, low amplitude fast activity and repetitive spiking. 10 different time domain features (Maximum, minimum, mean, median, area, linelength, activity, mobility, complexity (Hjort’s parameter) and number of inflexions) were applied channel wise to the EEG recordings.

Results

Sensitivity for the single features was between 62.8% and 76.4%. The range of the specificity was between 92.6% and 98.6%. Mean detection delay was between 20.32 s and 58.33. The best performing feature with respect to sensitivity (76.0%) and detection delay (22.3 s) was mobility. The number of inflexions gave the results with the highest specificity. The achieved detection delay of 33 s for inflection counting can be decreased by applying the algorithm to higher sampled data.

Conclusions

Simple time domain features were investigated on a huge database of invasive EEG recordings and candidates for a low complexity detection algorithms could be determined. To achieve shorter detection delays for the application in a closed loop system without loosing detection accuracy a patient specific strategy will probably be necessary.
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LP5

Electroencephalographic features of focal epilepsy with secondary bilateral synchronization on EEG among adult patients

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Question

Secondary bilateral synchronization (SBS) on EEG is characterized by features that are common either for focal or for generalized types of epilepsy. Distinguishing between focal and generalizes types of epilepsy is the most important task of diagnostics because focal and generalized forms of epilepsy require different incompatible approaches to treatment. The aim of our study was to investigate the electroencephalographic features of epilepsy with SBS on EEG among adult patients.

Methods

61 patients (36 women and 25 men) with focal epilepsy and SBS on EEG with age 18 years and older (the average age was 27.2±6.2 years) were studied with prolonged video-EEG monitoring. The duration of investigation was from 10 to 12 hours, procedure of study obligatory included night sleep time.

Results

Source of epileptic activity was in medial posterior zones of frontal lobe (47.5%), in deep medial zones of temporal lobe (42.6%) and in lateral zones of temporal lobe (9.9%). Roughly the half of patients (50.8%) had two or more sources of epileptic activity.

Patterns of SBS were found in wakefulness (50.8%), 1-2 stages of sleep (98.4%), during the rhythmic photic stimulation (19.7%), during the hyperventilation (14.8%), during the awakening (36.1%). During the deep and REM sleep patterns of SBS were not found.

Rhythmic photic stimulation caused the increase of quantity of pattern of SBS (photoparoxysmal response) only in 8.2% of cases. Hyperventilation caused the increase of quantity of pattern of SBS only in 4.9% of cases. During the awakening the increase of quantity of pattern of SBS was found only in 8.2% of cases.

Conclusion

Focal epilepsy with SBS on EEG is characterized by sources of epileptic activity in mediobasal zones of frontal and temporal lobes of brain, maximal detection rate during the 1-2 stages of sleep and low sensitivity to provocative activity of photic stimulation, hyperventilation and awakening.
Ictal Tachycardia in Childhood Epilepsy

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Question

A novel cardiac-based seizure detection (CBSD) algorithm has been incorporated in a Vagus Nerve Stimulation (VNS) device to allow closed-loop stimulation. A prospective multicenter trial in adult epilepsy patients (E36) demonstrated a high sensitivity and specificity to automatically detect ictal tachycardia (IcT). This study investigates the occurrence of IcT in children to estimate the potential candidacy for this novel VNS therapy.

Methods

Between 1.2011 and 12.2013, 34 children (age 10y [range 2-15], 18M/16V) with refractory epilepsy underwent video-EEG monitoring and simultaneous ECG recording at Ghent University Hospital. In patients with at least one seizure, baseline heart rate one minute before seizure onset was compared with heart rate during the seizure. IcT was defined as an ictal heart rate of at least 100 bpm and an increase of ≥35 bpm compared to the pre-ictal heart rate.

Results

Mean baseline heart rate was 92 bpm [range 60-160]. In 21 children (mean age 10y [range 3-15], 12M/9F) 99 seizures were evaluated. IcT was observed in 13 patients (62%) and in 20 seizures (20%). In 1 seizure IcT preceded ictal EEG or behavioral changes and in 4 other seizures IcT occurred in the first 10 seconds of ictal changes. When age-related tachycardia definitions were applied to define IcT (>133 bpm for 5-7 y, >130 bpm for 8-11 y and >119 bpm for 12-15 y), IcT was present in 8 patients (38%) and 13 seizures. In none of the patients the occurrence of IcT was consistent over all their seizures. IcT was associated with complex partial seizures originating from temporal, frontal, central or centro-parietal regions, with simple partial seizures in 1 patient and with generalized seizures in 3 (2 generalized tonic-clonic seizure and 1 tonic seizure). Two patients (9.5%) had an ictal decrease in heart rhythm of ≥35 bpm from baseline, but not below 60 bpm.

Conclusions

IcT, detectable by a novel CBSD algorithm, occurs frequently (62%) in children. The new VNS therapy system combining continuous intermittent VNS and closed-loop VNS based on CBSD may be indicated in a substantial number of children with refractory epilepsy who are not amendable for epilepsy surgery.
The comparison of resting state networks between normal children and adolescents with benign childhood epilepsy with centrotemporal spikes: A high density EEG study

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Abstract: Benign childhood epilepsy with centrotemporal spikes (BCECTS) is the most common idiopathic epileptic syndrome in childhood with characteristic EEG manifestations. In this study, we investigated the effect of interictal spikes on the resting state networks in children with BCECTS.

Methods: Nine children with right centrotemporal spikes and 9 healthy adolescents were included for both eyes-closed (EC) and eyes-open (EO with no fixation) resting state analysis. From each subject, 63-channel EEG was recorded and segmented into nonoverlapping two-second epochs, from which ten artifact-free epochs were randomly selected for further analysis, five for each EC/EO condition. Using low-resolution electromagnetic tomography (LORETA), distributed EEG sources were modeled for δ, θ, α₁, α₂, α₃, β₁, and β₂ bands. We compared regional normalized LORETA solutions from epileptic and normal subjects using paired t-tests for each frequency band and voxel. Cortical LORETA solutions (i.e. current source density at cortical voxels) accounting for scalp EEG spectral power densities were then computed at the group level.

Results: For both groups, current densities of α₂ and α₃ sources increased significantly from eyes-open to eyes-closed in frontal, parietal, temporal and occipital areas. Compared to the normal group, the epileptic group was characterized by (i) significant reductions in current densities of α₁-α₃ sources in occipital, medial and frontal areas in both conditions, (ii) significant increases in current densities of left parietal α₂ sources in both conditions, (iii) decreased alpha activity in bilateral frontal regions including the anterior cingulate and the superior and medial frontal gyri in the EC condition, and (iv) increased theta activity bilaterally at the medial temporal region in the EO condition. The normal group was mainly characterized by higher current densities of α₂ sources in bilateral frontal and occipital areas under the EC condition (Fig. 1).

Conclusion: Statistically significant (uncorrected P < 0.05) group differences in the anatomical distribution of cortical sources of resting-state EEG rhythms may be explained by anatomical/functional alterations due benign childhood epilepsy.

Figure 1: Spatial distribution of the statistically significant (P < 0.05) group differences of α₂ activity under the eyes-closed condition. Red and blue colors indicate greater activity in the control and the epileptic groups, respectively.
Abstracts of Poster Presentations – Poster Session 7 – Evoked potentials 1

P122
Normative Data of Visual evoked potentials in Eastern Region Population of Nepal
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Background
Visual evoked potentials (VEPs) assess the integrity of the visual pathways from the optic nerve to the occipital cortex. The VEP is very useful in detecting an anterior visual conduction disturbance however it is not specific with regard to etiology. It is very useful in evaluating visual function. It is non-invasive and has excellent temporal resolution. It can be used to assess the integrity or maturational state of the visual pathway in infants and preverbal children.

Objectives
To study VEPs in healthy subjects to prepare a normative data.

Methods
Pattern reversal and flash VEP tests were done in consenting 40 normal control eyes in Electrodiagnosis Lab II at BPKIHS, Dharan, Nepal. All subjects were taken from ophthalmology OPD of BPIKHS after ophthalmic assessments were found normal. Both pattern reversal and flash VEP were done to compare between these two. Statistical tests (paired t-test and Mann-Whitney test) were applied depending on distribution of observations.

Results
When ophthalmic variables were measured visual acuity [1.00±0.00], refractive error [1.88±1.11, D], foveal visual sensitivity [33.48±1.75, dB], cup disc ratio in percent [28.50±5.80], intraocular pressure [11.65±1.64, mmHg], automated visual field mean deviation [0.07±1.54, dB] automated visual field pattern standard deviation [1.64±0.45, dB] were measured. Among VEP variables pattern reversal latency N75 [67.30±5.09, ms], pattern reversal latency P100 [98.25±4.05, ms], pattern reversal latency N145 [137.52±15.20, ms], pattern reversal amplitude N75 [2.47±1.99, µV], pattern reversal amplitude P100 [6.07±1.44, µV], pattern reversal amplitude N145 [4.45±1.99, µV], flash latency N75 [66.85±6.13, ms], flash latency P100 [101.90±7.02, ms], flash latency N145 [146.62±13.22, ms] flash amplitude N75 [1.47±0.38, µV] flash amplitude P100 [2.78±0.42, µV] and flash amplitude N145 [1.43±0.38, µV] were measured.

Conclusion
Both pattern reversal and flash VEP values were found between normal ranges but flash VEP values were increased than that of pattern reversal.

figure 1
P123
The long-term effect of metabolic syndrome on cognitive event-related potentials

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Question

For the rapidly growing aging population and the consequent increase in dementia patients, to identify the putative factors and preventive strategies of cognitive impairment has become a major clinical and public issue. This two-year prospective study aimed to investigate the long-term influence of metabolic syndrome on cognitive event-related potentials (ERPs) and to determine whether there is a different effect of metabolic syndrome on early and late components of ERPs.

Methods

We recruited 53 healthy middle-aged and older adults (M:F=22:31). All participants were assessed for metabolic syndrome, cognitive function, and auditory event-related potential at baseline and at two-year follow-up.

Results

When the participants were stratified according to the cumulative exposure to metabolic syndrome (group of never, non-persistent, or persistent metabolic syndrome), there was no significant difference in demographic characteristics, scores of Cognitive Abilities Screening Instrument (CASI), and measures of ERPs at either baseline or two-year follow-up. Whereas, the participants with persistent metabolic syndrome displayed significant decrease in amplitude of P300 at Fz and Cz leads at two-year follow-up, compared with the baseline data, although their CASI scores showed no significant decline. Regarding the early components of ERPs at two-year follow-up, the N1 and P2 latencies revealed significant prolongation compared with the baseline data in all groups.

Conclusions

Our findings imply that only subjects with persistent metabolic syndrome are associated with cognitive decline in terms of lower P300 ERP amplitude. Based on the prolongation of N1 and P2 latencies at two-year follow-up, we postulate that attention and sensory processing are probably modulated by aging process.
P124
The value of VEP and OCT in Multiple Sclerosis

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Objectives

To evaluate the relative value of optical coherence tomography (OCT) and visual evoked potentials (VEPs) in assessing visual involvement in patients with multiple sclerosis (MS).

Methods

Cross-sectional study of 121 consecutive subjects with MS (34 clinically isolated syndrome, 69 relapsing-remitting, 15 secondary progressive, 4 primary progressive; age 36+10 years, disease duration 5.7+7.4 years, females 83, median Expanded Disability Status Scale-EDSS 2 (range 0.0-7.0). Of 242 eyes, 166 had no previous history of optic neuritis (ON), 22 had a single recent ON episode (<3 months); 54 had chronic ON (at least 1 episode >3 months before). All patients underwent assessment of EDSS, visual acuity (VA), OCT retinal nerve fiber layer (RNFL) thickness and VEP (checkerboard, size15'). VEP abnormalities were quantified according to a 4-graded conventional score (0 normal, 3 absent).

Results

In eyes with recent ON, the sensitivity of OCT was 5.6% considering only RNFL thickness increase, 38.9% considering also RNFL reduction, with a higher sensitivity of VEP (77.3%; McNemar p<0.0001 and 0.02). In eyes with chronic ON, no significant difference was found between OCT (68.5%) and VEP (81.5%) sensitivity (VEP/OCT 88.9%), as well as in eyes with previous ON within 6 (n=43) and 12 (n=34) months before (OCT 69.8% and 70.6 %; VEP 79.1% and 79.4%). Similar results were found excluding 13 eyes with repeated episodes of ON. In asymptomatic eyes, VEPs had a higher sensitivity (31.7%) vs OCT (19.9%; p=0.005); VEP/OCT combined detected abnormalities in 39.2%. In this subgroup, VEP score and global RNFL thickness were significantly correlated with EDSS (RNFL: Spearman ρ=-0.22, p<0.04; VEP score: p=0.30, p<0.0001), disease duration (RNFL r=-0.35, p=0.001; VEP score: p=0.25, p=0.001), not with VA.

Conclusions

The present findings confirm a higher sensitivity of VEPs in the subacute phases of optic neuritis (less than 3 months) and in asymptomatic eyes. This discrepancy fades off after more than 3 months from the ON episode, allowing for retrograde degeneration to occur and thus increasing OCT sensitivity. However, even at this stage the combination of the two exams allows to increase our overall sensitivity in detecting optic nerve damage. Finally, the correlation with disability and DD favours the usefulness of both techniques in monitoring MS patients, to be verified through longitudinal studies.
P125
Appraisal of the signal-to-noise-ratio of uni- and bipolar recordings of ocular vestibular evoked myogenic potentials
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Question
Vestibular evoked myogenic potentials (VEMPs) assess otolith function. Ocular VEMPs (oVEMPs) evoked by bone conducted vibrations or by air-conducted sound are a promising new diagnostic tool to evaluate utricular function.
In order to record oVEMPs various electrode configurations are used [1-3]. Most widely established is the bipolar recording with both electrodes placed inferior to the eye. A unipolar configuration using an electrode on the chin as reference was recently published [3]. Here we compared both configurations with respect to the signal-to-noise-ratio (SNR) in order to identify the superior method.

Methods
Extraocular muscle activity was measured in 12 healthy volunteers in response to otolith stimulation by bone conducted vibrations. Data were recorded both bipolar by means of surface electrodes placed 2 cm apart of each other beneath the eyes and unipolar using an electrode placed near the subjects chin as reference. We calculated the SNR by dividing the amplitudes of the N10 and P15 components by previously recorded noise.

Results
The average SNRs for the unipolar recordings was 0.327 and the SNR for the bipolar recordings was 0.479. The t-tests revealed a significantly better SNR during the bipolar recording for both the left (t-value: 2.48; p = 0.03) and right eye (t-value: 2.26; p = 0.04).

Conclusions
The lack of gold standards in the measurement of oVEMPs complicates a direct comparison of the results from different laboratories. Given our definition of signal- and noise we suggest the usage of a bipolar electrode configuration to record oVEMPs.

References

Supported by Deutsche Stiftung Neurologie, Graduate school for systemic neuroscience and Bundesministerium fuer Bildung und Forschung
P127
BRAINSTEM AUDITORY EVOKED POTENTIALS IN TYPE 2 DIABETES MELLITUS

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Methods

The study was conducted on consenting 30 type 2 Diabetes Mellitus (T2DM) patients comparing with 30 age and sex matched controls. The BAEPs and PTA were assessed. Independent samples T-test was used.

Results

In PTA, T2DM showed increase in auditory threshold at 250 Hz [21.5±4.18 vs 15.5±5.78 dB, p=0.000], at 500 Hz [20.83±5.09 vs 18±5.35 dB, p=0.04], at 1000 Hz [23.67±6.42 vs 18.33±5.92 dB, p=.001], at 2000 Hz [26.67±8.84 vs 20.83±4.93 dB, p=0.002], at 3000 Hz [34.83±8.66 vs 25.67±5.68 dB, p=0.000], at 4000 Hz [41.17±11.19 vs 30.17±7.59 dB, p=0.000], at 8000 Hz [47.5±11.04 vs 37.5±10.31 dB, p=0.000] in right ear and similarly significant increase in auditory thresholds was found in left ear. Significant increase in wave latencies I [1.85±0.22 vs 1.69±0.27 ms, p=0.011], II [2.97±0.27 vs 2.79±0.35 ms, p=0.026], III [4.25±0.37 vs 4±0.53 ms, p=0.045], V [6.86±0.5 vs 6.34±0.51 ms, p=0.000], and interpeak latencies III-V [2.61±0.53 vs 2.33±0.52 ms, p=0.045], I-V [5±0.51 vs 4.65±0.54 ms, p=0.011] in right ear and wave I [1.87±0.24 vs 1.75±0.21 ms, p=0.046], II [3.03±0.23 vs 2.81±0.23 ms, p=0.000], III [4.32±0.32 vs 4±0.37 ms, p=0.000], IV [5.53±0.39 vs 5.27±0.45 ms, p=0.002], V [6.72±0.46 vs 6.43±0.55 ms, p=0.028] and interpeak latencies I-III [2.45±0.3 vs 2.25±0.41 ms, p=0.031] in left ear at 40 dB. Significant increase in wave latencies I,II,III,IV,V and interpeak latencies I-III,I-V was found in T2DM at 60 dB and 80 dB bilaterally.

Conclusion

Asymptomatic diabetic patients showed significant increase in auditory thresholds, BAEP wave and interpeak latencies suggesting impairment of acoustic nerve function and CNS pathways in them.
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P129
ERP study on cerebral integration of audio-visual information in male and female

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Question

Lip-reading might improve speech perception in vocal communication under noisy environment. In daily life, visual information plays an important role to improve accuracy of auditory perception, and such phenomenon might be explained by audio-visual integration. However, audio-visual integration differs between genders, i.e., female tends to perceive voice with mouth movement more accurately. In this study, we examined gender differences of cerebral processing of audio-visual information.

Methods

9 male and 9 female right-handed volunteers participated in this experiment (mean age 22.0). White-noise and vowels pronounced by Japanese male were used as auditory stimulus (audio /a/ or /i/). Face image pronouncing a vowel was also used as visual stimulus (visual [a] or [i]). Experiment was done in the following conditions: 1) Auditory (A) condition: auditory stimulus was presented, 2) Visual (V) condition: visual stimulus was presented, 3) Audio-Visual (AV) condition: audio-visual stimuli were simultaneously presented. In AV and A conditions, participants were asked to press a button quickly with their right thumb for audio /a/ and noise. EEGs were recorded from 19 locations. In auditory ERP, subtracted ERPs (congruent: /a/[a]−[a], incongruent: /a/[i]−[i]) are compared to ERP due to auditory “alone” stimulus (audio /a/). In visual ERP, subtracted ERPs (congruent: /a/[a]−/a/, incongruent: /i/[a]−/i/) are compared to ERP due to visual “alone” stimulus (visual [a]).

Results

In auditory ERP elicited by “congruent” and “incongruent” stimulus, P2 amplitude in the male was smaller than that in the female (p<.05). And, P2 amplitude due to “congruent” and “incongruent” stimulus was smaller than auditory “alone” stimulus in the male (p<.05). Regardless of gender, P1 amplitude of visual ERP due to “congruent” stimulus was larger than visual “alone” stimulus (p<.05). Furthermore, N170 amplitude of visual ERP due to “congruent” stimulus was smaller than visual “alone” stimulus in the female.

Conclusions

Gender differences in electrophysiological data might suggest that face processing tend to be inhibited in the female when they receive congruent audio-visual information. On the other hand, attention in the male tends to be attracted to face image not only in incongruent stimulus but also in congruent one.
P130
Time domain of reversals in auditory brainstem responses

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Question
"Can Auditory Brain Stem Responses (ABR)¹ be a substitute for Electrocochleography (ECoG)² in the diagnosis of Auditory Neuropathy (AN)³/ Auditory Dysynchrony AD?"

Method
A clinical study including
Ø 16 patients and
Ø Age range, 9 to 43 months.
Inclusion criterion
Ø Healthy external and middle ear
Ø Diagnosed with AN/AD with severe-profound HL in ABR & BOA.
The assessments performed were-

1. The clinical assessment: Detailed physical and Otorhinolaryngological examinations before Audiological assessment.

2. The audiological assessment: BOA, Impedance Audiometry (IA), OAE and ABR were repeated to confirm AN.

Results
The TTD was computed and mean duration was calculated for the different peaks of CM. The mean duration of

1⁰ peak- 0.41ms; [range 0.21ms - 0.68ms]
2⁰ peak- 1.05ms; [range 0.61ms - 1.35ms]
3⁰ peak- 1.84ms; [range 1.08ms - 2.33ms]
4⁰ peak- 2.66ms; [range 2.01ms - 3.10ms]
5⁰ peak- 3.34ms; [range 2.80ms - 3.81ms]
6⁰ peak- 4.08ms; [range of 3.60ms - 4.36ms]

Conclusion:
The traces obtained in response to rarefaction or condensation clicks revealed that a low-amplitude oscillation, followed by first high amplitude of the CM⁴ and reversed in phase in response to stimuli of opposite polarity. This phase inversion means that this low amplitude activity is the CM itself, lasting longer than previously believed. So evaluation of CM duration by visual inspection represents a challenging if not impossible task.

CM can be obtained on ABR and this can provide a good replacement for ECoG.
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figure 1

TIME DOMAIN OF REVERBSAL IN AUDITORY BRAINSTEM RESPONSES

Question: Can Auditory Brain Stem Responses (ABR) be a substitute for Electrocochleography (ECochG) in the diagnosis of Auditory Neuropathy (AN)? Auditory Dysynchrony (AD)?

Method: A clinical study including
- 16 patients
- Age range, 9 to 43 months.

Inclusion criteria
- Healthy external and middle ear
- Diagnosed with AN/AD with severe-profound HL in ABR & BOA.

The assessments performed were:
1. The clinical assessment: Detailed physical and Otorhinolaryngological examinations before Audiological assessment.
2. The audiological assessment: BOA, Impedance Audiology (IA), OAE, and ABR were repeated to confirm AN.

Results: The TTD was computed and mean duration was calculated for the different peaks of CM. The mean duration of

- 1st peak: 0.41ms, [range 0.21ms - 0.63ms]
- 2nd peak: 1.05ms, [range 0.61ms - 1.35ms]
- 3rd peak: 1.84ms, [range 1.08ms - 2.33ms]
- 4th peak: 2.60ms, [range 2.01ms - 3.10ms]
- 5th peak: 3.34ms, [range 2.80ms - 3.81ms]
- 6th peak: 4.03ms, [range 3.60ms - 4.36ms]

Conclusion:
The traces obtained in response to rarefaction or condensation clicks revealed that a low-amplitude oscillation, followed by first high amplitude of the CM and reversed in phase in response to stimuli of opposite polarity. This phase inversion means that this low amplitude activity is the CM itself, lasting longer than previously believed. So evaluation of CM duration by visual inspection represents a challenging if not impossible task. CM can be obtained on ABR and this can provide a good replacement for ECochG.

References:

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P131
EVOKED POTENTIALS AFTER PAINFUL ELECTRICAL STIMULATION: PRELIMINARY RESULTS.

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Question

It is not known whether somatosensory evoked potentials after painful electrical stimulation (SEPpain) evaluate selectively the thermoalgesic pathway.

Methodology

Eighteen healthy adult subjects were recruited in the study. SEPpain were recorded in Cz to A1/A2 (10-20 EEG system), band-pass filter: 3-100 Hz. Stimuli were applied using ring electrodes in the right middle finger and in the right second toe. The stimulation protocol was double pulse, 1 ms pulse duration, ISI 5 ms, in trains of 10 stimuli at 0.1Hz. The electrical stimulation intensity used was chosen for each subject as the one that evoked a painful perception in the painful visual analog scale (VAS) (VAS 8 in 14 subjects, VAS 4 or more in 4). In 9 of the subjects we also recorded SEP using non-painful stimuli.

Results

Mean age was 36.3±12.3 years. In the upper limbs latencies were for N1=133.1±14.1 ms and for P1=192.7±17.9 ms. In the lower limbs latencies were for N1=155.8±14.8 ms and for P1=206.7±15.7 ms. In the 9 subjects with non-painful stimulation, we obtained SEPs of similar latency but smaller in amplitude (p=0.0039).

Discussion

Painful SEP is a simple and reproducible electrophysiological technique. SEPs of similar latencies are obtained with painful and non-painful stimuli, and there is an amplitude increase with higher intensity stimulation. In conclusion, painful SEPpain by electrical stimulation may not only evaluate the thermoalgesic pathway. *Fondecyt N°1120339: LAcevedo, GBarraza, MCampero, JLCastillo, RGuiloff, JHoneyman, RHughes, JMMatamala, EMullins, CRamirez, HRojas, ISazunic, RVerdugo, YWang.
P132
A Systematic Study of Vestibular Evoked Myogenic Potentials (VEMPs) from Upper and Lower Limb Muscles

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**Question**

From which upper and lower limb muscles can we reliably record VEMPs, including those that have not been reported previously, and what are their characteristics?

**Methods**

Twelve physiologically normal volunteers were recruited (age range 17-26 years, 4 males and 8 females). Together with the cVEMPs (from the sternocleidomastoid muscle) and oVEMPs (from the inferior oblique muscle), attempts to record VEMPs in response to moderate intensity (120 dB pSPL) tone (500 Hz) stimulation were done from the tonically active deltoid, biceps brachii (BB), triceps brachii (TB), flexor carpi radialis (FCR), extensor digitorum communis (EDC), abductor digiti minimi (ADM), vastus lateralis (VL), tibialis anterior (TA), gastrocnemius and abductor hallucis (AH) muscles.

**Results**

Reproducible responses were obtained from all muscles, with mean initial peak times of 15.4 msec (cVEMP), 8.6 msec (oVEMP), 12 msec (deltoid), 13.7 msec (biceps), 14 msec (triceps), 14.5 msec (FCR), 11.7 msec (EDC), 13.7 msec (ADM), 14.2 msec (VL), 18 msec (gastrocnemius), 16 msec (TA) and 20 msec (AH). All responses were unobtainable at 6Hz tone stimulation which is beyond the range of saccular stimulation. The AH was exceptional in being absent in some normal volunteers. Of the limb muscles, the highest corrected amplitudes were from the FCR and the lowest from the ADM and triceps.

**Conclusion**

It is possible to record VEMPs from all upper and lower limb muscles with different mean latencies and amplitudes. This should prove useful in evaluating lesions in the anterior funiculus of the spinal cord where the vestibulospinal tracts are located.
P133
Comparing statistics for objective detection of transient and steady state evoked responses in newborns.

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Question
The performance of automatic detection methods for auditory evoked responses is important for hearing screening. This study uses Receiver operating characteristic (ROC) methodology to compare the performance of different statistics in the automatic detection of multiple auditory steady state responses (MSSR) and click auditory brainstem responses (cABR) in neonatal hearing screening.

Method
Thirty five healthy newborns were tested within the first 2 weeks of birth. In each case cABR and MSSR (0.5 & 2 kHz) were recorded with and without acoustic stimulation, using the AUDIX equipment. With this test sample of recordings, ROC curves were evaluated separately for each statistic evaluated: 1) the standard deviation ratio (SDR) and the correlation coefficient ratio (CCR) for the cABR; 2) the Hotelling T2 (HT2) and circular T2 (CT2) for the MSSR.

Results
All objective detection methods performed well (areas under ROC (AUC) larger than 0.9). The MSSR statistics showed significantly larger AUCs at both frequencies (HT2: 0.98 and 1; CT2: 0.96 and 0.99) than the cABR measures (SDR: 0.91 and CCR: 0.92). The HT2 hits rate was the highest (97-100% at 0.5 & 2 kHz) for fixed false alarms rates of both 10 and 20%.

Conclusions
This superiority of performance of T2 like statistics, reflecting inherent advantages of MSSR analysis for automation, warrants serious consideration for further development of newborn screening technology.

Figure 1. ROC curves for HT2 and CT2 (at 0.5 & 2 kHz) are shown in the Figure 1 A. Figure 1 B shows ROC curves for CCR and SDR.
P134
Hearing screening using multiple auditory steady state responses to air and bone conducted stimuli

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Question

Minimizing the false positives rates is an important goal of the universal newborn hearing screening programs. An adequate way for reaching that goal could be differentiate between transient conductive hearing losses (false positives) and permanent sensorineural hearing impairments (true positives) by means of a methodology that study the electrophysiological responses to air and bone conducted stimuli. The aim of this study is to evaluate the efficiency of an automated hearing screening test based on Auditory steady state responses (ASSR) to air and bone conducted stimuli.

Methods

A sample of 80 high risk babies between 15 and 60 days were screened. A confirmatory clinical and electrophysiological evaluation was used as the gold standard.

Results

The estimated diagnostic efficiency of this screening test was equivalent or higher (100% of sensibility and 97.7% of specificity) than the efficiency reported for other hearing screening tests. The introduction of bone conduction in the screening reduced the false positives rate from 13.3% to 2.2%. The test duration was 5.3 (± 1.9) minutes. The 34% of babies need only 1 repetition of the test for raising the result.

Conclusions

This is the first time that ASSR was used in an automated screening test. The simultaneity principle of ASSR to present air and bone conducted stimuli at the same time was also introducing in this work. The screening test performed quite well in this initial clinical trial, differentiating transient conductive hearing losses from permanent impairments, and improvement the diagnostic efficiency of ASSR.
Caracterization of the occlusion effect in normal-hearing adults using MSSR

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**Question**

The occlusion effect (OE) is the increase in hearing sensitivity at low frequencies when the auditory system is stimulated by a bone-conducted signal and the ear canal (EC) is occluded. Are there any influence of the OE on the multiple auditory steady-state responses (MSSR) amplitudes and thresholds to bone conduction stimuli?

**Methods**

Bone conduction MSSR amplitudes and thresholds were obtained in 22 normal-hearing adults in two different conditions (occluded and unoccluded ears). The stimulus consisted of a combination of four continuous carrier tones (0.5, 1, 2, and 4 KHz) presented at the temporal bone.

**Results**

A repeated-measures ANOVA showed that EC occlusion had a significant effect $[F(3,63)=17.6, p<0.001]$ on thresholds. Multiple comparisons indicated that thresholds for occluded ears were significantly lower compared with unoccluded ears at 0.5 and 1 KHz. At 4 KHz occluded thresholds were significantly higher than unoccluded thresholds. The occlusion of the EC had no significant effect on the amplitudes (values between 0.017-0.16 µV for both test conditions across all frequencies at 40 dB HL). There was a significant correlation between the occluded and unoccluded thresholds for 0.5 and 1 KHz.

**Conclusions**

We confirmed the results of previous studies in a larger sample, corroborating the existence of OE for low frequencies during MSSR recordings. We do not recommend the EC occlusion when bone-conducted MSSR thresholds are determined. However, it is possible to use an electrophysiological correction factor for estimating threshold when the EC is occluded.
P137
Maturational changes in the human envelope following responses

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Question

Temporal auditory processing is deteriorated in old age, multiple sclerosis, auditory neuropathy, hearing loss, and developmental language disorders. Human envelope following responses (EFRs) is usefulness for electrophysiological measurement of auditory processing. In this study we evaluate the age-dependent changes of the EFRs during the first two years of live.

Method

The EFRs were recorded in 29 babies distributed into three groups: G1: 12 newborns, G2: 13 babies (1-12 months), and G3: 4 babies (24-35 months). EFRs were evoked by white noise carrier stimuli with a sweep of modulation frequencies (MF) from 20 to 200 Hz presented at 50 dB HL.

Results

The age related changes affected both morphology and EFRs detectability. These maturational changes are more evident in newborns. The main morphology differences were to expenses from frequencies below 50 Hz, were the first component P1 (located between 30-50 Hz) was not well defined in none of the 3 groups of ages. There was a significant effect of age over the EFRs amplitude. For all MF the newborns had significantly smaller responses than the two older groups. Also the EFRs amplitude was significantly larger for G3 than G2. The detectability of the response increased with age for all MF, reached a 100 % of detectability in G3.

Conclusions

This study provides the first evidences on the maturation of EFRs. Some understanding of normal EFRs development would facilitate a better use of this technique in clinically objective measurement of auditory temporal processing in infants who cannot provide reliable behavioral responses.
P138
Auditory gating function in common marmosets

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Question

Common marmosets, Callithrix jacchus, are small primates with a maximum body weight of only 500g. Although the marmoset brain is smaller than that of rhesus macaque, it has anatomical features similar to those found in other primates, including humans. However, the natures of the sensory processing of them have not been cleared. In this study, we examined the auditory gating function of marmosets and the effects of ketamine on it.

Methods

Five marmosets were implanted with 5 chronic electrodes on the brain. They were exposed to 2 identical consecutive auditory stimuli under awake and free-moving conditions. The potential differences between the positive and negative deflections, 40 and 80 ms after the stimuli, were measured. Ketamine (3mg/kg) was administered intramuscularly to the marmosets.

Results

When the interval between 2 consecutive stimuli was 0.5 s, the response to the second sound was about half of the size in comparison to the first one. On the other hand, when the interval was longer than 4 s, the amplitudes of both responses were the same. The responses differ significantly in accordance with the interval of the stimuli. Ketamine suppressed the response to the first auditory stimuli that resulted in the amplitudes of both responses becoming the same even in the smaller interval.

Conclusion

We therefore conclude that the auditory gating function in common marmosets is similar to humans. In addition, the deficit induced by ketamine suggests that it could be a model for the study of some psychiatric diseases.
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P139
Cortical activity in pausing of finger reactive movement: an ECoG study

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Purpose

We try to clarify the cerebral processing of motor control mechanism when reactive movement pauses.

Methods

A 25-year-old, right-handed patient with medically intractable epilepsy was participated. Subdural grid electrodes were placed over the left perirolandic and mid- to posterior temporal lobe for epilepsy surgery. Omission auditory stimuli: Auditory tone bursts were presented in fixed interval of 850 ms stimulus onset asynchrony. In the auditory sequence, 20% of the stimuli were omitted randomly. Paradigm:

1. ACTIVE condition. In a train of auditory stimuli, subjects were requested to move their right thumb in response to the tones as quickly as possible. Subjects should not move their thumb (= pause) when tones would be omitted.
2. PASSIVE condition. Subjects were requested just to listen to the same stimulus sequence.

Recording: Electric cortical stimulation disclosed his primary sensorimotor area (SI-MI) and negative motor area. Surface EMG of right thenar muscle was simultaneously recorded. ECoG and EMG epochs from -1.9 to +1.7 s with respect to the Omission onset were collected to contain four movement cycles, and 69 and 64 sweeps were averaged in ACTIVE and PASSIVE conditions, respectively. Signals were sampled at 2000 Hz with the bandpass filter of 0.10-600 Hz.

Results

In PASSIVE condition, a response to tones was found at 250 ms around the superior temporal gyrus (STG). No activity occurred in response to Omission. In ACTIVE condition, responses to tones were found in the SI-MI (400 ms in peak latency), inferior part of precentral gyrus (= ventral premotor, 460 ms) and STG (250 ms). These areas became active when movement paused in omission peaking at around 450 ms in latency, and additional activities appeared in inferior part of supramarginal gyrus and posterior temporal lobe.

Conclusion

The left SI-MI, ventral premotor and temporoparietal junction play some roles in pausing of reactive ongoing movement of right hand.
EARLY SENSORY EXPERIENCE AND MATURATION RATE OF NEONATAL VISUAL EVOKED POTENTIALS

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Introduction

The visual pathway maturation in neonates was studied mainly by long latency components. Very few data, however, exist on short latency VEP and their development.

Objective

The aim of this study was to compare the maturational process between premature and full-term neonatal short latency visual evoked potentials (VEPs), using flash stimuli.

Methods

Newborns at different age groups were tested, premature and full-term neonates. A total of 83 neonates were included in the study. They were divided into four post-conceptional age groups: 1-2 months, 3-6 months, 7-12 months and 13-24 months. Each group was subdivided into premature and full-term neonates. Responses from the retina and the optic pathways elicited by flashes were recorded using a Cz-Fz and Cz-O1/2 montage respectively.

Results

Immature retinal responses were observed in the first age-group and were characterized by a waveform roughly similar to that observed in adults but of a smaller amplitude as well as longer latencies. Decrease in wave latencies towards adult values occurred at 7 months and remained stable thereafter. Short-latency VEP in the first age-group showed marked morphological changes compared with adults, namely: increased latency and decreased amplitude of N1 wave and disappearance of the later components. The maturation process was characterized by a progressive decrease in the N1 latency, for each age-group and changes in response pattern and complexity. Interestingly, the maturation rate was affected by the duration of extra-uterine exposure to sensory experience.

Conclusions

Our results reveal that, early exposure to sensory experience presents differential effects on the peripheral and central components of short latency VEPs. Some of them are advanced while others are delayed.
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P141
MOTOR EVOKED POTENTIALS FROM MULTIPLE RECORDING SITES OF THE LOWER LIMBS AS A MONITORING TOOL OF CENTRAL MOTOR FUNCTION

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Question
Variability of MEP area hinders quantification of central motor conduction failure (CMCF), i.e. conduction block and axonal damage. MEP averaging, combined with objective control of voluntary facilitation, restrains intra-trial MEP variability1.

Objective
To achieve maximum stability of MEP area in subsequent recording sessions.

Methods
In 14 clinically stable Multiple Sclerosis (MS) patients and 8 healthy controls (HCs) MEPs to TMS with double cone coil1 and maximal CMAPs to High Voltage Electrical Stimulation of lumbosacral roots2 were recorded twice, 1-2 days apart, from Vastus Medialis and Lateralis (VM, VL), Tibialis Anterior (TA), Peroneus Longus (PL) and Flexor Hallucis Brevis (FHB) of both sides. The coil position, the vertebral stimulation point and all recording sites were marked with a dermographic pen. The two sets of Averaged MEP Areas and Area Ratios (MEP area/CMAP area, AR) were compared using the Coefficients of Variation (MEP- and AR-CV).

Results
The use of unchanged stimulation and recording sites significantly reduced inter-trial MEP variability, which was further restrained by AR in all muscles. The mean AR-CV were 9.3% ± 10.4% (VM); 7.9% ± 7.5 (VL); 3.5% ± 5.0 (TA); 9.3% ± 10.9 (PL) and 3.6% ± 4.4 (FHB). No significant differences were observed between MS patients and HCs.

Conclusions
The reduced inter-trial MEP variability makes the described technique a promising tool for CMCF monitoring. Moreover, trend analysis of the large number of available ARs in individual subject can sharpen the sensitivity of the method. When advised by clinical needs in selected patients, the vertebral recording point and stimulation sites can be fixed using small, almost unnoticeable tattoos, as commonly used in radiation therapy, making the method suitable for long-term follow-up.

P142
Visual evoked potentials preoperative in infant and children with congenital cataract

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Question

What are the abnormalities in visual evoked potentials (VEP) before surgery in children with congenital cataract and to determine its association with the development of infants and children?

Method

34 children with congenital cataract, 14 (.41) male and 20 (.59) female between 3 and 42-month (mean 10.5 ± 8.3) age, were studied. To obtain VEP, LED (Light Emitting Diodes) stimulus was used, averaging 100 stimuli in two occasions in right, left eye and binocular. We evaluated the amplitude, latencies and morphology of the cortical visual response.

Result

Eleven infant and children had normal visual response, 23 had abnormalities in the visual response. VEPs showed marked abnormalities, including small amplitudes (.13), prolonged latencies (.27), visual response absent (.06).

Moderate and severe delay in development was observed in 90% of infants and children.

A statistically significant association between the VEP and the global development of children (p<0.015) was found.

Conclusions

Congenital cataract is an important preventable cause of visual impairment and blindness in childhood. It is critical that children with abnormalities in visual response receive prompt treatment during the sensitive periods to decrease the risk of developing amblyopia or binocular abnormalities, producing irreversible changes in the visual system and consequently greater commitment the neurodevelopment.
P143
What do laser-evoked potentials (LEP) show in patients with functional non organic sensory disturbances: A report of 2 cases

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Question

In neurology daily practice sensory signs may occur due to nonorganic causes. Routine assessments normally include imaging and neurophysiological testing. Laser-evoked potentials (LEP) can be used to assess the integrity of spino-thalamic tract. We report 2 patients with suspected functional sensory disturbances in which LEP were performed.

Methods

2 chronic pain patients were referred to exclude a nerve lesion. A complete neurology clinical examination and LEP were performed including cortical recording of LEP and assessment of laser sensory and pain thresholds. Both patients had MRI, SEP and MEP done or measurements were completed.

Results

A 53 year old female developed left sided pain within 24 hours post car accident 4 years ago. On examination she showed left sided hypoesthesia to light touch and cold stimuli and hypoalgesia. Further, a 45 year old female presented with shoulder, neck and sacral pain since having a fall one year before. She showed sensory deficits sub C5 dermatome with hypoesthesia to light touch and cold stimuli and hypoalgesia. In both patients MRI, SEP and MEP were normal. Cortical LEP were normal but in patient 1 there were abnormal left sided laser sensory and pain thresholds while in patient 2 there were abnormal thresholds on both hands and feet.

Conclusion:

Despite of abnormal laser sensory and pain thresholds the cortical recorded LEP were totally normal. These results show, that the subjective reported and clinically objectified sensory disturbance was demonstrable with psychophysical methods but not with objective methods.
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P144
Contact heat evoked potentials (CHEPs) in healthy subjects - no laterality effect.

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Question
Contact heat evoked potentials (CHEPs), induced by brief cutaneous heat stimuli, provide objective information on the integrity of peripheral and central nociceptive pathways. The clinical use of CHEPs requires normative data collection. We investigated whether CHEPs are affected by hemi-body laterality (right vs. left differences).

Methods
Forty-eight neurologically normal adults were recruited to Neurology centers in Israel, Japan, Spain and USA. All underwent contact heat stimulation with a thermode (PATHWAY, Medoc, Israel) reaching a peak temperature of 51 °C, applied at 8 body sites (bilateral face, forearm, leg and C7 and L1). CHEPs were recorded over Cz, Fz and T3-T4, and the A delta N2-P2 amplitudes and latencies were analyzed after averaging 10-14 responses. Pain was rated using 0-10 verbal NPRS. We compared data (Cz) from left and right side stimulation using parametric (t-tests) or non-parametric (signed-rank tests) as appropriate.

Results
No significant laterality effect was observed for amplitude and latency of CHEPs, or pain scores: see Table below with means (SD).

<table>
<thead>
<tr>
<th></th>
<th>Amplitude (µV)</th>
<th>Latency (ms)</th>
<th>Pain score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>p value</td>
</tr>
<tr>
<td>Face</td>
<td>25.2(13.1)</td>
<td>26.1(12.6)</td>
<td>0.97</td>
</tr>
<tr>
<td>Forearm</td>
<td>23.8(14.9)</td>
<td>23.9(14.6)</td>
<td>0.26</td>
</tr>
<tr>
<td>Leg</td>
<td>17.5(9.8)</td>
<td>19.5(12.1)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Conclusions
CHEPs are not affected significantly by hemi-body laterality, for either latency or amplitude. These findings suggest that unilateral assessment is sufficiently reliable for normative data collection, and for the evaluation of symmetrical small fiber disorders.
P145
Neural correlates of subliminal affective priming effects: a high-density ERP study with ambiguous emotional faces

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Purpose

Affective priming effects refer to the phenomena that presentation of affective prime stimuli shifts subsequent affective evaluation to the target stimuli. Tsushima et al. (2006) revealed that unconsciously processed stimuli could more affect behavioral performance than consciously ones. However, neural correlates of subliminal affective face priming effects are largely unknown. Therefore, we investigated this issue using ERPs.

Method

Ten healthy volunteers (5 females, mean age 23.7±3.2 y.o.) participated. Stimulus sequences consisted of the 17 ms-subliminal prime faces (neutral or fearful) followed by a backward mask (SOA 300 ms) and 800 ms-target faces (neutral, emotionally ambiguous, or fearful) (Figure 1). ERPs were recorded by a 128ch EEG machine in the task in which subjects had to judge the expression of target faces as neutral or fearful. ERPs were obtained by averaging the responses for each target face.

Results

Behavioral data showed that subjects tended to judge ambiguous target faces as fearful at fearful face prime condition. ERPs data revealed that N170 and frontal P2 from the target faces were enhanced in fearful face prime condition. These results suggested that subliminal priming fearful face enhanced activation of extrastriate occipito-temporal cortex and frontal region as early as 200 ms post target stimuli onset. This might underlie the mechanism that emotionally ambiguous target faces were perceived as more fearful.

figure 1

![Neutral face - Ambiguous face - Fearful face](image)

Figure 1. Examples of target face stimuli
Visualization by magnetospinography of electrophysiological activity in the cervical spine evoked by peripheral nerve stimulation

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Purpose

We have developed a magnetospinography system that allows for non-invasive imaging of the magnitude and spatiotemporal spread of nerve-evoked currents in the spinal cord and spinal nerves. In this study, we aimed to visualize evoked currents from the cervical spine in response to median nerve stimulation.

Methods

Using a newly developed 120 channel SQUID fluxmeter, the neuromagnetic fields of 5 healthy volunteers were measured at the surface of the cervical spine in response to surface stimulation of the median nerve at the elbow. We also measured neuromagnetic fields after stimulation a few centimeters lateral to the median nerve and adopted a newly developed algorithm to reduce artifacts arising from surface electrical stimulation. Current sources were estimated using spatial filter techniques and the current field superimposed on X-ray images of the cervical spine.

Results

Neuromagnetic fields were successfully imaged in all subjects. Neural currents entered the lateral cervical spine and ascended in the spinal canal from caudal to cranial, followed by currents propagating in the opposite direction.

Discussion

We visualized neural activity patterns in the intervertebral foramen and spinal canal evoked by median nerve stimulation. Magnetospinography is expected to contribute to the clinical diagnosis and treatment of spinal cord and spinal nerve disorders.
P147  
SSEP revisited: The significance of absolute N20 amplitudes for prognosis following cardiac arrest  
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Question  
Absence of cortical SSEP (N20) after stimulation of the median nerves predicts poor outcome after cardiac arrest with high specificity. This may also apply to patients with minimally detectable N20, but cut-off levels for N20 amplitudes below which good outcome becomes very unlikely have not been determined.  

Methods  
Peripheral, spinal and cortical SSEP were recorded following stimulation of the median nerve at the wrist one to three days after cardiac arrest in patients treated with mild hypothermia (33°C for 24 hours). We measured N20P25 amplitudes and noise levels from all recordings and determined neurological outcome at discharge from the intensive care unit. Outcome was dichotomized in good outcome and poor outcome according to the cerebral performance category (CPC).  

Results  
SSEP from 297 consecutive patients were available. Preliminary analysis was performed on 117 patients. Of those, 51% had good outcome and 49% had poor outcome. Within this limited cohort, only one of 60 patients with good outcome had cortical amplitudes below 0.47 μV. Among patients with poor outcome, 24 of 57 patients had amplitudes below 0.4 μV or no detectable N20.  

Conclusions  
Our preliminary analysis of 117 cardiac arrest patients treated with hypothermia suggests that beyond the mere presence of a cortical potential, absolute amplitudes yield valuable prognostic information. Our data further indicate co-variation of outcome with N20 amplitudes and the existence of cut-off values, below which good outcome is improbable.
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P148
Air puff evoked potentials. Short latency response and long latency vertex response. Normative values

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Question
To determine normative values of the short latency evoked potentials (EP) and of the long latency vertex EP elicited with a pneumatic, innocuous and calibrated stimulation to the skin.

Material and methods
Twenty young healthy volunteers. Air puff stimuli were delivered through a home made device. The nozzle of the pneumatic stimulator (0.5 mm diameter outlet) delivered an air impulse (10ms duration, pressure 3,5 bars). It was placed perpendicularly to the skin at one cm. The noise of the air puff was masked. The cutaneous sites of stimulation were dorsum of hands and feet (right and left).

Short latency EP recording

Two series of 1000 stimulations delivered at 3Hz, band-pass (BP) : 0,3 to 3000 Hz, time of analysis (TA) : 100ms, reference electrode (RE) on the ear lobe and ground electrode (GE) on FPz. Latencies and amplitudes of the cortical response were measured on controlateral parietal or central region after stimulation of the hands (N1) and on Cz or Pz after stimulation of the feet (P1).

Long latency vertex EP recording

Two series of 20 stimulations delivered at 0,2 Hz, BP: 0,3 to 100 Hz, TA: 1s, RE on the nose and GE on FPz. Latencies and amplitudes of the responses N2 and P2 were measured on Cz. Normative values were defined as Mean + 2,5 SD.

Results
Short latency EP : A reproducible potential was obtained bilaterally in 10 subjects after stimulation of the hands and in 18 after stimulation of the feet. N1 and P1 mean latencies were 47,2 (SD 0,7) and 66 (SD 0,4) ms after stimulation of hand and foot respectively. Mean amplitude from baseline was 0,73 mV (SD 0,41) after hand stimulation and 1,1 mV (SD 0,9) after foot stimulation. When comparing the difference in latencies after hand or foot stimulation, the mean conduction velocity was 38 m/s consistent with a conduction of air puff related-responses by A beta fibers.

Long latency vertex EP : A reproducible potential was obtained bilaterally in 18 subjects after stimulation of the hands and in 14 after stimulation of the feet. N2 and P2 mean latencies were 139 (SD 7,1) and 196 (SD 22,5) ms after stimulation of hand and foot respectively. Mean N2/P2 pick to pick amplitude was 11 mV (SD 6,2) after hand stimulation and 10 mV (SD 3,8) after foot stimulation.

Conclusion
These normative data are useful for the assessment of patients suffering from neuropathic pain such as air-puff triggered allodynia.
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P150
A complex evoked cortical response is induced by the relief of air flow interruption

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QUESTION
To analyze brain electrical events elicited by the restoration of normal breathing after an air flow (AF) occlusion.

METHODS
Twenty nine subjects (21.6 ± 3.0 years) breathed through a shutter-equipped spirometer. AF was blocked for 20 seconds. Evoked potentials (EPs) were monitored after AF restoration. Amplitude and latency values were determined as a function of AF occlusion/restoration repetition. In parallel, the subjects self-evaluated their psychological discomfort (PS) at the end of the 1\textsuperscript{st} and 20\textsuperscript{th} AF occlusion.

RESULTS
EP were induced by AF restoration and consisted in consecutive negative (N1), positive (P1) and negative (N2) waves. N1 latency value, but not those of P1 and N2, decreased as AF occlusion/restoration was repeated. N1 and N2 amplitudes were decreased by AF occlusion/restoration repetition. P1 remained unchanged. PS decreased between the 1\textsuperscript{st} and the 20\textsuperscript{th} AF occlusion. No correlation was found between PS decrease and changes of N1 and N2 properties.

CONCLUSIONS
Apnea relief induced a complex brain electrical activity with latency and amplitude properties suggesting the adaptive contribution of various cortical and sub-cortical structures accompanying the relief feeling. These results reveal the modification of brain activity following apnea relief, a situation that occurs during sleep-associated breath troubles.
LP8
Vestibular myogenic and acoustical brainstem evoked potentials in neurologic practice

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Question

The clinical manifestation of central and peripheral vertigo sometimes very similar: in the acute period may be system vertigo, noise and hearing loss. MRI doesn't always reveal the impairment of the brainstem and cerebellum. The neurophysiologic tests (BAEP and VMEP) in combination with the otoneurology inspection make it possible to reveal the changes, which are significant for the peripheral and central level of the lesion of the vestibular and auditory system.

Methods

79 patients suffered from multiple sclerosis (MS) were under our observation, which had predominantly cochlear vestibular disturbance in the acute period of the disease, whereas 11 had the symptoms of unilateral hearing loss and the system vertigo similar to Meniere's disease.

Results

Comparison of the auditory dysfunctions with the vestibular symptoms in patients with the unilateral hearing loss always have retro cochlear lesion. Patients with the unilateral hearing loss and brainstem vestibular symptoms, which indicate the damage of auditory and vestibular pathways in the brainstem, have plural plugs in the brainstem on MRI. In case of the unilateral hearing loss up to the deafness, which is not combined with the brainstem vestibular symptoms, the plugs of demyelization on MRI in the usual regime may be not revealed. However, the signs of the disturbances of afferentation specific for MS could be reviled by the EP data.

Conclusion

The novelty of work consists in the complex use of objective methods of investigation the auditory and vestibular functions by EP and MRI in the regime of thin slices.
LP9
Central post-stroke pain explored by laser-evoked potentials and quantitative sensory testing: A multiple case study.

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²Swiss Paraplegic Centre, Centre for Pain Medicine, Nottwil, Switzerland

Question

After a stroke, central post-stroke pain (CPSP) i.e. a neuropathic pain syndrome can occur. Here, we described the neurophysiological assessments including laser evoked potentials (LEP) and quantitative sensory testing (QST) in single cases.

Methods

Five patients (3 males) with a mean age of 56 years (SD 7) were assessed with LEP and QST. All patients had a cerebral MRI and a neurological examination was performed. Stroke aetiology was embolic ischaemia (2), microvascular ischaemia (1), intracerebral hemorrhage (1) and subarachnoid hemorrhage in 1 case. LEP and QST performed according to the German Research Network on Neuropathic Pain were obtained in the painful area (3 patients on the hand and 2 on the foot). The following QST parameters were studied: Cold detection threshold (CDT), warm detection threshold (WDT), thermal sensory limen (TSL), paradoxical heat sensation (PHS), cold pain threshold (CPT), heat pain threshold (HPT), mechanical pain threshold (MPT), mechanical pain sensitivity (MPS), allodynia (ALL), wind up ratio (WUR) and pressure pain threshold (PPT) for STT function. DCS function was assessed by mechanical detection threshold (MDT) and vibration detection threshold (VDT).

Results

The mean age of patients at stroke was 52.8 years (SD 8.4). Patients had a mean pain history of 3.3 years (SD 2.0). The mean pain intensity was 82.6 (SD 16.3). LEPs were abnormal in 4 patients with reduced amplitudes in 2 and absent in 2 cases. Latencies were normal in 2 patients, increased in 1 and absent in 2. Pain thresholds to laser stimuli were respectively normal and abnormal in 3 and 2 patients. QST was abnormal for STT in all patients. Thresholds were increased for TSL (all patients), CDT (4), WDT (4), MPT (1) and MPS (1). PHS was present in 2 cases. Decreased thresholds were found for MPT (2) and MPS (1). Allodynia was present in 3 patients. DCS function in QST was abnormal in 4 patients showing increased VDT (3) and MDT (2). All MRI's showed a lesion within the somatosensory system as in insular cortex (2), white matter (1) and brainstem (2). STT abnormalities were consistent between LEP and QST in 4 cases.

Conclusions

Based on our results in patients with CPSP, a high rate of STT and DCS abnormalities measured by LEP and QST is found. A comparison to stroke patients without CPSP should further support the usefulness of both tools.
P151
High Accuracy Functional Neuromonitoring to Preserve the Facial Nerve during Robotic Direct Cochlear Access using a custom made Concentric Stimulating Probe

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Question

Minimally invasive direct cochlear access (DCA) is a computer assisted robotic approach to cochlear implantation [1]. The lack of direct visual control of the tool position puts structures such as the facial nerve (FN) at risk. Recently, neuromonitoring technology was integrated into a commercially available drill system enabling real-time monitoring of the FN [2]. Our group evaluated the feasibility of using this system combined with our robotic approach in a live sheep study [3]. The results of this study showed that the current implementation is neither sensitive nor specific enough to provide useful information during DCA procedures. This abstract reports on our initial efforts to model an optimal stimulating electrode. Additionally, the design of a second animal study with the improved tool will also be presented.

Methods

A concentric stimulating probe is proposed using the DCA drill geometry. The cathode electrode is located in the tool tip. 2 different anode configurations (d) and 2 different cathode heights (h) were studied (see Figure 1). Using a specialized software (Comsol Multiphysics, USA), the electrical field (E) between the cathode and the anodes was simulated for each of the 4 configurations.

Results

The electrical model predicted that the smallest cathode (h₂ = 0.3 mm) has a more focused electrical field in the radial axis (see Figure 2a). A cathode to anode distance of 1 mm (d₁) produced a more focused stimulation pattern at the tip than the 0.3 mm distance d₂ (Figure 2b).

Conclusions

We believe that a stimulation probe with 3 different anodes located at distances 0.4, 0.7 and 1 mm from the cathode will be a flexible design to evaluate the efficacy of the new stimulating tool in the robotic DCA approach. The exposed part of the cathode at the tool tip will be chosen as close as possible to 0.3 mm. To validate the stimulating efficacy of the new design, a live animal study has been organized and will be conducted in Bern from February to April 2014.

figure 1
figure 2
Continuous raw EEG recording during cardiopulmonary-bypass (CPB) surgery as a marker of hypoxia.

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Question

Raw EEG data are not routinely acquired during cardiopulmonary bypass (CPB) surgery, where processed data are preferred. Nonetheless, rEEG has a high specificity in detecting ischemic lesions (Florence et al., 2004). In awake patients, after CPB surgery, a global slowing of EEG frequencies has been reported (Zeitelhofer et al., 1988), but no data on continuous EEG during CPB have demonstrated a similar phenomenon.

Methods

16 patients undergoing mitral valve repair, without any other concomitant heart or valve defect, were selected (8 M, 6 F, mean age 64.3 years). 28 channels EEG was continuously recorded during surgery. Anesthesia was maintained stable (no bolus) for 10 minutes before the start of CPB, after sternotomy, 30 minutes after CPB beginning and during CPB weaning off (50% of pump activity). These intervals were selected off line, and 2 minutes periods analyzed with a Fast Fourier Transform to obtain the power spectrum density of the 3 periods. A multivariate analysis with Bonferroni correction was then run.

Results

Data from 12 were analyzed. A global slowing from T1 (pre-CPB) to T3 (post-CPB) emerged, with a diffuse increase of theta frequency (p=0.039). On frontal leads, delta increased with increase of time (p=0.005). Alpha and beta bands pointed to a reduction from T1 to T3 (alpha: temporal leads: 0.014; frontal: 0.003; beta temporo-parietal leads: 0.008), with tendency to appear on more anterior areas than physiological ones.

Conclusion

Continuous raw EEG recording during CPB surgery demonstrates a global frequencies slowing, with a higher susceptibility of frontal regions. EEG slowing is an indirect index of cortical dysfunction, possibly pointing in our series to hypoxia or riperfusion damage.

Figure 1

Power spectrum density ($\mu V^2/Hz$) for delta (1-4 Hz), theta (4-7 Hz), alfa (8-12 Hz), beta (13-30 Hz) bands at T1, T2 and T3. Vertical axis cut at 40 Hz to highlight the slower frequencies’ shift.
**P153**

Warning Thresholds for Motor Evoked Potential Monitoring During Surgery in Brain Motor Areas: Correlation with Neurological Outcome

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**QUESTION**

During brain surgery in or adjacent to motor areas, the goal of intraoperative neurophysiological monitoring (IONM) is to reduce the risk of neurological damage. Nonetheless different warning criteria for muscle motor evoked potentials (mMEP) are still under debate. The aim of our study was to analyze the early neurological outcome and the correlation with IONM in order to assess the value of different IONM criteria.

**METHODS**

Clinical data of 63 patients who underwent IONM assisted surgery for brain tumors in the motor areas, between January 2012 and August 2013, were collected prospectively in 24 patients and retrospectively in 39. Motor status on admission, early after surgery, at discharge and at follow-up was evaluated according to the Medical Research Council scale. IONM consisted of monitoring mMEPs elicited by transcranial electrical and/or direct cortical stimulation (DCS) of the motor cortex. Correlations between mMEPs and motor outcome were analyzed post hoc considering thresholds for significant amplitude decline set at 50% or at 80%.

**RESULTS**

Post-operatively 36% of patients (n=23) showed a worsening of neurological function. This rate dropped to 21% (n=13) at discharge and 8,5% (n=5) at the follow-up. Ninety-seven percent of patients (n=61) exhibited recordable mMEPs, and these were monitoring following DCS in 85% of the procedures (n=54). Considering the 50% amplitude reduction threshold, unaltered MEP recording occurred in 70% of patients (n=36) and none of them experienced a permanent paresis. Irreversible mMEP reduction occurred in 21,6% of patients (n=11); of these, 3 developed a new transient paresis and 5 a persistent paresis. One patient showed an irreversible MEP loss and developed a persistent new paresis. The rate of false positive results was 8% when threshold was set at 50% and 0% when set at 80%. Vice versa, the rate of false negative was 6% using a 50% threshold and 10% using a 80% threshold.

**CONCLUSIONS**

IONM reliably predicted motor outcome at discharge from hospital and especially at the follow-up. For mMEPs, an amplitude decline criterion of 50% exposes to some false positive but minimizes the risk of false negative results, while a 80% drop criterion seems to be too little sensitive.
Utility of Intraoperative Neurophysiologic Monitoring (IONM) in Altering Operative Management in the Endovascular and Surgical Treatment of Adult Cerebral Aneurysms

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Question

Can the use of IONM in surgical and endovascular treatment of adult cerebral aneurysms detect intraoperative cerebral ischemia, alter surgical management, and predict postoperative neurologic outcome?

Methods

Retrospective study of a consecutive series of 445 adult cerebral aneurysm cases, ages 25 to 84 years. Surgical and endovascular cases were monitored using somatosensory, brainstem auditory and motor evoked potentials; electroencephalography, and/or cranial nerve electromyography. Critical IONM changes were based on accepted criteria in the literature. Postoperative neurologic deficits were identified through chart review.

Results

88/445 (19.7%) cases demonstrated IONM changes; of these 73 (82.9%) had transient changes and 14 (15.9%) had persistent changes. 52/73 cases in the group with transient IONM changes showed no new deficits, 11/73 with transient deficits, and 10/73 with permanent deficits (total 21/73 with deficits). In the group with persistent IONM changes, 10 patients developed new permanent deficits, 2 with transient deficits, and 2 without new deficits (total 12/14 with deficits). 357/445 (80.2%) cases had no IONM changes; of these 7 (1.9%) had new postoperative deficits (5 transient, 2 permanent). Operative management was altered in all instances of IONM changes. The sensitivity and specificity of predicting postoperative deficits was 82.5% and 87.1%, respectively.

Conclusions

Persistent IONM changes predict a high risk for new postoperative deficits; and, in comparison, transient changes predict a low risk for new deficits. In addition, the data indicates that identification of IONM changes allows for intraoperative interventions. In general, IONM is a useful tool in accurately identifying intraoperative ischemia in time to alter operative management, and is likely to prevent cerebral injury and reduces the risk of new post-procedure neurologic deficits in the endovascular and surgical treatment of adult cerebral aneurysms. These results support the usefulness of IONM as an adjunct in cerebral aneurysm treatment.
P155
Alternative method of stimulation to elicit intraoperative bulbocavernous reflex

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2Hospital Ramón y Cajal, Neurofisiología Clínica, Madrid, Spain

**Question**

To describe an alternative method of stimulation for intraoperative recording of bulbocavernous reflex (BCR) and to assess its elicitability, feasibility and usefulness.

**Methods**

BCR is a widely accepted but not so extensively used technique, for continuous intraoperative monitoring of reflex lower sacral circuitry, stimulating pudendal afferents through surface electrodes. Available techniques show some limitations related to recording and stimulation methodology. To elicit the BCR, the pudendal branches (dorsal penile or clitoral nerves) were stimulated through a pair of monopolar needles. For dorsal penile nerve stimulation, needles were placed dorsal on each side of the base of the penis. For dorsal clitoral nerve stimulation, needles were placed at clitoris level on either side of labia majora.

Intraoperative recordings of BCR in 72 consecutives patients whom underwent neurosurgical or lumbosacral spinal procedures were collected.

**Results**

We reproducibly recorded BCR in 69/72 patients using a short train of 4/5 stimuli. We had not substantial differences in elicitability between genders. We had not intraoperative BCR loss related to neurosurgical procedures or attributable to stimulation technique. As far as possible elicitability and feasibility rates were compared to data from literature.

**Conclusions**

Preliminary results indicate that new technique could be considered as an useful alternative method, specially in those cases when superficial stimulation is not feasible (older patients, urogenital malformations).

Anatomical and physiological features of the new technique appears to resolve some methodologic limitations of superficial stimulation. However, elicitability rate improvement in females still need further investigation.
P157
Contralateral synkinesis of blink reflex in patients with hemifacial spasm

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Question

Some patients with hemifacial spasm (HFS) have synkinesis of the blink reflex (BR) not only on the ipsilateral but also the contralateral side. We determined whether contralateral synkinesis correlates with intraoperative findings of abnormal muscle responses (AMRs) and postoperative clinical course.

Methods

This study involved 72 patients (16 men and 56 women) who underwent microvascular decompression (MVD) for HFS. Patients were assigned to two groups according to the presence or absence of contralateral synkinesis obtained from preoperative BR (positive or negative synkinesis). With regard to AMRs, patients were divided into two groups on the basis of post-MVD disappearance or persistence of AMR (AMR disappeared or persistent AMR).

Results

Forty-three (60%) of the 72 patients had contralateral synkinesis recorded from preoperative BR (positive synkinesis group). Twenty-eight (39%) of the 72 patients had persistent AMR after MVD. Twenty-four of the 43 patients (56%) in the positive synkinesis group were assigned to the persistent AMR group, whereas 25 of the 29 patients (86%) in the negative synkinesis group were assigned to the AMR disappeared group (p < 0.001). Twenty-three of the 29 patients (79%) in the negative synkinesis group experienced immediate relief of their symptoms after the operation. In 29 of the 43 patients (67%) in the positive synkinesis group, HFS symptoms showed amelioration over time and eventually subsided (p < 0.001).

Conclusions

Contralateral synkinesis obtained from preoperative BR correlates with intraoperative persistence of AMR after MVD. The contralateral synkinesis-related findings may allow prediction of whether HFS disappears immediately after surgery or some time later.
P158
Usefulness of cranial nerve motor evoked potential monitoring during skull base surgery

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**Question**

To determine whether monitoring of facial, pharyngeal, and lingual motor evoked potentials (MEPs) elicited by transcranial electrical stimulation during skull base tumor surgery can predict postoperative function.

**Methods**

The authors analyzed facial MEPs in 104 patients during 112 surgical procedures, pharyngeal MEPs in 35 patients during 36 procedures, and lingual MEPs in 14 patients receiving treatment for skull base tumors. Corkscrew electrodes positioned at C3 or C4 and Cz were used to deliver supra-maximal stimuli. The correlation between the final to baseline amplitude ratio of each MEP and postoperative function was examined.

**Results**

Twenty-nine (94%) of 31 patients with amplitude ratios in facial MEP of less than 50% had poor facial motor function outcomes (House and Brackmann (HB) grade III-VI). In contrast, in 73 (90%) of 81 patients with amplitude ratios exceeding 50%, postoperative facial function was good (HB grade I-II). Twelve (86%) of 14 patients with amplitude ratios of less than 50% in pharyngeal MEP after tumor resection experienced deterioration of swallowing function, whereas 18 (82%) of 22 with amplitude ratios exceeding 50% showed no swallowing function changes. In lingual MEPs, all 4 patients with amplitude ratios of less than 50% experienced lingual palsy postoperatively, whereas 9 (90%) of 10 maintaining ratios of more than 50% showed no lingual function changes.

**Conclusions**

Intraoperative facial, pharyngeal, and lingual MEPs are potentially useful for predicting postoperative motor function after skull base surgery.
Transcranial Electric Myogenic Motor Evoked Potentials in Brain Tumor Surgery: An Exercise in Futility?

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Question

Are Transcranial Electric Myogenic Motor Evoked Potentials (TCEMEPs) useful for predicting motor deficits in brain tumor surgery?

TCEMEPs are standard of care in spine surgery. Frequent claims in the literature advocating for its application in brain surgery are found. However, when craniotomies are involved many factors will differ from the standard spine protocol.

Methods

We recorded TCEMEPs in 21 cases of frontal or parietal tumors during surgery. Stimulating electrodes were attached as close as possible to C1 and C2 as allowed by craniotomy. MEPs were recorded bilaterally from forearm, hand, leg and feet muscles. Stimulation for TCEMEPs was delivered on surgeon request to avoid patient movement interference with the surgery. SEPs from Median and Posterior Tibial nerves were also recorded. Disappearance of TCEMEPs, disappearance or 50% attenuation of SEP amplitude and a delay of 10% or greater of SEP latency from baseline were regarded as adverse changes. Clinical records were reviewed one month after the surgery to determine the presence or absence of new motor deficits or worsening of previously existent ones.

Results

Nine out of 21 patient had adverse TCEMEP changes during surgery. Only 3 of them showed new motor deficits. Conversely, 7 out of 12 patients with unchanged TCEMEPs showed new motor deficits. Thus, no association could be established between TCEMEP adverse changes during surgery and new motor deficits (p=0.245). Conversely, all 5 patients with adverse SEP changes had a new motor deficit, as were 5 out of 16 patient with unchanged SEPs. The association between SEP changes and motor deficits was thus significant (p=0.012).

Conclusions

IOM with TCEMEPs was not useful for predicting motor pathway damage during surgery for brain tumors and showed no added value over SEPs. Factors specific to craniotomies affecting TCEMEP sensitivity and specificity are discussed. Alternative procedures like direct cortical stimulation should be tried for assessing motor pathways in this context.

figure 1
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P160
THE ROLE OF INTRAOPERATIVE NEUROPHYSIOLOGICAL MONITORING DURING INTRAMEDULLARY SPINAL CORD TUMORS RESECTION: PROTECTION OF THE ANTERIOR HORN

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Question

The surgical removal of intramedullary spinal cord tumors (ISCTs) may lead to significant risk of iatrogenic damage and postoperative neurologic dysfunction. Intraoperative neurophysiological monitoring (IONM) combining motor and somatosensory evoked potentials (MEP and SSEP respectively) is usually employed to minimize this risk. However, anterior horn (AH) function cannot be adequately assessed by means of D-wave or MEP recorded at members. So the electromyography (EMG) can be helpful to protect AH.

Methods

IONM was performed in 19 patients (14 male and 5 female) who underwent surgical removal of ISCTs. A combination of SSEP/MEP/EMG was performed in all patients. The ASIA’s scale was used to assess the neurological outcome.

Results

The mean age was 46 ± 2.3 years. Total tumor resection was reached in 74% of cases. Pathology showed ependymoma (12) and hemangioblastoma (3) as the most frequent histological types. Significant MEP changes occurred in 11/19 (58%) and warning criteria for SSEP occurred in 17/19 (90%). Neurotonic discharges in EMG were seen in 11/19 (58%) during the attempt to detach the anterior part of the tumor from the spinal cord. All the changes were reversible and no new neurological deficit appeared, in fact, there was an improvement six months after the surgery in 6/19 patients.

Conclusions

During the ISCT resection there is a true risk to selectively injury the dorsal columns, the corticospinal tract and the AH, thus the combination of SSEP, MEP and EMG should be employed during ISCT resection to minimize the risk of neurological injury.

Figure 1. Dorsal ependymoma . A) Left: MRI showing the tumor. Right: intraoperative image during the surgery. B) Bilateral and reversible alteration of SSEP during opening the dura. C) Reversible alteration of MEP in thorax muscles, while in the lower limbs are reduced yet. D) Bilateral neurotonic discharges in intercostal muscles during resection, by irritation of AH (middle). Left side corresponds to the previous time and the right to the residual activity. ADM: abductor digiti minimi. AH: abductor hallucis. Blue: left side. Red: right side. Grey: warning criteria.
Elevated serum creatine kinase after intraoperative neuromonitoring in lateral position is associated with OP duration, BMI and age.

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Question

Highly elevated serum levels of creatine kinase (CK) following surgery may lead to renal dysfunction. High CK levels are known to occur after neurosurgical interventions, but a consensus on possible risk factors is still lacking. Here we investigate risk factors for excess CK in patients undergoing high risk surgical positioning with a special focus on the influence of motor evoked potentials (MEPs) as a modality of intraoperative neurophysiological monitoring (IONM).

Methods

We included all patients undergoing elective surgery in lateral position (park bench) between 2010 and 2012 and where IONM was performed. In these patients, the anesthesia regimen excluded muscle relaxation. Medical charts were reviewed retrospectively for patient characteristics, CK levels and indicators of renal dysfunction. The MEP response intensity was estimated by the RMS of the EMG signals. Data were analyzed by multivariate logistic regression.

Results

There were 96 patients (55 female, mean age 50 years) who met the inclusion criteria. The maximal CK level (CKmax) occurred on postoperative days 2 or 3 (mean 1763 U/L, range: 53-7172 U/L). In a multivariate linear regression model, log(CKmax) correlated positively with duration of surgery (p<0.001) and BMI (p=0.007), and negatively with age (p=0.007). There was no significant association between MEP response intensity of the muscles at risk and log(CKmax). We did not observe impaired renal function.

Conclusions

MEP was not among relevant risk factors for elevated CK levels. Surgical positioning should be especially careful for long surgeries on young patients with high BMI, in particular if operated in lateral position.
P162
Intraoperative monitoring of visual evoked potentials

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Question

During surgeries that put the visual pathway at risk of injury, continuous monitoring of the visual function is desirable. However, there is no consensus in the literature on the usefulness of intraoperative monitoring of visual evoked potentials (VEPs). Only recently have stimulating devices with high luminance been introduced.

Methods

We included 33 patients under total intravenous anesthesia for intraoperative VEP monitoring. Red LEDs provided flash stimulation at 1.1 Hz. VEPs were recorded at sites O1, O2, Oz against Fz, Cz, and linked A1 and A2 (A+). We analyzed the stability of the VEP features N75 and P100 and compared their distribution between patients with preoperative normal and impaired visual function. Their correlation to postoperative visual function was also examined.

Results

Intraoperative VEP monitoring was feasible in 27 patients (82%) and not feasible in 6 patients with severe preoperative visual dysfunction. N75 had median amplitude 2.6µV (range 0.8-7.7µV) and latency 84ms (57-142ms). P100 had median amplitude 2.0µV (0.5-7.0µV) and latency 102ms (75-161ms). N75 amplitude differed significantly between patients with preoperative normal and impaired visual function (P <0.05). Of all recording channels, Oz/A+ provided the largest number of stable VEPs (36/51, 71%). Of the 23 patients without N75 amplitude loss, 2 showed improved visual function postoperatively, 18 showed no change and 3 developed hemianopsia. This resulted in a specificity of 96% and a negative predictive value of 89%. Temporary VEP loss was observed in 3 patients and visual function was preserved. Permanent VEP loss was seen in 1 patient without new postoperative visual impairment.

Conclusions

Intraoperative VEP monitoring was feasible in all patients with intact preoperative visual function. Minor visual field defects such as quadrantanopsia did not affect VEP monitoring. Feasibility of intraoperative VEP monitoring depended strongly on the integrity of visual function. Patient selection should consider visual function.
Intraoperative monitoring of cranial nerves function in surgery of skull base tumours

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Question

Developing technique of mapping of cranial nerves (III, IV, VI, VII, IX - XII) along with their continuous intraoperative monitoring in surgery of skull base tumours and assesement of utility of this technique in clinical practice.

Material and methods

There were 16 patients (12 females and 4 men, mean age 50 years) with giant tumours of skull base (meningiomas: 5 petroclival, 2 of cavernous sinus, 1 of foramen magnum, 2 of petrous bone, 1 epidermoid in cerebello-pontine angle and in cavernous sinus, 2 chemodectomas, schwannomas: one of the IX nerve and one of the V nerve, inflammatory tumour in infratemporal fossa, ethmoid cells and sphenoid sinus. All the cases were operated on with mapping and monitoring of the cranial nerves: III nerve - 8 cases, IV - 11, VI - 11, VII - 12, IX - 8, X - 8, XI - 7 and XII - 4. The nerves were identified by means of nerve conduction velocity (NCV) and monitored with free run EMG recorded from muscles innervated by respective cranial nerves. Characteristic changes in recording and warning sounds heralded an imminent nerve damage thus providing warning to a surgeon.

Results

The mapping was successful in 15 patients. The failure happened in a giant petrous bone meningioma in which the monitoring of oculomotor nerves (III, IV, VI) and and facial nerve was attempted. Long-lasting and frequent irritation of a nerve, despite preservation of its anatomical integirity, resulted in the adequate neurological deficit present for up to a few months after surgery. Particularly, facial nerve was often affected in such a way. On the other hand, abducens nerve palsy occurring despite its identification turned out to be the most frequently encountered adverse event.

Conclusions

Intraoperative neurophysiological mapping of the oculomotor nerves (III, IV, VI) , facial nerve and lower cranial nerves is possible in almost all patients with skull base tumours. In majority of cases an early warning allows sparing of the affected nerve.
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P164
Intraoperative Neurophysiologic Monitoring of Surgical and Endovascular Treatment of Pediatric Arteriovenous Malformations

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OBJECTIVE

To analyze how intraoperative neurophysiologic monitoring (IONM) changes correlate with new postoperative deficits in the surgical and endovascular treatment of pediatric arteriovenous malformations (AVMs).

BACKGROUND

IONM aids in identifying neurological compromise during procedures that place the nervous system at risk. Cerebral AVMs are vascular anomalies that pose a risk for hemorrhage, stroke, or seizures. The utility of IONM in the treatment of pediatric AVMs has not been well documented.

DESIGN/METHODS

320 cases in 147 patients ages 10 days to 18 years were examined, including 213 endovascular embolizations and 107 surgical resections, all monitored with EEG, SSEPs, MEPs, EMG, and/or BAEPs. Preoperative and postoperative neurological deficits were analyzed using electronic medical records. IONM changes were defined as being either transient (resolving by the end of monitoring) or persistent (not resolving).

RESULTS

43 (13.4%) cases had IONM changes, 14 were persistent, and of those, 9 (64.2%) had post-operative deficits. 29 changes were transient, but only 6 (20.7%) of those had post-operative deficits. 277 (86.6%) cases lacked IONM changes, 6 (2.2%) of these had new deficits associated with cerebral hypoperfusion or edema after the end of monitoring, and 7 (2.5%) developed new deficits outside of the neurologic territory monitored. 28 (8.8%) cases presented IONM changes but did not have post-operative deficits; most of these were associated with alterations in surgical management or pre-embolization methohexital testing (performed to prevent permanent neurological injury).

CONCLUSIONS

Persistent IONM changes had a strong correlation with new post-operative deficits. Transient IONM changes, including those resolving after alterations in surgical management or pre-embolization methohexital testing, had a much lower risk of new deficits. Therefore, IONM can be a useful tool in pediatric AVM cases, not only in predicting neurological compromise, but also in identifying when to alter management.
P165
Spinal intradural tumours: a single centre experience

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**Question**

Primary spinal cord tumours represent 2% to 4% of all central nervous system neoplasms and are anatomically separable into two broad categories: intradural intramedullary and intradural extramedullary. We present our experience treating this kind of tumours in the last 10 years, with an especial focus on the use of intraoperative neurophysiologic monitoring (IOM).

**Methods**

We have performed a retrospective study within our institution, from an epidemiologic, clinical, radiologic and surgical point of view, including the use of IOM.

**Results**

A total of 93 patients, ages between 22 and 81 years old. The most frequent clinical presentation was motor deficit and pain. There was great histological variation, but neurinomas, meningiomas and ependymomas were more frequent. Multimodal IOM was used in 41% of the cases. We observed that in the group of monitorized patients the rate of neurological sequelae was lower that in the non-monitorized group.

**Conclusions**

The use of IOM in primary intradural spinal cord tumours reduces the incidence of neurological complications. IOM can identify neurological injury with excellent sensitivity.
Continuous dynamic mapping of the corticospinal tract during surgery of motor eloquent brain tumors

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Question

We developed a new mapping protocol to overcome the temporal and spatial limitations of classical subcortical mapping of the corticospinal tract (CST). The feasibility and safety of continuous (0.4-2 Hz) and dynamic (at the site of and synchronized with tissue resection) subcortical motor mapping was evaluated.

Methods

We prospectively studied 128 patients who underwent tumor surgery adjacent to the CST (<1 cm using diffusion tension imaging (DTI) and fiber tracking) with simultaneous subcortical monopolar motor mapping (short train, inter-stimulus interval (ISI) 4.0 ms, pulse duration 500 µs) and a new acoustic motor evoked potential (MEP)-alarm. Continuous (temporal coverage) and dynamic (spatial coverage) mapping was technically realized by integrating the mapping probe at the tip of a new suction device with the concept that this device will be in contact with the tissue where the resection is performed. Motor function was assessed one day after surgery, at discharge, and at 3 months.

Results

All procedures were technically successful. There was a 1:1 correlation of motor thresholds (MTs) for stimulation sites simultaneously mapped with the new suction mapping device and the classic fingerstick probe (24 patients, 74 stimulation points, r=0.996, p<0.001). Lowest individual MTs were as follows (MT, number of patients): >20 mA, n=13; 11-20 mA, n=27; 6-10 mA, n=18; 4-5 mA, n=27; 1-3 mA, n=43. At 3 months, 4 patients (3%) had a persisting postoperative motor deficit, three of which were caused by a vascular injury. One patient had a permanent motor deficit caused by a mechanical injury of the CST.

Conclusion

Continuous dynamic mapping was found to be a feasible and ergonomic technique for localizing the exact site of the CST and distance to the motor fibers. The acoustic feedback and the ability to continuously stimulate the tissue exactly at the site of tissue removal improves the accuracy of mapping, especially at low (<5 mA) stimulation intensities. This new technique may increase the safety of motor eloquent tumor surgery.
P167
Late Tongue Responses elicited by transcranial electric stimulation and peripheral median nerve stimulation

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Introduction

Motor responses in tongue muscles with latencies of > 50 ms elicited by transcranial magnetic stimulation have been described, although their origin remains unclear. We observed similar responses in anesthetized patients while performing transcranial electric stimulation (TES) but also peripheral median nerve stimulation (MN).

Objective

To describe the features of “late” tongue responses following TES and MN in anesthetized humans.

Methods

Patients undergoing neurosurgical removal of brain tumors with transcranially (TES) and direct cortically (DC) elicited motor evoked potentials (MEP) under total intravenous anesthesia without muscle relaxants were studied. MEPs were recorded from facial, Genioglossus (GG), upper and lower limb muscles following TES and median nerve (MN) electrical stimulation at the wrist (200 ms sweep length; 50-2500 Hz filtering bandpass, constant current stimulation). Responses were analyzed for onset and duration of long latency responses.

Results

In 9 patients (46.7±11 years of age; 4 female), TES elicited late GG responses with an onset of 56.1±9 ms and a duration of 41±7 ms. In 7 of those patients, ipsilateral MN elicited late GG responses with an onset of 37.3±5 ms, a duration of 35±12 ms.

In another group of 12 patients (47.83±19 years of age; 5 female), MN evoked long latency responses in bilateral GG in all patients, most prominent ipsilateral to the stimulated limb. Only the responses obtained on the non-tumor side were computed. The latencies ranged from 34.93 to 46.74 ms (onset 41.42 ± 5 ms). In none of the other limb muscles, nor in other facial muscles late responses were present. Further, late GG responses were not elicited by DC stimulation with a maximum intensity of 20mA.

Conclusion

These findings show “late” activations of the tongue muscles in response to stimulations delivered both to the motor cortex by transcranial electrical stimulation and to the median nerve at the wrist under general anesthesia. Since no late GG responses were observed from direct cortical stimulation of the motor cortex, we suggest that those responses are elicited by the activation of cutaneous sensory afferents. The nature of late GG responses deserves further investigation. We postulate that this response may be useful in neuromonitoring of the lower brainstem and cervical spinal cord.
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LP10
The warning sign hierarchy between quantitative subcortical motor mapping and continuous motor evoked potential monitoring during surgery of supratentorial brain tumors

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Question

Mapping and monitoring are believed to provide an early warning sign to determine when to stop tumor removal to avoid mechanical damage to the corticospinal tract (CST). The objective was to compare subcortical stimulation thresholds with direct cortical stimulation (DCS) motor evoked potential (MEP) monitoring signal abnormalities and to correlate both with postoperative motor deficits. We also sought to define a mapping threshold and DCS-MEP findings indicating a minimal safe distance from the CST.

Methods

100 patients underwent tumor surgery adjacent to the CST with simultaneous subcortical monopolar motor mapping and DCS-MEP monitoring. Evaluation was done regarding the lowest mapping threshold (train-of-five stimuli, interstimulus interval 4.0 ms, pulse duration 500 µs) and DCS-MEP changes (same parameters, 4-contact strip electrode). Motor function was assessed one day after surgery, at discharge, and at 3 months.

Results

Lowest motor thresholds (MTs) were as follows (MT, number of patients): >20 mA, n=12; 11-20 mA, n=13; 6-10 mA, n=20; 4-5 mA, n=30; 1-3 mA, n=25. DCS showed stable signals in 70 patients, unspecific changes in 18, irreversible alterations in 8, and irreversible loss in 4 patients. At 3 months, 5 patients had postoperative new or worsened motor deficits (lowest mapping MT 20 mA, 13 mA, 6 mA, 3 mA, 1 mA). All 5 cases showed DCS-MEP monitoring alterations (2 sudden irreversible threshold increases and 3 sudden irreversible MEP losses). Of these 5 cases, 2 had vascular ischemic lesions (MT 20 mA, 13 mA) and 3 had mechanical CST damage (MT 1 mA, 3 mA and 6 mA). 80% (75%) of patients with a very low mapping MT of 1-3 mA (1mA) showed stable DCS-MEP or unspecific reversible changes and none had a permanent motor worsening at 3 months. In contrast, 25% of patients with irreversible DCS-MEP changes and 75% of patients with irreversible DCS-MEP loss had permanent motor deficits.

Conclusions

Mapping should be the primary guide for resection of tumors adjacent to the CST. DCS-MEP is a useful predictor of deficits, but its value as a warning sign is limited because signal alterations were reversible in only approximately 60% of cases and irreversibility is a post-hoc definition. The true safe mapping MT is lower than previously thought. We postulate a mapping MT of 1 mA or less where irreversible DCS-MEP changes and motor deficits regularly occur. The limited spatial and temporal coverage of contemporary mapping may be a source of error and may contribute to false higher MTs.
Post-chirurgic preserved motor and sensory function in spite of transitory tibial SEP and MEP flattening during lumbar distraction in total disk replacement

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Anterior discectomy and total disk replacement (TDR) were performed with anterior approach, in 25 patients (34-59 years, 10 females) with degenerative disc disease of the lumbosacral level. Continuous electromyography (EMG) was recorded from muscles innervated by the nerve roots at the level above and below the surgery of lumbar and sacral segments; tibial and median nerve somatosensory evoked potentials, and motor evoked potentials of the legs were performed. Inter body distractions, during the prosthesis placement, ranged from 50-150% of the basal inter body distance. Desappearance of the tibial SEPs and MEPs occurred in 10 patients with 150% inter-body separations. Core temperature, blood pressure, anesthetic regimen, median nerve SEP’s, nerve peripheral signals and free running EMG remained unchanged. Distraction was continued up to 20 minutes in 5 cases, 10, 11, 15, 16 and 18 minutes in the other five. After distraction release, tibial SEPs and MEPs returned to normal; patients awaked without new neurological deficits. We hypothesize that interbody distraction caused stretching of the nerve roots, thus ischemia, causing temporal disruption of sensitive and motor signals. To the best of our knowledge, this is the first report of IOM during TDR with temporal lose of SEP and MEP during distraction, with a recovery of the signals after distraction release, resulting in preservation of motor and sensory functions after surgery. We encourage the use of multimodality monitoring during TDR.

Figure 1: Flattening of the both tibial nerves SEPs (center) for 20 minutes during intervertebral distraction. MEPs were also lost (lateral graphs) along with SEPs. After release of the distraction, the motor and sensory responses returned to base line. The patient awoke with no sensory deficits.

Figure 2: - Another example of tibial nerves SEPs flattening for 15 minutes, during intervertebral distraction. MEPs were also lost (not shown). As in figure 1, release of the distraction, motor and sensory responses returned to base line (blue). Patient awoke with no sensory deficits.
Abstracts of Poster Presentations – Poster Session 9 – Metabolic disorders

P168
Cardiovascular Autonomic Function in Hypothyroid Patients.
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Question
Hypothyroid patients have reduced parasympathetic and sympathetic activity and reactivity.

Method
The study was conducted on consenting newly diagnosed hypothyroid patients (n=30) and age and sex matched controls (n=30). For assessment of cardiovascular autonomic function activity, we used heart rate variability (HRV) tool and for reactivity, autonomic function tests (AFT). Statistics used were independent t-test for parametric and Mann-Whitney U test for non-parametric variables.

Results
Among cardio-respiratory variables, diastolic blood pressure (83.47 ± 5.65 - 78.87 ± 5.65) was significantly increased in hypothyroid patients as compared to the healthy control. Variables of the HRV representing parasympathetic activity: SDNN (57.7(47.4 - 74.4 - 43.75(34.8 - 56.82), RMSD 49.95(36.1 - 75.75) - 34.85(20 - 50.95), NN50 94.5(48.25 - 163) - 47.5(7 - 104.5) & pNN50 33.35(15.27 - 53) - 13.7(1.675 - 35.15) were significantly more are compared to the healthy control, where as variables of HRV representing sympathetic activity: LF power, LF percent and LF nu were comparable. LF/HF ratio which denotes the sympa-tho-vagal balance was also comparable between hypothyroid and healthy control. The Poincare plot, SD1 [16(11.2-20.9) vs. 24.7(14.18-36.13) ms, p=0.019] and SD2 [67.1(57.5 - 91) vs. 56.75(46.8 - 70.1]) ms, p=0.019] were more in hypothyroid patients. The parasympathetic reactivity: Valsalva ratio [(1.38 ± 0.22 vs. 1.48 ± 0.11) p=0.022], heat rate variation in deep breathing [(12.7 ± 5.1 vs. 16.74 ± 8.1) bpm, p=0.049] and E:I ratios [(1.16 ± 0.05 vs. 1.21 ± 0.1) , p=0.010] were significantly more in hypothyroid patients. But the sympathetic reactivity was comparable with the healthy controls.

Conclusions
The newly diagnosed hypothyroid patients have increased parasympathetic activity but reduced parasympathetic reactivity indicative of reduce stress coping ability of hypothyroid patients.
QUESTION

Deteriorating hepatic encephalopathy (HE) is known to result in both a gradual reduction of the critical flicker frequency (CFF) and a slowing of spontaneous oscillatory brain activity. This study aimed to characterize the link between the two.

METHODS

50 subjects were studied in 5 groups of 10 each: (i) healthy controls, (ii) cirrhotic patients without HE (HE 0), (iii) with minimal HE (mHE), and with manifest HE (iv) grade 1 and (v) grade 2. Using magnetoencephalography (MEG), spontaneous brain activity was recorded. The frequency of the dominant frequency in the extended alpha band (5-16 Hz) was determined. Additionally, the CFF was assessed.

RESULTS

Manifest HE patients showed a slower dominant frequency than healthy controls. In addition, the correlation between the dominant frequency and the CFF was found to be significant (R = 0.50, p < 0.01), indicating a parallel slowing of the CFF and the dominant frequency.

CONCLUSIONS

Our findings demonstrate that the purely behavioral measure of the CFF reflects the status of spontaneous oscillatory brain activity in HE. The present study thereby further strengthens the notion that the CFF is a meaningful parameter to quantify brain function and disease severity in HE.
P170
CYANOCOBALAMIN TREATMENT IMPROVES SENSORY PERIPHERAL NEUROCONDUCTION AND VITAMIN B12 STATUS IN DEFICIENT ELDERLY.

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Question
To evaluate possible neurophysiological abnormalities in asymptomatic elderly with vitamin B12 (B12) deficiency and their changes after an injection of 10,000 μg of B12.

Methods
Before-and-after study in 49 subjects recruited for an RCT on impact of B12 supplementation. All the subjects have a B12 below 148 pmol/dl, 28 received an injection of 10,000 μg of B12 and 21 did not. Motor and sensory conduction and somatosensory evoked potentials (SSEPs) were performed before and four months after injection.

Results
At baseline there was no significant difference in the level of B12. Significant improvements occur only in the intervened group for vitamin B12, MMA, tHocy and Holo-TC, without changes in the level of folic acid. Subjects that received B12 injection showed significant improvement in the latency of the sensory potential in the right median nerve and in both sural nerves. No changes were observed in the median and tibial SSEPs and motor conduction parameters.

Conclusions
Conduction velocity in large caliber afferents improves after a single injection of B12. Sensory central pathways seem more resistant to intervention.
P171
Fat-free mass predicts regional cerebral blood flow of brain regions associated with autonomic and homeostatic control - An H$_2$^{15}$O PET Study

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Question
Fat-free mass (FFM; i.e. all non-adipose tissues) is the major determinant of energy expenditure accounting for more than 80% of an individual’s energy needs and has been shown to predict food intake in humans. We aimed to investigate how interindividual variances in FFM relate to neuronal activity in humans and to identify a potential functional-anatomical link between FFM and the central regulation of food intake (i.e. perceived hunger).

Methods
64 healthy adults (21F/43M; age 31.3±9.1y; percentage of body fat [PFAT] 25.6±10.7%) underwent a 36h fast and subsequent H$_2$^{15}$O positron emission tomographic (PET) measurement of regional cerebral blood flow (rCBF), a marker of local neuronal activity.

Results
Voxel-wise multiple regression analysis revealed significant (p<0.05, FWE corrected) positive associations of FFM with rCBF within mesencephalic and adjacent diencephalic brain regions [cluster comprises parts of the periaqueductal gray (PAG), subthalamic nuclei, ventral tegmental area and hypothalamus], the left thalamus, left anterior and right midcingulate cortex, left insular cortex and right temporal cortical regions. Conjunction analysis of FFM and perceived hunger showed a significant (p<0.05 FWE corrected) overlap in the vicinity of the PAG and, at lesser significance levels, within the left hippocampal formation and the right frontoinsular junction. Mediation analysis highlighted an indirect effect of FFM on hunger with PAG rCBF as mediator.

Conclusions
Most of the regions associated with FFM are part of homeostatic pathways implicated in the regulation of basic bodily functions possibly indicating a potential role of these networks in the integration of FFM determined energy needs.
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VORICONAZOLE INDUCED HYPOKALEMIC PARALYSIS

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Question

Voriconazole (VOR), a broad-spectrum triazole antifungal agent, is an appropriate choice for the therapy of invasive aspergillosis and candidiasis. Is the asymmetrical proximal leg weakness in our patient caused by VOR-induced hypokalemia?

Methods

A 24-year-old male patient was admitted to the hospital because of myalgia for one week and difficulty in walking for four days. He had been diagnosed with acute myeloid leukemia 1.5 years ago and was on Fludarabine, ARA-C, Idarubicin treatment. VOR 400 mg/day was introduced 10 days ago because of the inadequate improvement of fungal lung abscess detected 1 month before. On neurological examination, there was slightly asymmetrical proximal muscle weakness in the lower extremities.

Results

Nerve conduction studies revealed decreased amplitude muscle responses to bilateral femoral and peroneal nerve stimulation. Needle EMG showed reduced recruitment and difficulty in sustaining muscle contraction in the weak muscles. Potassium level was low (2.6 mEq/L) and creatine kinase level was too high (12,000 U/L). VOR was stopped, hydration and potassium replacement was performed. His complaints were subsided by the 3rd day. Control neurological examination and nerve conduction studies were normal.

Conclusions

The most common side effects associated with VOR include transient visual disturbances, fever, rash, vomiting, nausea, diarrhea, headache, sepsis, peripheral edema, abdominal pain, and respiratory disorder. Hypokalemia and myopathy is very rare. If unreported signs and symptoms emerge in the course of a new treatment, clinicians must pay attention to the source of these findings, and ready to diverse the treatment accordingly.
Abstracts of Poster Presentations – Poster Session 9 – Metabolic disorders

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Seven-year follow up of two sisters with late onset Pompe’s disease: Effects and limitation of enzyme replacement therapy.

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Question

Enzyme replacement therapy (ERT) is available for Pompe’s disease since 2006. While ERT shows a better outcome in patients with relatively good condition, long term effects of ERT is not clear in late onset cases especially with severe muscle atrophy and respiratory failure.

Method

Patient 1, 38 yrs female, was unable to run at the age of 6. Gait disturbance, scoliosis and respiratory dysfunction gradually progressed. At the age of 15 yrs, she was diagnosed as Pompe’s disease and non-invasive ventilation was started. She became wheelchair bound at the age of 20 and required whole day mechanical ventilation at the age of 23. She developed dysphagia and needed gastric tube feeding at the age of 30. We started ERT (Myozyme, 20mg/kg, every 2 weeks) at the age of 30.

Patient 2, 31 yrs female, sister of patient 1, showed almost the same clinical course as her elder sister. Whole day mechanical ventilation support started at the age of 24. She had no dysphagia. We started ERT at the age of 24 with the same protocol as her elder sister.

We have evaluated body weight, serum CK, maximal tidal volume without ventilator support, scores of manual muscle testing and CMAP amplitude of both patients for 7 years. We also measured anti recombinant acid α-glucosidase (rhGAA) antibody.

Results

Fig1 and 2 demonstrate changes in parameters. Both patients felt beneficial effects of ERT soon after the treatment. Serum CPK decreased gradually. Body weight and CMAP amplitude increased for three years and became plateau. In patients 2, tidal volume increased for 2 years and declined or became plateau after 3 years. Patient 1, who could not breathe by herself, showed weak spontaneous breathing. Patient 1 showed almost no improvement in MMT scores. Patient 2, less affected younger sister, showed gradual improvements in some weakened muscles. Because both sisters showed almost the same clinical course before the treatment, the effect of ERT depends on the severity of symptoms at the time the therapy was started. Anti rhGAA antibody, increased initially and decreased after 3 years, seems to effect little on these improvements.

Conclusions

ERT provides long lasting improvement and maintenance even in severely affected patients with late onset Pompe’s disease. However, the effect depends on the severity of disease at the timing of treatment initiation.
No difference in neuronal and astrocytal densities of the striatum in obese humans - A post-mortem stereological study

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Question

Neuroimaging studies suggest that human obesity is associated with structural brain abnormalities, including the striatum. However, it remains unknown if and how these neuroimaging based findings are related to regional gray matter histology.

Methods

Neuronal (via cresyl violet staining) and astrocyte densities (via GFAP immunostaining) of formalin fixed post-mortem striatal brain samples (i.e. caudate-putamen) of 9 obese (BMI 40.2±6.1 kg*m⁻²) and 8 lean (BMI 24.4±1.0 kg*m⁻²) brain donors were assessed by using computerized unbiased stereology.

Results

No differences in mean neuronal (obese: 7.60E+06; SD 2.50E+06; lean: 7.85E+06; SD 8.26E+05; p=0.78) and astrocyte densities (obese: 7.42E+06; SD 2.27E+06; lean: 7.43E+06; SD 2.50E+06; p=0.99) were observed in the striatum. A significantly higher variance of striatal neuronal (p=0.007) but not astrocyte (p=0.72) counts was found in the obese group. No difference was found for the neuron/glia ratio between both groups (obese: 1.07; SD 0.39; lean: 1.15; SD 0.37; p=0.70), with an overall striatal neuron/glia ratio of 1.11 (SD 0.37) across the entire study population (n=17).

Conclusions

We found no differences in mean neuronal and astrocyte densities of the striatum between lean and obese. Further research is required to clarify how neuroimaging findings correlate with histological changes in obesity.
Objective To improve the sensitivity for the diagnosis of type 2 diabetic neuropathy with nerve conduction study by analyzing the characteristics of the type 2 diabetic neuropathy. Methods 2626 nerves of 213 patients meeting a criterion were performed nerve conduction, F wave, H reflex study. Results 2283 nerves were performed nerve conduction study (NCS). The abnormal rate of median nerve is highest in sensory nerve conduction (SNC), and the top abnormal rate of motor nerve conduction (MNC) is tibial and median nerve. The rate of abnormal nerve conduction of nervus tibial nerve, the longest nerve, is highest: 47.45%, then is median nerve which is vulnerable to pressure 46.83%. The lowest is sural nerve, 41.31%. 16 nerves in 21 with definite clinical features were abnormal. Cubital nerve with abnormal sensory nerve conduction were performed motor nerve conduction study. 57.14% of them were abnormal. The abnormal rate of sensory nerve conduction of median nerve (46.83%) is higher than that of motor nerve conduction (41.31%). 76.56% of motor nerve conduction of median nerve with abnormal sensory nerve conduction is abnormal. 89.63% of sensory nerve conduction of median nerve with abnormal motor nerve conduction is abnormal. F wave of cubital nerve, H reflex of nerves tibialis were performed. 25.83%, 52.24% of them were abnormal. Conclusion Type 2 diabetic peripheral neuropathy is length dependent, accordant with clinical manifestation. Sensory nerve is more vulnerable. Choosing nerves and performing NCS according to these characteristics can improve the sensitivity for the diagnosis of type 2 diabetic peripheral neuropathy with nerve conduction study.
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Combined use of functional magnetic resonance imaging and voxel-based morphometry in assessment of memory impairment in patients with cognitive disorders.

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Question
Cognitive impairment is one of the most common neurological disorders. Especially high prevalence of neurological disease with clinical cognitive impairment is among the senior people. Alzheimer’s disease (AD) and Vascular dementia (VaD) are the more common forms of dementia. The purpose of this study was to evaluate brain activation by visual memory task in patients with AD and VaD, and to determine correlation between memory impairment and atrophy of memory specific brain regions.

Methods
To investigate the organization of memory and localize cortical areas activated by visual memory task we used functional magnetic resonance imaging (fMRI) and to evaluate brain atrophy we used voxel-based morphometry (VBM). We studied 27 patients with AD (mean age 69,6±8,9 years), 29 patients with VaD (71,1±3,2 years) and 22 matched by age (68,8±4,3 years) volunteers without evidence of brain lesions as a control group. For test stimuli we used series of 12 not related images for "baseline" and 12 images with for "active". 6 images in “active" period have been already presented in “baseline”. Stimuli were presented 3 times with reduction of repeated images to 4 and 2. For VBM and functional data post-processing we used SPM8.

Results
Patients with AD showed less activation in hippocampal formation and parahippocampal gyri comparing to control group. The study also showed reduced activation in posterior cingulate cortex. VBM showed significant grey matter atrophy of both temporal lobes (fusiform and parahippocampal gyri), parietal lobes and cingulate cortex in AD patients. Patients with VaD showed less activation in posterior cingulate cortex and superior frontal gyri. VBM showed significant general atrophy of grey matter in VaD patients, especially of frontal lobes (superior frontal gyri) and posterior cingulate cortex.

Conclusion
Obtained data correspond to comprehensive conceptions of pathogenesis and general clinical features of AD and VaD. Combined use of fMRI and voxel-based morphometry allows to assess brain atrophy along with functional component of memory impairment and can be used in clinical practice in patients with cognitive disorders.

Fig. 1: Differences in activation between AD group and healthy controls (p<0.001).

Fig.2: Brain atrophy in AD patients comparing to the control group (p<0.001).
figure 1

figure 2
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Investigating the physiology of our sense of reality: experienced realness in healthy subjects and unreality feelings in depersonalization-derealization syndrome

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Question

The philosophy of mind postulates an affective background layer that relates us to the world as a whole and shapes all our specific experiences, beliefs, and thoughts (Ratcliffe 2008, Oxford UP). As a structural feature of consciousness, this bodily background layer is not necessarily always fully conscious but our sense of reality can vary in degrees (Gaebler, Lamke et al. 2013, J Conscious Stud), rendering it accessible to empirical investigation. A first 3T-fMRI study investigated emotional and self-related processes in patients for which the real world feels unreal: patients with depersonalization-derealization syndrome (DPDRS; ICD-10 F48.1, DSM-IV 300.6) are free of delusions but feel disconnected from their own mental processes, body, and surroundings. In a second 3T-fMRI study with healthy subjects, we modified the experience of realness through a manipulation of video stimuli.

Methods

In study 1, 22 patients with DPDRS and 22 matched, healthy controls either passively viewed aversive and neutral pictures or regulated the intensity of their negative emotional experience through cognitively reappraising the stimulus's self-relevance. In addition to brain activation, heart rate was assessed. In study 2, 25 healthy participants viewed videos that were more or less visually realistic while being equally complex. Subjects rated how strongly they experienced the situation depicted in the video (“immersion”) and correlations of brain activation across subjects were analyzed using multivariate techniques.

Results

In study 1, regulatory processes in both the autonomic and the central nervous system were found to be altered in patients with DPDRS. Abnormal regulation was associated with self-related processes such as interoceptive awareness, an index of conscious access to bodily functioning. In study 2, more realistic stimuli were associated with stronger immersion and higher synchronization of brain activation across subjects - both whole-brain and in specific regions, such as bilateral occipito-temporal cortices.

Conclusion

Self-related processes, both automatic and accessible to voluntary regulation, are associated with individual (un)reality feelings. In addition, our data support an intersubjective dimension in the experience of reality.
Abstracts of Poster Presentations – Poster Session 10 – MRI (functional and structural)

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\(^{23}\text{Na}, \, ^{35}\text{Cl} \text{ and } ^{39}\text{K} \text{ Magnetic Resonance Imaging at 7 Tesla}

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Introduction

The membrane potential of cells can be calculated via the Goldman-Hodgkin-Katz equation using the intra- and extracellular concentrations of sodium (Na\(^+\)), chlorine (Cl\(^-\)) and potassium (K\(^+\)) weighted by the membrane conductivity for each of these ions. Thus, a non-invasive measurement via magnetic resonance imaging (MRI) of these nuclei is desirable. However, they suffer from low in vivo concentrations, low MRI sensitivities and short relaxation times. Thus, SNR efficient pulse sequences that enable short echo times and high magnetic field strengths (e.g. 7 Tesla) are required to achieve sufficient image quality.

Methods

\(^{23}\text{Na}, \, ^{35}\text{Cl} \text{ and } ^{39}\text{K} \text{ MRI} \text{ was implemented on a 7 T whole body MR system (Magnetom 7 T, Siemens Healthcare, Erlangen, Germany). To enable ultra-short echo times (TE < 0.5 ms) and high SNR efficiency a custom-made density-adapted 3D radial pulse sequence was applied. Imaging of calf and thigh muscles was performed with a spin-density weighted sequence to measure the total concentration of the investigated ions. Acquisition parameters were adapted to the physical MRI properties of } ^{23}\text{Na}, \, ^{35}\text{Cl} \text{ and } ^{39}\text{K.}

Results

\(^{23}\text{Na}, \, ^{35}\text{Cl} \text{ and } ^{39}\text{K} \text{ MR images of the healthy thigh muscle were acquired in an acquisition time of 10 min for each data set. Nominal spatial resolutions of 3.8 x 3.8 x 10 mm}^3 (^{23}\text{Na MRI}), 8 x 8 x 16 mm}^3 (^{39}\text{K MRI}) \text{ and } 12 x 12 x 24 mm}^3 (^{35}\text{Cl MRI}) \text{ were achieved (Fig. 1). First results of combined } ^{23}\text{Na and } ^{35}\text{Cl MRI of patients with muscular diseases (hypokalemic periodic paralysis) show elevated Na}^+ \text{ and Cl}^- \text{ content compared to healthy controls.}

Conclusion

For the first time all ions of the Goldman-Hodgkin-Katz equation were non-invasively measured in humans by MRI. High-field (7 T) \(^{23}\text{Na}, \, ^{35}\text{Cl} \text{ and } ^{39}\text{K} \text{ MRI provide unique capabilities to non-invasively visualize (patho-) physiological cellular processes that are not visible in conventional } ^1\text{H MRI.}

**Figure 1:** \(^1\text{H, } ^{23}\text{Na, } ^{39}\text{K, and } ^{35}\text{Cl MRI of the healthy thigh muscle of a female volunteer. Each non-proton MR image was acquired in an acquisition time of 10 min. Nominal spatial resolutions of 3.8 x 3.8 x 10 mm}^3 (^{23}\text{Na MRI}), 8 x 8 x 16 mm}^3 (^{39}\text{K MRI}) \text{ and } 12 x 12 x 24 mm}^3 (^{35}\text{Cl MRI}) \text{ were achieved. The measured Na}^+, \text{ K}^+ \text{ and Cl}^- \text{ concentrations are within the expected range.}

![Figure 1](image-url)
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Cerebello-thalamo-cortical Connectivity in Essential Tremor: a Multimodal Imaging Study

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Essential tremor (ET) is a movement disorder characterized by action tremor mainly affecting the hands. ET is known to implicate the cerebellum and its connections to the cortex. However, how structural impairments can affect information flow within the cerebello-thalamo-cortical network is not well delineated. In the present study, we investigated structural and functional changes using 3T MRI in 20 ET patients compared with 20 age- and gender-matched healthy volunteers. Tremor severity was assessed using the Fahn-Tolosa-Marin scale (FTM), and tremor amplitude was measured with EMG recordings. Structural T1-weighted and diffusion images, and resting state functional MRI (rsfMRI) were acquired. We analyzed (1) grey and white matter volumes using voxel-based morphometry; (2) the structural integrity of the cerebello-thalamo-cortical tract using tractography; (3) and resting state connectivity in the cerebello-thalamo-cortical network, combining an independent component analysis and dynamic causal modelling. Compared to HV, ET patients presented increased grey matter in bilateral supplementary motor area (SMA), and decreased white matter in the cerebellum. Diffusion-based probability of connections was increased between the thalamus and the SMA bilaterally. Functional connectivity was increased between the SMA, thalamus and dentate nuclei, and decreased between the SMA and the primary motor hand areas, bilaterally. Structural and functional changes within cerebello-thalamo-cortical correlated with clinical scores and disease duration. Additionally, larger grey matter volumes in the SMA were associated with lower functional connectivity between SMA and the thalamus. Structural and functional changes in ET were observed along the cerebello-thalamo-cortical pathways, and particularly involved the SMA. The results suggest that SMA could play a role in modulating M1 activity by reducing the motor output in an attempt to improve the control of hand movements.
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Functional magnetic resonance imaging of central respiratory networks and peripheral physiological correlates during paced breathing

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Question

Slow breathing has been previously recognized to exert beneficial effects on cardiovascular parameters during hypoxia and is associated with states of subjective well-being. What is the effect of slow breathing on homeostatic and motivational brain centres during a hypoxic challenge?

Methods

Twenty healthy volunteers (Male=10, age= 33±8) were enrolled. Functional magnetic resonance imaging (fMRI) was undertaken during an experiment in which participants were prompted, over repeated blocks of one minute, to breathe at their own pace (free, un-paced, 3-12/min), slowly paced (6/min) or fast paced (10/min) in normoxic and hypoxic (13% inspired O2) conditions. Respiration was monitored using pneumotachography, capnography and pulse oximetry. Cardiovascular parameters were recorded using pulse oximetry.

Results

Heart rate was significantly faster under hypoxia (73±10) than normoxia (69±10) (p

Conclusions

Our innovative fMRI study contributes to the understanding of homeostatic and respiratory brainstem nuclei and their interaction with cortical centres controlling breathing function. Paced slow breathing interacts with hypoxic challenge by exerting distributed changes in brainstem and cerebral activity. Although beneficial effects of slow breathing were not replicated experimentally, our findings are relevant to well-being, yoga, mindfulness and self-regulatory processes.
Perilesional edema of inner capsule deteriorates nTMS-based fiber tracking results

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Question

Diffusion tensor imaging (DTI)-based fiber tracking (FT) is a commonly used method for function-preserving surgery of gliomas located within the white matter, e.g., adjacent to the corticospinal tract (CST). Recently, the results of navigated transcranial magnetic stimulation (nTMS) have been used to delineate the cortical seed ROI corresponding to M1. However, in some cases, nTMS-based FT of the CST remains challenging. Since DTI is highly susceptible for T2-alterations, tumor associated edema may confound FT of the CST.

Methods

We analyzed nTMS-based FT of body-area-specific CST in 31 patients with intracranial tumors. NTMS was performed using eXimia 4.2. MEPs were recorded by surface electrodes from the hand (APB), the foot (plantar muscle) and the tongue, whenever clinically relevant (82 body areas). To control for unspecific biases, hand mapping was performed on the contralateral side, also. NTMS-maps were exported in DICOM format, integrated in the iPlan-software and used as seed ROIs. A second ROI was placed on pontine level. The FT-results were checked for plausibility according to anatomical considerations (course on level of inner capsule and towards the brainstem). To investigate influencing factors, tumor vol., tumor edema vol. and edema within the inner capsule were analyzed.

Results

On the contralateral side, all CST-FT showed plausible results. However, on the tumor side, the rate of plausible CST-FT was 88% overall, with highly plausible results for the hand, whereas tracking the foot- and tongue-associated CST was more challenging (hand: 97%; foot: 84%; tongue: 77%). The contrast-enhancing tumor vol. (p=.61) and the vol. of the T2-hyperintense perifocal edema (p=.21) did not influence the plausibility of the tracking results. However, edema within the inner capsule seems to deteriorate the FT remarkably (fig.) and may serve as a, however poorly specific (35%) predictor for troubles with CST-FT (sensitivity: 65%).

Conclusions

NTMS-based FT of the CST leads to plausible results in the majority of cases. Tracking the CST of the hand seems to be less challenging than CTS of the foot or even the tongue. Tumor-associated edema within the inner capsule deteriorates the FT-results. In such cases, FT-results should be interpreted with caution, especially when using them for surgery planning.

figure 1
Cerebellar activity in cervical dystonia during a motor timing task: An fMRI study

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Question

Dystonia research has recently started to turn towards a new neural network node presumably playing a significant role in its pathophysiology - cerebellum. Even in the absence of traditional neurology signs of cerebellar dysfunction in most dystonia patients, more subtle indications of cerebellar abnormalities may still be found. In preliminary data of our fMRI study, we are presenting compelling evidence of its dysfunction in cervical dystonia patients.

Methods

Functional magnetic resonance imaging has heretofore been performed in 10 patients and 10 healthy individuals during interception of a moving target with simple button pushing - a task, known to engage cerebellum, involving complex predictive motor timing abilities, as the subjects has to react in advance according to the speed of the target to successfully intercept it.

Results

In addition to statistically significantly lower hit ratios than the healthy controls, cervical dystonia patients had substantial differences in activations during the movement estimation and motor timing in preparation for reaction - button pressing: there was lower activation in the ipsilateral cerebellar lobule VI and VII and in contralateral medial prefrontal cortex.

Conclusions

Our results suggest that the cervical dystonia patients suffer from impairment of predictive motor timing - dysfunction presumably directly attributable to changes in cerebellar activation.
Activity and functional connectivity of the premotor-parietal network modulate intrinsic power changes of mu rhythms: An EEG-fMRI study

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Mu rhythms refer to alpha-band (8-12 Hz) oscillations of electroencephalography (EEG) activities that are locally observed over the sensorimotor areas of the brain. Although motor demands can affect mu rhythms, the neural substrates that mediate intrinsic fluctuations of mu rhythms are still unknown. We hypothesized that activity in the inferior parietal lobe (IPL) and ventral premotor cortex (PMv), the key regions constituting the mirror neuron systems (MNS), might modulate fluctuations of mu rhythms at rest.

To identify the brain networks that underlie fluctuations of mu rhythms, we acquired brain activity from fifteen healthy participants (age range 21-35), by combining 32-channel MRI-compatible EEG and Siemens 3T-MRI systems. During data acquisition, the participants were awake and not engaged in any tasks with their eyes closed. BOLD-based fMRI signals and surface EEG data were recorded simultaneously for 20 min. Power of mu rhythms was calculated from EEG data at C3 and C4 electrodes within a 3-second time bin, corresponding to a single scan of MRI data (400 data points in total). Using SPM software, voxel-based general linear model analyses were performed in the whole brain to find regions correlated with spontaneous fluctuations of mu rhythm power physically at rest. We found that greater BOLD activities in the IPL and PMv were linked with suppression of mu rhythm power. Furthermore, we discovered that the functional connectivity between IPL and PMv was decreased when the power of mu rhythms was suppressed. We did not find any brain regions showing greater activities or functional connectivity in association with increases of mu rhythm power.

We conclude that greater activity but reduced functional connectivity of IPL and PMv are correlated with spontaneous suppression of mu rhythm amplitudes at rest. Our results may provide new insight into mechanisms of spontaneous fluctuations of brain activity or connectivity in a resting state.
Investigation of the neural correlates of tool use with activation studies in healthy subjects and lesion studies in brain damaged patients.

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Question

Results from brain activation studies in healthy subjects and lesion analyses in brain damage patients are expected to reveal a correspondence between areas activated by task performance with lesioned areas in case of deficits. We are planning to directly compare both approaches to study the neural network of tool use in as similar as possible and as realistic as possible conditions: On the other hand we examined tool use in healthy elderly subjects, during the realization of fMRI. On the other hand we plan to correlate the execution in this task in chronic stroke patients -with apraxia- with their damaged brain areas.

Methods

Both experiments used a tool carousel for controlled tool presentation (12 tools of daily life). The fMRI-data was analyzed with SPM8 in a factorial design (object and task) during the planning- and action-phase. In the lesion analyze study we score the execution according to an apraxic errors scale and use the voxel based lesion symptom mapping (VLSM), a method that includes mapping the lesion manually, normalizing brain image using cost function masking with SPM8 and making a voxelwise statistical analysis of neurological lesions to define the relationship between tissue damaged and behavior.

Results

Besides a clear left-sided lateralization, a wide spread network can be identified, specific for planning and executing the manipulation of tools. That includes parietal (superior and inferior parietal lobule and the intraparietal sulcus) and frontal cortex (dorsal and ventral premotor cortex and the middle frontal gyrus) as of regions of the temporal cortex and the lateral occipital complex. For the MRI data we are still working on the analysis.

Conclusions

The fMRI results show an activation-pattern representing semantic aspects, the processing of tool-knowledge and the realization of motoric actions, all important for executing complex actions like the usage of tools. It is expected that lesion analysis will reproduced the network, in particular the involvement of left parietal cortex, with some characteristic deviations. The use of the tool carousel supported better timing and more precise spatial control of stimulus presentation.

Figure 1: Statistical map of the contrast Tool vs. Bar (threshold of p < 0.001 with an extended threshold of 10 voxels per cluster)
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Brain tissue properties differentiate among motor and limbic basal ganglia circuits

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Question

Despite advances in understanding basic organisational principles of human basal ganglia, accurate in vivo assessment of their anatomical properties is essential to improve our understanding of cortico-subcortical disorders and optimise target planning in deep brain stimulation. Main goal of this study was the detailed topological characterisation of limbic, associative and motor subdivisions of the subthalamic nucleus (STN) in relation to corresponding cortico-subcortical circuits. Moreover, we aimed at investigating whether basal ganglia functional subregions are reflected in peculiar local tissue properties.

Methods

101 healthy subjects were examined on a 3T MRI system. Probabilistic tractography on diffusion weighted imaging was conducted on 13 subjects for estimation of STN connectivity to motor, associative and limbic cortices, aiming at parcellating the nucleus in subregions. Voxel based quantification on multi-echo FLASH acquisitions allowed for quantitative mapping of MT, R1 (1/T1), R2* (1/T2) in the whole cohort. We analysed the signal from STN subregions in the multi-parameter mapping dataset, and employed subregions as seeds to compute their covariance within motor associative and limbic basal ganglia circuits.

Results

In all 13 subjects we demonstrate STN connectivity pattern with a distinct antero-posterior gradient (from limbic to associative to motor (Fig.1). R2* maps (sensitive to iron) showed the highest covariance with motor STN in posterior putamen and posterior pallidum. MT maps (sensitive to myelin content) were most significantly covarying with limbic STN in dorsal, anterior and ventral caudate, anterior putamen, antero-ventral pallidum.(Fig. 2).

Conclusions

We confirm previous notion of topological specialisation within STN through diffusion tractography. We interpret the demonstrated covariance pattern as evidence for shared tissue properties within a functional circuit. Our findings open new possibilities for accurate diagnosis of basal ganglia disorders and prediction of treatment outcome.

Figure 1. Representation of averaged STN probabilistic connectivity gradients for motor, associative, and limbic cortical areas.

Figure 2. Covariance of multiparameter maps between motor and limbic/associative STN subregions and corresponding areas in basal ganglia.
Abstracts of Poster Presentations – Poster Session 10 – MRI (functional and structural)

**figure 1**

[Image of brain scans with color-coded regions]

**figure 2**

[Table with MRI images for Limbic/Associative and Motor regions for MT, R1, and R2*]
LP12

Construction of realistic neonatal head model based on co-registered CT-MR images

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Question

Creating accurate realistic head models is a critical step to increase the accuracy in electro-magnetic source imaging. Commonly used realistic head models include three conductive layers for scalp, skull and brain. In neonates, such models would lead to inaccurate EEG/MEG source reconstruction, mainly due to the existence of fontanels and significant anatomical differences between neonates’ head geometry. In this study, we used neonatal CT and MR images to create a realist head model including brain, CSF, skull and fontanel compartments.

Methods

For model creation we used five CT and five MR (T1-weighted) images acquired from nine newborns aged 39 to 42 weeks. From this dataset, the CT and MR images of one neonate were used as reference images for stereotaxic normalization. The other CT and MR images were aligned within their corresponding reference frame individually. The normalized CT images were segmented to identify cranial bones using simple thresholding and morphological operations. A signed distance function was first generated for each CT dataset based on its segmented cranial bones. A shape model for cranial bones was then reconstructed by applying the principal component analysis (PCA) on the signed distance functions. The fontanels were identified as gaps between the cranial bones in the shape model. Using a probabilistic atlas, the intracranial tissues (brain and CSF) were segmented from the normalized and averaged MR images. The scalp was then obtained by removing the segmented tissues from the averaged MR images. Finally, the segmented tissues were surface rendered and used to generate a realistic head model.

Results

Figure 1 shows the different compartments of the realistic neonatal head model including brain, CSF, scalp, cranial bones and fontanels (Fig. 1a) as well as their 3D reconstruction (Fig. 1b).

Conclusion

In this paper we developed a method to create a realistic neonatal head model based on the co-registration of CT and MR images from neonates. The model included the geometry of brain, CSF, scalp, cranial bones and fontanels. With a specific conductivity value assigned to each compartment, the model can be used for EEG/MEG source localization in neonates.
LP13
Activity in the brain network for dynamic manipulation of unstable objects is robust to acute tactile deafferentation: an fMRI study

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Question
The ability to manipulate objects with the fingertips (i.e. dexterity) involves different combinations of visual and tactile inputs and requires precise control of the fingertip forces. The aim of the study was to characterize reorganization of the neural network activity during dexterous task performance after tactile deafferentation.

Methods
Whole-brain functional Magnetic Resonance Imaging (fMRI) was conducted on 18 subjects aged 20-49 years, during compression of an unstable spring held with thumb and index finger of the right hand. Two sensory conditions were employed, i.e. with and without tactile feedback from the fingers. Local anesthetic was injected at the base of the thumb and index finger.

Results
The brain activity, observed with tactile input during task performance, was fully preserved after tactile deafferentation.

Moreover, without tactile input the brain activity was greater in the areas of the object manipulation network, preferentially involved in control of fingertip force vectors. This was accompanied by a significant increase of brain activity in the right dorsal premotor cortex.

Conclusions
The observed neural activity during performance of dexterous movements under anesthesia indicates robustness of the brain to acute tactile deafferentation. This study gives new insights to possible neural compensatory mechanisms during motor control in the absence of tactile information.

figure 1

Significant activations from the conjunction analysis between contrasts Tactile-Rest(T) and noTactile-Rest(noT) (FDR, p<0.05, number of voxels>10) on three-dimensional rendering of the anatomical template (SPM-96).
A. Contrast Tactile-noTactile (FWE, p<0.05). The significantly reduced activation in the right dorsal premotor cortex (area 6) is found, x=17, y=-14, z=63; Z-score=4.37. B - mean signal change under two sensory conditions compared to rest, p=0.005
P188
Using aftereffects to evaluate successful adaptation during myoelectrically (EMG)-driven neuromuscular electrical stimulation (NMES)-assisted locomotor exploration activity for post-stroke gait training

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Active participation of motor-cortex (and other cortical areas) may be facilitated by modulating neuromuscular electrical stimulation (NMES) with volitional effort where state-of-the-art prior works show that stimulation envelopes may be controlled [1] or triggered [2] with volitional electromyogram (EMG). Based on these prior works, we developed a Bayesian framework for sensor fusion that enforced normative muscle activity during post-stroke gait therapy (see Figure 1) [3]. We also developed an operant conditioning paradigm using visual biofeedback (see Figure 2), where post-stroke impaired reciprocal inhibition between Tibialis Anterior (TA)- Gastrocnemius (GAS) antagonist pair can be strengthened during transition from standing to walking on treadmill via increased presynaptic inhibition of group Ia-afferents. In fact, such operant conditioning has been shown possible for Soleus H-reflex in primates and for reciprocal Ia inhibition in rats where conditioning produced persistent anatomical and physiological changes at the motoneuron and several different synaptic populations on the motoneuron [4, 5]. In order to test successful adaptation during post-stroke gait training, we used aftereffects that occur in motor control when the visual or mechanical variables of the targets are perturbed in a systematic manner. Here, Held and colleagues [6, 7] have found aftereffects only with sensorimotor integration, which may then lead to motor adaptation [8]. In principal accordance, we found that only stroke subjects who showed aftereffects during systematic perturbation of the "EMG to NMES mapping" parameters (in Bayesian framework) at random catch-trials during the locomotor exploration activity, showed post-intervention changes in the EMG pattern during volitional (no NMES) treadmill walking.

References:

Figure 1: Bayesian framework for sensor fusion to volitionally (with EEG/EMG) drive NMES.
Figure 2: Operant conditioning paradigm shown during swing phase to improve tibialis anterior (flexor) - gastrocnemius (extensor) coordination. MRCP: movement related cortical potential, MN: α-motoneuron, IN: la-inhibitory interneuron, EMG: electromyogram, DRG: dorsal root ganglion.
P189
Does an intraneural interface short-term implant for robotic hand control modulate sensorimotor cortical integration? An EEG-TMS co-registration study on a human amputee


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**Purpose**

Following limb amputation central and peripheral nervous system relays partially maintain their functions and can be exploited for interfacing prostheses. Aim of this study is to investigate, for the first time by means of an EEG-TMS co-registration study, whether and how direct bidirectional connection between brain and hand prosthesis impacts on sensorimotor cortical topography.

**Methods**

Within an experimental protocol for robotic hand control, a 26 years-old, left-hand amputated male was selected to have implanted four intrafascicular electrodes (tf-LIFE-4s) in the median and ulnar nerves of the stump for 4 weeks. Before tf-LIFE-4s implant (T0) and after the training period, once electrodes have been removed (T1), experimental subject’s cortico-cortical excitability, connectivity and plasticity were directly tested via a neuronavigated EEG-TMS experiment.

**Results**

The statistical analysis clearly demonstrated a significant modulation (with t-test p<0.0001) of EEG activity between 30 and 100 ms post-stimulus for the stimulation of the right hemisphere. When looking at the individual latencies in that time range, a global amplitude modulation was present in most of the TMS-evoked potentials; particularly, the GEE analysis showed significant differences between T0 and T1 condition at 30 ms (p< 0.0404), 46 ms (p<0.0001) and 60 ms (p<0.007) latencies. Finally, also a clear local decrement in N46 amplitude over C4 was evident. No differences between conditions were observed for the stimulation of the left hemisphere.

**Conclusions**

The results of this study confirm the hypothesis that bidirectional neural interface could redirect cortical areas -deprived of their original input/output functions- toward restorative neuroplasticity. This reorganization strongly involves bi-hemispheric networks and intracortical and transcortical modulation of GABAergic inhibition.
Abstracts of Poster Presentations – Poster Session 11 – Neurobotics

P190
NEurocontrolled BIdirectional Artificial upper limb and hand prosthesisS (NEBIAS)

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Question

The hand is a powerful tool and its loss causes severe physical and often mental debilitation. Surveys on using artificial hands reveal that 30 to 50% amputees do not use their prosthetic hand regularly, due to its low functionality. The fundamental issue is therefore to improve the voluntarily-controlled dexterity to allow amputee to perform tasks that are necessary for activities of daily living and that cannot yet be done with the state-of-the-art artificial limbs. Starting from previous encouraging results, the NEBIAS (“NEurocontrolled BIdirectional Artificial upper limb and hand prosthesisS”) proposal aims at developing and clinically evaluating (in selected amputees) a neuro-controlled upper limb prosthesis intuitively controlled and felt by the amputee as the natural one.

Methods

The goal of the project will be achieved by combining microtechnology and material science and will allow, on one side, recording of the motor-related signals governing the actions of the amputated hand/arm for the motion control of a mechanical prosthesis, and on the other providing sensory feedback from tactile and kinesthetic sensors through neuromorphic stimulation of the adequate afferent pathway within the residual limb.

Results

The system will be implanted in one or more upper limb amputees enrolled for the study. The patients will undergo a complete clinical and functional neuroimaging study to verify the safety of the prosthetic system and its role in modifying cortical reorganizations following limb amputation and lack of sensory feedback. A clinical follow-up evaluation will be also performed 2 months after the electrode removal.

Conclusions

NEBIAS is a highly innovative, interdisciplinary project, combining forefront research from information technologies, smart bio-sensors, control theory, cognitive neuroscience, material sciences, electric design, measurements and robotics to solve a major social problem: the development of a prosthetic hand displaying all the basic features of a real human hand. The successful realisation of this highly visionary project requires crossing the boundaries of distinct scientific fields, merging forefront expertise of the consortium to improve quality of life of amputees.
P326
Robot-aided neurorehabilitation: Monitoring the effect of robot-assisted training on hand and elbow-shoulder movements by means of quantitative robot derived kinematic measurements

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Question

High intensity and early initiation of rehabilitation have been extensively demonstrated to enhance neural plasticity and motor recovery after stroke. Robot-aided training has the ability to perform, control and evaluate repeated voluntary movements. In this preliminary study we aim to answer these questions: (i) Evaluate motor outcomes in acute (< 6 months from stroke) and chronic (> 6 months after stroke) stroke survivors with moderate to severe upper limb paresis over a 1 month period of rehabilitation, (ii) demonstrate benefits of initiating robot-aided therapy distally.

Material & Methods

Retrospective study of 58 patients (69.2 ± 11.2 years) who had suffered either a first time ischemic or hemorrhagic stroke received robot-aided neurorehabilitation (MIT-Manus). Daily sessions of therapy lasted about 45 min (1000 movements). At the admission patients were evaluated using the Fugl-Meyer scale (F-M) and a Motor Status Score (MSS). Quantitative data based on kinematic and dynamic features included mean velocity, normalised length of the movement trace, accuracy error and finally an index of active movements.

Results

The results showed a gradual decrease in motor and functional impairments throughout the training period with a clinically meaningful increase in F-M and MSS. The overall improvements of kinematics robot data recorded during a squeezing relaxation task improved 21.4%. The overall elbow-shoulder analysis improvement was 27.8%. Both acute and chronic patients improved after robot-aided neurorehabilitation. The improvement of hand function continued during elbow-shoulder therapy, contrary to the improvement seen when performing elbow-shoulder therapy followed by hand therapy.

Conclusion

In this retrospective analysis of a relative small sample of patients, results suggested that a one-month period of intensive upper limb rehabilitation, resulted in significant improvements in patients with moderate to severe motor impairments. We believe that it is of outmost importance to begin therapy of the hand and fingers, and then continue therapy more proximally (shoulder-elbow).
Verification for clinical usage of glucocorticoid in migraine

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Spreading depression (SD) is a wave of depolarization, which passes through the brain and depresses neural activity. SD is a popular model for migraine disease and its correlation with various neurodegenerative disorders is approved. Clinical ECoG recording have showed SD wave in many neurological disorder. Various mechanisms have been postulated for SD neurotoxicity. Some of these pathways include ionic imbalances, intracellular calcium accumulation and electro potential changes. Hippocampus region is the most sensitive region of brain for SD cellular injuries, since; the first sign of damage appear in this area of brain. Correlation between hippocampal injuries and some neurodegenerative diseases have previously suggested. Inflammatory responses are possible execrative of hippocampal injuries following SD. In present study 36 Wistar rats were used to examine role of inflammatory responses in SD phenomenon by Dexamethasone treatment. Histological assessment after pretreatment of dexamethasone and SD induction was investigated. Our result indicated that neural cell death was significantly reduced by pretreatment of dexamethasone, which suggested an important role for inflammatory response in cell injuries after SD induction.

Key words: Spreading depression, Dexamethasone, Neuronal damage, inflammatory responses, Hippocampus.

Fig 1. Light-microscopic appearance (40× magnification) of coronal sections of the rat brain in SD, Sham, control treatment, and treatment with toluidine blue have been shown an increase of dark neurons in the dentate gyros, CA-3 and CA1 hippocampal tissues after SD induction.

Fig 2: The mean number of dark neurons in Hippocampal brain regions of SD, Sham, control treatment, and treatment rats indicates that significant increase in number of dark neurons, however treatment with dexamethasone could significantly decrease mean number of dark neurons. Number of dark neurons was compared between experimental groups and analyzed by one-way ANOVA followed by Tukey's multiple comparison tests. Values represent mean±SEM. *, **, and *** indicate significant P

figure 1

![Figure 1](image1)

figure 2

![Figure 2](image2)
Sympathetic skin response studies in patients with amyotrophic lateral sclerosis

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Question

To investigate the features of sympathetic skin response in patients with amyotrophic lateral sclerosis (ALS) and determine a possible involvement of the autonomic nervous system in ALS.

Methods

The data of outpatients and inpatients with definite ALS were collected in Peking Union Medical College Hospital from Jun, 2009 to Jun, 2012. Standard sensory and motor nerve conduction was performed in median nerve, ulnar nerve and tibial nerve in 95 patients with ALS. F-wave and sympathetic skin response were measured in median nerve. Parameters analyses mainly included sensory conduction velocity and amplitude, distal motor latency (DML), compound muscle action potential (CMAP) amplitude, SSR latency and amplitude. Findings were compared with those in 50 normal controls.

Results

The SSR was present in 100% of the controls but was absent in 5.3% in the hands and 12.6% in the feet in ALS patients. The mean amplitudes of the ALS patients (palmar SSR: 1.26±0.78 mv, plantar SSR: 0.76±0.66 mv) were lower than that of the controls (palmar SSR: 3.31±2.15 mv; plantar SSR: 1.73±0.98 mv) (P<0.01), while there was no significant difference in the latencies (P>0.05). The abnormality rate of SSR was 35.8% in 95 ALS patients, 13.5% in the hands, 35.8% in the legs. The abnormality of the plantar SSR is higher than that of the palmar SSR (P<0.01). The abnormality of SSR includes prolonged latencies, decreased amplitudes and wave absence. In limb-onset group the abnormality of SSR were increased. Logistic regression revealed a strong direct association between onset site and SSR abnormality. SSR latency and amplitude are not correlated to either the duration of the disease or the age of the patients.

Conclusions

An abnormal SSR can be observed in ALS. The autonomic nervous system in ALS patients may be early detected by the SSR.

Key words

amyotrophic lateral sclerosis; nerve conduction; sympathetic skin response
P194
Serum zinc level and disk degeneration

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Background
Lumbar disk herniation is one of the relatively common causes of Low Back Pain. It is now clear that mechanical factors alone cannot cause disk degeneration. The aim of present study was to estimate serum zinc levels in lumbar disk herniation patient as compare to control group.

Material and Methods
This case-control study was conducted during 17 September 2010 -17Jan. 2012 on sixty patients which were diagnosed as a"known case of Lumbar disk herniation" by the Neurosurgeon. Also57cases were chosen as a control with no disease. Assay was done based on single reagent direct calorimetric method.

Results
58 women and 59 men were observed in case and control groups.Serum zinc level was measured. Obtained results were analyzed by the help of SPSS with the confidence interval of 95 percent. Results showed that 21.7% of patients with Lumbar disk herniation were having high physical activity. On contrast to other 36.7% who have had low physical activity. Significant relation was found between Body Mass Index and Lumbar disk herniation in both sexes. The mean serum Zinc level in patients was 100.7± 49.2 µg/dl compared to 173.7± 73.7 µg/dl in control group.

Conclusion
The significant decrease in serum Zinc levels in patients with Lumbar disk herniation as compared to control group were observed(P< 0.001). Also relation between Body Mass Index and Lumbar disk herniation in both sexes were also observedP<0.002. We conclude that low level of serum zinc may also consider as one of the factor which cause disk degeneration
P195

The value of EEG in the neurophysiological diagnosis of the Creutzfeldt-Jakob disease. Our iconographic contribution on variable genotypes.

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**Question**

In the latest years a correlation between the codon 129 polymorphism and the type of the prionic protein (PrP) with variability of phenotypes in Creutzfeldt-Jakob disease (CJD) have been made.

The difficulty of identifying CJD ante mortem forces us to make use of all diagnostic approaches, including the search for the typical EEG pattern.

We also describe another EEG features in CJD and its correlation with variable genotypes. We approach some EEG-key elements to identify CJD and/or other CJ like syndromes.

**Methods**

We reviewed the EEGs of 19 patients with the diagnosis of CJD (17 sporadic, 1 familiar and 1 probable iatrogenic), and also the available data of the pathologic and genetic studies.

**Results**

16 patients were homozygotes at the codon 129 (11 MM; 4 VV) and only one was MV, the other three didn’t have the study. Only 9 patients had the determination of the PrP (3 PrP1, 5 PrP2, 1 not type 1 or 2).

11 patients have the typical periodic EEG pattern (all MM), but we also found other features with high prevalence such as the cyclic alternating pattern (11/16) and lateralization of anomalies (9/16).

**Conclusions**

EEG remains as an important diagnostic tool in CJD with excellent temporal resolution throughout the progressive stages of this disease. There is a correlation between polymorphism MM and type 1 PrP and the probability to find the typical EEG pattern. Even though the OMS criteria are used to make a neurophysiologic diagnostic, there are other features that allow us to suspect the disease. We have to keep other CJ-like syndromes in mind at the detection of periodic EEG patterns.
Abstracts of Poster Presentations – Poster Session 12 – Neurodegeneration

P196
The RISK FACTORS in the DEVELOPMENT of HYPOXIC ISCHEMIC ENCEPHALOPATHY IN CHILDREN

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Actuality
At the influence of harmful factors in early terms of pregnancy the damages of nervous system, heart, lungs and other systems of the fetus often occur. One of results of Central nervous system damages is hypoxic ischemic encephalopathy (HIE). Hypoxic level and tolerance of nervous system to hypoxic influence in every newborn is individual, and, in connection with that, the severity of cerebral disorders is also different.

The aim of study
To research extra genital anamnesis, complications of pregnancy course, deliveries in 30 women, and also evaluation of the newborns’ state with HIE.

Materials and methods of study
the data on extragenital anamnesis complications of pregnancy course and deliveries in 30 women, evaluation of their children with HIE were studied.

Result of the study
At analysis of anamnestic data it was determined that children with HIE were born mainly in young mothers, being in favourable age for the childbirth from 20 to 25 years (63.3%), after 1 pregnancy and 1 deliveries were 18 (66.7%). By the opinion of many authors in first time deliveries women the risk of the newborns trauma is highly possible. Analysis of frequency of some unfavorable antenatal risk factors for development HIE in the newborns revealed, that the examining women had overburdening gynecological anamnesis.

It is revealed that anemia (73.3%), gestosis (36.7%), chronic specific infections (33.3%) and endocrine disorders occurred with the highest frequency in comparison with other unfavorable factors. In many pregnant many combined several damaging factors were found, such as acute infectious diseases (26.7%), infections of genitourinary apparatus (26.7%), cytomegalovirus infection, toxoplasmosis, chlamydiosis (33.3%), hydramnon (16.7%).

Pathological deliveries were observed almost in 83.3% women, that proves the determined fact of active participation of fetus in occurance and development of delivery activity. The fetus, suffering for a long time in uterine, can be passive during delivery. It leads to disorder of delivery and is accompanied with intranatal damage of CNS.

Conclusions
This, in occurrences of HIE in the newborns the great significance has antenatal damaging factors. During anamnesis analysis the revealed presence of gestosis in mothers witness on factor of high risk for cranial damage of the child, as, the main pathogenetic chain of gestosis is microcirculation disorder and occurrence of tissue hypoxia.
Can symptoms be used to assess severity of CTS in elderly patients?

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Question

Clinical symptoms and signs have been used, traditionally, for diagnosis as well as severity assessment in Carpal Tunnel Syndrome (CTS). Age dependent changes were described related to median nerve. Late presentation of elderly people with CTS was reported in literature. Therefore the research question of the study was whether symptom can be used to assess severity of CTS in elderly patients.

Methods

Patients were selected based on clinical and nerve conduction study findings, out of the patients referred to the Department of Physiology, University of Ruhuna for nerve conduction studies. Detailed nerve conduction studies were performed in patients with CTS. Symptom assessment part of Sinhala translated Boston CTS questionnaire was used in the study to assess eleven symptoms.

Results

Total of 165 patients were included the study. They were divided into two groups; younger (n=81) and older (n=84) than 45 years of age. In younger group, distal latency was correlated (spearman rho p<0.05) with all the symptoms in the questionnaire except question No 7 and 8 while there was no such correlation in elderly group. A correlation was found between total symptom score and median motor distal latency (MMDL) in younger group (Spearman’s rho is 0.456, p < 0.001) while no correlation was found in elderly group. Mean total symptom scores and MMDL were not significantly different in two groups.

Conclusions

Symptoms do not correlate with severity of the median nerve compression. Therefore, symptoms should be used cautiously to assess severity of CTS in elderly patients.
P199
Neuroendocrine system condition in case of sudden sensorineural hearing loss

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Question

Recently, the problem of hearing loss is becoming more important as well as in the medical, so in the social plan. About 250 million people, or 4.6 % of the world’s population, according to WHO experts, suffer from hearing loss. The pathogenesis of sensorineural hearing loss (SHL) is still not well known, treatment and prevention of this disease are ineffective. Now the role of neuroendocrine system in the development of different diseases is actively studied. The most important factor of the neuroendocrine status is the pineal hormone’s melatonin level. Melatonin's spectrum of activity is sufficiently wide. There are antioxidant, stress protective, immune, geroprotective and vasodilating properties of this hormone.

Objective: to examine the level of urinary 6-SOMT (the main metabolite of melatonin) excretion in patients with sudden SHL, depending on the degree and duration of the disease.

Methods

The study involved 50 people, of whom 26 patients have sudden SHL. Control group consisted of 24 people with normal hearing. Standard ENT examination, acumeny study, tonal threshold audiometry, suprathreshold tests, acoustic impedance and examination of 6-SOMT-excretion was performed.

Results

The study of 6-SOMT-excretion level showed, that average values of this index in the urine of patients with sudden SHL were significantly higher, than the same parameters in the control group, regardless of the hearing loss degree. Also relationship between disease duration and the 6-SOMT-excretion level was found. Hormone’s level in patients with disease duration up to 1 week increased in 1,6 times, 1-2 weeks - in 1,4 times, 2-3 weeks - in 1,3 times, 3-4 weeks - in 1,1 times compared to the control group.

Conclusions

Patients with acute SHL have changes in the neuroendocrine profile, shown in raising of 6-SOMT-excretion level, regardless of hearing loss degree. There is relationship between disease duration and 6-SOMT-excretion level. The maximum hormone’s level occurs in patients with a short period of the disease (up to 1 week), which can be regarded as a compensatory and protective reaction. The results do not exclude the participation of melatonin in the pathogenesis of the SHL, and demonstrate the necessity for further research.
Abstracts of Poster Presentations – Poster Session 12 – Neurodegeneration

P200
Does MUNE reflect loss of lower motor neurons in aging?

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Motor unit number estimation (MUNE) is a tool for approximation of the real number of motor units.

**Objective**

to evaluate the multipoint incremental MUNE method in healthy population, to analyze if aging/sex/side of dominant hand have influence on motor units number and to assess reproducibility of MUNE by Shefner’s modification

**Material &Methods**

60 volunteers (mean age 47 yrs±17.7) in 4 groups in the ranges 18-30; 31-45; 46-60; over 60 yrs. MUNE was calculated in abductor pollicis brevis and abductor digiti minimi by dividing single motor unit action potential SMUP into supramaximal compound motor action potential (CMAP) amplitude.

**Results**

Test-retest variability was 7%. The mean value of MUNE for APB was 133.2 ± 43; for ADM 157.1±39.4 The significant differences between MUNE results were found between groups 18-30 and over 60 yrs and between groups 31-45 and over 60yrs. MUNE results correlated negatively with age of controls for both APB and ADM.

SMUP, reflecting the size of motor unit, increased with age of controls only in APB. CMAP amplitude correlated inversely with age of controls in APB and in ADM. The correlation between MUNE/ CMAP amplitude of APB /ADM muscles and the age of females but not of men was found.

**Conclusions**

multipoint incremental MUNE method in Shefner’s modification is a non-invasive, easy to perform method with high reproducibility. The loss of motor neurons due to aging, appears to be more pronounced in healthy people over 45 yrs, especially in females.
**P201**

Late midlife sleep pattern and sleep structure and the association to age-related changes in cognition

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**Question**

Advancing age is accompanied by changes in sleep pattern and increased prevalence of both sleep disturbances and cognitive impairment. Previous longitudinal studies exploring age dependent sleep and cognitive changes are scarce. Since disrupted sleep is linked to cognitive dysfunction we hypothesised that impaired sleep may be an early sign of cognitive deterioration.

**Methods**

Participants were healthy males born in 1953 and recruited from the Metropolit Cohort. Based on previous cognitive assessments in young adulthood and late midlife, the participations were selected for the study as cognitively unimpaired (N=97) or cognitively impaired (N=92). Overnight polysomnographic recordings were collected from a total of 189 subjects. A neuropsychological battery was administered to confirm group differences in cognitive functioning at the time when sleep data were collected. The battery included Mini Mental State Examination (MMSE), Addenbrookes Cognitive Examination (ACE) Digit Substitution Symbol Test (SDMT), Trail Making A and B-test, 15 word pairs, and Cambridge Neuropsychological Test Automated Battery (CANTAB). The main outcome measure was incident sleep polysomnographic characteristics

**Results**

Cognitive impaired males showed lower sleep efficiency than cognitive unimpaired males 78.5±12.8 (78.54±12.82 vs. 83.1±10.6, p=0.02) and increased nocturnal wakefulness (17.2±6.9 vs. 12.8±9.3, p=0.02). Percent stage REM sleep was slightly increased in cognitively impaired males compared with the cognitively unimpaired (17.6±7.0 vs. 15.7±6.3, p = 0.05). However, none of these polygraphic measures showed significant group differences after Bonferroni correction. Furthermore we found no strong correlation between sleep measures and cognitive test scores.

**Conclusion**

Subtle cognitive changes show few, if any, associations with sleep per se. Future research is needed to study the heterogeneity of cognitive aging and potential predictors of cognitive decline.
COMPARING OBJECTIVE MEASURES OF NEURODEGENERATION IN MULTIPLE SCLEROSIS (MS)

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Background

MS is a disease of the central nervous system (CNS) characterized by inflammation, demyelination and axonal loss. Neurodegeneration seems to be present from the beginning of the disease and is the main cause of progression of irreversible neurological deficits. Easy and low cost measures of axonal loss are lacking. Evoked potentials allows us the functional study of CNS. Visual (VEP) and motor evoked potentials (MEP) have already demonstrated good correlation with disability progression in MS. Optical coherence tomography (OCT) measures the retinal nerve fiber layer (RNFL) and the macular ganglion cell layer thickness (GCL).

Objectives

Investigate correlations between clinical measures of disability progression and OCT and evoked potential measures; and determine which objective measure correlates better

Material and methods

Prospective transversal study of 89 MS patients with PEV (latency p100; amplitude); MEP (magnetic stimulation; central conduction time-CCT, amplitude -average at least 3 supramaximal responses, and amplitude ratio with compound motor action potential-CMAP) and OCT (RNFL (µm); GCL((µm)))

Results

The mean age of our patients was 39 years (18-58) with a mean evolution time of the disease of 6 years and mean EDSS of 2,6(0-7). 31(49,2 %) patients had a relapsing-remitting form (EMRR). 27% had an episode of unilateral optic neuritis and 8% had a history of bilateral neuritis. We found statistically significant differences for OCT and PEV measures (latency p100 (ms) and amplitude) between MS eyes with optic neuritis (NO) and controls (p=0,0001), and between eyes of MS patients without ON and controls. GCL correlates better with EDSS measures than RNFL. OCT, PEV and PEM measures were also correlated between them. PEM amplitude ratio with compound motor action potential-CMAP, was the measure strongly correlated with progression (EDSS) in the multivariant analysis(p=0,0001), and ROC analysis showed a value of AUC of 0.8 for detecting progression EDSS>4. Conclusion: We detected axonal loss in patients with MS, either in eyes with NO or without it, with structural-OCT and functional-PEV and PEM measures. PEM measures are well correlated with OCT and clinical measures of neurodegeneration. PEM amplitude ratio was the most informative measure on disability progression.
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P203
Subjective sleep quality and daytime sleepiness in late midlife and the association to age-related changes in cognition

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Question

Poor sleep quality and cognitive changes are complex health issues, associated with increased frailty, morbidity and mortality and potential risk factor for further cognitive decline. Previous research on the association between self-reported sleep measurements and cognitive performance are somewhat inconsistent and leaves uncertainty with regard to the causal relationship of disrupted sleep and cognitive decline. Diminished sleep measures may be considered as early predictors of cognitive deterioration. We aimed to examine whether subjective sleep pattern is associated with change in cognition in middle-aged males.

Methods

189 healthy males born in 1953 and recruited from the Metropolit Cohort. Based on previous cognitive assessments in young adulthood and late midlife, the participants were selected for the study as cognitively unimpaired (N=97) or cognitively impaired (N=92). The Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) measured subjective sleep quality and daytime sleepiness. A comprehensive neuropsychological battery, including MMSE, ACE, Digit, Trail Making A and B-test, 15 world pairs, and Cambridge Neuropsychological Test Automated Battery (CANTAB) was administered to confirm group differences in cognitive functioning at the time when sleep data was collected.

Results

Overall, the prevalence of poor sleep quality (global PSQI score ≥5), was found to be 41% and excessive daytime sleepiness occurred in 15% (ESS ≥10). Compared to cognitive unimpaired males, the cognitive impaired males showed significant lower subjective sleep quality (5.40 ± 3.81 vs. 4.39 ± 2.40, p=0.03) Mean ESS score was (cognitive impaired 5.84± 3.42 vs. cognitive unimpaired 6.51± 3.15, p >0.05). There were few and weak correlations between sleep parameters and cognitive test performance in the combined sample.

Conclusion

Self-reported poor sleep quality was related to cognitive changes, whereas daytime sleepiness was not. Our results suggest that sleep quality may be an early marker of cognitive decline in midlife.
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P204
Electrophysiological Assessment of Dysautonomia in Multiple System Atrophy (MSA) and Progressive Supranuclear Palsy (PSP). A Comparative Study.

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Question

The aim of the study was to perform the electrophysiological assessment of the dysautonomia in MSA and in PSP using noninvasive tests: the sympathetic skin response (SSR) and R-R interval variation test (RRIV) and to answer to the question if autonomic profile specific for MSA and PSP defined by SSR and RRIV tests helps to distinguish between MSA and PSP.

Methods

The electrophysiological assessment of dysautonomia using SSR and RRIV, two noninvasive autonomic tests, performed according to the standard protocol was done in 59 patients with MSA (24 cases of MSA-C and 35 - MSA-P), among them 31 females, mean disease duration 4.2 +/- 2.7 yrs, mean age 60.3 +/- 8.4 yrs and in 37 patients with PSP (12 females, mean disease duration 4.6 +/- 3.6 yrs, mean age 67.5 +/- 6.1 yrs ) compared with the results obtained in 23 healthy controls matched for age and sex.

Results

In MSA patients SSR was abnormal in 64% of subjects whereas RRIV test was abnormal in 73% of cases. In PSP patients SSR was abnormal in 78% of subjects whereas RRIV test was abnormal in 81% of patients. According to our results SSR and RRIV tests were more often abnormal in PSP than in MSA patients. Electrophysiological testing revealed frequently subclinical autonomic damage in PSP patients.

Conclusion

In summary, sympathetic and parasympathetic involvement occurs in MSA and PSP in a various degree and may be assessed by non-invasive electrophysiological autonomic tests. Subclinical evidence of dysautonomia (abnormal SSR and/or RRIV tests) is more suggestive for PSP.
Background: Alzheimer's disease (AD) is a fatal neurodegenerative disorder. As a complex disease it is one of the six leading cause of dementia in the elderly. To identify the genetic alterations of AD by using the conventional cytogenetic techniques Trypsin G- banding. To conduct the biochemical parameters to analyzed by measuring the Neurotransmitters in AD patients. Apo E gene polymorphism in AD patients by using the PCR - RFLP was analyzed. Methods: Totally 70 AD patients blood was collected. The subjects were categorized in to two groups (31 Early-Onset AD) and (39 Late-onset AD) patients, in order to investigate the possible cytogenetic damage using PBLC, The MN assay was performed using the cytochalasin B technique, Biochemical analysis by HPLC with ECD and APO E gene polymorphism in AD patients by using the PCR - RFLP. Result: Comparative analysis of CSAs in Early-Onset AD patient and Late-onset AD patient. The Late-onset AD patient shows higher total CA level when compared Early-Onset AD patient. MN frequency was also found to be higher in Late-onset AD patients. A comparison of the frequencies for APO E genotypes among the Early-Onset AD and Late-onset AD subjects which demonstrates a significant difference between the two groups. Captivatingly in the study observed mutations in the chromosomes 10q, 9p, 9q, and 14p 19q and 21 was observed. Conclusions: The lack of evidence for interaction when the Apo E genotypes were used as covariates, despite the strong association of Apo E with Late-onset AD patients. Therefore, new treatments with the therapeutic target of improving mitochondrial function may prove to be promising. Key Words: CSAs- Chromosomal Type aberration, MN- Micronucleus Early-Onset Alzheimer's disease patient, Late- Onset Alzheimer's disease patients,
Background: Rett syndrome (RTT) is a postnatal neurological, pervasive development disorder, the vast majority of cases of classic RTT are caused by mutations in the MECP2 gene. A major source of the phenotypic variability associated with different MECP2 mutations and the pattern of X chromosome inactivation (XCI). The study mainly aims to identify case control study of genetic alterations by examining the effects of chromosomal and genotypic alterations in RS patients and their mothers, male subjects with RTT. Methods: A case control study of 2 male patients was evaluated based on the DSM IV-TR questionnaire and blood samples (5ml) were obtained from patients. The study was approved by the Institutional ethics board. Clinical profiles of the patients were recorded. Chromosomal, genotypic analysis and X chromosome inactivation (XCI) were carried out using standard protocol. Results: The Karyotype results of 2 male subjects were carried out by Giemsa-Trypsin banding and their results were confirmed by FISH. Higher degrees of chromosomal alterations were observed in X- chromosome includes 47, XXY and 46, XY, del(X) (Xp20.4-20.5). 316 C to T transition nucleotide changes and R106W amino acid changes was observed in 2 subjects. Higher frequency of XCI was observed in subjects with this RTT male subject (Max. 95.5%). Conclusion: Our present study reveals the most important and innovative work on RTT subjects. The recent studies demonstrating that neurological deficits resulting from loss of MECP2 can be reversed upon restoration of gene function are quite exciting. Thus, therapeutic strategies necessitate the identification of the molecular mechanisms underlying individual RTT phenotypes and picking out the candidates that can be therapeutically targeted. Keywords: Rett Syndrome; Chromosome alterations, X Chromosome Inactivation; MECP2
Bilateral ovariectomy (OVX) in female rats causes neurodegeneration in the nervous system of rodents and imitates systemic disorders in postmenopausal women's organism. Synaptic modulation by estrogen is essential to understand the molecular mechanisms of estrogen replacement therapy. The aim of present work was to determine the action of Sinestrol on rats' hippocampal synaptic transmission, plasticity and cell survival in condition of bilateral OVX. Electrophysiological and morphohistochemical (by revealing Ca2+-dependent acid phosphatase) studies by extracellular recording of hippocampal single-neuronal spike activity under high-frequency stimulation (HFS) of entorhinal cortex (EC) were performed on: 1) intact Albino rats, 2) after 8 week of OVX (placebo-control), 3) after 8 week of OVX (after 3 weeks i/m injection of Sinestrol- 0.1ml 2%). Our data suggest that OVX reduces hippocampal synaptic activity and failures the balance of excitatory and inhibitory responses of norm. After 8 week following OVX in hippocampal neurons dominate effects of tetanic depression in combination with posttetanic potentiation (45%) in response to HFS EC and typical of presence of areactive neurons (21%). Sinestrol promote the reorganization of neuronal circuitries of cortex-hippocampus by modulation of anomalous synaptic activity, as well as the balance of areactive and reactive units. Morphohistochemical analysis of studies by revealing Ca2+-dependent acid phosphatase testify that in whole Sinestrol enhances phosphorylation processes providing optimization of regeneration process following OVX.

Key words: Sinestrol, hippocamp, synaptic activity, phosphatase activity.
P208
Longitudinal quantitative EMG findings during reinnervation after complete nerve lesions

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OBJECTIVE

We investigated reinnervation of muscle fibers and subsequent remodeling of the motor unit after complete nerve lesions. EMG was carried out in ulnar or median innervated muscles after nerve-repair by suture or a collagen nerve guide.

BACKGROUND

After complete nerve lesions peripheral nerve fibers regenerate. Recovery is dependent of the rate of growth of fibers, the number of axons that regenerate, innervation of target tissue and maturation of regenerated fibers. Recovery is often incomplete, and patients have lasting motor deficits.

METHODS

In this randomized multi-center study two procedures for repair of complete nerve lesions were compared. The collagen nerve guide (NeuraGen™) was implanted in 22 of 43 patients and direct suture repair was used in 20 patients and a short graft in 1 patient. The outcome measures included clinical and electrophysiological studies at 1, 3, 6, 12, 18 and 24 months after repair. In a subgroup of 10 nerves repaired by suture and in 11 by nerve guide, quantitative EMG was assessed. A concentric needle was inserted in the muscle at up to 10 sites and the decomposition system EMGtools was used for analysis (IEEE TBE, 2011, 58:2707-2718). We measured denervation; durations, shapes and amplitudes of motor unit potentials (MUPs); and amplitudes and shapes of the recruitment patterns at maximal effort. The parameters were compared with normal controls and the contralateral normal muscle.

RESULTS

Denervation activity and absent voluntary activity occurred in all patients at 1 months. MUPs of small amplitude, long duration and polyphasic shape were first recorded after 3-6 months. Denervation gradually decreased and the amplitudes of the MUPs gradually increased while the duration remained unchanged. The amplitude and interference of the recruitment pattern increased. No differences at different repair types were detected.

CONCLUSIONS

Regeneration over short gap was supported as well by nerve guide as by suture and in the patient groups muscle reinnervation was similar.
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P209
Postural control in Lumbar Spinal Stenosis (LSS)
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Introduction

Patients suffering from lumbar spinal stenosis (LSS) present with stance and gait disturbances. However, it is not known yet which mechanisms contribute to these deficits. Moreover, it is not clear how surgical interventions and physiotherapy affect these altered mechanisms.

Aims

With the help of a model-based approach using parameter identification techniques, we aimed to identify components of stance and gait disturbance in LSS and compare these to those observed in healthy control subjects. Furthermore, we aimed to characterize the effects of therapeutic interventions using the parameter identification approach.

Methods

11 LSS patients were evaluated pre and post surgery and were compared to 15 age-matched healthy subjects. Postural control was assessed using external disturbances (tilting platform). We then calculated transfer functions between input (platform tilt) and output (body lean) and identified abnormal postural control mechanisms using a model-based approach.

Results

Amplitude, velocity and frequency range of LSS patients’ spontaneous sway is larger than that of healthy control subjects signaling larger ‘internal noise’ of the system. Characteristic features of patients’ transfer functions indicate abnormalities of postural control mechanisms. In particular, velocity feedback and sensor weighting seems to be affected. Surgery mainly influenced spontaneous sway, whereas transfer functions were less affected.

Conclusion

Postural control deficits in LSS patients are characterized by larger internal noise, altered velocity feedback control, and altered sensor fusion. The effects of spinal surgery and physiotherapy on velocity feedback and sensor fusion showed a clear tendency towards the values identified in healthy subjects. Surprisingly, these therapeutic effects clearly correlated with clinical measures of balance and gait stability. Measures of internal noise were significantly affected by therapeutic interventions. However, these measures poorly correlated with clinical scales of stability. We conclude that model-based parameters of postural control extracted from transfer functions of patients’ reactions allow for a precise picture of the individual postural control deficit. Parameters related to spontaneous sway, i.e. internal noise represent a more global, and less specific picture of abnormal postural control.
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P210
Preoperative functional mapping for rolandic brain tumor surgery

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Question

The resection of tumors within or close to eloquent motor areas is usually guided by the compromise between the maximal allowed resection and preservation of neurological functions. Navigated transcranial magnetic stimulation (nTMS) is an emerging technology that can be used for preoperative mapping of the motor cortex. In the present study we report the experience gained during the first year of systematic use of nTMS.

Methods

We performed pre-surgical mapping by using nTMS in 17 patients with lesions in or close to the precentral gyrus. The study was conducted on consecutive patients scheduled for surgical treatment. Preoperative mapping was performed with the eXimia navigated brain stimulation system.

Results

nTMS allowed to exactly localize the motor cortex in 88.2% of cases. In 70.6% it provided the surgeon with new unexpected information about functional anatomy of the motor area, influencing the pre-operative planning. Moreover, in 29.4% these functional information had a clear impact on surgery, making necessary a change of surgical strategy to avoid damage to the motor cortex.

Conclusions

nTMS has a large benefit in the treatment of rolandic brain tumors. It adds important information about spatial relationship between functional motor cortex and the tumor and reduces surgical-related post-operative motor deficits.
P211
MEP threshold evaluated by deterministic tractography and subcortical stimulation

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Objective
To validate the corticospinal tract (CST) illustrated by diffusion tensor imaging (DTI), we used CST-tractography integrated neuronavigation and direct fiber stimulation with monopolar electric currents.

Methods
Forty patients with brain lesions adjacent to CST were studied. During the operation, the motor responses (motor evoked potential; MEP) at the hand by the cortical stimulation to the hand motor area were continuously monitored. During lesion resection, direct fiber stimulation was applied to elicit MEP (fiber-MEP) to functionally identify CST. The threshold intensity for the fiber-MEP was determined by searching for the best stimulus point and changing stimulus intensity. The minimum distance between the resection border and illustrated CST was measured on postoperative isotropic images.

Results
Direct fiber stimulation demonstrated that CST-tractography accurately reflected anatomical CST functioning. There were strong correlations between stimulus intensity for the fiber-MEP and the distance between CST and the stimulus points. The results indicate that the minimum stimulus intensity of 20, 15, 10 and 5mA had stimulus points of approximately 16, 13.2, 9.6 and 4.8 mm far from CST, respectively. The convergent calculation formulated 1.8mA, which was much smaller than that of the hand motor area.

Interpretation
DTI-based tractography is a reliable way to map the white matter connections in the entire brain. By combining these techniques, investigating the cortico-subcortical connections in the human central nervous system could contribute to elucidating the neural networks of the human brain and shed light on higher brain functions.

Figure 1 (A) Postoperative image demonstrating the resection cavity (arrowhead) and ischemic lesions by surgical manipulation as high intense areas. (B) Isotropic image, (C) Volume calculation by segmentation of the resection cavity and CST. (D) Three-dimensional measurement of the minimum distance between the resection cavity and CST.

Figure 2 Scatter plot between the stimulus intensity of direct fiber stimulation and the distance between CST and the stimulus points on the postoperative isotopic images. Note that the minimum stimulus intensity with 20, 15, 10 and 5mA indicated that the stimulus point was approximately 16.0, 13.2, 9.6 and 4.8mm far from CST, respectively.

Reference
Neuroprotective effects of 17-beta-estradiol: A therapeutic potential drug for Alzheimer’s disease

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Objectives: Alzheimer’s disease (AD) is the most common form of dementia in the elderly. AD is characterized by the presence of amyloid plaques which are formed from deposits of β-amyloid protein (Ab). These changes increase during menopausal condition in females when the level of estradiol is decreased. The aim of the present study was to determine the effect of neuropeptide, neurokinin B (NKB) and amyloid beta fragment Aβ (25-35) on 17β estradiol (E2) treated aging female rat brain of 3 months (young), 12 months (adult) and 24 months (old) age groups.

Methods: The aged rats (12 and 24 months old) (n= 8 for each group) were given subcutaneous injection of 17b-estradiol (0.1 µg/g body weight) daily for one month. After 30 days of hormone treatment, experimental animals of all the groups were sacrificed and brains were isolated for further study.

Results: The results obtained in the present work revealed that increased activities of antioxidant enzymes, membrane bound ATPases and decrease in level of calcium levels , monoamine oxidase activity and lipid peroxidation in presence of NKB and combined NKB and Aβ in vivo estradiol (E2) treated ageing rat brain. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain. An in vitro incubation of E2 treated synaptosomes with Aβ showed toxic effects on all the parameters, while NKB showed stimulating effects and the combined NKB and Aβ showed a partial effects as compared to Aβ (25-35) and NKB alone.

Conclusions: Present study elucidates an antioxidant, neuromodulatory and neuroprotective role of tachykinin peptide NKB against the beta amyloid induced toxicity in E2 treated female rats. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain.
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LP14
Comparison of motor skills and behaviour in B6CBA and C57BL/6 mice

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Introduction

The strain differences in the neural functions and other strain derived properties in laboratory mice can influence the results of experiments performed in mouse models of the various pathological states.

Aim

The aim of the experiment was to compare the motor capabilities and behaviour in B6CBA and C57BL/6 mice.

Methods

Adult mice of the B6CBA and C57BL/6 strain were used and the spontaneous motor activity and anxiety were examined in the open-field for 3 days. The object-recognizing test was performed. Finally, motor capabilities were evaluated using the rotarod and coat-hanger tests.

Results

In the open field C57BL/6 mice moved significantly more than B6CBA mice on the 1\textsuperscript{st} day. During the following days the C57BL/6 mice decreased the length of their trajectory, while B6CBA did not. There were no differences in preference of the arena periphery. In the object-recognizing test B6CBA mice spent more time exploring the novel object than the familiar one. In C57BL/6 mice the difference in the reaction to both of the objects was insignificant. The mean distance to the novel object was significantly shorter in B6CBA than in C57BL/6 strain. In the rotarod and coat-hanger test no differences were found.

Conclusion

We found moderate strain differences in behavioural characteristics. C57BL/6 mice showed higher exploratory activity which decreased during repetitive exposure as the environment became familiar. B6CBA mice showed better differentiation between the novel and already explored object. Motor capabilities of B6CBA and C57BL/6 mice did not differ.

*Supported by the research project VZ MSM 021620816.*
LP15
EEG Slowing and Cognitive Domains in Non-Demented Patients with Parkinson’s Disease

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Question
Cognitive deficits in Parkinson’s Disease (PD) are heterogeneous and can be classified into neuropsychological domains. EEG has been shown to be related to cognitive status and can predict development of dementia. In this study, we investigate the relationship of cognitive domains and slowing of the EEG in PD patients without dementia.

Method
Data of 52 patients with idiopathic PD were analysed. Domain scores were calculated combining z-scores of cognitive test variables. Slowing of EEG was measured with median EEG frequency. Linear regression was used for the correlational analyses and to control for confounding factors.

Results
Deficits in overall cognitive performance and more specifically the domains memory, attention, fluency and executive functions performance correlated with EEG slowing. These domains were correlated to similar EEG patterns.

Conclusions
EEG is discussed as a surrogate marker for cognitive performance. The biomarker based investigation of cognitive domains in non-demented PD patients is important for a potential early detection of different forms of dementia and their clinical management.
Clinical spectrum of sensory ganglionopathy in eight patients

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Question

Sensory neuronopathies or ganglionopathies, or dorsal root ganglion disorders, represent a subgroup of peripheral nervous system diseases, frequently associated with dysimmune or neoplastic disorders and with toxic agents. A degeneration of both central and peripheral sensory projections is present. Patients typically show early ataxia, loss of deep tendon reflexes and positive sensory symptoms present both in proximal and distal sites of the body.

Methods

We retrospectively studied 8 patients with a final diagnosis of subacute sensory neuronopathy (SSN).

Results

In all patients the presenting symptom suggested a SSN with symmetrical distribution. Paresthesias in upper limbs and both feet were a predominant manifestation (100%). Other presenting symptoms were: gait ataxia (5/8), pain (4/8) and perioral paresthesias (2/8). Electrophysiology showed sensory axonal neuronal pattern with reduced or absent SNAPs with normal CMAPs in all cases. Final diagnosis was acquired sensory neuronopathy, associated with Sjögren’s syndrome in 3 patients, paraneoplastic syndrome in 2 patients (one patient had small cell lung cancer with positive anti-Hu antibodies, and other one had epidermoid lung cancer) and idiopathic SSN in 3 patients. Five patients were treated with immunotherapy, high dose intravenous methylprednisolone and/or intravenous immunoglobulin (IVIg), with poor response in 3 cases and neurologic improvement in 2.

Conclusions

Sensory neuronopathies or ganglionopathies are a distinct category within sensory neuropathies. The present work shows the typical clinical and electrophysiological pattern of SSN and the relevance of early treatment, which could stop or reverse the damage to the dorsal root ganglion, improving final prognosis.
P213
Bifid Median Nerve is not associated with Carpal Tunnel Syndrome or hand/wrist configuration

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Question
The etiology and predisposing factors of idiopathic carpal tunnel syndrome (ICTS) is a matter under investigation. Bifid median nerve (BMN), an anatomical variation of the median nerve has been studied in relation to CTS, but the results of the relevant studies are conflicting. Aim of our study was to assess the frequency of BMN in a cohort of patients with ICTS and a group of healthy controls to determine whether it comprises a predisposing factor.

Methods
50 patients (40 women) with clinically and electrophysiologically confirmed CTS and 50 age and sex-matched healthy controls underwent ultrasonographic imaging of their carpal tunnel in both wrists for BMN detection, measurements of carpal tunnel ratio and cross sectional area of median nerve. Their height, weight, body mass index, external dimensions of hand and wrist (hand ratio, wrist ratio) were noted.

Results
BMN was found by ultrasonography in 4 out of 50 subjects (8%) in both groups. In the ICTS groups there were 3 women and in the control group 2 women, while in both groups 1 subject had bilateral BMN and 3 had unilateral. Subjects with BMN in the two groups did not differ significantly as regards to height, weight, body mass index and the anthropometric, external or ultrasonographic measurements, except for electrophysiological findings (sensory conduction velocity and distal motor latency) that discriminated the two groups.

Conclusions
BMN does not seem to constitute a risk factor for ICTS nor is associated with a particular hand/wrist shape.
P214
STUDY OF SYMPATHETIC SKIN RESPONSE IN DIABETIC PATIENTS WITH SOFT TISSUE RHEUMATISM OF THE HAND

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Background

Physicians have long recognized the association between diabetes mellitus (DM) and several pathologic conditions of the hand. The most commonly recognized conditions are trigger finger, tenosynovitis, Dupuytren's disease (DD), carpal tunnel syndrome (CTS), and limited joint mobility (LJM). However, there is a paucity of data regarding the presence of a possible relation between those hand lesions and diabetic autonomic neuropathy.

Aim

To investigate the relationship between sympathetic dysfunction and diabetic hand soft tissue lesions.

Patients

Group 1 contained 20 diabetic patients with one or more hand soft tissue lesions. Group 2 contained 20 diabetic patients without any hand pathology and 20 healthy control subjects.

Methods

Patients with DM were thoroughly evaluated clinically and assessed for the presence of diabetic autonomic neuropathy (DAN) using tilt table test before proceeding to the electrophysiological tests which were (1) Sensory and motor conduction studies of median, ulnar, and radial nerves.(2) Sympathetic skin response (SSR).

Results

5 patients had trigger finger, 2 had tenosynovitis, 1 had Dupuytren's contracture, 6 had CTS, 2 had LJM and 4 had combined CTS and trigger finger. Abnormal SSR was detected in 10 patients in group 1 and in 11 in group 2(in the form of absent response or delayed latencies). There was no statistically significant difference between group 1 and 2 regarding the frequency of SSR abnormalities. There was a statistically significant relationship between the presence of CTS in group 1 patients and abnormal SSR results. There was statistically significant relationship between positive tilt table test results in group 1 patients and abnormal SSR in the same group. There was statistically significant relationship between the duration of DM and abnormal SSR results in group 1 patients.

Conclusions

diabetic patients with CTS tend to have prolonged SSR of the hand .further studies are recommended to study other factors responsible for the occurrence of diabetic soft tissue lesions

References


Key words

diabetic hand soft tissue lesions, diabetic autonomic neuropathy, sympathetic skin response.
P215
Anti-ganglioside complex IgM antibodies and immune-mediated neuropathies: a novel case of acute motor conduction block neuropathy (AMCBN)?: a case report

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Introduction

Acute motor conduction block neuropathy (AMCBN) has been described as unusual presentation of different immuno-mediated peripheral nerve pathologies: Guillain – Barré syndrome (GBS), acute motor axonal neuropathy (AMAN), multifocal motor neuropathy (MMN). Diverse anti-ganglioside antibodies associations were observed, but anti-GM1/GT1A/GT1B IgM complex has never been reported.

Objective

to report a patient with acute motor neuropathy, conduction blocks and anti-GM1/GT1A/GT1B IgM complex antibodies.

Methods

A 24-year-old female was admitted to our department complaining about recent onset of tingling and weakness in both hands. Three months earlier she was diagnosed with type 1 diabetes arising after a journey in Eritrea, were she complained fever, diarrhea, and ambulation difficulties treated with antibiotics. Neurological examination showed mild heel ambulation impairment, bilateral lower limb hyporeflexia, mild bilateral hand-grip weakness, mild stocking-glove hypoesthesia; cranial nerve exam was normal, nor patient complained about dysphagia or dyspnea. Nerve conduction study evidenced a primary motor polyneuropathy with segmental demyelination, conduction blocks and F-wave abnormalities. No significant involvement of sensory conductions nor reduction of distal compound motor action potential (CMAP) were observed. Lumbar puncture revealed increased proteins (97.8 mG/dL) with normal count cell; immunoblotting disclosed elevated titer of IgM anti-GM1, anti-GT1A and anti-GT1B. Patient was treated with IvIG (0.4 mg/kg/day) for 5 days without a significant benefit till two months later when, after an initial clinical and instrumental motor worsening, she reported clinical recovery and nerve conduction improving.

Conclusions

In our patient clinical course and electrophysiological findings were not suggestive of AMAN, GBS or GBS-variants, nor typical for MMN. AMCBN remains the most plausible explanation of her symptoms and nerve conduction features. Immunological profile suggests new possible AMCBN anti-ganglioside associations.

figure 1
Carpal tunnel syndrome in pediatric mucopolysaccharidoses

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2Murdoch Childrens Research Institute, Melbourne, VIC, Australia
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4University of Melbourne, Department of Pediatrics, Melbourne, VIC, Australia

Background

Carpal tunnel syndrome (CTS) is rare in children but is a recognised complication of the mucopolysaccharidoses (MPS). Clinicians should have a low threshold of suspicion for carpal tunnel syndrome in this group as symptoms may be atypical or minimal, especially in those with intellectual disabilities secondary to mucopolysaccharidoses. If untreated, CTS can cause significant, potentially permanent loss of hand function. We present findings in 11 children with MPS and suspected CTS, and propose guidelines for screening for carpal tunnel syndrome in children with these disorders.

Methods

Clinical and electrodiagnostic data of 11 children with confirmed MPS by enzymatic +/- molecular testing, who were suspected on clinical grounds to have carpal tunnel syndrome, was reviewed. All subjects underwent motor and sensory conduction studies of bilateral median and ulnar nerves. The presence of CTS and its severity was determined. Subsequent details of intervention(s) and recurrence were noted.

Results

Three children had Hurler syndrome (MPS I), five had Hunter syndrome (MPS II), one had Sanfilippo syndrome (MPS III) and two had Morquio syndrome (MPS IV). Seven had motor and three sensory features referable to median nerve compression. Nine of the eleven children (2/3 with MPS I, 5/5 with MPS II, 0/1 with MPS III, 2/2 with MPS IV) had median neuropathies at the wrist, (eight bilateral, one unilateral) which were mild in three, moderate in five, and severe in one. Three children presented with symptoms at age five years age. Six underwent median nerve decompression. Four of these had recurrent symptoms several years after surgery. Recurrent carpal tunnel syndrome was confirmed on nerve conduction studies in two cases. To the best of our knowledge, this is the first report of carpal tunnel syndrome in MPS IV.

Conclusion

Some children with MPS experience early development of at least moderately severe CTS. We recommend screening for CTS from age 5 years for children with MPS, particularly types I, II and IV, irrespective of symptoms or specific treatment received for the storage disorder. Those with no evidence of CTS and those having undergone surgery should be assessed annually by a neurologist and at regular intervals for evolution of compressive median neuropathy.
P217
Electrophysiological features of demyelination and axonal loss in POEMS syndrome: distribution and relation to weakness

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2Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Neurology, Beijing, China

Question

POEMS syndrome is a rare cause of demyelinating and axonal mixed neuropathy. The distribution of axonal loss and demyelination, the correlation between electrophysiological abnormalities and weakness has rarely been studied in patients with POEMS syndrome.

Methods

We reviewed medical records of 89 patients with POEMS syndrome for the pattern of weakness and electrophysiological abnormalities. Difference in electrophysiological abnormalities in lower arm and lower leg segments as well as that among different segments of upper limb nerves was assessed. Multivariate logistic regression analysis was used to determine the independent determinant to axon loss and weakness.

Results

Axonal loss was prominent in distal lower-limb nerves. Distal motor latency compatible with definite demyelination was found predominantly in arm nerves. Conduction slowing consistent with demyelination was more predominant in proximal and intermediate nerve segments; Conduction block (CB) was detected in 20% of nerves and more frequently in proximal nerve segments. Motor conduction velocity compatible with definite demyelination, CB and axonal loss were independently correlated with each other. Furthermore, axonal loss was an independent determinant of weakness.

Conclusions

In patients with POEMS polyneuropathy, EMG features consistent with axonal loss was more common in distal lower-limb nerves, whereas electrophysiological abnormalities consistent with definite demyelination was more significant in upper-limb nerves, with the predominance of conduction slowing in proximal and intermediate nerve segments, and CB in proximal nerve segments. CB and axonal loss correlate with each other. Pathophysiological mechanisms leading to axonal loss play an important role in weakness in the patients.

Figure legend

Fig.1 Electrophysiological abnormalities in lower leg vs. forearm nerves

Fig.2 Logistic regression analysis for the determinants of weakness
Abstracts of Poster Presentations – Poster Session 13 – Neuropathies 1

**figure 1**

![Bar chart showing lower leg and forearm percentage values](image)

**figure 2**

<table>
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<td>Prolonged DML</td>
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<tr>
<td>Reduced MCV</td>
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<tr>
<td>CB</td>
<td>0.61 (0.51 - 1.61)</td>
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<tr>
<td>TD</td>
<td>0.98 (0.28 - 3.45)</td>
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<tr>
<td>Axonal loss</td>
<td>3.51 (1.45 to 8.52)*</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.00 (0.99 - 1.01)</td>
</tr>
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* P<0.001
P218
Preliminary reports of use of low intensity laser for entrapment neuropathy
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¹Botucatu Medical School, Neurology, Psychology and Psychiatry, Botucatu, Brazil

Introduction

The carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. After surgery different types of complication may occur, than search for new clinical forms of treatment is necessary. There are controversies about the efficacy of laser on CTS [1,2,3] . The aim of this study was to test the effectiveness of low intensity laser therapy in patients with CTS.

Methods

Patients with clinical and ENMG diagnosis of CTS never previously treated were included. Sensory and motor conduction studies were performed by conventional described techniques. Low intensity laser treatment was by 660 nm wave length, average power of 30 nw, continuous operation area of 0.06 cm², fluence of irradiation of 10 J/cm², exposure of 10 seconds per point, totaling 6 points of irradiation on the carpal tunnel, from the proximal to the distal sense. Laser was positioned at 90° to the skin, 2 sessions per week during 3 months were performed (24 sessions).

Results

To this moment 12 hands of 9 patients were studied, all reported clinical improvement. Improvement of the different parameters of the conduction studies was observed in 11 hands, worsening was detected in one. The patient with worsened hand evaluated by conduction studies informed clinical improvement.

Discussion

In our opinion low intensity laser therapy is a new, no expensive and easy to apply encouraging treatment for CTS.

References


Legends

Tab1-Clinical data of the 9 patients. VAS=Visual analogical scale; ROM=range of movement of carpal flexion; GS=grip strengh.

Tab2-Conduction studies values of the 12 hands.
### figure 1

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### figure 2

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Applicability of electrophysiological registers in the study of BMMC-mediated remyelination after sciatic nerve crush.

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Question

Our group has previously reported histomorphological changes associated with rat peripheral remyelination induced by the transplant of bone marrow mononuclear cells (BMMC) after sciatic nerve crush\textsuperscript{1}. Functional evaluation and the correlation between electrophysiological and histomorphological parameters has generated controversy. In order to evaluate whether the electrophysiological registers are suitable for the study of peripheral remyelination, these registers were adapted and the effect of the lesion was evaluated, together with the treatment of latencies and the amplitude of compound motor action potentials.

Methods

Adult Wistar rats were submitted to sciatic nerve crush and sacrificed 7, 14 and 21 days post injury. The ipsilateral nerve was dissected in proximal, crush and distal areas. BMMC were isolated from rat tibia and femur and injected intravenously immediately after crush. Motor Conduction Velocity (MCV) was evaluated through a Cadwell Wedge Sierra II device (Cadwell Labs, Inc., Kennewick, WA, EEUU), stimulating the contralateral or ipsilateral sciatic nerve with needle electrodes in the distal stump with pulses of 8 to 40 mA. The differences were evaluated using ANOVA.

Results

The stimulation of the naked nerve and the comparison of MCV between groups demonstrated better register quality and replicability. Animals receiving BMMC transplant at the time of lesion showed faster distal latency recovery as compared to non-transplanted animals (p = 0.007, ANOVA with Bonferroni's correction for multiple comparisons).

Conclusion

The electrophysiological register is suitable for the evaluation of this model and its findings correlate with a higher degree of peripheral remyelination in BMMC-transplanted animals.

\textsuperscript{1}“Bone marrow mononuclear cells migrate to the demyelinated sciatic nerve and transdifferentiate into Schwann cells: an attempt at an endogenous repair mechanism after nerve injury”. Vanina Usach, Belén Goitia, Lucía Lavalle, Rocio Martinez Vivot and Patricia Setton-Avruj. Journal of Neuroscience Research 89:1203-1217 (2011).
The clinical and neurophysiological features of acute autonomic and sensory neuropathy

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²Huashan Hospital, Shanghai, China
³Upstate Medical University, Department of PMR, Syracuse, United States

Introduction

Acute autonomic and sensory neuropathy is a very rare disorder. Early diagnosis and proper treatments of this disease are of very important significance.

Methods

We characterized the clinical, neurophysiological, and prognostic features in two patients early diagnosed with this disease.

Patient 1. A 49 year old male was previously healthy except a sore throat six days ago. On the day of onset, he suffered from lower abdominal pain and distention. Then, he felt numbness and touch pain in the median side of both hand and felt unsteady when walking, and developed to difficult to stand on the 10th day. After IVIG, his gastrointestinal symptoms resolved and he was able to stand and walk but still felt numbness in both hands.

Patient 2. A 67 year old male reported a gastrointestinal tract infection one week before he began to complain of faintness upon standing and later numbness of fingers and toes on both sides. Blood pressure was 116/73mmHg in supine position and immediately dropped to 66/44 mmHg after standing up. After IVIG, he was able to sit up.

Neurophysiological measures: Sensory function: SNCS, soleus H reflexes from stimulation distally at the knee (tibial H reflex) and proximally at the S1 foreman (S1 H reflex). Motor function: MNCS, F waves, EMG. Autonomic function: the coefficient of variation of the R-R intervals on electrocardiography (ECG).

Results

Clinical: Both patients presented antecedent events, with the initial symptoms related to autonomic disturbance and superficial sensory impairment while the deep sensory impairment accompanied by sensory ataxia and wild spread loss of tendon reflexes subsequently. With the early diagnosis and application of IVIG, the autonomic dysfunction was ameliorated to some degree within several months, although the recovery of sensory function was less significant in the early stage.

Neurophysiological measures: In both patients: severely reduced amplitude of SNAPs with preserved conduction velocities relatively. Absent tibial and S1 H reflex. Normal MNCS, F waves and EMG. Abnormal coefficient of variation of the R-R intervals on ECG.

Conclusions

Neurophysiological measures including H reflex to distal and proximal stimulations are essential in the early diagnosis and management of acute autonomic and sensory neuropathy, which might affect the sensory axons more distally and sensory neurons proximally.
Detection of Early Abnormalities in Familial Amyloidotic Polyneuropathy by Quantitative Sensory Testing (QST)

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Introduction

The small fiber neuropathies alter myelinized Aδ fibers and non-myelinized type C fibers, involving autonomic functions, nociception, thermal perception and sweating. Genetic mutation TTR-Val30Met is the etiologic factor in the Portuguese variant of Familial Amyloid Polineuropathy, compromising earlier the small nerve fibers. Conventional neurophysiological studies are unable to detect those abnormalities, delaying specific treatments.

Objective

The main goal of the present study was to evaluate the Quantitative Sensory Testing -QST, as an early diagnostic tool, identifying abnormalities in patients with the genetic mutation Val30Met in transthyretin (TTR) gene.

Methods

Patients were classified in 3 groups according to symptoms and neurological examination. Thresholds for cold perception, heat-pain (onset (HP 0.5), intermediate pain (HP 5.0), stimulus response slope (HP 5.0 - 0.5)) and vibration were assessed in the different groups, compared to healthy controls.

Results

33 cases and 18 controls, divided in asymptomatic (24.2%), symptomatic with normal neurological examination (42.4%) and symptomatic with abnormal neurological examination (33.3%). There were no differences between asymptomatic patients and healthy controls. The abnormalities on cold threshold detection and intermediate severity of heat-pain response (HP5), can occur before changes in the neurological examination. In patients with abnormal neurological examination differences also include the stimulus-response slope (HP 5-0.5) between intermediate severity (HP 5.0) and onset perception of pain with heat (HP 0.5).

Conclusions

Cold, heat pain 5.0 and stimulus response slope (HP 5-0.5) thresholds are the most useful parameters showing differences between symptomatic and asymptomatic patients, including those without neurological abnormalities.

The Quantitative Sensory Testing showed to be a useful tool in the detection of small fiber abnormalities in patients with TTR Val30Met mutation.
Figure. Quantitative Sensory Testing in Patients with Val30Met Mutation

- **Heat Pain 5.0**:
  - G1: Not symptomatic (Norfolk = 0)
  - G2: Symptomatic, normal neurological examination (Norfolk > 0, Utah – Michigan B = 0)
  - G3: Symptomatic, abnormal neurological examination (Norfolk > 0, Utah – Michigan B > 0)

- **Heat Pain 5.0 - 6.5**:
  - Similar to Heat Pain 5.0

- **Cold Threshold**:
  - Similar to Heat Pain 5.0

- **Vibration Threshold**:
  - Similar to Heat Pain 5.0
P222
Sensory Axonal Dysfunction in Asymptomatic Diabetic Patients

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\textsuperscript{1}Wan Fang Hospital, Taipei Medical University, Neurology, Taipei, Taiwan
\textsuperscript{2}Neuroscience Research Australia and Prince of Wales Clinical School, University of New South Wales, Sydney, Australia
\textsuperscript{3}Translational Neuroscience Facility, School of Medical Sciences, University of New South Wales, Sydney, Australia

Objective

Diabetic is a worldwide problem, and presence of diabetic neuropathy contributed toward increasing morbidity and mortality in diabetic patients. Utilizing the novel nerve excitability test (NET), previous studies have demonstrated that the motor nerve properties changes precede the development of neuropathy in diabetic patients. However, given the fact that diabetic patients suffer more sensory symptoms than motor, the present study, we aim to further elucidate the early pathophysiology of axonal dysfunction in diabetes by studying the excitability of sensory nerve in different stages of diabetes.

Methods

A total of 63 type 2 diabetic patients are studied and sub-grouped based on Total Neuropathy Score (TNS) and HbA1c estimated into Grade 0 (G0; TNS 0-1, n=24), Grade 1 (G1; TNS 2-8, n=28) and Grade 2 (G2; TNS 9-24, n=11). Patient underwent standard nerve conduction studies and NET of sensory and motor axons. G0 patients were asymptomatic and had normal routine nerve conduction study.

Results

Compare to healthy controls, sensory NET data of G0 group showed significantly increased threshold and latency, down-shifting of recovery cycle (RC) with increased superexcitability (p < 0.001) and decreased late subexcitability (p < 0.001), and increasing TEd(10-20 ms) (p<0.001). Changes in above parameters have trends as the disease progressed. (Figure 1) Meanwhile, motor NET data in the same G0 patients also had significant increase in threshold and latency. However, of the trends of change was opposite to sensory with decrease in superexcitability and subexcitability, and decrease in TEd(peak) and S2 accommodation. Motor axonal changes also progressed with disease progression but not as significantly as sensory axons at early stage. (Figure 2)

Conclusions

More significant excitability parameter changes in sensory NET in G0 group suggest axonal dysfunctions from nodal to internodal areas in sensory axons precede motor axons. The fact that these abnormalities can be detected by sensory NET prior to clinical evidence of neuropathy suggested that sensory NET may provide an effective biomarker to further elucidate the pathophysiological mechanisms producing axonal dysfunction in patients with diabetes at early stage.
Abstracts of Poster Presentations – Poster Session 13 – Neuropathies 1

figure 1

Figure 1. Motor nerve excitability changes in different TNG groups.

figure 2

Figure 2. Sensory Nerve excitability changes in different TNG groups.
Axonal membrane dysfunction in IgM neuropathy

M. ten Kate¹, N. Notermans¹, L. van Schelven¹, *H. Franssen¹
¹UMC Utrecht, Utrecht, Netherlands

Question

IgM neuropathy is a chronic slowly progressive symmetrical distal sensorimotor polyneuropathy. Pathological studies reveal damage to the myelin sheath and axonal degeneration. Current treatment strategies, directed at decreasing serum-IgM levels, have little or no effect. This may be explained by the occurrence of irreversible axonal damage. Mechanisms responsible for this are unknown. We suggest a mechanism involving paranodal and internodal demyelination that alters the density of specific ion channels and causes impairment of impulse propagation and axonal degeneration. In this study, we investigated axon membrane and ion channel function in patients with IgM neuropathy.

Methods

Excitability tests were performed in 17 patients with IgM neuropathy and 15 healthy volunteers. Stimulus response curves, strength-duration relation, threshold electrotonus, current-threshold relation and recovery cycle were investigated. The MEMFIT model was used to interpret the results of the excitability studies.

Results

In IgM neuropathy, stimulus current for a 50% CMAP was increased, stimulus-response curve slope decreased, rheobase increased, refractoriness decreased, and super- and subexcitability were less prominent. Threshold electrotonus and current-threshold relation showed no abnormalities. Modeling showed that excitability results were best explained by increased fast K current.

Conclusions

In patients with IgM neuropathy, axolemmal ion channel function is altered, possibly due to paranodal demyelination.
P224
Cauda equina conduction time in GBS, CIDP, and MMN

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¹Japanese Red Cross Medical Center, Neurology, Tokyo, Japan
²University of Tokyo, Neurology, Tokyo, Japan
³School of Medicine, Fukushima Medical University, Neurology, Fukushima, Japan

Introduction
To investigate the conductions of proximal and distal parts of peripheral nerves in Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), and multifocal motor neuropathy (MMN), we measured cauda equina conduction time (CECT) and motor conduction velocity (MCV).

Methods
Patients were 12 GBS (8 axonal and 4 demyelinating types), 14 CIDP, and 5 MMN patients. Compound muscle action potentials (CMAPs) were recorded from the abductor hallucis muscle. To measure MCV, electrical stimulation was conducted. To obtain CECT, magnetic stimulation was performed using a MATS coil (magnetic augmented translumbosacral stimulation coil).

Results
CECT was normal in all axonal GBS patients but prolonged in all demyelinating GBS patients, whereas MCV was normal in all GBS patients. CECT was prolonged in 12 CIDP patients (85.7%), whereas MCV was delayed in 5 CIDP patients (35.7%). Both CECT and MCV were normal in all MMN patients.

Conclusions
CECT is frequently prolonged in demyelinating GBS and CIDP, whereas it is usually normal in axonal GBS and MMN. MATS coil stimulation method can detect the conduction delay of cauda equina in some types of demyelinating polyneuropathy.
Small fiber Neuropathy associated with hyperlipidemia: Utility of Cutaneous Silent Periods and Autonomic Tests

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Objective

This study investigated the relationship between hyperlipidemia and small fiber neuropathy. Established electrophysiological methods have limited clinical utility in the diagnosis of small-fiber sensory neuropathy (SFSN). The cutaneous silent period (CSP) may be useful as a method for the evaluation of smaller and unmyelinated fiber dysfunctions. In this study, hyperlipidemia and SFSN in symptomatic patients with normal nerve conduction studies were evaluated with autonomic tests and cutaneous silent periods (CSPs).

Methods

Twenty-five patients with clinically suspected SFN and 23 healthy volunteers were included. CSP latency and duration, as well as CSP latency difference of the upper and lower extremities, were examined. Two tests were used to assess the autonomic nervous system, namely the R-R interval variation test in basal and profound breath conditions (RRIV) and the sympathetic skin response (SSR).

Results

Twenty-five patients with clinically suspected SFSN and normal nerve conduction studies were compared with 23 controls. In the upper extremities (UE), patients had prolonged CSP latencies (p= 0.034) and shortened CSP durations (p=0.039), whereas, in the lower extremities (LE), patients had shortened CSP durations (p= 0.001). The expiration-to-inspiration ratios were also reduced in patients groups. There was no significant difference between sympathetic skin response latencies and amplitude of the case and control groups.

Conclusions

Our findings indicate that CSP may become a useful technique for the assessment of small fiber neuropathy in hyperlipidemic patients.
LEPROSY AS A NEW ETIOLOGY OF MALE SEXUAL DYSFUNCTION.

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¹Botucatu Medical School, Neurology, Psychology and Psychiatry, Botucatu, Brazil
²Botucatu Medical School, Dermatology, Botucatu, Brazil
³Botucatu Medical School, Urology, Botucatu, Brazil

Introduction

Leprosy is endemic in our geographic region (São Paulo State, Brazil) and is a common cause of mononeuropathy multiplex, usually with sensory loss on the ulnar, median, peroneal and tibial nerve territory [1, 2]. In this work we describe 2 male patients with leprosy and sexual dysfunction with probable mononeuropathy of the pudendal nerve as etiology.

Methods

From 10 patients with leprosy treated in our University Hospital in the current year, 2 referred sexual dysfunction based on the *International Index of Erectile Function (IIEF-5)*. Neurological examination, conduction studies of the 4 limbs and of the pudendal nerve were performed. Somato-sensory evoked potentials (SSEP) by pudendal stimulation were obtained.

Results

The 2 patients with sexual dysfunction were classified as multibacillary. The neurological examination showed typical leprosy loss of thermal sense in different body areas, one of them had genital hypoesthesia. Conduction studies of the 4 limbs showed sensory mononeuropathy multiplex. The conduction studies of the pudendal nerve showed absence of the pudendal reflex, marked low amplitude of the sensory penile potential and SSEP showed temporal dispersion of the lumbar potential and absence of the cortical response.

Discussion

Pudendal nerve conduction studies abnormalities are expected among the general mononeuropathy multiplex of the leprosy, however, as far as we know this is the first report of leprosy as probable etiology of male sexual dysfunction.

References


Legends

Fig.1 - Conduction study of the pudendal nerve (ground was positioned on the right forearm).

Fig.2 - Pudendal nerve sensory action potential (very low amplitude and slow conduction velocity).
Figure 2
Three CIDP Cases Presented with Clinical Diabetic Amyotrophy

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Question

The most common chronic autoimmune neuropathy is chronic inflammatory demyelinating polyneuropathy (CIDP). Diabetic amyotrophy is a syndrome that consists of unilateral or bilateral, but asymmetrical marked weakness and aorophy, it primarily affects the pelvifemoral muscles and is generally accompanied by pain in back and thighs. There has been suggested by some clinicians that immune-mediated microangiopathy causes diabetic amyotrophy. In this report we described 3 patients presented with clinical diabetic amyotrophy and meeting CIDP diagnosis criteria.

Cases

The 1ˢᵗ and 2ⁿᵈ cases met probable CIDP and 3ʳᵈ case met definite CIDP diagnosis criteria. Common properties of the three cases with CIDP have been their being new diagnosed diabetic, starting of their neuropathic complaints with severe pain, their pain’s disappearing dramatically with immune modulatuar treatment, their having asymmetric muscle strength loss and their having loss in weight accompanied by pains.

Conclusion

The co-occurrence of autoimmun diseases has been a well-known phenomenon. Thus, we thought this patients might be not only mimic diabetic amyotropy clinic but also they have overlap CIDP and diabetic amyotrophy.
A perplexing case of progressive “dangling arm” phenotype with hypoglossal involvement secondary to MADSAM

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Background

The underlying pathology of bilateral upper extremity weakness is diverse and can represent a diagnostic challenge.

Objectives

To document a case of tongue pseudohypertrophy associated with a dangling arm syndrome.

Case report

A 40-year-old woman presented with significant muscle weakness and atrophy of both arms. She also noticed worm-like movements and “fluctuating” swelling of the left tongue. Clinical examination revealed a left hypoglossal nerve palsy (Fig 2A). Her early clinical course, at age 37, was marked by right median sensory symptoms and a sudden onset of painless right shoulder girdle paresis which gradually extended at the arm. Her symptoms were getting worse and gradually progressed in both upper extremities with inability to move her arms. A diagnosis of neurofibromatosis was made based on imaging studies showing multifocal nerve root and brachial plexus enlargements (Fig. 1A,B,D). However, the nerve conduction studies revealed a multifocal pattern of motor and sensory loss with motor conduction blocks (Fig. 1C), secondary axonal changes on needle EMG involving the brachial plexus and roots and subclinical unilateral phrenic nerve compromise. Left hemitongue EMG study showed prominent complex repetitive and myokymic discharges (Fig. 2C). Tongue MRI findings were consistent with denervation pseudohypertrophy (Fig. 2B). CSF analyses and autoimmune antibody tests were normal. Demyelination and remyelination changes with onionbulb formation and inflammatory infiltrates were confirmed in a nerve fascicular biopsy.

Result

A diagnosis of multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) was made. Partial improvement was observed following immunosuppressive therapy (IVIG and prednisone).

Conclusion

This report illustrates an unusual case of unilateral tongue pseudohypertrophy involved in a chronic multifocal upper limb demyelinating neuropathy which may mimic a variety of clinical conditions. Cervical nerve root hypertrophy can be a useful distinctive feature. Early diagnosis and treatment are essential for a successful treatment response. A comprehensive electrodiagnostic examination, including proximal nerve segments, should be encouraged even when isolated nerve dysfunctions are suspected.
A 53-year-old woman was admitted to our hospital for difficulty walking and numbness in the four limbs for two years, which gradually worsened in last two months. Two years earlier, she presented with unsteady gait and numbness started in the peripheral portions of both lower limbs, which then gradually spread to the both hands. Difficulty walking progressed until she was unable to walk independently. Family history was unremarkable.

Neurological examination revealed normal superficial sensation, severely impaired joint position sense and vibration sense in the lower limbs from the hips, a positive Romberg sign, and normal Manual muscle testing (MMT) results for the upper and lower limbs. Deep tendon reflexes were absent in the lower limbs and decreased in the upper limbs. Her gait was unsteady and she was unable to perform tandem walking test. There was no autonomic dysfunction.

CSF analysis, chest-CT, cranial and cervical MRI was normal. Laboratory findings were normal except for positive Ro/SSA-antibodies of 1:100 and antinuclear antibodies of 1:320. There was no evidence of impaired glucose tolerance.

The patient complained a dry mouth recently, which led to the habit of drinking water frequently. Ophthalmologic examination confirmed dry eyes, Schirmer’s test was pathological with 4mm/5min.

Patients underwent electromyography and nerve-conduction studies of the tibial, peroneal, ulnar and median nerve. The SNAP (sensory nerve action potential) was not elicited and somatosensory evoked potentials (SEPs) amplitudes could not be derived from the peripheral neural components. Motor nerve conduction studies and needle electromyelogram (EMG) examination were normal including F-wave latencies.

Sjoegren’s syndrome was diagnosed based on a positive anti-SSA antibody and mouth and eye dryness. The objective clinical signs and abnormal electrophysiological findings indicated the diagnosis of pure sensory neuronopathy. Patient had sensory ataxic neuropathy that was characterized by impairment of deep sensory nerves without substantial motor symptoms. SS-associated sensory ataxic neuropathy was suspected, the site of disturbance was consistent with dorsal root ganglionopathy, based on the absence of motor neuropathy.

Sjoegren’s syndrome is a recognized cause of sensory ataxic neuropathy and dorsal root ganglionitis leading to prominent loss of kinaesthesia and proprioception.
P232
Does flexing the arm really affect ulnar motor conduction velocity across the elbow?

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Objective

The aim of this study is to determine whether extension of the elbow or flexion at 45 or 90 degrees from the horizontal affects ulnar nerve motor conduction velocity in patients with symptoms and signs of ulnar nerve entrapment. Furthermore, the study aims at determining the lowest ulnar motor conduction velocity across the elbow below which pathology of the ulnar nerve should be considered.

Material and methods

We performed electrophysiological evaluation of the ulnar nerve in 23 patients with symptoms of ulnar nerve entrapment and compared them to 24 controls. We compared the conduction velocity across the elbow with the arm extended and flexed at 45 and 90 degrees to the horizontal, in both groups. We performed statistical analysis on the different values in both groups and across all angles.

Results

We found a statistically significant difference in the conduction velocity of the ulnar nerve across the elbow in all patients, in comparison to controls, at all the examined angles. Furthermore, there was no statistical significant difference in the conduction velocity, across the different angles, in both patients and in controls. A conduction velocity of 46.5 m/sec was determined as the cut-off value, below which the conduction velocity of the ulnar nerve across the elbow is considered abnormal.

Conclusion

We conclude that conduction velocity of the ulnar nerve across the elbow is independent of the position of the arm, and its measurement should be independent of the angle in which the arm is placed. Nevertheless, consistency is recommended to preserve reliability of the technique and results.

We conclude that conduction velocity of the ulnar nerve across the elbow of less than 46.82 m/sec should be considered abnormal.

Key words: ulnar nerve, conducing velocity, entrapment, nerve conduction studies, elbow position.

figure 1

Speed of Nerve Conduction at different angles for Patients (p) and Controls (c)

figure 2

Probability Curve of being a Patient according to Speed of Nerve Conductivity for each measured Angle
P233
Gender differences in intraepidermal nerve fiber density in healthy individuals and in patients with polyneuropathy

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Question

To evaluate whether sex differences in intraepidermal nerve fiber density (IENFD) described in healthy individuals also persist in persons with clinical suspicion of small fiber neuropathy (SFN) or/and when a potential cause of SFN is present.

Methods

Specimens were obtained through 3 mm punch skin biopsy 5-10 cm above the lateral malleolus and sections were immunohistochemically stained for PGP 9.5. Analysis of IENFD was performed according to published guidelines. Data from patients (n=551, 313 females and 238 males) and healthy individuals (n=134, 77 females and 57 males) were available.

Results

Mean IENFD in the controls was 12.4 ± 4.5 and in the patient material 5.7 ± 3.0 (p<0.001). Healthy females had significantly higher IENFD (13.6 ± 4.7) than men (10.9 ± 3.8, p=0.001), but this difference did not persist after adjustment for age (p=0.2). In the total patient group a significant gender difference in IENFD (in females 6.5 ± 3.1; in males 4.8 ± 2.5) existed also after adjustment for age (p<0.001). A similar difference between genders was also observed in the patients with abnormal IENFD (n=324), p=0.02, but not in patients with normal IENFD (n=227).

Conclusions

In healthy individuals mean IENFD at the lower calf was lower in men than in women, but this difference did not persist after adjustment for age. However, in the total group of patients, as well as in those with abnormal IENFD depletion, males had significantly lower IENFD values than females.
Autosomal dominant intermediate Charcot-Marie-Tooth disease and nephropathy: clinical presentation and long-term follow-up

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Question

Mutations in IFN2 and its interaction with formin related proteins might underlie the association of Charcot-Marie-Tooth disease (CMT) and nephropathy. The usual phenotype is a neuropathy with intermediate conduction velocity range (25-45m/s) and nephrotic syndrome due to focal segmental glomerulosclerosis (FSGS). It is currently unknown if the neurological deficits precede the renal disease and long term descriptions of the outcome are lacking.

Methods

We report the clinical and neurophysiological findings in three patients with CMT and nephropathy and a follow-up of ten years.

Results

The probands, a 29 year old woman and her brother, aged 27, reported gait imbalance and feet deformities since infancy. Both had developed end-stage renal disease, steppage gait, severe atrophy of distal muscles of the forearm and legs and areflexia. Nerve conduction studies (NCS) revealed absent sensory nerve action potentials (SNAPs), absent motor potentials in lower limbs and intermediate motor nerve conduction velocities (MNCV) in upper limbs. The brother died of sepsis at age 39. His elder son, evaluated at age 6, had frequent falls and NCS revealed slight reduction of SNAPs amplitudes and conduction velocities. After ten years, he developed feet deformities, steppage gait and renal failure. Kidney biopsy revealed diffuse glomerular sclerosis. All SNAPs were absent and MNCV was reduced to intermediate range. No mutations were found in PMP22, MPZ, EGR2 or GJB1.

Conclusions

The mechanisms underlying neurological and renal disease in CMT/FSGS are currently unknown, although both diseases seem to progress together in an inexorable way to end-stage renal failure and severe neurological compromise.
figure 2
P235
Cervical myelopathy masked by sensorymotor polyneuropathy

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BACKGROUND
Peripheral nerve disorders due to polyneuropathy can alter the signs of myelopathy.

METHODS
This study is a case description and analysis of 4 consecutive cases with the diagnosis of cervical myelopathy coexisting peripheral nerve disorder identified during the sixth years.

RESULTS
All our 4 cases had compressive cervical myelopathy due to disc herniation C4-5 in association with sensorymotor polyneuropathy, in three cases with diabetes mellitus and in one case with hypothreoidism. There were three man and one woman, average age of 59 year. They suffered from weakness and numbness legs during one or two years. Previously present data for diabetes mellitus and hypothyroidism. Neurological examination revealed hipotrophy of legs, enhanced one or both PR while AR were reduced. Extensor plantar response in three patients but asymmetrical and flexor in one patient. Electrophysiologic fundings showed markedly reduced amplitude of the distal sensory and motor evoked response of both peroneus and tibialis nerves with reduced motor and sensitive conduction velocity, without signs of denervation (EMNG) and reduced amplitude with prolonged distal latency of N9 and asymmetricaly decrease amplitude of N13 (SSEP n medianus). Cervical spine MRI showed herniates disc C4-5 and signs of myelopathia with stenosis of spinal canal.

CONCLUSION
It is important to continually question whether the working diagnosis of peripheral nerve disorder explains the clinical findings. Electrodiagnostic tests and neuroimaging methods can identified myelopathy whose adequate treatment offers a better outcome.
P236
Neurophysiological changes in CIDP patients treated with subcutaneous immunoglobulin

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**Question**

Do electroneurographic parameters and Motor Unit Number and Size Index (MUNIX, MUSIX) change during treatment with subcutaneous immunoglobulin (SCIG) in patients with chronic inflammatory demyelinating polyneuropathy (CIDP)?

**Methods**

We analyzed neurophysiologic data from a randomized, placebo-controlled, double-blind parallel-group trial, testing SCIG in 30 patients with CIDP (Markvardsen et. al 2013). This trial had showed an improvement in isokinetic muscle strength in the SCIG group.

Neurophysiological evaluation was performed before and after the 12 weeks treatment period. We assessed the distal motor latency (DML), motor conduction velocity (mCV), amplitude and duration of the compound muscle action potential (CMAP) as well as F-wave minimum latency in one peroneal, median and ulnar nerve. MUNIX and MUSIX were assessed in the abductor pollicis brevis muscle.

**Results**

Data from 23 patients could be analyzed. Changes in MUNIX were greater in the SCIG treated group compared to placebo (p

**Conclusion**

MUNIX values increased during treatment with SCIG. This might be due to an increase in CMAP amplitudes. There were no changes in DML, mCV or F-wave latencies during treatment with SCIG.
Neuropathic complications in patients after unilateral varicectomy - comparing the yield in neurography, clinical sensory tests and subjective symptoms.

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Question

The aim of the study was to investigate occurrence and risk factors of sensory nerve injuries and neuropathic pain in patients undergoing varicectomy, and to evaluate the diagnostic sensitivity of sensory neurography and clinical sensory tests in detecting the neuropathic complications.

Methods

All 38 patients (33 women) were prospectively studied before and within 30 days after varicectomy. The patients who showed neuropathic symptoms or signs were further investigated after 3 and 6 months. Symptoms were evaluated using a symptom chart drawing and Visual Analogue Scale (0-100) for pain. Clinical sensory tests included warm/cold discrimination using thermal rolls (Somedic) and tactile as well as mechanical pain detection thresholds measured with Semmes-Weinstein monofilaments and method of limits. Pain wind-up was tested with the monofilament giving the first slight sensation of pricking pain. Sensory neurography of the sural, saphenous, and superficial peroneal nerves was done bilaterally with standardized protocol.

Results

Five of the 38 patients (13.2%) reported postoperative neuropathic symptoms: neuropathic pain and altered sensibility: two patients within saphenous, one within superficial peroneal and saphenous, and two patients in all 3 studied nerve distributions. In 4 patients, sensory alterations and pain symptoms disappeared by 6 months after surgery. In one patient (2, 6 %), neuropathic pain persisted after severe partial axonal saphenous nerve lesion. Neurography findings were in line with subjective symptoms and confirmed all nerve injuries (demyelinating), severity of the lesion was moderate/severe), while clinical sensory tests were able to detect 3 out of 7 injured nerves.

Conclusion

Varicectomy may cause neuropathic complications but it rather infrequently gives rise to persistent neuropathic pain. Subjective sensory symptoms should be verified with neurophysiologic recordings as clinical sensory testing may remain falsely negative in these iatrogenic injuries.
P238
Does Cross-Training balance strength asymmetry in healthy subjects? A proof-of-concept trial

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**Question**

We investigated whether a unilateral, maximal isokinetic strength training of the stronger leg may balance strength asymmetry between sides, inducing in the contralateral untrained side a worthy strength-transfer, i.e. a cross-training effect (CT) as well as cortico-spinal adaptations.

**Methods**

Ten healthy volunteers (25.2±4.3yrs) underwent: i) bilateral measurements of the tibialis anterior (TA) strength with isokinetic dynamometry; ii) assessment of both cortical and spinal drives to the untrained TA, through recordings of central motor conduction time, input-output curve, short-interval intracortical inhibition, intracortical facilitation, short-interval intracortical facilitation, cortical silent period (cSP), short-latency afferent inhibition, H-reflex, V-wave and M-wave. Dynanometric and neurophysiological tests were performed before and after a 4-week maximal isokinetic training (16 sessions) of the stronger leg.

**Results**

The trained TA showed a maximum strength increase of 24.8% ($p=0.008; d=0.8$) at 90°/s angular velocity and 21.5% ($p=0.001; d=0.7$) at 40°/s, whilst the untrained TA showed respectively 30.2% ($p=0.014; d=0.8$) and 23.9% ($p=0.001; d=0.6$) increases in strength. Notably, after training no significant difference in strength output was anymore detectable between sides at 90°/S (pre: $p=0.004$; post: $p=0.558$). A significant increase in cortico-spinal drive to the untrained TA was revealed by reduction of cSP duration ($p=0.01, d=0.5$) and by increase of the V-wave amplitude ($p=0.01; d=0.8$).

**Conclusion**

In our cohort, the CT-effect was remarkable and capable of significantly balancing strength asymmetry. These findings disclose new potential implications for CT as a promising approach to neurological conditions where unilateral muscle weakness does not allow or makes difficult performing a conventional strength training of the weaker limb.
Clinical Research on Improving the Brain Microcirculation of Children with Cerebral Palsy by Acupuncture

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Objective

To investigate the therapeutic action and value of acupuncture in Cerebral Palsy rehabilitation.

Methods

150 spasm Cerebral Palsy patients from 1.5 to 7 years old are randomly divided into three groups. Acupuncture group (group A): 50 patients are treated with head acupuncture and body acupuncture; Rehabilitation-training group (group B): 50 patients are treated with physical therapy of Bobath and Vojta methods. Acupuncture add rehabilitation-training group (group C): In this group 50 patients are investigated.

Results

The total effective rate of group A and group C are obvious higher than that in group B. After treatment the DQ value of group A and group C are higher than that in group B (p<0.01). The improve rates of CT brain dysphasia and atrophy in group A and C are significantly higher than that in group B (P<0.05－0.01) .The recover to normal rates of ECT brain blood stream in group A and C are obviously higher than that in group B(P<0.01) .The results of TCD after therapy are better than those before therapy in group A [PI: 1.19±0.19 and 1.10±0.16; VP: (132.92±17.14)cm/s and (139.63±14.64)cm/s]and group C [PI: 1.18±0.24 and 0.91±0.19; VP: (131.84±15.93)cm/s and (139.68±15.66)cm/s](P P<0.01).

Conclusions

Acupuncture can obviously increase cerebral circulation, improve cerebral cell metabolism, promote partial or complete compensation of cerebral function and the restoration and function of plasticity of cerebral tissue in children with cerebral palsy.
Brain correlates of sustained pressure stimulation in healthy subjects: an fMRI perspective

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QUESTIONS

The aim of this study was to assess the changes in brain activation patterns in healthy volunteers after sustained manual pressure stimulation according to Vojta therapy. Although the efficacy of this rehabilitation treatment has been supported by clinical studies, the underlying physiological processes at the central nervous system level remain largely unknown. We hypothesize that the stimulation effects include changes in task-related cortical activation as well as in resting state networks.

METHODS

Twenty healthy volunteers (2 males, mean age 24.8) were included and divided into two groups: Group A (n = 11) receiving stimulation in the Vojta right heel zone and Group B receiving sham stimulation of the right ankle. All subjects underwent a single fMRI session using a 1.5T Siemens scanner, including 6 experimental runs employing 3 different conditions: rest (6min); dominant hand finger tapping alternating with rest (6 min); intermittent pressure stimulation applied by an experienced therapist (10 min). Both rest and finger tapping tasks were tested before and after two consecutive stimulation runs. Statistical analysis was carried out using FEAT and MELODIC, parts of FSL 5.0, to compare the task-related activation and the functional connectivity, respectively.

RESULTS

In Group A, the post-hoc contrasts of stimulation data revealed significant activation in the right fronto-temporal perisylvian and insular cortex, in the right striatum, brainstem, and cerebellum, as well as in bilateral pallida and anterior thalami as compared to Group B. In contrast, the latter group activated the bilateral precentral and postcentral gyri, left prefrontal cortex, and bilateral occipital cortices. In the finger tapping task, a significant group by time interaction was detected in the right middle and superior frontal gyrus, and in the right central sulcus. No difference was observed in the resting-state networks.

CONCLUSION

Our findings during the stimulation and the voluntary motor task performance before and after the treatment provide evidence that the sustained pressure stimulation according to Vojta therapy is associated with specific changes in cortical and subcortical brain activation when compared to sham stimulation.

ACKNOWLEDGEMENT

Supported by grant IGA MH CR NT13575.
P241
Change of cerebral cortex excitability after Electromyogram triggered electrical stimulation combined with mirror visual feedback in healthy elderly subjects

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In this study, we used Electromyogram (EMG) triggered electrical stimulation (ETES) to move unilateral hand synchronously with contralateral voluntary hand movements while performing mirror visual feedback therapy and investigated relationships between hemodynamic responses and neural activities by functional near infrared spectroscopy (f-NIRS) in 16 healthy elderly subjects. The regions of interest (ROI) were the superior parietal gyrus (SPG), angular gyrus (AG), superior temporal gyrus (STG), precentral gyrus (PrG), postcentral gyrus (PoG), supramarginal gyrus (SMG), middle occipital gyrus (MOG)and middle frontal gyrus (MFG). The subjects performed 7 tasks as below: observation of mark without movements (Rest), observation of a mark with only left hand extension movements (Task1), observation of resting right hand added to Task1 (Task2), observation of mirror reflection of left hand movements added to Task1 (Task3), observation of a mark and right hand movements induced by ETES (Task4), observation of passively moving right hand added to Task4 (Task5), and observation of mirror reflection of left hand movements added to Task4 (Task6) (Fig.1). The results showed that the bilateral SMG, PoG, MOG, the left SPG, AG, STG, PrG and MFG were activated in Task6 compared with Rest (Fig. 2). No other task was statistically significant compared with rest. These results suggested that in elderly subjects, the combination of visual feedback through the mirror and afferent feedback by electrical stimulation to superimpose the voluntary moving hand might induce the brain activation like the mechanisms of motor observation (R Hari, 1998), motor illusion (C Keinrath, 2006) or both. Furthermore, it was suggested that mirror neuron system consisted of SMG, STG and ventral premotor cortex was more activated by combination of mirror visual feedback and electrical stimulation.

figure 1
Fig 1. Schematic illustration of the experimental setup. The arrow in each task represents where the subjects were asked to look. The shading portion indicates the area which can not see from subjects.

Figure 2

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<th>Visual direction</th>
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* : p<0.05
Discriminate visual neglect from hemianopia by semantic priming effect: a clinical study

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There is a wide agreement concerning spared abilities in implicit information processing for patients with neglect. We then hypothesized that a priming word in the neglected space should produce a semantic activation effect even when it is not consciously perceived. On the contrary, if the priming word occurs in a blind field, as it would be in case of homonymous hemianopia, this should not entail any facilitation effect. We here discuss the results of a 72 y.o. patient with a bilateral hemispheric lesion (right fronto-temporal and left occipital ischemic area) affected by left visual neglect and right homonymous hemianopia in order to study the differences in implicit information processing among neglected space and hemianopic field. After a clinical assessment the patient underwent to an experimental observation by means of a visual priming task. A prime related, unrelated or neutral to the target, occurred for 200ms on the horizontal central line in six different positions of the screen (three on the left and three on the right). This task was previously tested on 69 control subjects and it determined in each prime position a semantic activation effect, in accordance with literature. As expected, the patient showed a priming effect in the neglected space whilst no facilitations was observed in hemianopic field. Furthermore, we studied patient's eye movements to support behavioural data. He presented some saccades and fixations only in the neglected side; this evidences are in line with some theoretical accounts concerning a spared automatic attention orientation even towards neglected space. In conclusion these results, even observed on a single case study, seem to support our work hypothesis. Further steps of the research are now ongoing, specifically involving the application of experimental paradigm to group of patients with neglect or with hemianopia.

References


P243
Rehabilitation of Drop-Foot with Maximal Isokinetic Cross-Training: a case report

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**Question**

We wondered whether an unconventional intervention, the Cross-Training, could improve the performance of dorsiflexor muscles in an inveterate iatrogenic drop-foot. We investigated whether unilateral, maximal isokinetic training of the normal leg would induce, in the contralateral affected side, a worthy strength-transfer, with cortico-spinal and gait adaptations.

**Methods**

A 59-year-old man who suffered in childhood a surgical-induced damage of the left common peroneal nerve at the head of the fibula, performed a 4-week training (16 sessions) of the normal leg, at 40°/s-angular velocity. Before and after training, the subject underwent a test-retest assessment procedure including: 1) bilateral isokinetic dynamometry of the dorsiflexors’ performance; 2) stance and gait-analysis; 3) recording of cortical and spinal drives to the affected leg, through measurement of central motor conduction time, input-output curve, cortical silent period (cSP), SICI, ICF, SICF, H-reflex, V-wave and M-wave.

**Results**

The untrained-affected dorsiflexors showed considerable increases in strength (peak-torque: *pre*=23N/m; *post*=31N/m), power (*pre*=14W; *post*=22W) and total-work (*pre*=9J; *post*=22J). Ankle dorsiflexion increased from 4 to 11 degrees. Overall gait pattern was unchanged, however a better stance performance was suggested by changes in heel-to-forefoot contact-time % of stance-time (*pre*=0.5%; *post*=3.4%) and mean step-length (*pre*=30cm; *post*=34cm). An increase in cortico-spinal drive to the untrained-affected leg was revealed only by reduction of cSP duration (120%RMT: *pre*=154ms; *post*=144ms; 150%RMT: *pre*=196ms; *post*=182ms).

**Conclusions**

Maximal isokinetic cross-training induced considerable improvements in the performance of the untrained-affected leg with a parallel increase in its cortico-spinal drive. In this report cross-training was a viable and effective rehabilitative approach to drop-foot.
Rubber hand and rubber foot illusion: a comparison and perspective in rehabilitation

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**Question**

In literature several reports about dissatisfaction and psychological maladaptation with lower limb prostheses in amputees could be observed. Because the functional adaption of the prosthesis to the body schema starts within two weeks after wearing it and becomes only close to normal after two years, this period is critical for the satisfaction with the prosthesis and a possible psychological maladaptation. Due to new technological perspectives (e.g., user in the loop concept) in rehabilitation of lower limb amputees, we investigate the mechanism of how to integrate an artificial limb (foot) into the body scheme. The basic paradigm was the rubber hand illusion (RHI), which describes an illusionary perception of an artificial "rubber" hand as one’s own hand after the visually covered real hand and the seen rubber hand were stimulated synchronously with a brush. This paradigm was transferred experimentally to the lower limb and compared to the upper limb.

**Method**

N=39 subjects participated in the study. The stimulated and unstimulated limb was located on a table. An artificial “rubber” foot or hand was located beside the real hand or foot (see figure). The stimulated limb was covered and both the real and the artificial limb were stimulated with a brush in a time range of 0.5 Hz in a synchrony, asynchrony or only visual condition.

**Results**

Data from questionnaire and proprioceptive drift reveal results from literature in both extremities. Data from temperature measurements showed inconsistent results.

**Conclusion**

We discuss the development of new technological improvements in the rehabilitation of prosthetic users and the use of certain indicators for a successfully induced illusion in body scheme. A brief overview for further experiments are presented.
Electroencephalographic determinants of school difficulties

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Examine the features of brain activity in school children with minimal brain dysfunction (MMD) in comparison with that of the control group using electroencephalography. The study included 166 pupils aged 7-15 years, of which 115 children (study group) with MMD and 51 healthy children (control group). EEG recording was carried out on the International circuit 10/20 N. Jasper using a computer complex "Neuron -Spectrum- 3". The order included the registration of EEG background activity, samples of "opening", "closing" of the eye", photic stimulation, hyperventilation. Comparative evaluation of brain activity was based on the classical data on semiotics and age characteristics of the EEG groups: 7-9 years, 10-12 years and 13-15 years. Electroencephalographic study of children with MMD showed normal type of EEG in 48.70% of cases (in the control group - 76.47%), the delay in the formation of age-electrogenesis 30.43% of the cases (in the control group - 7.85%); gipersinchronizirovanny type in 13.04% (control group - 9.80%), low amplitude type in 7.82% of cases (in the control group - 5.90%). In children with MMD on becoming a normal age-related rhythms, there is a violation of differentiation zone differences, reducing the frequency of the alpha rhythm. At 1.33 times more likely to have children in the main group noted gipersinchronizirovanny version of EEG with the advent of the provocative test of irregular frequency of epileptiform activity. Thus, changes in the EEG of school-age children with MMD are nonspecific and reveal a violation of the processes of normal autoregulation mechanisms of maturation and the formation of brain activity and retain pathological mechanisms for responding to external negative influences.
How to test anosognosia in stroke patients?
Improving the reliability and validity of VATA-M and VATA-L psychometric measures

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Anosognosia is a pervasive disturb which includes a specific impairment in the meta-cognition about patient’s own morbid state, and which can totally compromise the efficacy of neuropsychological rehabilitation and treatment. From the neuropsychological point of view a reduced number of psychometric measures was used to explore this relevant construct. The present contribution explores the validity and reliability of some existing measures (VATA-L; VATA-M) which respectively test the patient’s self-awareness of language and motor deficits. The total score of these tests included the subtractive rating (caregivers/patient score) as a significant cut-off to discriminate between high vs. low anosognosia profile. VATA-L and VATA-M measures were administered to 45 patients (M 20/F 25, age 70.20±14.1) and their caregivers (M 15/F 30, age 51.8±14.4). Secondly, these psychometric indexes were correlated with caregiving strain (FSQ-SF), caregiver’s perceived difficulties in assisting the patient and level of awareness attributed to the patient (both rating on a visual analogue scale), and level of functional dependence (FIM). Results indicate possible directions to improve the validity and reliability of both tests, taking into account some specific features of patients’ profile (i.e. left/right hemisphere lesions distinction), the comprehensibility of some items (in relationship with the cognitive effort they induce), the direct link and comparability between patients’ and caregivers’ evaluations, and the ecological validity of the selected measures. These include a proposal of an integrative measure (pre-VATA-M) to discriminate between high vs. low reliable items.
Brain-Machine Interface training combined with transcranial direct current stimulation in patients with chronic severe hemiparesis: Proof of concept study

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Question

Brain-machine interface (BMI) has been applied to stroke patients to improve motor function. However, the long-term effects have not been reported. Event-related desynchronization (ERD) during motor imagery used for a BMI trigger is sometimes difficult to detect in stroke patients. Anodal transcranial direct current stimulation (tDCS) is known to increase ERD. This study investigated the long-term effects of BMI training and the adjunctive effects of anodal tDCS for BMI training in patients with severe hemiparesis.

Methods

Eighteen participants with chronic stroke were divided into a BMI and tDCS-BMI group and conducted a 10-day BMI training. ERD was detected in the affected hemisphere during motor imagery of the affected fingers. The tDCS-BMI group received anodal tDCS before BMI training. The Fugl-Meyer Assessment upper extremity motor score (FM-U) was assessed before, immediately after and 3 months after intervention. ERD was evaluated before and after intervention.

Results

The FM-U was significantly increased in both groups and the improvement was maintained at 3 month. There was no interaction of Time and Intervention (tDCS-BMI and BMI). ERD was, however, significantly increased in the tDCS-BMI group.

Conclusions

BMI training induced a long-lasting effect to improve motor function in patients with severe hemiparesis. Anodal tDCS could increase ERD for BMI application.
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Effect of the intensive rehabilitation on functional recovery and motor neuron excitability after stroke

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The purpose of this study was to test the relationship between the effects of the intensive rehabilitation on functional recovery and motor neuron excitability of the paretic upper limb in post-stroke patients by electrophysiological examination. Thirty-nine post-stroke patients with upper limb hemiparesis were studied (age, 58.6 ± 11.6 years; time after stroke, 29.9 ± 28.3 months). All patients received the repetitive facilitation exercise (Kawahira 2010, Shimodozono 2013). 24 patients received low frequency repetitive transcranial magnetic stimulation (Etoh 2013). 16 patients received the continuous electrical stimulation (Simodozono in press) and the direct application of vibratory stimuli (Noma 2012). Fugl-Meyer Assessment (FMA), Action Research Arm Test (ARAT) were used to evaluate upper-limb function. The Modified Ashworth Scale (MAS) were measured to evaluate spasticity. F-waves were recorded in the abductor pollicis brevis muscle following stimulation of the median nerve in both the affected and unaffected upper limbs. FMA, ARAT, MAS and the F-wave persistence, F-mean/M ratio (the ratio of mean F-wave amplitude to M-response amplitude) were measured before and after the 4-week rehabilitation. FMA and ARAT scores improved significantly. MAS scores did not change. The intensive rehabilitation significantly decreased the persistence of F-wave in the affected upper limb, but not in the unaffected limb. F-mean/M ratio in the affected upper limb did not change. The F-wave persistence gains were significantly correlated with FMA score gains. The intensive rehabilitation improved the function of affected upper limb, and changed F-wave parameters in stroke patients.
Electrophysiological testing of visual function after mirror telescope implantation

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Objective

Implantation of an intraocular telescope increases life quality of patients with end-stage age related macular degeneration (AMD), which is the most common cause of blindness with estimated prevalence up to 8 % in white population above 40 years. The aim of the presented study was to monitor changes of electrophysiological markers of visual processing after implantation of a novel telescope based on mirror lenses, and to contribute to discussion about brain plasticity in elderly.

Methods

Visual evoked potentials (VEPs) were recorded to high contrast pattern-reversal, low contrast motion-onset stimuli and to target detection in the odd-ball visual paradigm. The responses were collected before the mirror lens implantation and then at least seven times during seven months in two patients (OV - male 90y, MZ - female 70y) with a final-stage form of the AMD.

Results

The mirror lens offers resolution boost by zoom of 2.4, it, however, concurrently decreases contrast of the retinal image and its luminance at least by factor 5.8. During whole monitoring we found reliable responses only to low contrast motion-onset stimuli outside of central 20 deg (M20-VEP) in both patients. The post-implantation luminance and contrast drop was reflected in the dominant M20-VEP peak latency prolongation, the expected gain for higher spatial frequencies was not visible in pattern-reversal VEPs, partially also because of their high variability even during one session. The M20-VEPs amplitude degraded for about one month after surgery and then it started to return to pre-implantation values, however, with prolonged latency.

Conclusion

The development of the electrophysiological responses to peripheral stimuli and psychophysical measurements demonstrates distinct CNS plasticity in the visual information processing after telescope implantation in the elderly.

Supported by the project GACR P407/12/2528 and Charles Univ. project PRVOUK - P37/07.
Cortical excitability modifications in subacute stroke patients after upper limb rehabilitative treatment

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Question

More than 50% of stroke patients show a persistent impairment of affected upper limb. There is no univocity about the rehabilitative approach.

Our aim was to test the efficacy of a combined treatment for upper limb in subacute stroke patients using rTMS on unaffected hemisphere and conventional physical therapy and to assess modification of cortical excitability.

Methods

We recruited one subcortical and one cortico-subcortical stroke patient, both with left hemiparesis.

A 2-week rehabilitation protocol for upper limb was administered (5 sessions/week). Every session included 20 min-rTMS (1 Hz) on the contralesional M1, followed by 30 min of conventional physical therapy.

Before (T0) and after (T1) the training, subjects underwent: 64-channel EEG at rest, motor evoked potentials (MEPs), inhibitory and facilitatory paired pulse TMS (ppTMS) protocol. Sub-scores of upper limb part of Fugl-Meyer Assessment (FMA) scale, Bimanual Activity Test (BAT) and Modified Ashworth Scale (MAS) were administered to assess the upper limb function.

Results

EEG showed an unbalance in cortical activity between the two hemispheres. MEPs were bilaterally present in both patients at T0. At T1 a considerable amplitude reduction of MEPs by single pulse TMS and by ppTMS on unaffected hemisphere was observed in both subjects (Figure 1). These results are associated to an improvement in FMA and BAT in affected side.

Conclusions

We observed a cortical excitability reduction in the stimulated hemisphere coupled with functional improvement in the affected upper limb. This extensive approach should became a routine for the evaluation of stroke rehabilitation effects and may contribute to a better understanding of the mechanisms underlying the functional recovery induced by rehabilitation.

Figure 1. MEP and facilitatory ppTMS pre and post rehabilitation treatment
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Central effects of NeuroMuscular Electrical Stimulation applied to healthy subjects and stroke patients.

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Modern neurorehabilitation aims at motor recovery by limiting compensatory strategies. For this purpose it is essential to strengthen the muscles involved in daily activities and let the patients relearn motor strategies similar to those of normality. The NeuroMuscular Electrical Stimulation (NMES) is used to regain, maintain or increase muscular strength and function. By applying a paradigm of Transcranial Magnetic Stimulation (TMS) we investigated whether the peripheral electrical stimulation of upper-limb muscles functionally modulates the cortical excitability. The study was first conducted on healthy subjects and, at a later stage, on stroke patients. Single-pulse TMS was applied to the motor cortex and motor evoked potentials (MEPs) were recorded from contralateral upper-limb in extensor carpi radialis (ECR), extensor digitorum (ED) and first dorsal interosseus (FDI) muscles. MEPs were obtained by sequences of 12 TMS pulses delivered within a 1-min time window at 3-min intervals both before the NMES protocol (baseline) and within 15 minutes following it. NMES was applied to extrinsic extensor muscles of the hand for 15 minutes using 30-sec cycles of single pulses and a 2 sec - 50 Hz tetanic contraction allowing the extension of wrist and fingers. Results revealed changes on peak-to-peak MEP amplitudes which occurred immediately after NMES, in ED and FDI muscles. This pattern of modulation reached baseline values on mean within 4 minutes following the electrical stimulation protocol. By contrast, no change of MEP amplitude was observed in ECR muscle. Thus, the peripheral electrical stimulation of skeletal muscles induces effects on the excitability of the motor cortex, which, noteworthy, is affected in a specific manner, being the distal muscles controlling hand movements the main target of the observed modulations. This suggests the potential role of NMES in shaping cortical reorganization after stroke.
The combined effects of anodal tDCS and patterned electrical stimulation on spinal inhibitory interneurons and motor function among patients with incomplete spinal cord injury

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Question

Supraspinal modulation and phase-related sensory input might play an important role for the modulation of spinal reflex and functional recovery of locomotion among patients with incomplete spinal cord injury (SCI). The present study examined the combined effects of anodal transcranial direct current stimulation (tDCS) and patterned electrical stimulation (PES) on the spinal inhibitory interneurons and lower extremity motor function in patients with incomplete SCI.

Methods

Eleven patients with incomplete SCI participated in this single-masked, sham-controlled cross-over study. They randomly participated in the following two sessions: (1) anodal tDCS combined with PES; (2) sham tDCS combined with PES. We applied PES to the common peroneal nerve with a train of 10 pulses at 100 Hz every 2 s for 20 min. Anodal tDCS (1 mA) was simultaneously applied to the primary motor cortex for 20 min. In sham condition, tDCS was delivered for only the first 15 s. We assessed disynaptic reciprocal inhibition (RI) and presynaptic inhibition (D1 and D2) using a soleus H-reflex conditioning-test paradigm. The conditioning-test stimulus interval was set at 2 ms (RI), 20 ms (D1), and 100 ms (D2). The magnitudes of inhibition was assessed before, immediately after, 10 min and 20 min after the stimulation. We measured ankle movement speed before and 20 min after the stimulation.

Results

Simultaneous combination of anodal tDCS and PES persistently increased the magnitude of RI and D2 until 20 min after the stimulation, but the D1 inhibition was not changed at each time point. Sham tDCS and PES increased the magnitude of RI immediately after the stimulation. Anodal tDCS and PES significantly increased the number of ankle movement in 10 s. This improvement was significantly correlated with that of the amount of RI and D2.

Conclusion

Anodal tDCS combined with PES could modulate reciprocal inhibitory interneurons and improve the ankle movement in patients with incomplete SCI.
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Myoelectric control by auricular muscles - an alternative human-machine-interface

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Introduction
Electric wheelchairs improve mobility and quality of life of individuals with tetraplegia. However, a reliable wheelchair control remains challenging. We present a novel myoelectric user interface based on ear muscle activation. Advantages of this approach are that no ear muscle task is known that would interfere with a control activity and that it can be applied even in high-level tetraplegia. This pilot study investigates whether intentional auricular muscle activation can be learned by training and particularly, whether bilateral selectivity can be achieved in humans.

Method
10 healthy subjects trained activation of their M. auricularis posterior over 5 days, first using visual feedback, then specific computer tasks for 60 min each day. EMG-signals were sent wirelessly to specially developed software. In each session 6 parameters of the ear-muscles’ control capacity were evaluated (e.g. duration of contraction, contraction frequency, bilateral selectivity, speed and accuracy in a virtual obstacle course). On day 5, all subjects had to steer a wheelchair through a real obstacle course (including slalom and turns).

Results
All subjects learned to activate their auricular muscles voluntarily. Control capacity improved on average 174% compared to day 1 (s. Fig. 1, all criteria p<0.05). Speed (p=0.001) and accuracy (p<0.0001) in the virtual obstacle course increased (s. Fig. 2). In addition, the bilateral selectivity improved substantially (p<0.0001), so that all subjects were able to navigate a wheelchair through a real obstacle course on day 5.

Discussion
The results of the feasibility study show for the first time that side-distinct ear muscle activation can be trained and subsequently used for electric wheelchair control. This is in particular noteworthy since half of the subjects initially declared not to be able to generate ear movements. In conclusion, the auricular myoelectric control system has an immense potential to serve as an alternative human-machine-interface for robust control of rehabilitation devices.

Figures
Fig. 1 Control capacity improves linearly over 5 days to 174% of baseline.

Fig. 2 Subjects’ paths (black lines) in a virtual obstacle course with auricular control on day 1 (a). Decrease of turns and reduction of deviance from the theoretical path (green line) on day 5 (b).
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figure 1

![Training Effect on Control Capacity](image1)

figure 2

![Navigation Patterns](image2)
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Neural activity modulation employing Real-time fMRI-based Neuro-feedback

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Neuro-feedback refers to the method whereby a subject monitors his/her own neural activity in a particular brain region of interest, and gains the ability to willfully control the level of neural activity. Recently, self-monitoring of neural activity in subcortical and other deep brain areas, as well as areas related to higher-order brain function, became possible with the development of real-time fMRI. The purpose of this research is to determine whether fMRI-based Neuro-feedback training holds promise for improving the emotional and social cognition of individuals with psychiatric disorders which have been difficult to treat using drugs alone. This is a nascent research area as there have been few reports so far on fMRI-based neuro-feedback training for the treatment of psychiatric disorders such as those mentioned above.

This study was approved by the Ethical Committee of Tamagawa university. In addition, each subject’s written consent was obtained after thoroughly explaining, both verbally and in writing, the contents of the experiment as well as foreseeable risks, merits, compensation and the like (informed consent).

Thirty subjects aged 18-22 years (mean age: 20.93 years) participated in this study. A real-time fMRI system and MR-compatible eye-tracker were installed. In addition, the following task protocols were developed for both neuro-feedback training and for evaluating the affects of training. We had four tasks: 1) amygdala localization task, 2) conditioning task, 3) training task with neuro-feedback, 4) evaluation task (same as localization task).

After three training sessions, subjects were able to increase neural activity in the amygdala at will, even when no emotion-eliciting stimulus was provided. When a subject was able to successfully control amygdala activity under neurofeedback, a Psycho-physiological Interaction (PPI) analysis seeded on the activated amygdala voxels revealed significant activity in the MPFC and insula. In other words, the time-courses of activity in the MPFC and insula were correlated with that of the willfully controlled amygdala activity.

It is evident that subjects are able to increase amygdala activity through neuro-feedback training, and that in order to willfully control amygdala activity, simultaneous activity in the insula and MPFC are necessary.
Evaluation of lower limb voluntary motor recovery with clinical, biomechanical, electromyographic and neurophysiological measures: a longitudinal study during subacute spinal cord injury

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QUESTIONS

Longitudinal studies of recovery of voluntary motor function are required to highlight robust objective measures of neuroplasticity and motor recovery after incomplete spinal cord injury (iSCI). The aim of this study was to quantify motor recovery during subacute iSCI employing different measurement techniques.

METHODS

A longitudinal study that included 4 testing sessions at 2 week intervals was performed in 22 subjects between 2-6 months after motor iSCI. Fifteen healthy subjects represented the control group. Testing sessions included clinical (muscle testing, WISCI II scale), biomechanical (dorsiflexion maximal voluntary torque, DMVT) and neurophysiological (Tibialis Anterior motor evoked potentials, TA-MEP) evaluations. A protocol to quantify the duration of TA electromyography (EMG) acquired during auditory-paced dorsiflexion movements was also performed.

RESULTS

Clinical and biomechanical measures demonstrated general improvement of motor function during the longitudinal study. TA-MEP amplitude and latency parameters failed to demonstrate motor recovery during the study within the iSCI group. In contrast, significantly longer TA EMG activation duration in the iSCI compared to the healthy group measured during auditory-paced dorsiflexion movements demonstrated recovery of voluntary motor function.

CONCLUSION

Duration of TA EMG activation during the auditory-paced dorsiflexion protocol detected recovery of lower limb motor function compared to the neurophysiological measures of TA-MEP during iSCI, suggesting that simple controlled motor tasks combined with electromyographic measures have diagnostic potential to assess residual motor neuroplasticity.
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Neuropathological and neuroprotective features of vitamin B\textsubscript{12} on the dorsal spinal ganglion of rats after the experimental crush of sciatic nerve: an experimental study

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**Background**

Spinal motoneuron neuroprotection by vitamin B\textsubscript{12} was previously reported; the present study was carried out to evaluate neuroprotectivity in the dorsal root ganglion sensory neuron.

**Methods**

In present study thirty-six Wister-Albino rats (aged 8-9 weeks and weighing 200-250 g) were tested. The animals were randomly divided into 6 groups which every group contained 6 rats. Group A: received normal saline (for 42 days); Group B: vitamin B\textsubscript{12} was administered (0.5 mg/kg/day for 21 days); Group C: received vitamin B\textsubscript{12} (1 mg/kg/day for 21 days); Group D: received vitamin B\textsubscript{12} (0.5 mg/kg/day for 42 days); Group E: received vitamin B\textsubscript{12} (1 mg/kg/day for 42 days); Group F: received no treatment. The L5 Dorsal Root Ganglion (DRG) neurons count compared to the number of left and right neurons. Furthermore, DRG sensory neurons for regeneration were evaluated 21 or 42 days after injury (each group was analyzed by One-Way ANOVA test).

**Results**

(1): The comparison of left crushed neurons (LCN) number with right non-crushed neurons in all experimental groups (B, C, D and C), indicating a significant decline in their neurons enumeration ($p<0.05$).

(2): The comparison of test group’s LCN with the control group’s LCN revealed a significant rise in the number of experimental group neurons ($p<0.05$). (3): Moreover, comparing the number of right neurons in experimental groups with the number of neurons in crushed neurons indicated that the average number of right neurons showed a significant increase in experimental groups ($p<0.05$).

**Conclusion**

Consequently, the probability of nerve regeneration will be increased by the increment of the administered drug dosage and duration. On the other hand, the regeneration and healing in Dorsal Spinal Ganglion will be improved by increase of administration time and vitamin B\textsubscript{12} dose, indicating that such vitamin was able to progress recovery process of peripheral nerves damage in experimental rats. Finally, our results have important implications for elucidating the mechanisms of nerve regeneration. Moreover, the results showed that vitamin B\textsubscript{12} had a proliferative effect on the dorsal root ganglion sensory neuron.

**figure 1**
Clinical symptoms and EEG markers of dopamine deficiency in patients with TBI

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Neurochemical systems suffer from a lesion in direct anatomical structures containing dopaminergic neurons - due to the high sensitivity of these neurons to hypoxia after TBI [Chen Y, Shohami E, et all., 1998]. Bales JW, Wagner AK, et all, 2009 emphasize the high importance of the state of the dopaminergic system in the course and outcome of TBI.

Objectives

1) to identify patients with clinical signs of dopamine deficiency (DD) after TBI, 2) to analyze the dynamics of symptoms of DD 3) to analyze the EEG and reveal the characteristic of DD.

Materials and Methods

Among the 98 studied patients identified 35 patients with clinical signs of dopamine deficiency syndrome in the form of increased muscular tone of extrapyramidal type, resting tremor, specific autonomic disorders. Analyzed the dynamics of clinical symptoms and the level of consciousness and outcome one year. Concomitant EEG study included 19 - channel recording, visual and spectral- coherent analysis, as well as equivalent dipole source (EDS) localization of the most typical EEG- components.

Results

It is revealed that DD after TBI is more common for the early stages of mental recovery. Developed clinical picture of this syndrome is accompanied by changes in the EEG as a gain in the pattern of synchronized beta activity rate of 13-14 Hz, accentuated in the frontal and anterior temporal areas ( with EDS of subcortical and cerebellar fronto-basal localization ) as well as increased compared with the normal right- brain coherent relations theta and beta components. DD regression is accompanied by increased frequency of beta- activity (from 13 to 16 Hz), but the persistent abnormal enhancement of right- hemisphere of coherence, especially in the occipital- temporal areas.

Conclusions

Shown in this study contingency manifestations beta EEG activity with the state of the dopaminergic system after TBI may contribute to an objective diagnosis of DD syndrome, as well as assessing the effectiveness and impact of the elucidation of mechanisms aimed therapeutic interventions.
P258
Prognostic value of ERP for simple tones and complex stimuli in successful mental recovery after severe head injury

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The aims of studying were to analyze mechanisms of the long-term posttraumatic unconscious state development and regression and to outline prognostically significant markers. ERP were recorded with the oddball paradigm for simple tones and complex stimuli (names and music fragments) at 22 patients in vegetative state and mutism as well as to predicting their possible psychic recovery. The control group consisted of 32 healthy examinees.

The amplitude, latency and mapping of N100, N200 and P300 components of ERP for simple tones were analyzed. Wavelet-synchrony was calculated for ERP for complex stimuli. The obtained results were analyzed and compared to the data of MRI of 10 patients.

Patients with predictive mental recovery up to clear consciousness revealed all three components for target tone even being in the vegetative state. The instruction to count improved its expressiveness. Moreover, the interhemispherical wavelet-synchrony of response for the complex stimuli was marked between the frontal and temporal areas. Patients who recovered to minimal consciousness showed all components to standard tone and only N100 and N250 components to the standard tone while performing the task to count. We marked that amplitude seemed to be more correlate with outcomes than latency. These correlations were most expressed for N100 and N200 components than for P300. The diffuse decrease of wavelet-synchrony for the instrumental music was revealed.

At early stages of mental recovery, response of the left hemisphere to the instruction to count was prognostically more significant compared to sagittal structures which seemed to be more involved in performing the task to listen to sounds.

We revealed a close correlation between the obtained ERP-changes and findings of the DT-MRI. Patients in chronic unconscious state revealed a combination of damage of the corpus callosum. The data specify in one of the key role of frontal lobe structures and it disconnections determines to a great extent the degree of mental recovery.
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P259
A role for dysfunctional bbb in neurovascular coupling impairment: evidence from cortical injury models in the rat

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Introduction

Cerebral venous thrombosis (CVT) represents an often under diagnosed cause for acute or slowly progressive neurological deterioration. Patients with CVT present with a remarkably wide spectrum of signs and symptoms. Focal or generalized seizures, including status epilepticus for example, are observed in 30% - 40% of patients with CVT (4,5). The underlying pathophysiological basis is not well understood, but seems to differ from that of arterial occlusion, reflecting the different anatomical and physiological features of the cerebral venous system. The blood-brain barrier (BBB) is the regulated interface between the peripheral circulation and the central nervous system (CNS). Accumulated studies suggest the role of BBB dysfunction in epileptogenesis (2). In the present study we establish a rat model for venous thrombosis and investigate the effects of such pathology on vascular permeability and neuronal activity.

Methods

The open cranial window method was used in anesthetized rats. Cortical vein infarction was induced by photoactivation of Rose bengal via laser-optic illumination. For BBB permeability and cellular injury assessment, sodium fluorescein and propidium iodide were injected (respectively) intravenously before and following photothrombosis. High frequency (30/s) images were acquired during injection using a CCD camera to allow for the quantification of dye leakage (1). Image analysis was performed offline using home-made Matlab scripts. Electrocerticogram (ECoG) recordings were performed to measure cortical activity dynamics following treatment.

Results

Pixel-permeability maps reveal that venous infarction induces a gradual spread and increase in BBB permeability over time (30, 60 and 120 minutes) and associated with cell damage as noted using propidium iodide. ECoG showed reduced threshold for the induction of seizures and impaired neurovascular coupling.

Conclusions

We demonstrate that selective venous infarction is associated with a robust increase in vessel permeability in the surrounding cortex, even when arterial perfusion remains intact and in the absence of increased intracranial pressure. We suggest that BBB dysfunction and associated impaired neurovascular coupling is associated with cellular injury (3). On-going studies are performed to underscore the mechanisms underlying BBB dysfunction, cellular injury and their functional significance.
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P260
Cutaneous silent period in brachial plexopathy and root avulsion

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OBJECTIVES

The cutaneous silent period (CSP) is a spinal inhibitory reflex mediated by small-diameter A-delta nociceptive fibers. Nociceptive impulses enter the spinal dorsal horn and suppress activity in spinal motor nuclei in neighboring myotomes. The aim of the study was to determine if CSP testing may serve as a useful aid in evaluation of brachial plexus injury involving upper and middle trunks, and in the diagnosis of root avulsion.

METHODS

In 23 patients with traumatic brachial plexus injury (16 males, age 18 - 62 years) we performed clinical examination, imaging studies (MRI or CT myelogram) and neurophysiologic testing. Needle EMG was obtained from muscles supplied by C5-T1 myotomes. CSP was recorded after painful stimuli were delivered to thumb (C6 dermatome), middle (C7) and little (C8) fingers while subjects maintained voluntary contraction of intrinsic hand muscles.

RESULTS

Electrodiagnostic and imaging studies confirmed severe brachial plexopathy maximally involving upper trunk or corresponding C5, C6 roots in all patients, although 10 also had axonal loss injury in middle and lower trunks and lower cervical roots. In 7 subjects, the CSP following thumb stimulation was absent, but in the remaining 16, a well defined CSP was present, even in cases of presumed Erb’s palsy with root avulsion.

CONCLUSION

In brachial plexopathy with presumed avulsion of upper or middle trunks, the CSP can provide quick physiologic confirmation of preserved conduction through damaged trunks and roots. In the majority of cases of brachial plexus avulsion, based on EMG and imaging studies, the CSP is preserved.

SIGNIFICANCE

CSP is a robust protective plurisegmental spinal reflex, which can document residual continuity in severe brachial plexopathies, when continuity cannot be detected by standard electrodiagnostic or imaging studies.

Supported by Research Projects of Charles University PRVOUK P34, Grant Project of Czech Ministry of Health NT12282, NT13693
Transcutaneous direct current stimulation on cervical spinal cord: effects on H-reflex and Spinal Reflexes.

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Question

In the past 5 years non-invasive transcutaneous weak direct currents (tsDCS) applied over the thoracic spinal cord (SC) has been shown to be able to modulate the progression of sensory inputs, motor outputs and SC activity at segmental level. Aiming to increase the possible application sites of tsDCS, we investigate the effects of tsDCS applied on the cervical SC on H-Reflex Recruitment Curve (HR-RC), Reciprocal Inhibition (RI) and Presynaptic Inhibition (PI).

Methods

Twenty-two subjects were randomized in two groups. Anodal/SHAM (A-tsDCS, 10 subjects) or cathodal/SHAM stimulation (C-tsDCS, 12 subjects) were applied for 25 minutes on the cervical SC (2 mA, active electrode on C7, reference electrode on the right deltoid area). HR-RC from the left median nerve (MN) at the elbow, RI and PI (conditioning stimulus on the left radial nerve (RN) at ISI 1 ms for RI and 20 ms for PI, H-reflex amplitude set at the 30% of the H-max on the ascending slope of the curve) were assessed before, during, immediately after and 30 minutes after the DC offset. CMAP and F-wave from MN, CMAP and SAP from RN were assessed at the same time intervals as a measurement of nerve excitability (NE).

Results

C-tsDCS induced a progressive leftward shift of the HR-RC during stimulation and the effects persisted after stimulation offset. Indeed, C-tsDCS induced a significant reduction of RI at all the times points. Both A-tsDCS and SHAM had no significant effects on HR-RC and RI. None of the stimulation polarities showed an effect on PI and NE.

Conclusions

tsDCS can modulate cervical SC excitability. The orientation of the spinal interneurons and motoneurons with respect to the electrical field (EF) seems to be important in establishing the final effects. Further studies are needed to elucidate mechanisms of tsDCS, with respect to polarity and geometry of EF.

Reference

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**figure 1**

![H-Reflex Baseline vs H-Reflex T0](image1)

**figure 2**

![Reciprocal Inhibition 1 ms](image2)
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High-Definition transcranial Direct Current Stimulation (HD-tDCS): a TMS study to investigate focal motor cortex (M1) excitability

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Questions

HD-tDCS with electrodes arranged in a 4x1 ring configuration has been proposed as a focal, non-invasive neuromodulatory technique.¹² Computational models have predicted that the 4x1 ring configuration is the most effective in focusing stimulation under the central electrode.¹ In the present study we tested the effects of HD-tDCS on MEPs evoked in FDI and Biceps muscles in 15 subjects. We explore whether (1) the focality of HD-tDCS leads to differential effects on the two muscles, and (2) whether displacement of the ring from the targeted hotspot leads to further changes in MEPs.

Methods

TMS intensity was adjusted to produce MEPs of approximately 1 mV peak-to-peak amplitude. Twenty MEPs for each muscle were collected before and after anodal DC (2mA, 10 min). HD-tDCS (Neuroelectrics, Spain) was delivered through 5 electrodes (area 3.14 cm²), arranged according to a 4x1-ring using a home-made flat sponge with a 3.5 cm distance between each electrode. The central electrode was always used to deliver anodal DC; return current was distributed evenly through the surrounding four electrodes. The protocol consisted of 3 different stimulations: (1) anodal DC over the FDI hotspot; (2) the entire ring was moved backwards, so that one of the peripheral electrodes was placed over the FDI hotspot; (3) sham stimulation.

Results

Anodal HD-tDCS increased M1 excitability compared to sham (Stimulation 1, FDI Pre 1,16 ± 0,33 mV, Post 1,60 ± 0,61 mV; Stimulation 2, Pre 1,15 ± 0,29 mV, Post 1,72 ± 0,92 mV; SHAM, Pre 1,15 ± 0,53 mV, Post 1,14 ± 0,32). No differences in excitability were observed between the two muscles and the two configurations.

Conclusions

These results suggest that HD-tDCS is able to increase M1 excitability similar to conventional TDCS, but it fails to produce focal effects. Finally, modulation of excitability did not seem to correlate with the distribution of the electrical field expected from computational models. Further investigations are needed to elucidate the physiological mechanisms of HD-tDCS.

References

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figure 1

![HD-tDCS - FDI Hotspot](image1)

figure 2

![FDI vs Bic MEP Amplitude Changes](image2)
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Effects of transcranial direct current stimulation in children and adolescents: TMS/EEG Study

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Introduction

Transcranial direct current stimulation (tDCS) has been demonstrated as a promising and well tolerated therapeutic tool for neurological and psychiatric disorders. However, the effects of tDCS on the developing brain and the therapeutic potential of the method in children and adolescents are still unknown. Therefore, the aim of the present study was to investigate systematically the physiological effect of the anodal, cathodal or sham tDCS (10 min) on the motor cortex excitability in 19 healthy children and adolescents (11-16 years old). To detect changes in cortical excitability, motor evoked potentials (MEPs) and TMS evoked potentials (N100) were analysed before and after 10 minutes of tDCS by using 1 mA and sham stimulation over the primary motor cortex. To explore the dependency of tDCS effects from stimulation intensity, two control experiments with 0.5 mA anodal and cathodal stimulation for the same duration were conducted.

Methods

tDCS was delivering by a battery driven stimulator (NeuroConn GmbH, Ilmenau, Germany) through conductive-rubber electrodes. The minimum period between sessions for a single subject was 7 days, and sessions (anodal vs. cathodal vs. sham tDCS) were applied in randomized order. EEG for TMS-evoked N100 and EMG for MEPs were recorded simultaneously with TMS before, immediately after as well as every 10 min up to 60 min tDCS.

Results

In all subjects the tDCS was well tolerated. This study reveals the following main findings: 1) Both the 1 mA anodal as well as cathodal tDCS resulted in a significant increase of MEP amplitudes compared with baseline recordings and sham stimulation; 2) The 0.5 mA cathodal tDCS caused a significant decrease of cortico-spinal excitability, whether the 0.5 mA anodal tDCS did not induce significant MEP changes; 3) 1mA cathodal stimulation, significantly suppressed N100 amplitudes compared to baseline and sham stimulation; 4) in contrast to the effect of 1 mA cathodal stimulation, 1mA anodal tDCS did not modify the N100 amplitudes significantly, when compared to sham stimulation. 5) TMS-evoked N100 amplitude did not correlate with MEP amplitudes of the target muscle. This suggested that MEP and TMS-evoked N100 are two independent parameters.

Conclusion

Our results suggest that tDCS effects differ in children compared with adults. This should be taken into account for applications of the stimulation technique in treatment of childhood neurological and psychiatric disorders.
Regional personalized electrodes to select transcranial current stimulation target

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Personalizing transcranial stimulations promises to enhance beneficial effects for individual patients.

We aimed at 1. developing a procedure to bend and position custom shaped electrodes to stimulate specific cortical regions; and 2. probing that different effects on cortical excitability are produced when the properly customized electrode is targeting different cortical areas.

An ad-hoc neuronavigation procedure was developed to shape and place the personalized electrodes on the basis of individual brain magnetic resonance images (MRI) on bilateral primary motor (M1) and somatosensory (S1) cortices. The transcranial alternating current stimulation (tACS) protocol (Feurra et al., 2011) was used to test the effects on cortical excitability of the personalized electrode when targeting S1 or M1.

Changes in neuronal excitability assessed by tACS differed when targeting M1 or S1, with the General Estimating Equation model indicating a clear tCS Effect (p < 0.001), and post-hoc comparisons showing solely M1 tACS20Hz reducing M1 excitability with respect to baseline and other tACS conditions.

The present work hones knowledge that transcranial current stimulation (tCS) can be focused by properly shaping and positioning the stimulating electrodes according to the target regions.

Through multimodal brain investigations continuous efforts in understanding the neuronal changes related to specific neurological or psychiatric diseases become more relevant as our ability to build the compensating interventions improves. A relevant step forward on this path is the ability to target the specific cortical area of interest, as documented by the present work.


FIGURE 1 | Regional Personalized Electrode shaping.

FIGURE 2 | Experiment to probe differential effects of stimulation target.
figure 2
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Inhibitory vs. excitatory neuromodulation by regional personalized electrodes

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**Background**

Transcranial stimulations with amplitude modulated currents are promising to enhance neuromodulation effects by neuronal activity entrainment. Concurrently, the development of customized electrodes opens the path to target predetermined regions of interest enabling adjustment of the intervention to compensate for the alterations of specific networks. New electrode shaping implies new configurations with inhibition/excitation effects to be properly defined.

**Objective/Hypothesis**

We used a 20 Hz transcranial alternate current stimulation (tACS\(_{20Hz}\)) to bilaterally target the primary motor cortex (M1) via an individually shaped and positioned electrode. We assessed the dependence of the cortical excitability modulation on the current amplitude changes.

**Methods**

Inhibitory and excitatory effects were obtained with current amplitudes of respectively nearby 25 µA/ cm\(^2\) and 62.5 µA/ cm\(^2\) peak current superficial densities. M1 excitability was tested through motor-evoked potentials (MEPs) by transcranial magnetic stimulation (TMS), and the effects of tACS\(_{20Hz}\) were tested online. Excitability modulation was assessed for each current’s intensity through a non-paired t-test of the MEPs collected with and without stimulation, from eight healthy subjects.

**Results**

MEP amplitude showed a reduction for low densities and an increased for high current densities.

**Conclusions**

Our findings document that by properly setting the current density it is possible to induce either inhibition or excitation using tACS while targeting the bilateral M1 via a customized electrode. Neuromodulation techniques, promising to enable neuronal activity entrainment without anode/cathode distinction, can be applied to obtain inhibition or excitation effects, depending on current superficial density. These data are especially useful in determining the tACS ‘reference’ electrode size that will fall into the ‘no effect’ current density.

*Figure 1: Experimental setup*

*Figure 2: Cortical excitability modulation induced by customized electrode in dependence on current intensity*
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figure 1

TMS delivered through tCS electrode customized to target a specific cortical area

A

B

C
tCS

OFF

ON

OFF

ON

1.5 min

TMS

OFF

ON

Rest

Baseline 1

Rest

Baseline 7

Rest

Baseline 3

figure 2
Investigating the effect of current flow on cortical excitability using bipolar tDCS

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Question

High-Definition transcranial Direct Current Stimulation (HD-tDCS) has been proposed as a new non-invasive neuromodulatory technique that uses small electrodes placed in a 4x1 configuration to localise the electrical field to a targeted area.¹,² Neurophysiological effects are thought to depend on the intensity and polarity used, as with classic tDCS.³ No clear studies have been published on the possible contribution of current flow direction to the final effect. In 11 subjects, we explore whether the orientation of the current flow, parallel or perpendicular to the FDI hotspot, has differential effects on motor cortex (M1) excitability.

Methods

TMS intensity was adjusted to produce MEPs of approximately 1mV peak-to-peak amplitude. Twenty MEPs from the FDI were collected at each time point (Baseline, 0, 10, 20, 30, 40 minutes after stimulation), with the TMS coil oriented perpendicular to the central sulcus. HD-tDCS (Neuroelectrics, Spain; 1mA, 10min) was delivered via circular sponge electrodes (area 3.14cm²), each placed 3.5cm from the FDI hotspot. Two were positioned parallel to the TMS coil to induce posterior-anterior current across the hotspot (PA). Two were perpendicular to the coil (PP stimulation) to induce a mediolateral current. The protocol involved 3 different sessions: (1) stimulation with AP tDCS, (2) stimulation with PP tDCS, (3) sham stimulation.

Results

PA tDCS significantly reduced the M1 excitability compared to PP and sham stimulation. PP stimulation showed no significant change in motor cortex excitability compared to sham.

Conclusions

These results suggest that a current flow oriented parallel, but not perpendicular to TMS over M1 hand is able to change corticospinal excitability. Further investigations are needed to elucidate the physiological mechanisms of HD-tDCS.

References

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The effects of bilateral transcranial direct current stimulation over posterior parietal cortices on visuospatial attention bias

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Question

TDCS over parietal cortex has previously been found to induce a transient, neglect-like effect in healthy participants, and more so with dual (Left-anode: Right-cathode) parietal than unilateral right (cathodal) parietal tDCS (Giglia et al., 2011). We employed dual parietal tDCS (including the reversed left-cathode: right-anode montage) to further study the time-course of these effects using an online approach.

Methods

A computerised landmark task was presented to 40 right-handed adults, which involved deciding which end of a pre-bisected horizontal line appeared shorter. Participants completed a total of 10 blocks (1 pre-tDCS, 6 on-line tDCS, 3 post-tDCS). Each subject performed 3 sessions >24 hrs apart: 1) Left-anode right-cathode 2) Left-cathode right-anode 3) Sham. Half of the participants were administered 1mA stimulation and half were administered 2mA stimulation over P5/6 for 20 minutes.

Results

We found a significant overall rightward shift in bias over time, in line with a previous study showing a rightward shift in visuospatial attention bias with increased time-on-task/decreased arousal (Benwell et al., 2013). However, in line with Giglia et al. (2011), we found the left to rightward shift in spatial attention to be more pronounced for the left-anode: right-cathode montage. The left-cathode: right-anode montage did not drive a bias shift significantly different from sham stimulation.

Conclusions

We conclude that only left-anodal: right cathodal dual tDCS over the posterior parietal cortex can shift the attentional vector in healthy participants. The rightward shift with this montage is likely to be driven by a reduction in the dominance of the right hemisphere during task processing. The effect is additive to the already established rightward bias shift with time-on-task.

References


Investigating the duration effects of transcranial near infrared light stimulation (tNILS) on cortical excitability of healthy subjects

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Introduction

Transcranial low level near infrared stimulation (tNILS) is a non-invasive stimulation techniques that can penetrate the scalp and skull that could allow modulation of biochemical processes in targeted neuronal populations (Hashmi et al. 2010). Result from recent human studies show that the application of tNILS over the primary motor cortex (M1) for 10 minutes can decrease cortical excitability. However, there have been no studies reporting the effects of different stimulation durations in either patient or healthy populations.

Methods

13 healthy subjects participated in the study. tNILS was administered over the left M1 using a 4 acupuncture needle configuration held in place via 4 wire holders attached to a crown which is placed around the head. The laser acupuncture needles were percutaneous and did not penetrate the skin of the head. They are approximately 2 mm in diameter and emit a maximal output of 100 mW per diode on full power, 810 nm. The stimulations were administered for 5 and 20 minutes. The changes in cortical excitability were measured using transcranial magnetic stimulation (TMS)

Results

There were no significant differences between sham and 5 minutes of tNILS. Using 20 minutes stimulation duration, there was a marked facilitation of the MEP amplitudes in 11 out of 13 subjects.

Conclusion

These preliminary findings will help in determining the optimal duration for therapeutic intervention using tNILS in future studies and clinical settings.

References


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Effects of parietal continuous theta burst stimulation on episodic memory

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Although the parietal lobe is not traditionally thought to support declarative memory, recent fMRI studies and electroencephalography evidence during episodic memory tasks have consistently revealed a range of memory-related influences on activation in lateral posterior parietal cortex (PPC) and Precuneus. Therefore, we aimed at investigating the possible causal role and the specific involvement of PPC and Precuneus in episodic memory. To this aim continuous theta burst stimulation (cTBS) was applied to modulate the activity of these areas between the study phase and the test phase of an episodic memory task. Thirty healthy right-handed subjects took part in the study and were randomly assigned to one of three groups according to the stimulated target (Precuneus or left PPC; Sham). During the study phase subjects viewed 160 pictures half outlined in green and half in red. During the test phase, 160 previously presented items and 80 new pictures were outlined in black and subjects were asked to indicate for each items if it was an old/Red, Old/Green or New item. cTBS was delivered offline over the target regions before the test phase. The data were analyzed in terms of hit; false alarms; source errors and omissions. The main results showed a decrease of source errors after stimulation of Precuneus but not after Left parietal posterior cortex and after sham simulation. This result suggests the role of precuneus in memory process and its involvement in episodic contextual associations.
Short-term effect of different tDCS intensities on motor cortex excitability

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Objective

To evaluate the on-line and short-term effects of different intensities of anodal and cathodal transcranial direct electric stimulation (tDCS) on the human motor cortex.

Methods

14 healthy subjects received anodal and cathodal tDCS in a random order on two separate sessions using a 35 cm² electrodes positioned over the left M1 and the contralateral supra-orbital region. During each session tDCS was randomly delivered at 0.5, 1, 1.5 and 2 mA with a wash out period of 25 min between intensities. The duration of stimulation was varied so that the total charge transferred was 4 mA.min for all intensities. Twelve motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) were recorded from the right first dorsal interosseous muscle before (baseline), at the beginning (on line 1), at the end (on line 2) and immediately after (post) each stimulation. Data were analysed with a repeated measures ANOVA using polarity (anodal/cathodal), intensities (0.5-1-1.5 and 2) and time (baseline, on line 1, on line 2 and post) as within subject factors. Paired t tests were used for post hoc comparisons.

Results

the ANOVA showed only a significant effect of time on MEPs amplitude (F:8.7, p<0.001). MEPs were significantly higher during (on line 1 p=0.001, on line 2 p=0.002) and immediately after either polarity of stimulation (p=0.02) compared with baseline

Conclusions

short duration application of both anodal and cathodal tDCS facilitates corticospinal output during and immediately after application. The effects are independent of the intensity and the duration of stimulation if the total amount of charge delivered is constant.
Transcranial direct current stimulation (tDCS) and vision restoration training (VRT) in post-acute stroke rehabilitation - safety, applicability and preliminary results

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Question

Stroke in posterior cerebral artery usually results in visual field defects varying in size and extent of the blind field and areas of residual vision (ARV). Vision restoration training (VRT) may reduce visual field impairment. Combined application of transcranial direct current stimulation (tDCS) together with VRT indicates that tDCS may accelerate VRT-effects in the post-acute stage. We investigated safety, applicability and efficacy in 7 post-acute stroke patients.

Methods

Four Patients with homonymous field defects bordered with ARV and 3 patients with homonymous clear-cut hemianopia without ARV were treated with up to 10 tDCS-sessions (2mA, 15-20 minutes, cathode: Cz, anode: O1/O2) combined with VRT. Data of safety monitoring as well as a survey of side effects was collected. Perimetric detection thresholds at post were compared to baseline to investigate training effects.

Results

Referring to the safety monitoring no clinical abnormalities whatsoever as well as negative side effects apart from skin itching beneath the anode where reported. Significant improvement of detection accuracy in all cases could be measured. However there was a higher effect size in the patients with presence of ARV.

Conclusions

Concerning our pilot study, the application of tDCS combined with VRT in sub-acute stroke is safe and might facilitate rehabilitation of visual field loss. Effects on visual field defects bordered with ARV seem to be even stronger than without.
P272
Probing changes in corticospinal excitability following continuous theta burst stimulation of the human motor cortex

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Question

The long-term depression-like reduction in corticospinal excitability induced by continuous theta burst stimulation (cTBS) of the human motor cortex can vary considerably between individuals and between studies. This may be related to the methods used to probe excitability changes following cTBS. Whereas most studies use single-pulse transcranial magnetic stimulation (TMS) at single, intermediate test intensities to evoke motor evoked potentials (MEPs) with amplitudes that lie within the linear portion of the sigmoidal input-output curve, it is unclear whether this method is optimal for detecting cTBS-induced after-effects. Therefore, we constructed input-output curves before and following cTBS to determine the range of test intensities that are most sensitive to the effects of cTBS.

Methods

Single-pulse TMS was applied to the left motor cortex and MEPs were recorded from the right first dorsal interosseous muscle. To construct input-output curves, eight TMS pulses were applied at ten different stimulus intensities between 90% and 180% of resting motor threshold (RMT) in a pseudo-randomised order. Curves were measured five times: twice at baseline and at 0, 15, and 30 min following cTBS.

Results

There was no effect of cTBS on MEPs evoked using near-threshold stimulus intensities, nor was there a change in MEPs at intermediate stimulus intensities above threshold. However, MEPs evoked using intensities between 150% and 180% RMT (corresponding to the upper end of the sigmoidal input-output curve) were depressed following cTBS.

Conclusions

These results suggest that test intensities higher than those conventionally used may be required to detect cTBS-induced changes in corticospinal excitability.
Fast induction of alpha entrainment with bandwidth confined electric and photic stimulation

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Introduction

Brain stimulation is emerging as a fundamental tool in the clinical repertoire of a neurologist. Whereas invasive approaches are well established in clinical practice, non-invasive approaches are quickly gaining on importance. Independent of the type of stimulation, it is becoming remarkably clear that a better understanding of the neurophysiological mechanisms of interactions between patterns of stimulation and patterns of subject specific neural activity is necessary. The aim of this pilot study is to address if short periods of stimulation can entrain brain-rhythms. More explicitly, due to striking neurophysiological similarities between “photic driving” and “transorbital alternating current stimulation”, we compare short term photic- and electric stimulation. The hypothesis is that 30 seconds of bandwidth confined stimulation will evoke entrainment of the central alpha rhythm.

Methods

To address this question, we stimulated 10 healthy subjects with retinofugal alternating current stimulation at 10 Hz for 30 seconds. In direct comparison, we induced steady-state visual evoked potentials at 10 Hz for 30 seconds. Sessions were applied in randomized order with baseline EEG recordings prior, during and after stimulation. EEG analyses were defined by clinical standards to identify “photic driving”.

Results

In this framework we investigated: if a subject was susceptible to 10 Hz photic stimulation (DRIVING), if carry over effects exist for visual (VIS POST) and electric (ELC POST) stimulation. Results show that entrainment (DRIVING) could be induced and that alpha-entrainment persisted in both VIS POST and ELC POST conditions. All effects were significant in one-sided paired t-tests against baseline (p < 0.05).

Discussion

These findings show that short terms of brief stimulation can evoke significant entrainment of central rhythms. Remarkably, this was the case for both electric and photic stimulation. This provides a method to investigate quick changes in central rhythms induced by stimulation. One perspective is Brain-Computer-Interface driven stimulus optimization (DFG grant Nr: BR 1691/8-1).
Influence of slow oscillating transcranial direct current stimulation (so-tDCS) on sleep EEG with focus on spindle density and cognitive performance on healthy subjects

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Introduction

Previous experiments with transcranial direct current stimulation before sleep on healthy subjects showed a tendency towards an increased spindle density during sleep. So we performed a randomized, sham-controlled and double-blinded study on 10 male subjects between 20-30 years.

Methods

We stimulated subjects with a frequency of 0.2 Hz and a sinusoidal waveform with a current of 550 µA and a DC offset of 275 µA. Stimulation electrodes were placed bilaterally on C3, C4, left and right mastoids. We stimulated 30 min with a 1 min free interval after every 5 minutes in the evening before subjects underwent polysomnography. Before and after the night in the sleep laboratory subjects had to perform several tests.

Results

Final results according spindle density are still outstanding. Visual spindle counting leads to a high intra- and inter-rater variability. Therefore we needed to establish a reliable counting method first. We found no significant difference in cognitive performance or sleep stage distribution. But subjects reported more sleepiness after a night with evening stimulation.
Bilateral Sequential Motor Cortex Stimulation and Skilled Task Learning with Non-dominant Hand

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Objective

Increase of excitability/activation of the primary motor cortex (M1) can be achieved either by direct M1 stimulation with an excitatory TMS protocol or by stimulation of contralateral M1 with an inhibitory TMS protocol. The study’s aim was to check whether bilateral sequential stimulation of the primary motor cortex (M1) with an excitatory protocol over non-dominant M1 and inhibitory one over dominant M1, would be able to improve performance on a skilled task with non-dominant hand more than unilateral stimulations could do.

Methods

40 right-handed healthy subjects (mean age 24.8±3.4y, 16 women) were divided into 4 matched groups (10 subject each) according to the intervention they had: 1) facilitatory, intermittent theta burst stimulation TBS (iTBS) over non-dominant M1 - the iTBS group; 2) inhibitory, continuous TBS (cTBS) over dominant M1 - the cTBSc group; 3) contralateral cTBS followed by iTBS over target M1 - the cTBSc/iTBS group, and 4) placebo, sham iTBS - Placebo group.

Learning was evaluated by comparing scores (number of pegs positioned) on Purdue peg-board test (PPT), before (T0) and immediately after (T1) experimental interventions.

Results

In all groups, the PPT scores increased at T1 in comparison to T0 showing clear learning effect (Fig. 1). The ANOVA showed significant Group effect (F(3,36)=3.57, p=0.023) for relative increase in number of pegs positioned at T1. However, although increase in PPT score following both iTBSi and cTBSc was clearly higher than following placebo, post-hoc t-tests showed as significantly different from placebo only increase following bilateral sequential cTBSc/iTBSi protocol. The increase following cTBSc/iTBSi was significantly higher than increase following either iTBSi or cTBSc, as well.

Conclusion

Neither direct stimulation of the target M1 nor indirect stimulation through release from contralateral M1 inhibition (by inhibiting contralateral M1) were able to increase motor skill learning significantly above the level seen with placebo. Only bilateral sequential stimulation consisting of inhibition of contralateral M1 followed by stimulation of target M1 was able to significantly improve learning of a skilled motor task with non-dominant hand. The findings may lead to development of new TMS interventional approaches in neurorehabilitation.

figure 1
P276
Asymmetrical Sensitivity of the Primary Motor Cortex to the Functional Inhibition by Continuous Theta Burst Stimulation.

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Objective

Motor control is asymmetrically organized within brain cortex with one hemisphere, usually left, typically having a dominant role. Given their different position in the hierarchy, the two hemispheres may have different functional susceptibility to the inhibitory effects of the noninvasive cortical stimulation (NCS) techniques. The aim of this study was to check this hypothesis on the model of motor learning, and to evaluate it related to the NCS effects on the primary motor cortex (M1).

Methods

As inhibitory NCS, continuous theta burst stimulation (cTBS), was used. During cTBS protocol, short bursts of 50Hz stimulation (3 pulses of 80% aMT) were applied at 5Hz continuously, for a total of 600 pulses.

Participants were 30 right-handed healthy subjects (mean age 25.5±4.5y, 15 women). They were divided into 3 matched experimental groups (10 subjects each) according to the intervention they had: 1) cTBS over dominant M1 - the cTBS-D group; 2) cTBS over non-dominant M1 - the cTBS-nD group, and 3) no intervention at all - Control group.

The outcome measure was change of the scores (number of pegs positioned with a hand contralateral to the side stimulated) on Purdue peg-board test (PPT). The scores were measured before (T0), immediately after (T1), and 30 min after (T2) the experimental interventions.

Results

In control group, both hands showed clear up-ward going learning curves, with the curve for the dominant, right, hand being steeper (Fig. 1). However, following cTBS, the two groups showed quite distinctive behaviors (Fig. 1). In cTBS-nD, scores at T1 were slightly below the ones at T0, only to start improving at T2; at both post-intervention time points the scores of the group were clearly below the Control group's scores, significant for T1 ($t_{(18)}=2.91$, $p=0.01$). In cTBS-D, the learning curve was similar to the one in the control group with scores only slightly lower.

Conclusion

In right handed healthy young subjects, the dominant M1 has much lesser functional susceptibility to the inhibitory effects of the cTBS that the non-dominant M1. The results may help in better understanding of the physiology of motor learning.

figure 1
P277
The Role of the Cerebellum on Motor Imagery

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Introduction

It’s thought that the cerebellum plays a role in motor imagery (MI). Although there are some neuroimaging evidences support this, limited number of data investigated the role of the cerebellum on MI, in terms of neurophysiology. The aim of the this study is to explore the role of the cerebellum on MI. Cerebellar transcranial direct current stimulation (ctDCS) was used to modulate cerebellar excitability.

Method

11 healthy subjects were recruited the study (3 female, aged between 27-47, mean 33.3 ±8. 7).

Subjects were instructed to image two different motor task. Abduction of the index finger was the simple task, while tell one’s beads was the complex one. MEPs were elicited from right first dorsal interosseous muscle. The basal MEP amplitude was calculated average values of 30 MEPs. The effect of MI on motor cortical excitability was measured by MEPs amplitude changes. Resting motor threshold (rMT), threshold for 1 mV motor evoked potential (MEP) and silent period (SP) were measured before and after ctDCS.

Each subject underwent two different cerebellar modulation study: anodal stimulation and sham stimulation. The interval between experiments was at least one week.

tDCS was delivered through two sponge embedded in a saline-soaked solution. Active electrode was centered on the right cerebellar cortex, 3 cm lateral to the inion. Reference electrode was positioned on the right masseter muscle. The intensity of stimulation was set at 2 mA for 20 min. Sham cTDCS consists of 30 seconds current stimulation.

Results

- Anodal ctDCS:
  - Before ctDCS: basal MEP values: 976.4 ± 425. µV, after simple MI: 1858.2 ± 743.7 µV (p=0. 000), after complex MI: 1014.2 ±724.8 µV (p>0,05).
  - After ctDCS: basal MEP values: 952.4 ± 719.2 µV, after simple MI: 1202.9 ± 376.4 µV (p>0,05), after complex MI: 934.8 ±724.8 µV (p>0,05).

- Sham ctDCS:
  - Before ctDCS: basal MEP values: 1102.6±290. 5 µV, after simple MI: 1970.2 ± 989.9 µV (p=0.009), after complex MI: 1446.9 ±615.3 µV (p=0.0016).
  - After ctDCS: basal MEP values: 1090.1 ± 339.6 µV, after simple MI: 1857.5 ± 930.2 µV (p=0, 016), after complex MI: 1421.7 ±785.8 µV (p=0. 001).

Conclusion

The results of the study indicate that the cerebellum modulates MI. The finding that suppression of MEP amplitude increase during MI with anodal ctDCS indicates that it has an inhibitory effect on MI.
Facilitatory effects in a perceptual learning task through an “inhibitory” stimulation

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Question

In the cognitive neuroscience domain no clear correlation emerges between transcranial direct current stimulation polarity (anodal a-tDCS vs. cathodal c-tDCS), and behavioural performance (improvement vs. impairment). Contradictory results are present mainly for c-tDCS. Therefore our aim was to investigate if and how some variables i.e., c-tDCS timing, pauses during c-tDCS and duration of c-tDCS affect performance, in the healthy adult brain. We applied c-tDCS before or during a task execution (before vs. during - timing), continuous vs. paused c-tDCS (yes vs. no pauses) and different c-tDCS durations (22 vs. 9 min), to evaluate if and how these parameters may alter its effects.

Methods

1.5mA c-tDCS was delivered by a battery-driven stimulator through an active electrode applied on primary visual cortex (16 cm²), and a reference electrode on the right arm (60 cm²). 82 subjects executed an orientation discrimination task (ODT) in a between-subjects design. They had to decide whether the presented stimulus was tilted clockwise or counterclockwise relative to the previously presented one. We measured the percentage of accuracy (d’ values).

Results

rmANOVAs showed an improvement of the performance when c-tDCS was applied before the task whereas with online c-tDCS performance was similar to sham. The presence of pauses during c-tDCS and a different duration of the stimulation did not modify the facilitatory induced effect.

Conclusions

We demonstrated that not necessarily c-tDCS induce behavioural inhibition, but the effects should be considered in relation to the timing of application and the executed task.

The same protocol of “neuroplasticity induction” can provoke different effects depending on the excitability level of the stimulated neurons. We speculate that offline c-tDCS could induce metaplasticity mechanisms functional to obtain an “optimal” neural activation when consequently the cortical area is involved in a specific task.
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P280
Effects of different repetitive Transcranial Magnetic Stimulation treatments and the role of attentional bias in complex Focal Hand Dystonia: a case-report.

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Question

Focal hand dystonia (FHD) is a movement disorder characterized by involuntary muscle contraction, causing abnormal postures. Its symptoms are associated with deficient cortical inhibition. Previous studies suggest that inhibitory low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) over contralateral premotor cortex (PMC) might ameliorate FHD, although no clear evidence of significant improvement has been shown. In this study we investigated the effects of different rTMS protocols on complex FHD of the right hand and associated symptoms in a 41-year-old man.

Methods

Two different experiments were conducted. In experiment 1, the patient underwent eight daily sessions of rTMS over left PMC. In experiment 2, in order to investigate the role of rightward attentional bias and the effects of lower doses of stimulation we compared the effectiveness of a weekly three days treatment over PMC with a three days treatment over left PPC (Posterior Parietal Cortex). RTMS over left Occipital cortex and sham stimulation over PPC constituted two control conditions. Clinical and behavioral evaluation comprised the patient’s self-estimation of dystonic symptoms, handwriting, finger tapping, and the use of everyday objects. In experiment 2, a line bisection task was also administered.

Results

Taken together the findings of the experiments suggest that: 1) lower doses of rTMS over PMC, more distributed in time, may induce better clinical outcomes than higher doses; 2) the rightward attentional bias played a role in this patient’s FHD and was improved by rTMS over PPC; 3) rTMS over PPC induced longer term beneficial effects than rTMS over PMC.

Conclusions

Our findings suggest that both PMC and PPC represent effective sites for rTMS treatment of FDH. Future double-blind placebo-controlled studies on groups of patients are needed to further explore the differential role played by the two sites in the pathophysiology of FHD and optimal doses of stimulation.
Modulation of cortical activity after anodal transcranial direct current stimulation during motor task: An fMRI study

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Question

It is known that offline anodal transcranial direct current stimulation (AtDCS) increases cortical activation by motor task. However, it is still unclear how AtDCS during motor task modulates the brain activity.

Methods

AtDCS over the non-dominant hand area of the primary motor cortex was applied in 11 healthy subjects. Each subject participated in 2 experimental sessions (either AtDCS with an intensity of 1mA for 10 minutes or sham tDCS) in pseudo-randomized crossover design with an interval of at least 1 week. Each tDCS was applied while performing finger tapping task using non-dominant hand. Before and 10 minutes after each tDCS, BOLD signals for finger tapping task were recorded in a block design manner.

Results

Brain activities in the contralateral primary sensorimotor cortex during the task were reduced after AtDCS. There was no significant change after sham tDCS.

Conclusions

This finding supports that AtDCS while performing motor task decreases the motor cortex excitability as measured with transcranial magnetic stimulation (TMS). This study clarified that AtDCS in combination with the motor task induced effects different from AtDCS alone.
P282
Effect of coil orientation on strength-duration time constant with controllable pulse parameter transcranial magnetic stimulation

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Question
Controllable pulse parameter transcranial magnetic stimulation (cTMS) devices are now available. Is it possible to adjust pulse width to more selectively stimulate neuronal populations with different time constants? How does this impact on the evoked EMG responses?

Methods
10 young healthy subjects participated in the experiment (5 men/ 5 women). Single pulse stimulation over the hand motor area was performed using a cTMS device that generates monophasic pulses with independent control of the pulse width, connected to a figure-of-eight coil. We tested the effect of coil orientations (i.e. posterio-anterior (PA)/anterior-posterior (AP)) with three different pulse widths (30, 60 and 120 μs) on the strength-duration curve, the input-output (IO) curve and the latency of the motor evoked potentials (MEPs) in the first dorsal interosseous muscle.

Results
During a weak background contraction, strength-duration time constants were estimated from both motor threshold and IO data for PA and AP orientations. When estimation was based on motor threshold data, the mean strength-duration time constants were 231 and 294 μs (t(9) = 3.39; p = 0.008) whereas time constants were 252 and 296 μs respectively (t(9) = 8.74; p < 0.001) for estimation from IO data. Repeated measure ANOVA on MEP latencies to AP and PA stimulation (during active contraction) revealed a significant interaction between pulse width and orientation (F(2,18) = 9.97; p = 0.001), due mainly to longer onset latencies following AP stimuli of short duration.

Conclusion
The data suggests that PA and AP orientation activate neural populations with different time constants. The long time constant element activated by short duration AP pulses has a more indirect connection with the corticospinal output neurones than the PA activated population probably because it tends to recruit later I-waves.
P283
TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) IN PARKINSON'S DISEASE


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**Question**

Transcranial Direct Current Stimulation (tDCS) is a promising noninvasive technique for adjunctive treatment of movement disorders. The aim of the study is to assess whether daily tDCS over the cerebellum (tcDCS) and over the motor cortex (M1-tDCS) can improve patients with Parkinson Disease (PD).

**Methods**

10 patients (aged 37-85) (female=4) (Hoehn & Yahr 1.5-3) diagnosed as having idiopathic PD were recruited from two Movement Disorders Clinics. To evaluate the effect of tDCS (tcDCS or M1-tDCS) on motor function in PD, we delivered bilateral anodal (2 mA, 20 minutes, five consecutive days) and sham tDCS, in random order, in two separate experimental sessions at intervals of at least 1 month. In each session, the Unified Parkinson's Disease Rating Scale (UPDRS-III and -IV) was administered before (baseline) and after the treatment (T1).

**Results**

After five days of anodal M1-tDCS but not tcDCS improved the UPDRS IV (dyskinesias section) by 35\% ±4.7 (p=0.001). tcDCS and sham tDCS failed to significantly change the UPDRS IV. Sham tDCS, tcDCS and M1-tDCS failed to significantly influence the UPDRS III score (p>0.05).

**Conclusion**

Despite the small sample size, our preliminary results show an improvement of dyskinesias after five days of anodal tDCS over the cortical motor areas persisting for at least four weeks after the end of the stimulation protocol.
**P284**

**Impact of the α₄β₂ nicotinic receptor partial agonist on transcranial direct current stimulation-induced plasticity in the human motor cortex**

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**Question**

The neuromodulator nicotine is shown to alter cognitive functions in animals and humans. The physiological basis of this effect might be alterations of plasticity. Recently, in principal accordance, a modulatory effect of nicotine on neuroplasticity induced via transcranial direct current stimulation (tDCS) of the human motor cortex was demonstrated. tDCS induces calcium-dependent plasticity of the glutamatergic system. Therefore, an impact of nicotine on respective receptors with calcium channel properties is probable. We aimed to test this hypothesis by exploring the impact of the partial α₄β₂ nicotinic receptor agonist varenicline on tDCS-induced plasticity.

**Methods**

We administered low (0.1mg), medium (0.3mg) and high (1.0mg) single doses of varenicline or placebo medication before anodal or cathodal tDCS to the left motor cortex of 12 healthy non-smoking individuals. Corticospinal excitability was monitored by single-pulse transcranial magnetic stimulation (TMS)-induced motor evoked potential (MEP) amplitudes every fifth minute for up to 30 min after stimulation, 60, 90, and 120 min, at the evening of the stimulation day (approximately at 18:00), and next morning (~9:00), noon (~12:00), and evening (~18:00).

**Results**

After administration of low dose (0.1mg) of varenicline, tDCS-induced plasticity is not affected, while it is completely abolished by medium dose (0.3mg). High dose (1.0mg) of varenicline causes a delayed onset of anodal tDCS-induced excitability enhancement and prolongs cathodal tDCS-induced excitability diminution up to the same evening after the end of stimulation.

**Conclusions**

The results of this study show that activation of nicotinic α₄β₂ and possibly, α7 receptors has specific and dosage-dependent effects on tDCS-induced neuroplasticity in healthy human non-smoking individuals. These results might help to further explain the involvement of the above mentioned receptors in the nicotinic impact on neuroplasticity and cognitive functions.
Introduction: Cluster headache is included in the group of trigeminal autonomic cephalalgias. Although the pathophysiology of cluster headache has not yet been sufficiently established, the theory of a central origin tells us that this headache is produced by hypothalamic dysfunction. More than 50 patients have been treated with deep brain stimulation of the posterior nucleus of the hypothalamus from 2001. The results show clinical improvement in more than 60% of the cases, opening a promising issue for the treatment of the cluster headache persistent after medical treatment. The surgical targets that have been used until now are based on the origin of the cluster headache in the hypothalamic dysfunction. Method: Patients: we report five patients with refractory chronic cluster headache on whom stimulation of modified target. Surgical technique: the stereotaxic coordinates used were: 4mm lateral to the third ventricle wall, 2mm behind the midintercommissural point and 5mm under the intercomisural line. A minimum of three recording were conducted in all patients. The recording was locate the subthalamic nucleus, the second was situated the anterior edge of subthalamic nucleus, and the last one was to look for activity in target point. Conclusions: review of the target used and propose another surgical target. The value of neurophysiological intracerebral records for its location.
Modulation of cortical excitability by grouped electrical stimulation protocols

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Question

Theta burst stimulation (TBS) is a variant of repetitive transcranial magnet stimulation (rTMS). Huang et al., (2005) demonstrated that TBS is able to produce a long lasting effect on cortical excitability following only a short time of stimulation. Here, we try to validate the electrical form of this theta burst stimulation (eTBS).

Methods

The effects of 3 eTBS protocols on cortical excitability were investigated on healthy subjects: intermittent TBS (iTBS), intermediate TBS (imTBS) and continuous TBS (cTBS). Each eTBS pattern consists of 3 pulses of stimulation given at 50 Hz, repeated every 200 ms. iTBS uses a 2 s train of TBS, repeated every 10 s. imTBS uses a 5 s train of TBS, repeated every 15 s. The cTBS pattern consists of a 40 s train of uninterrupted TBS. eTBS was applied over the left primary motor cortex (M1) with a reference electrode over the contralateral orbit in 15 healthy volunteers at an intensity of 5 mA. Monophasic single-pulse transcranial magnetic stimulation (TMS) was used to measure changes in corticospinal excitability before and after eTBS in the right hand muscle. Inactive sham stimulation was used as a control.

Results

It could be shown that 5 mA eiTBS resulted in a marginally significant inhibition of the amplitude of muscle evoked potentials (MEP’s) compared to a sham control. Furthermore, cTBS showed a tendency to an inhibitory effect as well.

Conclusion

eTBS is able to achieve a modulation of the activity in the motor cortex but faster and with less intensity, thus providing a cheaper alternative to the common TBS. Moreover, the technical possibilities of eTBS (e.g. applied frequency) are far less limited than for TMS.
Dosage-dependent effect of D2 receptor activation on motor cortex plasticity in humans

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The neuromodulator dopamine plays an important role in synaptic plasticity depending on subreceptor specificity, concentration level and the kind of neuroplasticity induced. In animal experiments, D2-like receptor stimulation revealed seemingly opposing results on plasticity which might be explained by dosage-dependency. In humans, blocking D2 receptors abolishes any kind of plasticity, highlighting its relevance for this function. However, the dosage-dependent impact of this receptor on plasticity in humans has not been explored so far. To this aim we applied the selective D2 receptor agonist bromocriptine (2.5mg, 10mg and 20mg) or placebo medication combined with anodal and cathodal transcranial direct current stimulation (tDCS) which induces non-focal plasticity and paired associative stimulation (PAS) for a more focal kind of plasticity in the motor cortex of healthy human volunteers. 24 volunteers were included and plasticity was monitored by transcranial magnetic stimulation (TMS)-induced motor evoked potential amplitudes (MEP). Our results reveal that D2 receptor activation produces a clear inverted U-shaped dose-response curve on plasticity induced by inhibitory tDCS, excitatory and inhibitory PAS. However, for excitatory tDCS, the direction of after-effects was reversed. These data support the assumption that modulation of D2-like receptor activity exerts a dose-dependent effect on neuroplasticity in the human motor cortex.
The selective influence of rhythmic cortical versus cerebellar transcranial stimulation on human physiological tremor

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Purpose

The influence of central neuronal oscillators on human physiological tremor is controversial and there is a paucity of interventional studies examining the neural networks involved.

Methods

Transcranial alternating current stimulation (TACS) was delivered at peak tremor frequency to 12 healthy volunteers in a 2x2 crossover study. Two sites were stimulated (contralateral primary motor cortex, M1 versus ipsilateral cerebellum) whilst participants performed two types of task designed to probe the different manifestations of physiological tremor of the hand - kinetic and postural tremor. Tremor was measured by accelerometry. Cortical coherence with the accelerometry signal was also calculated in the absence of stimulation. The phase synchronisation index, a measure of the phase entrainment of tremor, was calculated between stimulation and tremor waveforms. The amplitude modulation of tremor was similarly assessed.

Results

There was significant phase entrainment that was dependent both on tremor type and site of stimulation: M1 stimulation gave rise to phase entrainment of postural but not kinetic physiological tremor, whereas cerebellar stimulation increased entrainment in both cases. There was no effect on tremor amplitude. Tremor accelerometry was shown to be coherent with the cortical EEG recorded during postural but not kinetic physiological tremor.

Conclusion

Physiological tremor has proven differentially susceptible to transcranial stimulation. This novel experimental approach has allowed for separation of the influences of central and peripheral mechanisms in tremorogenesis. TACS modulates the phase of physiological tremor, and its effects are dependent both on tremor type and stimulation site. The present study is the first to demonstrate that tremor can be entrained by TACS over the cerebellum, with a potency that at least matches that of stimulation over M1. The absence of an effect on tremor amplitude suggests that factors downstream of the stimulation sites dominate amplitude modulation. We conclude that central oscillators play a significant role in two of the major manifestations of tremor in health.
Cortical atrophy features in Parkinson's disease patients with depression

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Objectives

To determine cerebral cortex atrophy features and their prognostic significance in Parkinson's disease complicated by depression

Materials and methods

49 patients with idiopathic Parkinson's disease were examined according to British Bank of the brain criteria. The study involved patients with stage 3 by Hoen/Yahr, 31 of which had an akinetic-rigid form of the disease (63.3 % ), the other had a mixed form of PD (36.7 %). Assessment of mental function was carried out using Beck Depression Scale. The main group consisted of patients with depression of moderate and higher severity. The controls were PD patients with no depression. MRI (1.5T Siemens scanner) was performed, T1-WI, T2-WI, were obtained, as well as DTI, which was analyzed using FreeSurfer. 243 subjects underwent statistical analysis. Correlations were calculated using Spearman's test. Data processing was performed using Statistica 8.0 of package StatSoft using Mann-Whitney test.

Results

We have identified significant differences in the thickness of the cortex in both left and right brain hemispheres. Patients with depression suffer lesion of the lingual area, parahippocampal areas on both sides and gyrus rectus.

Discussion

Our data indicate the presence of few structures involved to the pathogenesis of depression in patients with PD. First of all, it is worth paying attention to the lesion of the lingual area and some of its components, particularly s. occipital-temporal medial, pars Lingualis, which has got significantly reduced thickness of the cortical layer in both hemispheres. Besides, we observed strong negative correlations of lingual cortical areas thickness on both sides and a total score of Beck Depression Scale. The combination of these facts allows to talk about usage of the lingual cortex thickness (of the middle occipital-temporal sulcus), as a predictor of depression in PD patients.

One of the most important aspects of the study was to identify markers predicting the occurrence of depression in patients with Parkinson's disease. It was found three most important areas - the right and the left parahippocampal area and the average occipital- temporal sulcus. The most valuable is the left parahippocampal region, which increases the risk of depression in 46.8% patients cortex thickness goes below 2,597 mm.
Mild cognitive impairment (MCI) in Parkinson’s disease (PD) is not explained by reduced alertness - a quantitative EEG study

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Question

About 30% of patients with PD suffer from dementia, and 34% from MCI. Dysfunction of sleep-wake cycle is also common in PD and might have an impact on alertness. To investigate whether reduced alertness is a surrogate of PD-MCI, we compared the alpha reactivity (the ratio between the alpha power during eyes closed and eyes open) as a quantitative measure of alertness between PD-MCI patients, PD patients with normal cognition (PD-NC patients) and age-matched healthy controls.

Methods

256-channel EEG were recorded from 17 PD-MCI patients (median age: 70y, range: 60y-79y), 9 PD non MCI patients (median age: 72y, range: 60y-84y) and 17 healthy subjects (median age: 73y, range: 68y-79y). Alpha frequency power (8-13Hz) was calculated only for occipital electrodes to avoid eye blink artifacts. Alpha power was determined during 8 periods of 4 seconds in each condition (eyes closed/eyes open). ANOVA was applied to compare the three groups.

Results

There were no differences in alpha reactivity between PD-MCI patients, PD-NC patients and healthy controls (p=0.8).

Conclusions

Reduced alertness as measured by alpha reactivity is unlikely to cause MCI in PD.
Assessment of hand force coordination in unimanual manipulation tasks in patients with moderate Parkinson’s disease without levodopa-induced dyskinesias

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Question

To evaluate hand force (i.e., grip [G] and load force [L]) coordination in various unimanual manipulation tasks related to specific aspects of functional impairment in Parkinson’s disease (PD) patients without levodopa-induced dyskinesias (LID).

Methods

Ten patients (age range 40-55 years, mean ± SD 49.2 ± 6.9) with moderate PD (Hoehn and Yahr 2.5-3) and ten age-matched healthy controls performed various static (ramp-and-hold and oscillation force producing) and dynamic (simple lifting) manipulation tasks with an instrumented device that recorded the grip and load force performed unimanual by each hand. All PD patients were tested in ON-condition exclusively.

Results

Parkinson’s disease subjects has consistently shown differences between more affected hands vs. healthy controls regarding the lifting task at holding phase (CV of L - PD 1.51% ± 0.58 vs controls 0.81 ± 0.33; G/L ratio PD 1.27 ± 0.21 vs. control 0.90 ± 0.18), as well as the oscillation task (G/L ratio - PD 2.03 ± 0.83 vs. control 1.03 ± 0.22; offset G/L - PD 6.21 ± 5.83 vs. controls 1.23 ± 1.16).

Conclusions

Impairment of hand function observed in lifting and oscillation task in the tested PD patients without LID, suggest subtle force dysregulation that underlie the clinical features of PD, even in ON-condition.
P288
ACUTE NEUROPATHY IN DUOENAL LEVODOPA TREATED PARKINSONIAN PATIENT. ELECTROPHYSIOLOGICAL DESCRIPTION

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Question
Peripheral neuropathies have been described in duodenal levodopa (duo-dopa) treated parkinsonian patients. However acute severe neuropathy is not frequently reported. The relationship with vitamin B12 and B6 deficit has been postulated in some cases.

Methods
We report clinical and electrophysiological assessment of a parkinsonian patient who developed a severe acute neuropathy during duo-dopa treatment. A severe vitamin B6 deficit was detected

Case Report
A 63-year-old female with diabetes mellitus and long-term Parkinson’s disease under duo-dopa treatment began mild distal paresthesias in legs and arms four months before. The last two weeks developed severe worsening, with inability to manipulate objects and gait instability. Tendon reflex were absent in lower limbs. Electrophysiological studies showed a severe mixed sensorymotor neuropathy, with abolished sensory potentials, and minor decreased motor potentials. Blink reflex, jaw reflex, skin sympathetic response, RR variability, quantitative sensory test and somatosensory evoked potentials were reported. Severe vitamin B6 deficit were detected and treated. Serial electrophysiological studies were done to assess outcome.

Conclusions
We describe a patient with Parkinson’s disease under duo-dopa treatment who developed an acute sensorymotor polyneuropathy by vitamin B6 deficit. Electrophysiological characterization and outcome is discussed.
P289
Functional connectivity of Sub-thalamic and Pedunculopontine rhythms in Parkinson’s disease

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Question

There is anatomical connectivity between sub-thalamic nucleus (STN) and pedunculopontine nucleus (PPN) in humans. However, the functional linkage between the two has not been fully elucidated. Two questions were asked: 1. through which frequency band(s) are the two nuclei bridged? 2. Which nucleus leads the other one if there is functional connectivity between them?

Methods

Three patients with Parkinson’s disease (PD) underwent bilateral STN and left PPN deep brain stimulation (DBS) were recruited for the investigation on the 2nd day after operation. The local field potentials (LFPs) were recorded from the externalized electrodes in resting states during patients’ ‘off’ and ‘on’ states . The coherence and cross-power spectral density estimates were conducted for signal analysis.

Results

There is a strong coherence at alpha frequency between STN and PPN LFP. The analysis of phase spectra over the alpha frequency showed significant coherence between STN and PPN and PPN led STN at this frequency by 5.9, 7.3 and 5.1 ms, respectively, in three subjects were detected. After levodopa treatment, the leading time increased in subject 2 and 3 (13.7 and 9.5 ms).

Conclusions

There is functional connection between PPN and STN with PPN in leading position through alpha frequency band in PD. Levodopa administration lengthened the leading time of PPN. It seems that faster alpha input from PPN to STN would perturb the motor capability in PD and this hypothesis should be further tested by motor tasks.
Blood pressure and heart rate regulation is already disturbed in prodromal α-synucleinopathy due to peripheral autonomic denervation.

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Question

Impaired blood pressure (BP) and heart rate (HR) regulation including orthostatic dysregulation is a prominent feature in α-synucleinopathies. Peripheral vasoconstriction and increased HR as major cardiovascular adjustments to orthostatic challenges are primarily mediated by the arterial baroreflex, which is the major determinant in BP/HR regulation (Ichionose, Front Physiol 2012). Baroreflex regulating cerebral areas such as the vagal dorsal nucleus are early involved in synuclein-mediated neurodegeneration (Braak, Neurobiol Aging 2003). However, it is unclear, whether BP/HR regulation is already disturbed in prodromal α-synucleinopathies such as REM sleep behaviour disorder (RBD). We hypothesized that BP/HR dysregulation is present and mediated by baroreflex dysfunction in RBD.

Methods

We determined BP/HR response to orthostatic challenge, HR variability (HRV) and BP variability (BPV) in the frequency domain [HRV: high frequency (HF), low frequency (LF), very low frequency (VLF) band power; BPV: HF, LF band power] to assess cardiac/vascular autonomic innervation and baroreflex sensitivity (BRS) to assess baroreflex function in 17 patients with “idiopathic” RBD (i.e. without further neurodegenerative symptoms) and 20 healthy controls.

Results

RBD patients and controls were comparable in age, gender, motor function, cognitive function and presence of autonomic symptoms (SCOPA-AUT score). Resting BP and HR did not differ between RBD and controls. During the orthostatic challenge, increase in systolic (p≤0.04) and diastolic BP (p≤0.04) was diminished in RBD patients but HR response was unchanged compared to controls. HRV band power was lower in all spectral bands (total p≤0.02, HF p≤0.05, LF p≤0.04, VLF p≤0.007) in RBD compared to controls, indicating cardiac autonomic denervation. BPV LF (p≤0.01) but not HF band power was also diminished in RBD patients, indicating peripheral vascular autonomic denervation. BRS did not differ between RBD patients and controls.

Conclusions

Autonomic dysregulation is already present but - in contrast to our hypothesis - baroreflex function is preserved in prodromal α-synucleinopathy. Diminished orthostatic BP/HF response must arise from peripheral autonomic cardiac/vascular denervation as indicated by lower HRV and BPV in RBD patients.
P291
Effective connectivity of the default mode network in Parkinson's disease and Parkinson's disease dementia

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Introduction
There is inconsistent data available for the default mode network (DMN) connectivity in Parkinson's disease (PD) and PD with dementia (PDD).

Objectives
The DMN effective connectivity was studied when switching from baseline to the cognitive task condition. We used fMRI and 3 groups of participants: PD, PDD, and age-matched healthy controls (HC).

Methods
In all, 14 PDD, 18 PD, and 18 HC were studied. The cognitive task was designed to test visual processing. Effective connectivity analysis was conducted using the seed-based functional connectivity analysis and psychophysiological interaction method with the posterior cingulate cortex (PCC) as a seed. The threshold was set at $p < 0.05$ FWE corrected.

Results
We observed task-induced activations in areas engaged in the ventral visual and dorsal attention networks in all groups without any significant differences among them.

HC showed greater PCC connectivity with bilateral middle temporal/ middle occipital gyri during the baseline than during the task condition. The correlation changed from positive to negative indicating that the ventral visual network switched on during the task condition. In PDD similar changes of PCC connectivity were observed with the left precentral gyrus/premotor cortex, i.e. areas involved in the dorsal attention network. This was also the only region with significant PCC connectivity changes between PDD and HC/PD groups while no significant difference was observed between HC and PD.

Conclusions
Our results show increased engagement of the dorsal attention network in the PDD group as compared to both PD and HC when switching from baseline to the simple visual processing task condition. This result may reflect increased top-down control in the PDD group.

Acknowledgement: The study was supported by the grant of the Czech Ministry of Health NT13499.
P292
FEATURES OF PATELLAR PENDULUM TRIGGERED BY PATELLA T REFLEX IN RIGIDITY

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Parkinson's disease is a movement disorder characterized by an increase in muscle tone. Rigidity affects motor capacity and daily functions of the patients. Aim of the study is analyzing electrophysiologically and kinesiologically features of the patellar pendulum that was triggered by patella T reflex in the Parkinson patients with rigidity.

Method

We stimulated patella T reflex by an electronic triggered reflex hammer and recorded muscle action potenteials by surface electrodes from quadriceps femoris and biceps femoris muscles. We analyzed electrophysiological features of patellar T reflex and also analyzed characteristics of the patellar pendulum during the reflex motion in patients with rigidity and normal subjects. Joint angle changes and instantaneous angular velocity during reflex was measured with a goniometric approach.

Results

Twenty five normal subjects included study as a control group. Patella T reflex had 17.9±1.9 milliseconds latency and 6404.1±2860.0 microvolt amplitude. Initial time of joint motion was 51.5±9.9 milliseconds and it was measured with an accelerometer. The pendulum count was 4.8±1.5. Angle of joint motion was 18.3±5.6°; extension time was 317.4±23.4 milliseconds; instantaneous angular velocity was 58.0±16.6 degrees/second; frequency was 1.0±0.1. Damping ratio of the pendulum was calculated as 0.6±0.2. A parameter was developed using by significant kinesiological findings and it was 60.3±16.1 degrees/second*Hz.

There were 45 Parkinson's disease patients in the rigidity group. Patella T reflex had 17.9±2.4 milliseconds latency and 4467.7±2528.4 microvolt amplitude. Bf-LLR response had 94.2±17.0 milliseconds latency, 770.8±488.0 microvolt amplitude and it was seen in 28 cases. Initial time of joint motion was 61.7±5.7 milliseconds. The pendulum count was 1.8±0.7. Angle of joint motion was 9.2±4.2°; extension time was 274.5±39.3 milliseconds; instantaneous angular velocity was 33.7±15.5 degrees/second; frequency was 1.3±0.2. Damping ratio was calculated as 0.2±0.2. The parameter value was calculated as 27.5±13.9 degrees/second*Hz.

Conclusion

Kinesiologic features of patellar T reflex change significantly in Parkinson's disease. The most striking changes occur on the pendulum count and angle of the first movement. The parameter that generated by using kinesiologic scales can distinguish between Parkinson's disease and normal subjects.
Effects Of Transcranial Direct Current Stimulation On Dual-Task Gait Performance In Patients With Parkinson’s Disease

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Background

Non-invasive stimulation such as transcranial direct current stimulation (tDCS) has gained more popular application in neuro-rehabilitation. Previous studies reported that a single session of tDCS enhanced upper limb motor function and 8 sessions of tDCS enhanced complex upper limb motor and gait performance in patients with Parkinson’s disease (PD) (Benninger et al. 2010)

Objectives

The study aimed to examine the immediate and accumulative effect of tDCS on dual-task gait performance in patients with patients with PD

Methods

Eighteen PD patients were randomly assigned into an intervention and a sham group. Each group received 5 treatment sessions of tDCS in one week. Each session lasted for 20 minutes. The outcome measures were gait velocity, stride length and cadence when subjects walked at their natural speed and did calculation using a GAITRite walking mat. Subjects were assessed at baseline (T<sub>day0</sub>), after first treatment session (T<sub>day1</sub>), and completion of 5-day treatment (T<sub>day6</sub>). Two-way repeated measures ANOVA was used to examine the within-group and between-group differences.

Results

There was no significant between-group difference for any outcome measures at baseline. After 1 day of treatment, there was no significant change in all gait parameters in both subject groups. After completion of 5 days of tDCS, there were significant group x time interactions for gait velocity (p=0.048) and stride length (p=0.026). PD subjects in the intervention group had significantly faster gait velocity (by 17% p=0.022) and longer stride length (by 11%, p=0.023). In contrast, subjects in sham group did not have any significant changes in gait parameters after 5 days of treatment.

Conclusion

The positive outcomes in gait velocity and stride length in the intervention group suggest that 5 consecutive days of tDCS could improve gait performance under dual cognitive-walking condition.

Reference

Neuronal oscillatory patterns in the subthalamic nucleus in parkinsonian patients with off-period dystonia

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Objective

To explore neuronal oscillatory activity in the subthalamic nucleus (STN) in Parkinson’s disease (PD) with levodopa induced dyskinesia (LID).

Background

The dysfunction of the basal ganglia has been proposed to be involved in the pathophysiology of LID.

Methods

Eighteen patients with PD who underwent STN DBS were studied. Their Hoehn and Yahr score was 3.1±0.6 and UPDRS III score was 27.7±6.4 when off. Nine patients had LID and their UPDRS IV score was 6.4± 1.6. Another 9 patients did not present any sign of LID and were defined as a control group. Microelectrode recordings in the STN together with electromyogram from the upper and lower extremities of the body side contralateral to surgery were recorded. Single unit behavior, the interspike interval (ISI), coefficient of variation (CV) of ISI, ISI histograms, and spectral analysis were performed. Coherence analysis was used to study the neuronal oscillations in relation to dyskinesia.

Results

Two hundred and fifteen neurons were identified from 30 STN (Each group n=15). Of total neurons, in addition to 18.1% neurons (n=39) with tremor frequency oscillation (TFB), 26.5% neurons (n=57) with β frequency oscillation (βFB) and 46.5% neurons (n=100) without oscillation, there were 8.8% neurons (n=19) showing low frequency oscillation (LFB) at peak power of 1.2± 0.5 Hz. These neurons were often coherent with off-period dystonia. A majority of them were localized in the dorsal STN the same localization as neurons with TFB and βFB oscillation. Notably, 17 of 19 neurons with the pattern of LFB oscillation were found in the LID group (p<0.05). The age of onset of PD, duration of disease and L-dopa consumption were statistically different between the two groups (p<0.05).

Conclusion

Neurons with LFB oscillation in the STN are important in the generation of off period dystonia in PD. The earlier onset of PD, duration of disease, and L-dopa daily consumption are risks in the development of LID.
P295
Increased motor activity during REM sleep is linked with dopamine-function in idiopathic REM sleep behaviour disorder and Parkinson’s disease.

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Question

Rapid eye movement sleep behaviour disorder (RBD) is a parasomnia characterized by impaired motor inhibition during rapid eye movement sleep, and dream-enacting behaviour. RBD is especially associated with α-synucleinopathies, such as Parkinson’s disease (PD), and follow-up studies have shown that patients with idiopathic RBD (iRBD) have an increased risk of developing an α-synucleinopathy in later life. Imaging studies have shown that iRBD is associated with a reduced volume of the putamen, as well as a reduced density of the striatal dopamine transporters. Although abundant studies have associated the striatal dopamine system with daytime motor function in Parkinsonism, only few studies have focused on this system in relation to motor activity during sleep. Therefore the objective of this study was to investigate the relationship between the nigrostriatal dopamine system and muscle activity during sleep in iRBD and PD.

Methods

10 patients with iRBD, 10 PD patients with PD (PD+RBD), 10 PD patients without RBD (PD-RBD), and 10 healthy controls. All participants were assessed with 123I-FP-CIT SPECT, neurological examination, and polysomnography.

Results

Patients with iRBD and PD+RBD had increased phasic EMG-activity compared to healthy controls. 123I-FP-CIT uptake in striatum was highest in controls, followed by iRBD, and lowest in patients with PD. In iRBD patients EMG-activity in the mentalis muscle was correlated to 123I-FP-CIT uptake in striatum. In PD patients EMG-activity was correlated to anti-Parkinson medication.

Conclusions

Our results support the hypothesis that increased EMG-activity during REM sleep is associated with the nigrostriatal dopamine system in iRBD, and with dopaminergic medication in PD.
Sensorimotor gating deficits in multiple system atrophy: comparison with Parkinson's disease and idiopathic REM sleep behavior disorder.

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Question

Prepulse inhibition (PPI) of the auditory blink reflex is a measure of sensorimotor gating, which reflects an organism's ability to filter out irrelevant sensory information. PPI has never been studied in patients with multiple system atrophy (MSA), although sensorimotor deficits are frequently associated with synucleinopathies. We investigated whether alterations in PPI were more pronounced in MSA compared with Parkinson's disease (PD), idiopathic rapid eye movement sleep behavior disorder (iRBD) and healthy controls.

Methods

10 patients with MSA, 12 patients with iRBD, 40 patients with PD, and 20 healthy controls completed the study. A passive acoustic prepulse inhibition paradigm was applied with prepulses 5 dB and 15 dB above background noise at 30-, 60-, 120- and 300-ms intervals.

Results

Non-parametric analyses showed that MSA patients had significantly lower prepulse inhibition, as measured with max-amplitude, than PD patients and iRBD patients on the 60 ms-85 dB and 120 ms-85 dB inter stimulus intervals. The same relation was found when using area under the curve. No differences were found between groups for the 30 ms-85dB and 300 ms-85dB. Furthermore, blink reflex characteristics such as habituation did not differ between patients and controls.

Conclusions

The present study showed that sensorimotor gating, as measured with PPI, is markedly reduced in MSA. This may be due to the pronounced severity of striatal and brainstem dysfunction, as well as the degeneration of other structures related to the PPI modulating pathways in MSA. PPI may be a non-invasive neurophysiological measure that can aid in the differential diagnosis between PD and MSA.
P297
SPONTANEOUS SWALLOWING IN PARKINSON’S DISEASE- A Polygraphic study

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Question

The oral and pharyngeal phases of voluntary swallowing in Parkinson’s disease (PD) are affected. Spontaneous swallows (SS) in patients with PD were not systematically studied. The aim of this study is investigated that SS in PD by using polygraphic recording systems.

Method

We studied 27 PD patients and 22 controls. The polygraphing investigations were performed with an electroencephalography apparatus and twelve channels were used. Polygraphic recording consisted of surface electromyography of submental, orbicularis oris, oculi(OC), masseter muscles, a laryngeal and nasal sensor for respiration, parieto-occipital electroencephalogram, electrooculogram and electrocardiogram (figure1).

Results

SS frequency rate was very variable and arrhythmic in both group during wakefullness and slow wave sleep. In PD patients, the number of SS per minute increased when compared to normal controls (0.95 SS per minute vs 0.6 SS per minute) during wakefullness. SS frequency rate was decreased significantly in PD patients during slow wave sleep (4.0 SS per minute vs 2.0 SS per minute). A novel finding was the salvo type of consecutive swallow bursts with more than 4 SS in PD patients (figure2). Decrease of SS at the slow wave sleep and salvo type swallow bursts were the major findings in patients with PD. Furthermore an activation was observed in OC muscle during swallowing unrelated to blink reflexes.

Conclusions

We conclude that this finding might be related to the delayed triggering of accumulated SS at the pharyngeal spaces. This can be due to insufficient sensory inputs to the central nervous system. The activation in OC is probably related with gustato-facial reflexes.

figure 1
Abstracts of Poster Presentations – Poster Session 17 – Parkinson disease

Identification of spontaneous swallows (SS) - One hour recording

figure 2
Imaging pain anticipation and pain perception in drug-naïve patients with idiopathic Parkinson’s disease.

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Question

Pain is a frequent non-motor symptom in Parkinson’s Disease (PD). Its prevalence seems to be significantly higher in PD patients compared to healthy adults or patients suffering from other neurodegenerative diseases. Alterations in central processing or a dysfunction of descending pain control have been proposed to explain the high prevalence of pain in PD.

Method

Here we aimed at investigating brain mechanisms associated with pain anticipation and pain perception in drug-naïve PD patients. To this end, we applied 15 painful heat stimuli to the participant’s volar forearm. Participants provided pain intensity ratings for each stimulus. Imaging data from 23 PD patients (Hoehn&Yahr 1-3, 12 male, 64.9±9.6 years) and 23 healthy controls (HC, matched in age, gender, education; 12 male, 64.9±8.3 years) were analyzed. 21 patients were drug-naïve to avoid confounding drug effects.

Results

PD and HC did not differ in heat pain thresholds, stimulation temperatures, and perceived pain intensity. First imaging analyses indicated that during pain perception PD patients showed stronger activity in the medial cingulate cortex, thalamus and amygdala. In addition, they seem to suffer from a reduction in anticipatory activity in DLPFC, rACC and RVM.

Conclusion

Our preliminary results suggest a combination of reduced anticipatory activity in key regions of the descending pain modulatory system and an altered activation of the medial pain system in drug-naïve PD patients compared to age-matched healthy controls. These findings might shed light on the neural underpinnings of pain in PD.
Abstracts of Poster Presentations – Poster Session 17 – Parkinson disease

P299
Cognitive and cortical variables accompanying early markers in Parkinson's Disease: a nested case-control study

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Question

Hyposmia and an increased hyperechogenic area of the substantia nigra (SN) are known preclinical markers of Parkinson's Disease (PD). Up to now it is unclear, if the sole presence of these biomarkers is associated with changes in cognitive and brain-morphological variables as well.

Methods

From a prescreened sample of 711 volunteers we selected 30 showing either hyposmia (percentile ≤ 15, N=21) or an increased hyperechogenic area in the SN (≥0.25 cm², N=12). For each selected person we contacted several participants from the same cohort showing neither one of these markers, resulting in an experimental and a control group matched for age, sex, handedness, and years of education. All participants underwent a neuropsychological examination comprising tests for executive function, memory, word fluency, verbal learning, and impulsivity first. The subsequent structural and functional MRI recording included T1-, diffusion tensor, and magnetization transfer imaging as well as a 178 volume resting state sequence and a finger-tapping task.

Results

Cognitive tests indicated subtle, but significant differences between groups, e.g. decreased phasic alertness in the experimental group. Moreover, in the experimental group some biomarkers are linearly related to cognitive abilities (e.g. r(hyposmia,alertness)=−.32; r(echogenic area substantia nigra, action control)=-.34).

Conclusions

The presence of preclinical biomarkers for PD is accompanied by changes in the participants’ cognitive capacity. This aspect will be discussed in relation to structural and functional imaging parameters.
P300
Effective connectivity in Parkinson's disease and the impact of dopaminergic medication

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Introduction

Patients suffering from Parkinson's disease (PD) typically feature motor as well as non-motor symptoms, which distinctly improve under dopaminergic medication [1,2]. A possible explanation might lie in the differential modulation of dopaminergic motor and cognitive pathways [3]. Therefore, we here used analyses of effective connectivity for functional magnetic resonance imaging (fMRI) to investigate brain network interactions involved in basic motor tasks as well as executive functions in PD on and off medication and healthy controls.

Methods

12 PD patients (scanned twice, on and off medication) and 12 healthy controls underwent fMRI performing 4 different tasks: (i) index finger-tapping at maximum speed, (ii) button presses at a self-chosen time point, visually cued reaction time task (iii) without and (iv) with pre-determined response lateralization. Hence, conditions 2-4 systematically varied in terms of action selection and initiation. Dynamic Causal Modeling (DCM) was used to estimate effective connectivity between key areas of the motor system.

Results

Behaviourally, patients were significantly slower compared to healthy controls, except for the externally triggered movement selection task (iv). Exclusively motor performance (i) improved under dopaminergic medication. DCM revealed a significant reduction of endogenous (task-independent) connectivity in PD, especially for cortico-subcortical connections. Furthermore, PD patients off medication featured increased coupling between prefrontal and lateral premotor areas during external triggered movements (iv) compared to controls. Dopaminergic medication increased endogenous coupling between prefrontal and mesial premotor areas, as well as task-related coupling between premotor and putaminal areas during finger-tapping (i).

Conclusions

Our data suggest a disruption of motor networks in PD, reflected by the global reduction in endogenous connectivity. Dopaminergic medication seems to increase the coupling between cortical premotor and putaminal, as well as prefrontal and mesial premotor areas. These changes in connectivity seem to impact on basic motor functions but not executive dysfunction.

References:

[1]: Michely et al., 2012. Neuropsychologia. 50: 2506-2514
P301  
Efficacy of high-frequency repetitive transcranial magnetic stimulation on depression in Parkinson’s disease

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Objectives: To investigate whether high-frequency repetitive transcranial magnetic stimulation (rTMS) is effective on depression in patients with Parkinson’s disease (PD).

Methods: Nine depressed patients with Parkinson’s disease participated in this study. Depression was diagnosed when they experienced more than five symptoms from the DSM-IV criteria for a major depressive disorder. rTMS was applied over the dorsolateral prefrontal cortex. For 10 days, 600 stimulations a day were applied with an intensity of 90% of the resting motor threshold of (RMT) with 5 Hz frequency. Rating scales were measured at the “drug-on” stage of the patients and at the same time on each visit day. The Unified Parkinson’s Disease Rating Scale (UPDRS) motor part (III), Beck depression inventory (BDI), Montgomery-Asberg Depression Rating Scale (MADRS) and the Hamilton Rating Scale (HRS) were compared before rTMS, immediately after stimulation, and 4 weeks after the last stimulation.

Results: The mean age of the patients was 69.2±7.5 and their disease duration was 8.44±8.57 years. Repeated measures ANOVA analysis showed that the BDI, MADRS and HRS after rTMS significantly decreased compared to those before rTMS. The BDI was 30.0±5.7, 21.0±4.6 and 18.7±5.0 before, immediately after and 4 weeks after rTMS, respectively (mean±standard error). The MADRS was 20.6±1.3, 9.7±4.3 and 12.3±3.2, and the HRS was 12.7±1.3, 6.5±1.3, and 5.8±1.5 before, immediately after and 4 weeks after rTMS. In addition, the UPDRS part III was significantly different at each visit (14.2±2.8, 9.0±2.9 and 10.8±3.1).

Conclusions: Our findings demonstrate that rTMS can reduce the severity of depression as well as of motor symptoms at the “drug-on” stage in PD patients. In addition, the efficacy of rTMS continues for a long period of time. rTMS may be an option for treatment of depression in PD patients.
Abstracts of Poster Presentations – Poster Session 17 – Parkinson disease

**P302**
Basal ganglia metabolism changes assessment according to levodopa therapy in involved Parkinson’s Disease patients.

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**Objective**

To evaluate levodopa therapy affect to general metabolism in basal ganglia and substantia nigra in PD patients by means of MR spectroscopy.

**Materials and Methods**

In total 21 patients with idiopathic Parkinson's disease were examined. The study included patients with stages 2,5 and 3 by Hoen/Yahr, 7 patients had an akinetic -rigid form of the disease (33.5 %), the rest had a mixed form of PD (66.5 %). The study included patients who did not have dopaminergic therapy before. 14 patients were with right-sided lateralization were and 7 patients - with left onset of the disease. According to the obtained native MR images (T1-WI, T2-WI) multivoxel spectroscopy of the basal ganglia was performed. Metabolic maps were postprocessed then with the following levels of the major metabolites analyzed: N- acetylaspartate, choline, creatine, creatine, inositol, glutamate, lactate and citrate. Two studies were held in total. First - just before the start of levodopa therapy, and the second - in 3 months after that.

**Results**

Significant differences in N-acetylaspartate concentration in substantia nigra of subjects with levodopa treatment (p <0,05) were obtained. Significant differences were detected for all other metabolites (p > 0,05). There was a significant increase in the concentration of N- acetylaspartate in the contralateral onset of the disease of the substantia nigra.

**Discussion**

The findings suggest that levodopa affects cellular metabolism of nigral neurons positively. The basic fact is expressed by an increase in the concentration of N- acetylaspartate in the projection of the substantia nigra, which leads to increased functional activity of neurons.

One of the highlights is the improvement of axonal transmission through the accumulation of N-acetylaspartate in the presynaptic pools, as well as its distribution in the course of white matter pathways.

Besides mitochondrial function improves in nigral neurons, responsible for the production of N-acetylaspartate. As a result processes of aerobic respiration increase the viability of neurons. Perhaps this is one of the factors responsible for slowing the death of cells of the substantia nigra and providing increased survival of patients while taking levodopa therapy.
P303
Alteration of the autonomic nervous system in initial stadiums of Parkinson's disease, and his modulation for L-Dopa.

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Hypothesis
Disautonomía is present in the patients with Parkinson's disease (PD) in the initial phases and it progresses with the evolution of the same one. The treatment with L - Dopa might help to stabilize the autonomic function.

Background
PD is a multisystemic process that it affects not only to somatomotor, cognitive and limbic systems, but also to the autonomic nervous system. Disautonomía affects negatively patients quality of life and a precocious detection of the same can orientate the treatment and help to establish differential diagnoses.

Objective
1) To study the appearance of disautonomía in patients with PD, his progression and the effect of the treatment with L - Dopa.; 2) To design two simple protocols of analyses that could be used of precocious form in the daily clinic.

Methods
50 healthy subjects and 50 patients with PD have been studied. Patients with reasons and treatments that could alter the autonomic function are excluded. The patients were in phase "ON" and were divided in 3 groups according to the time of evolution (0-5 años, 5-10 > 10 years or complicated PD) and in 2 groups according to the treatment (as receive or not L-Dopa). To study the sympathetic dysfunction analyzes the cutaneous-skin response (CSR). To study the parasympathetic function (P) analyzes the variability of the cardiac frequency (HRV) in rest, deep breathing to 6 cycles / minute and during Valsalva's maneuver. In the analysis of the HRV parameters are valued for the Time-domain and for Frequency-domain. In patients with PD we analyzed the evolution of these parameters according to the time of evolution, stadium of Hoehn and Yahr and treatment. The obtained variables were analyzed using the statistical program SPSS.

Results
The analysis of the CSR was showing statistically significant differences (p

Conclusions
Patients with PD present alteration of the ANS (S as P) in the initial stadiums of the disease before to clinic. The affection worsens with the time of evolution of the disease and is correlated by the stadiums of H & Y. The treatment with L-Dopa has a stabilizing effect of the autonomic function (more significant in the P. CSR and HRV are two useful, simple tools and inócuas for his precocious detection.
P304
Striatal dopamine depletion lead to altered functional connectivity with the thalamus in Parkinson disease: a PET and fMRI study


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Introduction

Parkinson Disease (PD) is characterized by loss of nigrostriatal dopaminergic neurons that results in motor symptoms. Although the cortico-basal ganglia circuit model explains some of the motor symptoms in PD, there remains some discrepancy. For example, the model is difficult to reconcile with the fact that thalamic lesions were found to produce benefit, rather than disbenefit, for the treatment of parkinsonism. To investigate reasons for this discrepancy, we examined the effect of dopamine depletion in the striatum on functional connectivity of the cortico-basal ganglia circuit. We assessed altered functional connectivity between patients with PD and age-matched healthy controls using functional magnetic resonance imaging (fMRI).

Methods

17 PD patients and 16 healthy control subjects (HC) have underwent [11C]-2-β-carbomethoxy-3-β-[4-fluorophenyl] tropane (CFT) PET (FOV 250 mm, voxel size 1.95×1.95×4.25 mm 35 slices, 5mCi). Whole brain BOLD fMRI (voxel size 3×3×3 mm; TR = 3 sec; the paradigm consisted of self-initiated, sequential finger-to-thumb opposition movement of right and left hand, 21-s blocks consisted of 16 rest conditions and 15 finger-thumb opposition movements), T1 weighted image (voxel size 1×1×1 mm, 160 slices) and field map data were acquired on a 3T scanner. Analyses were performed using FMRIB Software Library (FSL) v4.1.9 tools.

Results

The binding of 11C-CFT in PD was compared with HC. The area showing reduction in 11C-CFT binding in the striatum were identified and defined as striatal seed regions of interest (strROIs). Then, we compared the functional connectivity of the strROIs between PD and HC by using fMRI. As a result, we found decreased correlation between the strROIs and thalamus in PD. (P < 0.05)

Conclusion

According to the cortico-basal ganglia circuit model, it is expected that dopamine depletion in the striatum lead to increased inhibition of thalamic neurons. Based on the present findings, we suggest that dopamine depletion in the striatum in PD lead to decreased functional connectivity with the thalamus.
Electrophysiological implementation for the prevention and management of Levodopa induced dyskinesia in Parkinson’s disease.

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Objectives

Parkinson’s disease is one of the common and complicated movement disorders. Successful therapeutic management is available since decades in the form of Levodopa. The most complicated adverse effect of this drug is induction of dyskinesia after chronic treatment for 4-10 years. After the induction of dyskinesias the positive effects of the drug almost disappear. In the present review, mechanism and probable electrophysiological changes which cause the induction of Levodopa induced dyskinesia (LID) are elaborated. Electrophysiological implementation regarding this complicated condition have no major coverage and never been studied at massive level.

Methods

This is a review in which up-to date probable mechanism and causes of electrophysiological related possibilities for the mechanism and management of L-Dopa induced dyskinesia will be covered.

Results

The two most important factors which cause L-DOPA induced dyskinesia are increased activity of the kappa opioid receptor by dynorphin and increased GABA formation by glutamic acid decarboxylase. Both these chemical changes are caused by up-regulation of prodynorphin mRNA and glutamic acid dehydrogenase mRNA, respectively, after chronic L-DOPA therapy as a result of gene expression.

Conclusion

The electrophysiological implementation of these changes for the L-Dopa induced dyskinesia are not only uncovered field but also it could lead to our improved understanding for the development of new therapeutic approaches for the prevention and management of LID. Here, I am going to propose the possible electrophysiological targets as future therapeutic regimes to prevent and manage LID.
Abstracts of Poster Presentations – Poster Session 17 – Parkinson disease

P306
Association of subthalamic activity with clinical and demographical parameters in a large cohort of Parkinson’s disease patients

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Question

The implantation of stimulators in the subthalamic nucleus (STN) of Parkinson’s disease patients has allowed the recording of local field potentials from this structure in the postoperative period. Our aim was to assess the relationship of the oscillatory activities found in these recordings with different clinical and demographical parameters, in a large series of PD patients.

Methods

We found 58 patients with good-quality recordings from the STN obtained at rest during a minimum continuous period of 300 seconds, off or on-medication. Relative peak power and peak area in the theta (4-10 Hz), low beta (10-20 Hz), high beta (20-30 Hz) and gamma bands (60-80 Hz) were measured in the power spectrum. Clinical (UPDRS-III scale) and demographical (gender, age at surgery, age at onset) variables were correlated with the different oscillatory activities.

Results

There were no gender-related differences in beta activity. The frequency of the low-beta peak typical of the off state correlated inversely with age at surgery. Low beta peak relative power and area off-medication correlated with the UPDRS rigidity subscore, while high beta peak and area correlated positively with UPDRS axial symptoms and inversely with the tremor subscales. Both low and high beta areas off-medication correlated with total UPDRS-III scores.

Conclusions

Our results confirm in a large series the association of beta activity with the UPDRS-III total score, and with the rigidity subscale. Additionally, we found an inverse association of high-beta activity with tremor and a positive association with axial symptoms that had not previously been reported.
P307
Levodopa responsiveness of blink reflex recovery index – an objective method of differentiating Parkinson disease from Parkinson plus syndromes

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Background
Parkinson’s disease is primarily diagnosed by clinical examination. The Parkinson plus syndromes especially PSP are hard to differentiate from PD before the classical clinical signs appear. To date, there is no objective tool for differentiating Parkinson’s disease from Parkinson plus syndromes. Blink reflex recovery abnormality due to hyperexcitability of brainstem interneurons has been demonstrated by Jun Kimura. A comparison of levodopa responsiveness of the blink reflex in Parkinson disease and Parkinson plus syndromes has not been done before.

Aim
We attempted to find an objective, possibly even quantifiable tool in the form of “levodopa responsiveness of the blink reflex recovery” to differentiate between PD and Parkinson plus syndromes.

Materials and methods
25 patients with clinically probable Parkinson disease, 10 clinically Probable progressive supranuclear palsy and 3 clinically probable MSA patients, 1 patient with clinically probable CBD, 4 patients with drug induced parkinsonism, 2 patients with vascular parkinsonism underwent the study. Two electrical stimuli were applied at interstimulus intervals of 500msec and 1000msec after a conditioning stimulus, before and 90min after administering 100 mg of levodopa. The ratio of test response to conditioned stimuli of pre and post levodopa responses were compared.

Results
Patients with clinically probable PD showed a statistically significant decrease in R2 recovery index post levodopa, clinically probable PSP patients did not show any response and patients with clinically probable MSA showed a paradoxical increase in R2 recovery index post levodopa.

Conclusion
Among PD and Parkinson plus syndromes, only Parkinson disease patients show significant response to levodopa in blink reflex whereas PSP patients do not show response and MSA patients show a paradoxical increase in excitability. This is a simple, non invasive, least expensive bedside study to objectively confirm the diagnosis of Parkinson’s disease and to differentiate it from Parkinson plus syndromes.
**Abstracts of Poster Presentations – Poster Session 17 – Parkinson disease**

**P309**
**Motor planning improvement in Parkinson’s disease after excitatory deep repetitive transcranial magnetic stimulation with H-coil: evidence from sensorimotor rhythms event-related desynchronization.**

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**QUESTION**

In this pilot study, we aimed at defining a new approach of repetitive transcranial magnetic stimulation (rTMS) in patients suffering from Parkinson’s disease (PD) that would induce efficient, stable, and reproducible symptom relieves. Since it has been demonstrated that primary motor cortex (M1) and prefrontal cortex (PFC) induce striatal dopamine release, we proposed a new stimulation approach combining PFC-M1 rTMS using a new coil: the Hesed coil (H-coil) which is designed to generate deeper and wider magnetic field without increasing the stimulation intensity. Our objectives were thus to investigate the clinical and neurophysiological effects of non-invasive, deep rTMS in PD, using the H coil.

**METHODS**

Twenty patients (3F; 63±9 y.o.; PD duration: 6±3 y) were included and underwent 12 deep rTMS sessions in 4 weeks. Excitatory 10 Hz rTMS was applied over M1 contralateral to the patient’s worse side (WS) and over the bilateral prefrontal cortices. Motor control was assessed before and after deep rTMS, OFF medication, using clinical (UPDRSIII, lateralized scores, timed arm tapping, and Nine-Hole Peg Test) and neurophysiological measurements (Event-Related Desynchronization (ERD) of the mu and beta sensorimotor rhythms during self-paced WS wrist extensions).

**RESULTS**

No drop-outs or adverse events were recorded. Our results showed that UPDRSIII (global and subscores) and timed tests significantly improved after treatment (p<0.001). Mu and beta ERD latency onsets were also significantly increased after treatment (Mu: -1237±177 ms before, and -2024±215 ms after; beta: -1247±151 ms before, and -2229±179 ms after; p<0.01). DISCUSSION: Deep rTMS is a safe treatment that improved motor symptoms and modulated the cerebral activity related to motor planning. The delayed mu and beta ERD shows that deep rTMS facilitated the activity of hypofunctioning cortico-striato-thalamo-cortical circuits, probably through dopamine release. This study highlights the importance of the use of the H-coil for rTMS in PD, and the importance of repeating the sessions for more than two weeks. Further placebo-controlled, randomized studies are needed to assess the therapeutic efficacy deep rTMS and its consequences on cortical motor control.
Abstracts of Poster Presentations – Poster Session 17 – Parkinson disease

P310
Quantitative Sensory Testing (QST) in patients with Parkinson’s disease and chronic pain.

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Background and aims

Pain is a frequent non-motor symptom of Parkinson’s disease (PD). Studies strongly suggest that basal ganglia and the dopaminergic system are involved in central pain processing. There is no consensus regarding the mechanisms and classification of pain in PD. The aim of this study was evaluate pain characteristics in PD patients with chronic pain.

Methods

Thirty-five patients with PD and chronic pain (mean age, 69.09 ± 8.6 years) and 25 healthy controls (63.33 ± 7.6 years) were included in this study. All PD patients were in mild or moderate stages of the disease (UPDRS 51). Parkinson’s disease Questionnaire (PDQ-39) for access the quality of life and Hamilton Rating Scale for Depression (HRSD) were used. Pain and allodynia were assessed (in the ON-medication condition) by administering the McGill Pain Questionnaire and the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale. Mechanical sensory and pain thresholds were assessed using von Frey monofilaments and a pressure analog algometer. Thermal sensory and pain thresholds were evaluated in the thenar eminence (TE).

Results

Reported pain intensity was 3.6 in average (0-10 VAS). The higher values of VAS interfere in life activities and in quality of sleep. There is a significantly association between pain intensity and higher values in the HRSD. Allodynia as defined by the LANSS scale was found in 14 patients (40%). The legs were the most frequent location of pain (40%), followed by the back (25%), arms and shoulders (8.6%), feet or neck (5.7%), and head or abdomen (2.9%). The TE showed increase in warm, cool detection and cold pain thresholds but decreased heat pain thresholds compared to controls.

Conclusions

Allodynia appears to be unrelated to thermal thresholds in patients with PD, suggesting different central mechanisms of nociceptive processing. Our PD patients in mild stage of disease presents impaired heat perception but increased mechanical and cold pain perception compared to controls. Our findings are supported by the involvement of basal ganglia abnormality in pain perception.
LP19
Electrophysiological activity of the subthalamic nucleus in response to emotional prosody: an intracranial ERP study in Parkinson’s disease


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Background
Using intracranial recordings of local field potentials (LFPs) in Parkinson’s disease (PD) patients undergoing deep brain stimulation (DBS), previous studies have consistently reported event-related desynchronization of alpha activity within the subthalamic nucleus (STN) in response to emotional stimuli, suggesting that the STN is involved in emotion processing. However, these studies focused on the influence of visual stimuli, and it has yet to be determined whether the STN’s electrophysiological changes in response to emotional stimuli are modality-specific, possibly arising from specific oculomotor activities during visual emotion processing, or supramodal, as it was previously shown in behavioral studies.

Objective
In this context, we set out to explore the STN’s electrophysiological activity in response to both positive and negative emotional stimuli in the auditory modality (i.e., emotional prosody).

Methods
To this end, we recorded LFPs within the STN in response to angry, happy, and neutral prosodies, as well as to nonhuman, synthesized auditory stimuli, in four patients with PD who had just undergone bilateral implantation of electrodes for high-frequency DBS.

Results
We observed i) a specific modulation of the right STN in response to the human voice, as opposed to synthesized stimuli, both early and later on post-onset, and ii) a specific modulation of the STN in response to angry and happy prosodies, as opposed to neutral ones, occurring both early and later on post-onset.

Conclusion
Taken together with previous reports of modulated STN activity in response to visual stimuli, the present results appear to confirm that the STN is involved in emotion processing, irrespective of stimulus valence (positive or negative) and sensory modality (visual or auditory), suggesting that the STN’s role in emotion processing goes beyond a simple oculomotor effect.
LP20
High frequency stimulation of the Subthalamic Nucleus improves graft survival and functional outcome in a rat model of Parkinson’s disease

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Background

Current surgical treatment for Parkinson’s disease (PD) by neuromodulation of the subthalamic nucleus (STN) can temporarily improve motor symptoms. Alternative regenerative approaches are under research to restitute dopaminergic neurotransmission and offer a more extensive and long lasting repair. The aim of our project was to test whether the high frequency stimulation within the STN can act synergistically with dopaminergic grafts in reversing functional deficits.

Methods

Rats were rendered parkinsonian by unilateral injection of 6-OHDA into the right medial forebrain bundle (MFB). The MFB lesioned animals were assigned into two groups (STN-TX and TX-only). All animals were given striatal grafts of rat E14 ventral mesencephalic (VM) tissue into the ipsilateral striatum. Behavioral tests and post-mortem immunohistochemistry were performed.

Results

Survival of transplanted VM cells and functional recovery were observed in both transplanted groups, however the STN-TX group presented a significant increment in the number of grafted TH positive cells in comparison to the TX-only group (p=0.017). Other than that, the “STN Group” showed better outcome than the TX group in the Amphetamine-induced rotation test (p=0.047), in the Cylinder test (p=0.009), as well as in the Stepping test (p<0.01).

Conclusions

The read-outs as host re-innervation and behavioural recovery showed that dopaminergic grafts and DBS can act synergistically in the experimental model of PD. These findings suggest that cell therapy could be combined with STN neuromodulation. Further studies should be performed to confirm and extend these findings.
P311
The development of sensorimotor reflexes in albino mice; albino rats and black-hooded rats

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The present investigation aimed to show the differences in the development of sensorimotor reflexes and their relationship to the structural changes in spinal cord, cerebellum and cerebral cortex in three rodent species. The three species are albino rats (A-Rats), black-hooded rats (B-Rats) and albino mice. The development of selected reflexes was examined from day (D1) to D21. The structural changes were investigated at D7, D14, and D21. The following reflexes were analyzed: fore-limb/hind-limb grasp, surface body righting, fore-limb hopping, chin tactile placing, visual placing and body righting in the air. The developmental pattern of the reflexes was different in three rodent species. Although the black-hooded rats and albino rats belong to the same species, they are different in their appearance and developmental pattern. The development of external features and sensorimotor reflexes appeared earlier in mice than in A-Rats and B-Rats. At D7, differentiation of neurons was observed in the spinal cord while in cerebellum and cerebrum the neurons were found to be undifferentiated. At D14 and D21, the differentiated neurons were observed in spinal cord, cerebellum and cerebrum. Our data indicate that the developmental pattern of the reflexes in rodents may not be species specific but may be related to the animal strain.
P312
Cortical Relay Time in Assessment of Apraxia

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Introduction

Our goal is to investigate the use of cortical relay time (CRT) as a neurophysiological method in the assessment of the functional status of associative pathways passing from frontal lobe to parietal lobe in apraxia which is thought to be caused by the dysfunction of those pathways. For that purpose, we used idiopathic Parkinson's disease (PD) as a model as it is the most common degenerative movement disorder and the presence of ideomotor/ideational apraxia is known although it is not the most common cause of apraxia.

Subjects and methods

We analyzed F-responses, long latency reflexes (LLR) and somatosensorial and motor evoked potentials recorded over abductor pollicis brevis muscle in four different situations (rest, imagination of the movement, observation of the movement and active movement) in eight PD patients with apraxia, 11 PD patients without apraxia and age and sex matched eight healthy volunteers.

Results

None of the patients and healthy volunteers had LLR responses during rest, imagination of the movement and observation of movement. LLR II was determined in all participants during active movement, mean latencies of LLR II and CRT were found to be the shortest (53.3 ± 3.9 ms) in the control group and the longest (60.4 ± 4.2 ms) non-apraxia group (p=0.031).

Conclusions

LLR II responses and CRT did not distinguish healthy individuals and PD patients with apraxia. In the presence of normal MEP and SEP latencies, we think that prolongation of LLR II and cortical relay time in PD without apraxia reflects a deficit in PD probably other than dopaminergic deficit because we examined our cases under optimum dopaminergic treatment when they do not have PD symptoms. However, in PD apraxia functional magnetic resonance imaging studies also showed overactivity of default mode which may be the underlying factor of shortening of cortical relay time.
Abstracts of Poster Presentations – Poster Session 18 – Refex studies

P314
Excitability changes in spinal reciprocal inhibitory circuit induced by periodical sensory inputs
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Question
Our question is how sensory inputs from antagonist muscle influence the excitability changes in reciprocal Ia inhibitory circuit.

Methods
The degree of reciprocal Ia inhibition and the conditioning effects of transcranial magnetic stimulation (TMS) on the Soleus (Sol) H-reflex were examined in ten healthy subjects. The degree of reciprocal Ia inhibition was determined via short-latency (condition-test interval: 1, 2, 3ms) suppression of the Sol H-reflex by conditioning stimulation of common peroneal nerve (CPN). The TMS-conditioning effects on the Sol H-reflex was measured at short-latency condition-test intervals (-3, -2, -1, 0ms). Negative condition-test intervals indicate that the conditioning stimulus was applied after the test stimulation. The stimulus position for TMS was defined as the site where TMS consistently resulted in the largest Sol motor evoked potential. The periodical electrical stimulation was applied on CPN every 1sec (100Hz-5train) at motor threshold intensity of tibialis anterior muscle. The degree of reciprocal Ia inhibition and the TMS conditioned H-reflex amplitude were assessed before, immediately after, and 15 minutes after of the electrical stimulation.

Results
The degree of reciprocal Ia inhibition and the amplitude of the TMS-conditioned H-reflex around -1ms were increased by periodical sensory inputs from antagonist muscle, which were not concomitant with the change in Sol motoneuron excitability.

Conclusions
Our results indicated that Ia inhibitory interneurons are sensitive to periodical sensory inputs, because the change in the amplitude of the TMS-conditioned H-reflex was only observed in the specific condition-test interval which is assumed to be mediated by Ia inhibitory interneurons.
P315
INFLUENCE OF LIMB TEMPERATURE ON CUTANEOUS SILENT PERIODS

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OBJECTIVE

The cutaneous silent period (CSP) is a spinal inhibitory reflex mediated by A-delta fibers. The effect of limb temperature on CSPs has so far not been assessed.

METHODS

In 27 healthy volunteers (11 males; age 22 -58 years) we recorded median nerve motor and sensory action potentials, median nerve F-wave and CSPs induced by noxious digit II stimulation in thenar muscles in a baseline condition at room temperature, and after randomly submerging the forearm in 42°C warm or 15°C cold water for 20 minutes each.

RESULTS

In cold limbs, distal and proximal motor and sensory latencies as well as F-wave latencies were prolonged. Motor and sensory nerve conduction velocities were reduced. Compound motor and sensory nerve action potential amplitudes did not differ significantly from baseline. CSP onset and end latencies were more delayed than distal and proximal median nerve motor and sensory latencies, whereas CSP duration was not affected. In warm limbs, opposite but smaller changes were seen in nerve conduction studies and CSPs.

CONCLUSION

The observed CSP shift “en bloc” towards longer latencies without affecting CSP duration during limb cooling concurs with slower conduction velocity in large-diameter efferent and small-diameter afferent myelinated fibers. Correlation of small- to large-diameter fiber slowing reveals a similar sensitivity to temperature of both fiber types relative to their conduction at normal temperature, which, however, results in a differential delay in corresponding latencies.

SIGNIFICANCE

Limb temperature should be taken into account when testing CSPs in the clinical setting, as different limb temperatures affect CSP latencies more than large-diameter fiber conduction function.
P316
SYMPATHETIC AUTONOMIC INVOLVEMENT IN CLUSTER HEADACHE: IS IT A SYSTEMIC OR CRANIAL PHENOMENON?

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QUESTION

To investigate the extent of sympathetic autonomic involvement in cluster headache (CH) using face in contrast to extremity sympathetic skin responses (SSR) during attack and remission phases.

MATERIAL AND METHOD

Nineteen drug-free CH patients (16 male, 3 female) and 20 gender and age matched, healthy volunteers were included. SSR recordings of the forehead, hand and foot, and R-R interval variations (RRIV) were evaluated both in attack and remission phases.

RESULTS

Mean latency of face SSRs was longer and amplitude was lower on the symptomatic side compared to the asymptomatic side and controls (p=0.005, p=0.068); although SSR was obtained from both face and extremities during attack and remission periods, there were no differences in latency or amplitude of extremity SSRs compared to controls. Only three patients were determined to have orthostatic hypotension (OH) during attacks (16%), and none had OH in remission. No significant difference was determined for RRIV values during attack and remission in patients or controls. No significant association was identified between SSRs, RRIV, OH and duration of illness, average number of episodes per year, average duration of cluster periods in days, average number of attacks per day, pain duration.

CONCLUSION

SSRs recorded from the face are more sensitive than extremity recordings and RRIV in CH suggesting that sympathetic autonomic dysfunction in CH might mostly be limited to the cranial area.
THE EFFECT OF LEMON JUICE AND WATER ON OROPHARYNGEAL SWALLOWING AND THE GUSTATO-FACIAL REFLEXES IN HEALTHY ADULT SUBJECTS

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2Invited researcher, Neurology, Izmir, Turkey

Question

It is well known that the sour taste can improve the oropharyngeal dysphagia. However, the effect of increasing volumes of lemon juice and water on oropharyngeal dysphagia and gustato-facial reflexes has not been evaluated yet.

Method

Twenty-one healthy adult subjects were investigated in our study. Respiratory signals, submental, orbicularis oculi (OC) and orbicularis oris (OR) muscles EMG activities were recorded simultaneously during swallowing of 5, 10, 15 and 20 ml lemon juice and water. Recordings were made consecutively during 60 seconds. The synchronization of OR and OC muscles was evaluated.

Results

Increased of volumes of both lemon juice and water lead to increase of frequency and duration of swallows and duration of submental muscle EMG activities. Effects of pure lemon juice were more prominent than water (p<0.05). Synchronization of OR and OC muscles during swallows was proportional to increase of volume. There was no difference between lemon juice and water concerning the effects of volume increase.

Conclusions

The sour taste significantly facilitates the swallowing when compared to water. The increase of the volume may cause the rise of the gustato-facial reflexes during the water and lemon juice.
Abstracts of Poster Presentations – Poster Session 18 – Reflex studies

P318
The Effect of Cold on Trigeminal Conduction System

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Question

Trigeminal nerve can be studied electrophysiologically by trigemino-trigeminal reflex methods such as masseter inhibitory reflex; somatosensorial evoked potentials (SEP) and motor evoked potentials (MEP). Nerve cooling is a well known technique used to investigate whether or not the short and medium latency components of the stretch reflex are mediated by the same muscle spindle afferents. The aim of this study is to study the effects of cooling of masseter muscle onto the trigemino-trigeminal reflex pathway in normal subjects and display which kinds of muscle afferents are responsible for this reflex circuit.

Methods

12 healthy subjects (7 females and 5 males, aged 25-44 years) were included in the study. Electrical masseter inhibitory reflex (MIR), jaw tendon reflex (JTR), trigeminal SEP and trigeminal MEP were studied. After cooling the masseter muscle to 18 °C by applying cold pack over mouth mucosa inside and outside, the same studies were repeated. Pre- and post-cooling values of latency and amplitudes of the responses and the latency and duration of the silent periods together with suppression percentages were compared.

Results

The latencies of silent periods were longer and durations shorter on the cold side. Silent periods were absent in 4 subjects. Increase in the amplitude of reflex responses was recorded. Trigeminal MEP studies also revealed that silent period latencies were longer and durations were shorter on the cold side. Post-cooling N1, P1, N2, P2 wave latencies were slightly longer but showed no statistically difference.

Conclusions

Post-cooling changes in the responses of reflex and silent period studies of masseter muscle in our study validate the preceding ones reported in the literature proposing that group I afferent fibres mediate the short-latency responses and group II afferents mediate the long-latency responses in the stretch reflex studies carried out by cooling the extremity.
P319
Auditory Startle Response In Patients With Epilepsy

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¹cerrahpasa, cerrahpasa medicine faculty, Istanbul, Turkey

Purpose

The auditory startle response (ASR) is a generalized motor response caused by sudden, loud acoustic stimulus mediated by brainstem. To date no study has investigated ASR characteristics in patients with epilepsy (PWE).

Subjects and Methods

Total of 53 patients with epilepsy were investigated, (30 males and 23 females; age:31.08±11.42). Twenty patients were idiopathic generalized epilepsy (IGE) and 33 patients were partial epilepsy (PE). Thirty one healthy volunteers served as controls (CS, 11 males, 20 females; age:36.52±15.47). ASRs were elicited by binaural high-intensity auditory stimuli. Reflex electromyographic (EMG) activity was recorded simultaneously with surface electrodes left sides from orbicularis oculi (O.oc), masseter, sternocleidomastoid (SCM), biceps brachii (BB) and tibialis anterior (TA) muscles.

Results

ASR probability was higher and latencies of O.oc muscle was shorter in controls than PWE (%26.3±8.22 versus %21.99±8.67 and 36.1±7.68ms. versus 39.12±13.6ms. respectively), but there were no significant difference between IGE and PE groups and mono or polytherapy groups.

Discussion

Reduced ASR in PWE may reflect defective function of pontomedullar reticular nuclei in PWE, or suppressive effect of antiepileptic drugs on this region.

Keywords

Auditory startle response, epilepsy
Neurophysiological assessment of C7 radiculopathy using reflex tests.

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**Question**

Reflex tests are important electrophysiological tools to assess proximal segments of peripheral nerves. Among the methods available, two of them stand out: the H reflex (HR) and T reflex (TR). These techniques are useful and have clinical applicability in the detection of radiculopathies. The aim of this study was to compare these techniques, to correlate them with EMG abnormalities and to determine their reliability and sensitivity in the evaluation of C7 radiculopathy.

**Methods**

Twenty one patients with diagnosis of unilateral C7 radiculopathy were evaluated. All patients had some degree of radicular compression on magnetic resonance imaging studies. A second group consisting of 25 health adults, was also evaluated. Nerve conduction studies and electromyography were performed in both groups. HR on the flexor carpi radialis muscle was performed stimulating the median nerve at the elbow using bipolar surface electrodes, whereas TR from triceps muscle was obtained using an electronic reflex hammer. The abnormality criteria used was a difference of 2 msec between the sides and the presence or absence of responses. Amplitudes were not considered because of their great variability. To avoid the habituation phenomenon, nerve or tendon was stimulated at intervals of 3 seconds. The presence of fibrillation potentials and chronic neurogenic changes (increased duration and amplitude and poliphasic potentials) were considered as EMG abnormalities.

**Results**

TR could be elicited in all subjects. The use of facilitation techniques (FT), as mild voluntary contraction to prime the motor neuron pool for reflex activation, was necessary in 40% of all subjects to obtain the HR. The mean latency for TR and HR were 11,31 ±0,40 ms and 16,69±0,37 ms respectively. The TR was abnormal in 14 patients (five patients with prolonged latencies and nine with absent responses - sensitivity 66,7%) while HR was abnormal in 11 patients (two patients with prolonged latencies and nine with absent responses - sensitivity 52,7%). EMG abnormalities were found in all cases with a major predominance of them in the triceps muscle when compared to the flexor carpi radialis muscle.

**Conclusion**

Both methods proved to be useful in assessing C7 radiculopathy, but TR showed to be more sensitive than HR for its detection. This increased sensitivity could be directly related to a greater amount of fiber nerves from C7 nerve root serving the triceps muscle. TR could easily be performed, did not require FT, and consequently revealed a greater technical practicality.
Objective

We aimed to establish the utility of long latency reflexes (LLR) examination and area measurements of corpus callosum (CC) in the diagnosis of Multiple Sclerosis (MS) and in the determination of irreversible disability caused by axonal degeneration.

Patients and methods

This study was performed with 23 MS patients who had the diagnosis of ‘definite MS’ according to Poser and McDonald’s diagnostic criteria and a control group including 15 healthy individuals, at the Neurology Clinic of Şişli Etfal Education and Research Hospital, prospectively. Neurologic examination of the control group and MS patients were done and EDSS scores of the patients were estimated. For all the individuals, LLR examination and callosal area measurements were performed.

Results

In the MS group, LLR latencies were longer than that of the control group and corpus callosum areas were smaller in MS patients when compared with healthy individuals. In the MS group, we found a significant correlation between Expanded Disability Status Scale (EDSS) and CC area. Although there was no significant correlation between LLR and callosal area measurements in the MS group (p=0.38), the normal and abnormal CC area measurements corresponded in 15 patients with normal and abnormal LLR parameters.

Conclusion

Only the patients with mild deficits were included in this study and nearly half of the patients had normal LLR tests and corpus callosum area measurements, so the probability of finding significant correlation between them was thought to be low. However, our findings suggested that LLR examination could be included in the evaluation of irreversible disability in MS patients. Both the LLR examination and CC area measurements may be used together or alone in the diagnosis of MS and in the estimation of irreversible disability as safe and easy tests.
Abstracts of Poster Presentations – Poster Session 18 – Refex studies

P322
Vestibular ocular reflex dynamics with head-impulses in hereditary cerebellar ataxias

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Question
The vestibular ocular reflex (VOR) dynamic changes occurring with head impulses are poorly understood. VOR function can now be non-invasively and easily assessed with the video head-impulse test (vHIT), allowing the quantification of VOR dynamic parameters and the characterization of quick eye movements (QEM) triggered during and/or after the impulses. Our aim was to determine if the involvement of central vestibular pathways caused differential disturbances in VOR dynamic changes during vHIT, which could contribute not only to the differential diagnosis of patients but also to the understanding of VOR control mechanisms.

Objective and Methods
We explored patients diagnosed with spinocerebellar ataxia (SCA) type 3 (n=15), type 1 (n=4) and type 2 (n=4), Friedreich’s ataxia (FA) (n=9) and healthy controls (n=40). We calculated the regression (VOR₉₀) and instantaneous VOR gain at 40, 60 and 80 ms (VOR₄₀, VOR₆₀ and VOR₈₀) and determined the latency, peak-velocity and occurrence rate of the QEM triggered during (covert saccades) and after (overt saccades) the head-impulse.

Results
VOR₉₀, VOR₄₀ and VOR₆₀ were significantly lower in FA and SCA3 in comparison to SCA2 and controls (p<0.01 for all comparisons). Only SCA3 VOR₈₀ was significantly lower then controls (p<0.01), as VOR instantaneous gain increased from 40 to 80 ms in FA in comparison to controls (p=0.01). Covert saccades were only triggered in SCA3 but with low occurrence rate and peak velocity (11.1±28.5; 77.50±15.30°/s). On the contrary, overt saccades were present in all groups, with significantly higher occurrence rate in SCA3 then controls (p=0.001).

Conclusions
Our findings suggest that vHIT is a suitable clinical device for VOR evaluation in ataxic patients. Although the presence of diffuse cerebellar and extracerebellar lesions limit specific anatomical correlations, the combination of bilateral VOR dissociated lesions, the absence of covert saccades and/or the lack of vestibular dynamic control are suggested as centrality signs that could be used for topodiagnosis.
Abstracts of Poster Presentations – Poster Session 18 – Refex studies

P323
Anticompensatory quick eye movements after head impulses: a peripheral vestibular sign in spontaneous nystagmus.

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²German Center for Vertigo and Balance Disorders, Department of Neurology, Munich University Hospital, Germany, Germany
³Hospital Clínic, Neurology Department, Universitat de Barcelona, Spain
⁴Brandenburg University of Technology, Cottbus-Senftenberg, Germany
⁵Hospital Clínic, EMG and Motor Control Unit, Universitat de Barcelona, Portugal
⁶Institute for Clinical Neurosciences, Munich University Hospital, Germany

Question

Differentiating central from peripheral origins of spontaneous nystagmus (SN) is challenging. Looking for a simple sign of peripheral disease with the video Head Impulsive Test we noticed anti-compensatory eye movements (AQEM) in patients with peripheral etiologies of spontaneous nystagmus (SN). Here we assess the diagnostic accuracy of AQEM in differentiating peripheral from central vestibular disorders.

Methods

We recorded the eye movements in response to horizontal head impulses in a group of 43 consecutive patients with acute vestibular syndrome (12 with central, 31 with peripheral disorders), 5 patients after acute vestibular neurctomy (positive controls) and 39 healthy subjects (negative controls). AQEM were defined as quick eye movements (peak velocity above 50°/s) in the direction of the head movement.

Results

All patients with peripheral disorders and positive controls had AQEM (latency 231±53ms, amplitude 3.4±1.4°, velocity 166±55°/s) when their head was moved to the opposite side of the lesion. Central patients did not have AQEM. AQEM occurrence rate was higher in peripheral patients with contralesional (74±4%, mean±SD) in comparison to ipsilesional (1±4%) impulses (p<0.001). Overall diagnostic accuracy for differentiating central from peripheral patients was 96% (95% CI for AUC ROC curve: 0.90 to 1.0) for VOR gain and 100% (95% CI: 1.0 to 1.0) for AQEM occurrence rate.

Conclusions

These results suggest that AQEM are a sign of vestibular imbalance in a peripheral deficit. In addition to VOR gain they should be added to the evaluation of the head impulse test.
P324
CNE STUDY OF H REFLEX TOPOGRAPHY IN HUMAN CALF MUSCLES DISCLOSES A DYNAMIC FIELD OF MOTOR UNIT POTENTIALS (MUPs) IN HEALTH AND DISEASE

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The physical examination of tendon reflexes and muscle tone still stands as the principal method to address αMN excitability in clinical practice. Hmax/Mmax assessment using surface electrode, despite many adjustments did not provide a sensitive individual reference. Concentric needle electrode (CNE) offers a superior view of MUPs, however, early notes on Hmax variability in gastrocnemius-soleus (GM-SOL) probably precluded its clinical use without a thorough study of the cause.

We used CNE for Hmax assessment in selected calf muscles and muscle layers in prone resting subjects. Presented are the results of 86 control subjects and 95 patients with segmental afferent or UMN lesions. Starting with Hmax in SOL, CNE was set in the medial or lateral GM at defined recording depth, Mmax range and sharp Hmax or Mmax configuration. The tibial nerve stimulation (0.1-0.2 Hz, 1ms) using hand held bipolar electrode was kept at the lateral popliteal position. Hmax amplitude was taken from the highest of 3-5 approximates in the recruitment series.

In control subjects, Hmax and Mmax in SOL range respectively 6.5-35 mV (µ 17.34; SD 6.63) and 17-43 mV (µ 30.98; SD 6.38). The dispersion of Hmax/Mmax values inside SOL (µ 0.58; SD 0.14) seems unrelated to the recording depth (Fig 1). On the contrary, medial or lateral GM show lower or no Hmax that independently of Mmax, increase with the deeper recordings up to SOL values (Fig 2). The patients with S1 radiculopathy or polyneuropathy show in SOL lower Hmax, transient H/F, or no low threshold late potential, in correlation with clinical TSR. The patients with UMN lesion or physically trained subjects exhibit significantly higher Hmax/Mmax and/or Hmax, distinctively in GM surface layer.

In conclusion, as the main source of calf Hmax variability, CNE records uncovered a gradient like changes, from GM surface layer minimum to the SOL maximum. The lower range of Hmax values exhibit a little relation to Mmax. Relative to the extent of reflex MU recruitment, Hmax records probably reflect the density of active muscle fibers. Based on heteronymous SOL to GM facilitation, Hmax spectrum could represent a parcel of dynamic MUPs field monitoring αMN excitability changes in health and disease.

figure 1
Abstracts of Poster Presentations – Poster Session 18 – Refex studies

Figure 2

H recruitment curves relative to the recording depth in SOL

H recruitment curves relative to the recording depth in GM
Effectiveness of different treatment modalities on spasticity management of spinal cord injury: An H-reflex study

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2Mutah College of Medicine, Physiology, Al-Karak, Iraq

**Objective**

To evaluate the effectiveness of oral antispasticity drugs, Transcutaneous electrical nerve stimulation (TENS) and physical therapy alone on management of spinal cord injury (SCI) spasticity by using the H-reflex.

**Methodology**

This study was performed on 107 cases with traumatic spinal cord injury suffering from spasticity. They were 88 male and 19 female ten with an age range from 18-73 years and a mean ± SD = 33.96 ± 11.12 years. In addition we include a Positive controls, and a Negative control group. The positive control group includes 12 male who were not taking any type of treatment or performing a regular previous physical exercise program. While the Negative control group includes 31 normal volunteers. They were 30 male & 1 female with an age range from 21-66 years and a mean ± SD = 38.96 ± 13.24 years. All of them were able to follow instructions and had no history of any disabling diseases.

Spasticity of these patients was evaluated electrophysiologically by H-reflex including H latency, H duration, H-reflex conduction velocity and H max/M max ratio in addition to the F wave latency.

**The Patients groups:**

- **Group (I):** included 31 patients who were subjected a regular physical therapy program which was performed as 1 session/ daily for about one month, without any other type of treatment.

- **Group (II):** included 30 patients who were taking oral anti-spasticity drugs in the form of Baclofen and performed physical therapy program.

- **Group (III):** included 33 patients who were subjected to TENS therapy applied to spastic lower limbs once before the examination lasting for 10 minutes and performed the same previous physical therapy program.

- **Group (IV):** included 13 patients who were taking oral anti-spasticity drugs in the form of Tizanidine and were subjected to the same previous physical therapy program.

**Results:** There was a highly significant difference (p

The F wave and other H-reflex parameters showed no significant statistical difference among all the groups.

**Conclusion**

Spasticity can be effectively treated but a multidisciplinary approach. The study showed that combination of more than one method of treatment is required since they showed a better response than single type of treatment in most of the patients. The best combination of treatment was found to be Physiotherapy and central muscle relaxant drugs. No clear difference was found between the response of the two muscle relaxant drugs used (Baclofen, Tizanidine).
Table (1). Showing the H & M latency, H duration, HCV and F wave latency in patients and controls with their P value.

<table>
<thead>
<tr>
<th></th>
<th>H latency</th>
<th>M latency</th>
<th>H duration</th>
<th>HCV</th>
<th>F wave latency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Patients</td>
<td>32.62±1.35</td>
<td>6.39±0.35</td>
<td>15.02±1.17</td>
<td>52.48±2</td>
<td>38.45±2.73</td>
</tr>
<tr>
<td>N=107</td>
<td>59</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>32.19±1.63</td>
<td>6.25±0.42</td>
<td>15.73±2.32</td>
<td>53.04±1.84</td>
<td>39.76±2.73</td>
</tr>
<tr>
<td>N=31</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table (2) shows highly significant improvement in the H/M ratio when comparing the positive controls to the other groups while the H/M ratio in the negative controls shows no significant difference with group II and group IV and a significant difference with the other groups.

<table>
<thead>
<tr>
<th>The parameter</th>
<th>+ve versus −ve control</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>H/M ratio</td>
<td>Mean±SD</td>
<td>+ve control</td>
<td>−ve control</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group III</td>
<td>Group III</td>
</tr>
<tr>
<td>Mean±SD</td>
<td></td>
<td>72.94±11.92</td>
<td>35.54±13.82</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
MuSK antibody positive Myasthenia Gravis in association with Waldenstrom`s Macroglobulinemia. A case report.

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Question

To report a unique, to our knowledgment, case of Musk-antibody positive myasthenia gravis (MG) in association with Waldenstrom`s macroglobulinemia (WM).

Methods / Results

A 49-year-old man presented in January 2006 with a 15 days history of fluctuating diplopia that worsened at the end of the day. Examination shown limited left eye abduction without other motor symptoms. Neurological and ophthalmologic exploration were, otherwise, normal. Tensilon test was weakly positive. Nerve conduction studies and repetitive nerve stimulation test (RNST) of a limb muscle (ADQ) were normal. Single fiber EMG on orbicularis oculi revealed slightly increased MCD whithout blocking. Laboratory testing revealed hyperproteinemia and quantification of immunoglobulin disclosed IgM of 26,4 g/l (&lt;2,58). Antibody determination was: Anti-AChR: 0,21 nmol/l (&lt;0,5)) and anti-MuSK antibodies: 0,4 nmol/l (&lt;0,05). Bone marrow biopsy showed clusters of mature lymphoid cells with immunohistochemical staining positive for CD20. WM and MG were diagnosed and treatment with pyridostigmine and corticosteroids was prescribed. Two months later, the patient developed severe generalized weakness and required mechanical ventilation. At that time, RNST was abnormal in ADQ. Treatment of WM with Rituximab dramatically improved symptoms and led to a progressive and sustained decrease of IgM and anti-MuSK titres. Six years later, patient remains stable without treatment.

Discussion

Neurophysiological features studies allowed to rule out a peripheral neuropathy, played a role the diagnosis of MG and, more on, its features correlated with clinical status. Response to rituximab could throw additional light on the role of B cells as therapeutic targets in anti-MuSK positive MG.
The development of sensorimotor reflexes in albino mice; albino rats and black-hooded rats

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2Beni-Suef University, zoology, Beni-suef, Egypt

The present investigation aimed to show the differences in the development of sensorimotor reflexes and their relationship to the structural changes in spinal cord, cerebellum and cerebral cortex in three rodent species. The three species are albino rats (A-Rats), black-hooded rats (B-Rats) and albino mice. The development of selected reflexes was examined from day (D1) to D21. The structural changes were investigated at D7, D14, and D21. The following reflexes were analyzed: fore-limb/hind-limb grasp, surface body righting, fore-limb hopping, chin tactile placing, visual placing and body righting in the air. The developmental pattern of the reflexes was different in three rodent species. Although the black-hooded rats and albino rats belong to the same species, they are different in their appearance and developmental pattern. The development of external features and sensorimotor reflexes appeared earlier in mice than in A-Rats and B-Rats. At D7, differentiation of neurons was observed in the spinal cord while in cerebellum and cerebrum the neurons were found to be undifferentiated. At D14 and D21, the differentiated neurons were observed in spinal cord, cerebellum and cerebrum. Our data indicate that the developmental pattern of the reflexes in rodents may not be species specific but may be related to the animal strain.
Abstracts of Poster Presentations – Poster Session 18 – Reflex studies

LP22
The use of blink reflex study in determining the clinical recovery and quality of life in Bell’s palsy patient.

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2Ministry of Health, Medical Department, Kuala Lumpur, Malaysia

Question

Acute facial nerve palsy causes inability to control facial muscles of expression on the affected side. We conducted this study to determine the clinical recovery and neurophysiological outcome in patients with acute lower motor neuron facial nerve palsy and the effect on the quality of life of these patients.

Methods

We prospectively analyzed facial nerve conduction test and blink reflex in 21 patients attended the Neurology clinic UKM Medical Centre, who were having facial nerve palsy up to 10 days of the onset and compare them with House-Brackmann scale, visual analogue and Facial Clinimetric Evaluation (FaCE) score. The correlation between neurophysiological studies, clinical recovery and quality of life were evaluated at presentation up to 10 days (baseline), 1 month and 3 months. We used prednisolone 25mg twice daily without acyclovir as the standard form of treatment for our patients. [1]

Results

This study demonstrated a significant improvement in House-Brackmann Scale, visual analogue score as well as total FaCE score over 3 months (Table 1). There was significant difference between severity of axonal degeneration and ipsilateral R1 and R2 components of blink reflex at 3 months (p=0.005, p=0.05 respectively) Table 2. Significant differences were observed in the total FaCE score in most of the components of the blink reflex at baseline, 1 month but not at 3 months. The clinical outcome and quality of life was statistically significant.

Conclusions

This study showed the blink reflex can determine the clinical outcome and quality of life in patients with acute lower motor neuron facial nerve palsy. The neurophysiological studies can provide quantitative information regarding the extent of axonal degeneration as well as nerve latency to predict clinical outcome and recovery as well as long term prognosis.

![Figure 1](image-url)
### Table 2: Comparison between axonal degeneration and blink reflex at 1 month and 3 months

<table>
<thead>
<tr>
<th>Blink Reflex</th>
<th>1 month Visit 2</th>
<th>p value</th>
<th>3 months Visit 3</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50% degeneration n=15</td>
<td>&gt;50% degeneration n=6</td>
<td>&lt;50% degeneration n=12</td>
<td>&gt;50% degeneration n=4</td>
</tr>
<tr>
<td>Ipsi R1</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt; 13.1 ms</td>
<td>12 (57.1%)</td>
<td>4 (19.0%)</td>
<td>0.998</td>
<td>12 (75.0%)</td>
</tr>
<tr>
<td>&gt; 13.1 ms/absent</td>
<td>3 (14.3%)</td>
<td>2 (9.5%)</td>
<td>0.014</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Ipsi R2</td>
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<tr>
<td>&lt; 41.0 ms</td>
<td>9 (42.8%)</td>
<td>1 (4.8%)</td>
<td>0.014</td>
<td>12 (75.0%)</td>
</tr>
<tr>
<td>&gt; 41.0 ms/absent</td>
<td>6 (28.6%)</td>
<td>5 (23.8%)</td>
<td>0 (0.0%)</td>
<td>2 (12.5%)</td>
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<tr>
<td>Contra R2</td>
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<tr>
<td>&lt; 43.0 ms</td>
<td>14 (66.7%)</td>
<td>6 (28.6%)</td>
<td>1.000</td>
<td>10 (62.5%)</td>
</tr>
<tr>
<td>&gt; 43.0 ms</td>
<td>1 (4.8%)</td>
<td>0 (0.0%)</td>
<td>2 (12.5%)</td>
<td>0 (0.0%)</td>
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P327
The disturbance of the relations between temporal parameters of early and late evoked potentials components in schizophrenic patients

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The aim of this work is to investigate the relations between the latencies of early and late ERPs components during the process of passive perception of verbal stimuli with different significance (words/non words) in the norm and schizophrenia.

Methods and participants

60 patients with schizophrenia with the predominance of positive symptoms and 58 healthy subjects were presented with 80 words and 80 non words consisting of 5-6 letters on the monitor screen in random order. EEG from 19 derivations was obtained with the amplifier “Neuroscan Synamps”. The latency of components P100, N170, P200 and P300 was studied.

Results

It was revealed that the latency of early ERPs components P100 and N170 was shorter in the group of patients than in the control group. That means that sensory analysis of words in norm was more complete than in patients. In the latters the sensory processing was deficient resulting in the difficulties for recognition and categorization of these stimuli.

The negative correlations observed in the norm between the latencies of the early components- P100 and N170 from the one side, and the late components - P200 and P300 from the other side point to the opposite relations between the latencies of early and late components. In patients these correlations are only positive.

Conclusion

Deficient sensory analysis observed in schizophrenic patients creates the difficulties for recognition and categorization of the stimuli at the later stages of their processing.
P328
Spectral composition of wake EEG and cognitive functions in patients with schizophrenia

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Question

MATRICS Consensus Cognitive Battery (MCCB) is a contemporary standard for assessment of cognitive functions in patients with schizophrenia. Seven cognitive domains (speed of processing, attention and vigilance, working memory, verbal and visual learning, reasoning and problem solving, social cognition) may be assessed with ten tests which are included in MCCB. The aim of this study was to assess the association between resting EEG spectra values and MCCB results in patients with schizophrenia.

Methods

39 patients (12 females, mean age 28.2 +/- 5.2) diagnosed with schizophrenia according to the ICD10 criteria were assessed with standard 19-channel EEG. The patients were treated in monotherapy with second generation antipsychotics (n=23), perphenazine (n=1) or a combination of two antipsychotics (n=15). Patients underwent assessment with the MCCB within 9±6.3 days following the EEG recording. Participants were divided into four groups according to their overall MCCB score. Power spectra for each electrode were extracted from EEG recording with EEGLAB toolbox. Mean power values in eight frequency ranges (delta to beta3) were compared between the group of patients characterized by the superior cognitive functioning (quartile with best MCCB scores) and the group of most cognitively deteriorated patients (quartile with worst MCCB scores).

Results

Significant differences between the groups were observed for delta and theta band activity recorded mainly from the frontal and frontotemporal electrodes.

Conclusions

Superior cognitive functioning is associated with less frontal and frontotemporal slow-waves in EEG recording in patients with schizophrenia.
P329
Functional connectivity of predictive coding in schizophrenia

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2University College London, Institute of Neurology, London, United Kingdom
3Technion, Faculty of Medicine, Haifa, Israel
4University of A Coruna, Physical Education, La Coruna, Spain

Question

We tested the hypothesis that patients with schizophrenia have a deficit in selectively attending to predictable events.

Methods

We used dynamic causal modelling (DCM) of electrophysiological responses - to predictable and unpredictable visual targets - to quantify the effective connectivity within and between cortical sources in the visual hierarchy in 25 schizophrenia patients and 25 age-matched controls.

Results

Bayesian model comparison showed that there were profound differences in the strength of extrinsic backward connections, from higher hierarchical levels to lower levels, when comparing schizophrenic and control subjects. In addition controls exhibited significant differences between recurrent inhibitory connections during the processing of predictable and unpredictable stimuli, which were markedly attenuated in schizophrenia patients.

Conclusions

The findings suggest that the pathology in schizophrenia involves an aberrant encoding of precision in terms of the excitability of superficial pyramidal cells reporting prediction error. In addition, schizophrenia patients are impaired in their ability to modulate the sensitivity of neurons responsible for passing sensory information (prediction errors) up the visual cortical hierarchy.
Visual mismatch magnetic responses to a windmill pattern stimulus in schizophrenia: an MEG study


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Background

Schizophrenia is one of major neuropsychiatric disorders and shows cognitive or attention deficits. Auditory mismatch negativity (aMMN), one of well-known event-related potentials (ERPs), is a predictive error signal and considered to be a candidate biomarker of schizophrenia. Though there have been quite few studies on visual counterpart of aMMN (vMMN) in schizophrenia, it was smaller than that in healthy control (NC) in our previous study. The aim of this study was to investigate magnetic fields for vMMN (vMMF) in schizophrenia by using 306-ch whole head MEG because it has higher spatial resolution than that of EEG equipment.

Method

Subjects consisted of 10 long-term schizophrenics (ChS), 6 first episode schizophrenics (FES) and 14 NCs. They were instructed to look at the screen in front of them while listening to a story via earphones. Two round windmill patterns and one white circle stimulus were randomly presented with probability 8:1:1. The two windmill pattern stimuli were adopted as standard or deviant stimuli and white circle was a target stimulus (Figure 1). Brain magnetic fields were recorded throughout the experiment. Evoked response was averaged by each stimulus, and vMMF was observed by subtracting the responses from the deviant stimuli to those from standards.

Result

Behavioral performance (i.e. accuracy of tracking context of story, correctness and reaction time for target detection) in the both patient groups was worse than that of NC. vMMF was observed during the period between 100 and 200 ms from stimulus onset in all participants. vMMF in ChS group was smaller than that of FES or NC group.

Conclusion

MEG is preferable than EEG to elucidate event-related neural activities in schizophrenia and vMMF can be a potential biomarker of schizophrenia.
Neurophysiological markers of multisensory processing in schizophrenia

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**Question**

Synchronized oscillations are important for successful neuronal communication during multisensory processing. Behavioral studies have suggested abnormal multisensory integration in individuals with schizophrenia. Moreover, neurophysiologic studies showed impaired neuronal communication during the processing of unisensory stimuli. Here, we addressed whether altered oscillatory activity, measured by the EEG, contributes to impaired multisensory processing in schizophrenia. We examined oscillatory activity during the sound induced flash illusion (SIFI) in patients with schizophrenia and a non-psychiatric control group. The SIFI is an effective audiovisual paradigm, whereby multiple auditory stimuli presented alongside a single visual stimulus can induce the illusory percept of multiple visual stimuli.

**Methods**

The psychopathology of the patient group was assessed by using the Positive and Negative Syndrome Scale (PANSS). Cognitive capabilities were measured using the Brief Assessment of Cognition in Schizophrenia (BACS). EEG was monitored using a high-density setup with 128 electrodes. The focus of EEG analysis was on the comparison of oscillatory activity in response to illusory compared to non-illusory trials.

**Results**

We expected differences in multisensory perception between the two groups. These differences should be paralleled by modulation of oscillatory activity, which is presumably source-localized to primary sensory and higher-order cortical areas. Our preliminary data indicate an enhanced illusion rate in patients, compared to the control group. This enhanced illusion rate tended to be accompanied by deviances in oscillatory activity. Further results on the relationship between the psychopathology and severity of cognitive deficits and the behavioral and neurophysiologic findings in the SIFI study are presented.

**Conclusions**

We propose that the study of multisensory integration is a promising new approach to further our understanding of neurophysiological mechanisms underlying the psychopathology and cognitive deficits obtained in schizophrenia.
P332
Dysfunctional hippocampal novelty processing correlates with orbitofrontal salience response in acute psychosis

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2Charité Universitätsmedizin Berlin, Berlin, Germany
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4Otto von Guericke University, Magdeburg, Germany

Patients with psychotic states commonly attribute abnormal salience to novel, but otherwise unimportant events. Here, we aimed to assess potential neural mechanism underlying this phenomenon, using functional magnetic resonance imaging (fMRI) in 16 unmedicated patients with paranoid schizophrenia and 20 age-matched healthy controls. All patients experienced positive symptoms at time of participation. Participants performed a visual target detection task with complex scene stimuli in which novel and familiar rare stimuli were presented randomly intermixed with a standard and a target picture. Presentation of novel relative to familiar images elicited hippocampal activation in both patients and healthy controls, but novelty-related hippocampal activation correlated with 24-hour delayed recognition memory performance in controls only. Patients, but not controls, showed a robust neural response in the orbitofrontal cortex (OFC) during presentation of novel stimuli that was positively correlated with hippocampal activation, but not indicative of a behavioral performance advantage. Functional connectivity analysis in the patients further revealed a novelty-related increase of functional coupling between the OFC and the insula and, to a lesser extent, also the ventral striatum. Our results suggest that in patients with acute psychosis, hippocampal novelty processing is inefficient with respect to long-term memory encoding, but instead engenders atypical activation of brain structures that have previously been linked to salience processing.
Cerebral oxygenated hemoglobin changes using Shiritori tasks in patients with schizophrenia

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\(^2\)Kurume University, Cognitive and Molecular Research Institute of Brain Diseases, Kurume-City, Japan

**Objective**

We performed near-infrared spectroscopy (NIRS) during shiritori tasks. Shiritori is a very popular Japanese language game, involving saying a word that begins with the last character of the preceding word. In this study, we used two kinds of shiritori task (standard, creature category) and investigated the characteristics of patients with schizophrenia in comparison with healthy subjects.

**Methods**

The subjects consisted of 24 outpatients with schizophrenia (30.4 ± 5.6 years) and 24 age-matched healthy controls (31.6 ± 7.4 years). Oxy-Hb changes were measured during the tasks using 44-channel NIRS machine (ETG-4000; Hitachi, Tokyo). All subjects were instructed to perform two conditions (standard, creature category). They were asked to immediately say a word starting with the last character of the written Japanese word shown in front of them, and this procedure was repeated 20 times. During control condition, they repeated the vowels “A, I, U, E, O”. Grand mean waveforms of the 20 responses were produced and changes in oxygenated hemoglobin (oxy-Hb changes) from the control state were converted to numeric values every 100 ms. The approximated value of area, peak amplitude and latency after performance were determined as data. Left channel 11 and right channel 12 in midfrontal area, left channel 19 and right channel 22 in frontopolar area were selected as the regions of interest (ROIs) and oxy-Hb changes in the ROIs was evaluated. This study was performed with the approval of the Ethical Committee, Kurume University and informed consent obtained from all subjects after a written explanation of the contents of the examination.

**Results**

In ROIs, Patients showed decreased oxy-Hb changes compared with healthy subjects in both tasks. In addition, the peak amplitude was larger and latency was earlier in healthy subjects than those in patients during creature category shiritori task. There was significant correlation between the negative syndrome scales of the PANSS and oxy-Hb changes.

**Conclusion**

These results suggest the usefulness of NIRS using shiritori tasks for evaluating psychophysiological indices.
P334
EEG spectral power at rest and in mental arithmetic task performance in first episode of schizophrenia and schizoaffective disorder

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Background
Abnormal neural oscillations in schizophrenia and their relation to cognitive deficits have been broadly discussed in existing literature. Assuming clinical and diagnostic overlap between schizophrenia and schizoaffective disorder as well as distinct nosological characteristics, it remains unclear whether patients with schizoaffective disorder possess similar or different EEG abnormalities during cognitive processing.

Method
We analyzed EEG spectral power (SP) in the resting state and while performance of the arithmetical task (subsequent subtraction of 7 from 200) in 32 acute/subacute patients with first episode of schizophrenia (SCH, n=32), 32 patients with first episode of schizoaffective disorder (SAD, n=32) and healthy controls (HC, n=40). Behavioral parameters such as accuracy and counting speed were also evaluated.

Results
No difference was obtained in accuracy and counting speed in patients groups. Both SZ and SA patients were slower in counting in contrast to HC. As compared to healthy controls, in the rest conditions in SP was higher in theta and gamma bands and lower in alpha band in SCH group, while in SAD group SP was higher only in beta² band. Comparison of task performance with resting state in HC showed an increase of SP in theta and gamma bands in anterior midline sites. In SCH we observed a significant reduction of SP in theta, alpha and beta bands, whereas SAD group demonstrated a growing trend of SP in gamma band (Fig.1 and Fig.2).

Conclusions
Our findings indicate distinct neurophysiological mechanisms of cognitive task processing in schizophrenia and schizoaffective disorders and provide the basement for further research.

Figure1: Changes in theta SP in the rest condition and while performing a cognitive task
Figure2: Changes in gamma 2 SP in the rest condition and while performing a cognitive task

figure 1
figure 2
Hypothesis in short:

Schizophrenia and autism are two sides of the same coin. There exists in healthy as well as schizophrenic and autistic brains two major high level cognitive processes; namely the Thought Process and the Impulse Process. These two higher-level processes are functionally mapped onto two lower level neural circuits.

The thought process is responsible for reasoning about all the things one can reason about and the impulse process is responsible for impulse (the strong urge and desire to execute an action, whether sexual, anger rage, other miscellaneous actions). Both processes are not independent but affect each other mutually. You can feel impulsive on what you think about, e.g. sexual thoughts. Or you think of what you already feel an impulse on. It is assumed that in a healthy individual there is a healthy balance between the relative strengths of these higher level processes in the consciousness and so one can exert control over actions and also feel desire that keeps the person healthy, e.g. social behavior, romantic relationships, etc.

In schizophrenic patients a malfunction in the lower level circuits leads to a break down of the thought process and a surge of strength in the impulse process. Hence the psychosis, hallucinations, as well as strong impulse leading to the popular symptom 'someone else controlling me / my thoughts'. In autistic patients however, a different but similar malfunction leads to a surge of strength in the thought process but a break down in the impulse process. Hence the popular genius symptom of autistic patients a long with the lack of social impulse.

The hypothesized mechanism of this pathophysiology is that genetic expression in brain cells leads to certain neural circuits consuming excessively extra amounts of Ca²⁺ ions for conducting action potential intracellularly. This leads to decreased amounts of extracellular Ca²⁺ ions in the brain, and hence other neural circuits are not able to consume the Ca²⁺ they need for healthy conduction. Hence a surge of strength in some neural circuits due to excess intracellular Ca²⁺ ions while a break down in others due to deprivation of intracellular Ca²⁺ ions. In schizophrenia, the impulse neural circuit is responsible for excess consumption of Ca²⁺ and deprivation in other regions. While in autism the thought neural circuit is responsible for excess consumption of Ca²⁺ and deprivation in other regions.

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LP23
Association among extrastriatal dopamine D_2 receptor binding, idea fluency and depersonalization: A positron emission tomography study

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Question

Fluency tasks have been widely used to evaluate executive functions mainly implemented in the frontal lobes. Meanwhile, a recent PET study showed that divergent thinking, which was associated with fluency tasks, was related to dopamine D_2 receptor densities in the thalamus, but the role of D_2 in the frontal lobes remains unclear. In the current study, we were interested to understand how dopaminergic neurotransmission in the frontal lobes and thalamus were associated to fluency performance, in relation with a specific psychiatric symptom of depersonalization.

Methods

We performed PET studies on 24 healthy male subjects. Extrastriatal dopamine D_2 receptor bindings were measured by 60 min PET scans using \[^{[1]}\text{C}\]FLB457. For each PET scan, BP\textsubscript{ND} were calculated using SRTM using the cerebellum as a reference region. Outside the scanner, all participants performed ideational and word fluency tasks and 15 subjects fulfilled Cambridge Depersonalization Scale (CDS).

Results

Voxel-by-voxel analysis revealed that dopamine D_2 receptor binding potentials (D_2 BP\textsubscript{ND}) in the right prefrontal cortex were negatively correlated with performance of idea fluency task, but no region was found for word fluency. We conducted an additional ROI analysis for thalamus using thalamic connectivity atlas to investigate whether a specific thalamo-cortical connection played a role in idea fluency. Negative correlation between D_2 BP\textsubscript{ND} and idea fluency performance was found in the thalamic region that had projections onto prefrontal cortex. We further revealed performance of ideational fluency was positively correlated with CDS scores.

Conclusions

Tendency of depersonalization scale was related to idea fluency, which was associated with dopaminergic transmission in the prefrontal cortex and its anatomically connected region in the thalamus.
Impairment of neuromuscular transmission in Transient Global Amnesia- does it really exist?

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Background. The main hypotheses on transient global amnesia (TGA) mechanisms are ischemia in hippocampal structures, epileptic genesis and migraine. According to the hypothesis of the shared, common pathophysiological mechanism in both, TGA and migraine, the neuromuscular transmission (NMT) abnormalities, found previously in migraine, were also suspected in TGA. Objective The aim of our study was to analyze NMT in TGA patients to reveal the subclinical impairment of neuromuscular transmission, as a possible indicator of underlying chanellopathy, as in shared etiology with migraine. Material & Method. The group under study consisted of 15 patients (6 males) with TGA (mean age 69.5 years ± 7.4). The duration of amnesia differed from 1 to 6 hrs (mean 4.4 hrs). Single fibre electromyography (SFEMG), the most sensitive tool for NMT assessment, of the voluntarily activated frontal muscle was performed in 1 to 5 days after TGA incident. Results. Abnormal SFEMG was found in 1 patient (6.6%). SFEMG in all other patients was in normal range. Conclusion. Our neurophysiological study does not confirm the signs of neuromuscular transmission defects in TGA. The role of channelopathy with NMT dysfunction in pathogenesis of TGA is rather improbable, whereas in migraine subclinical NMT abnormalities were certainly proven.
Stimulated single fibre electromyography using concentric needle electrode in organophosphate insecticide poisoning in Sri Lanka

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Question

Could stimulated single fibre electromyography using concentric needle electrode be used to study the neuromuscular dysfunction in organophosphate insecticide poisoning?

Methods

A study was conducted at the neurophysiology unit of the Teaching Hospital, Peradeniya and Faculty of Medicine, University of Peradeniya, Sri Lanka. In 27 patients with self poisoning caused by organophosphate insecticides, within the first week of poisoning, stimulated single fibre electromyography was recorded from the orbicularis oculi muscle using concentric needle electrode after the facial nerve branch was stimulated using a monopolar needle electrode. Square wave pulse stimulation with 0.05 - 0.2 ms duration, 0.05 - 2 mA strength and 10 Hz frequency was used. Data were acquired with frequency filters with bandwidth of 1 to 10 kHz. A single fibre potential was identified with a sharp rise time of less than 200 us and an amplitude of more than 100 uV.

Results

There were 22 males and 5 females. Age range was from 17 to 80 years. Mean day of recording was 3.5. There was one patient who had complete blocking during the time of recording with the clinical suspicion of intermediate syndrome. Mean jitter for all the other patients was 30.3 us. Range was from 10.8 to 61.0 us. Nine patients showed jitter values exceeding the upper limit of normal reported in the literature.

Conclusions

Stimulated single fibre electromyography using concentric needle electrode is a useful technique to delineate the neuromuscular junction dysfunction seen during the first week in organophosphate insecticide poisoning.
INVESTIGATION OF NEUROMUSCULAR JUNCTION ABNORMALITIES IN MYOTONIC DYSTROPHY 1 BY SINGLE FIBRE AND DECREMENTAL STUDIES

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BACKGROUND

Myotonic Dystrophy type 1 is the most common Dystrophy in adult people. It has a broad spectrum of EMG manifestations like myotonic discharges, fibrillations, positive sharp waves, and myopathic pattern. It can also presents mild abnormalities on nerve conduction studies.

Some experimental studies have shown neuromuscular junction structural lesions, and few studies show a decremental response to high rate repetitive nerve stimulation, SF-jitter abnormalities haven't been investigated as far.

METHODS

The aim of this work is to investigate neuromuscular junction abnormalities in 10 patients affected by Myotonic Dystrophy 1 by single fibre-jitter study (jitter medium and abnormal pairs) and high repetitive stimulations studies (3 Hz, 10 Hz and 20 Hz).

RESULTS

A decrementing response occurred in 2 patients, only at a stimulation frequency of 20 Hz. The SF-jitter resulted abnormal in the all patients. There wasn’t concordance from neurophysiological abnormalities and the CTG expansion value.

CONCLUSIONS

A decrementing response doesn’t appear constant finding of Myotonic Dystrophy 1 patients. Abnormal muscular membrane excitability is disclosed only by high frequency stimulation in Myotonic Dystrophy 1 patient. The abnormalities revealed by SF-jitter could be related to neuromuscular junction structural lesions as shown by histochemical studies.
P339

NORMATIVE JITTER VALUES ON VOLUNTARY ACTIVATED PERIOCULAR MUSCLES WITH
CONVENTIONAL (37 MM) CONCENTRIC NEEDLE ELECTRODE

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2Private Nisa Hospital, Neurology, Istanbul, Turkey

Question

The aim of this study was to get normal values of jitter in 37 mm concentric needle electrode (CNE) regardings for voluntary activated periocular muscles.

Method

We retrospectively re-evaluated the recordings of 130 healthy subjects whose periocular muscles [m. Frontalis (n=119) and m. Orbicularis oculi (OOc) (n=19)] were investigated between the years of 2010 and 2013. There were 86 women and 44 men with a mean age of 43.6 ± 15.3 years (19-81). They had no symptom of any medical condition, they were free of any medication and their neurological examination was normal. A disposable CNE (37mm x 0.46 mm, 26G) was preferred for acquisition with 2 kHz low-cut filtering. The mean consecutive difference (MCD) was accepted as a jitter. Twenty jitters and the mean value of these were calculated from each muscle.

Results

Overall 2760 jitters were calculated from 138 muscles. The mean value of these jitters was 22.6 ± 10.3 μs. The calculated mean value of mean jitters was found 22.6 ± 3.8 μs. To determine the cut-off value, we looked for 18th highest out of 20 jitters of each muscle (n=138, %95 CI). Mean value of these 18th highest jitters was 31.44 ± 6.5 μs and cut-off limit was 45 μs.

Conclusion

Jitter values higher than 45 μs calculated from periocular muscles with 37 mm CNE with 2 kHz low-cut frequency filtering may suggest neuromuscular transmission disorder and further investigation should be performed.
P340

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²Antwerp University Hospital, Department of Medical Statistics, Edegem, Belgium

Question

single fiber EMG (SFEMG) is preferentially done with a reusable single fiber needle electrode (SFN), but for practical reasons, a single use concentric needle EMG-electrode (CN) is often used. Limited reference values are available for CN-SFEMG.

Methods

we performed stimulated SFEMG of the Orbicularis oculi muscle (OO) from 1990 on. In 2009 we switched from a SFN to a CN. We reviewed the data of the first two years with the CN with the last two years with the SFN. All examinations were done by the same investigator in a similar way except for the low frequency filter and the required minimum amplitude of the signals.

Results

the CN group included 103 patients of whom 33 had a final diagnosis of MG, the SFN group 112 patients with 39 MG. The mean and median of the mean jitter values were 24.8 µs and 18.0 µs for the complete CN group and 22.1 µs and 17.5 µs for the complete SFN group. After exclusion of MG and ALS patients the data were normally distributed. Mean ± standard deviation were 16.8 ± 2.0 µs for the CN group and 16.5 ± 2.1 µs for the SF group. Statistical analysis showed that measurements in the CN and SFN group were equivalent (95 % confidence intervals within an equivalence margin of ±1 µs).

Conclusion

our results suggest that stimulated CN-SFEMG of the OO can be interpreted with similar reference values as stimulated SFEMG with SFN.
Serial Single Fibre Electromyography Studies in Myasthenia Gravis

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Question

Are serial Single Fibre Electromyography (SFEMG) studies useful in “restricted” form of Myasthenia Gravis (MG)?

Methods

14 patients with MG (ocular-13; ocular/mild generalised-1) underwent SFEMG of Frontalis-14 patients, Orbicularis Oculi (OO)-14 patients, and Extensor digitorum communis (EDC)-1 patient for initial diagnostic evaluation (Tb). SFEMG was done using Medtronic’s SF electrode and Keypoint.NET EMG system. In each muscle, 20 potentials pairs were sampled for jitter analysis. After starting treatment (Prednisolone 0.7 mg/kg/day), repeat SFEMG of the more abnormal muscle (Frontalis-7, OO-6, EDC-1) was performed (32 studies over 35 months). Quantitative MG scores (QMGS) were also assessed.

Results

Mean age, gender ratio, and mean duration of symptoms were 37.1 (15.7) years, 12:2, and 2.4 (1.7) months. Repeat QMGS assessment and SFEMG studies were performed at: T1(4-8 months) -10 patients; T2 (8-12 months) -7 patients; T3 (12-15 months) -7 patients; and T4 (15-35 months) -5 patients. Relapses were observed in 5/9 patients with poor drug compliance. At Tb, T1, T2, T3 and T4, mean QMGS were 1.5(0.9), 0.5(0.9), 2.1(4.4), 1.1(2.2), 0.6(0.6) and QMGS was “0” in 1/14, 7/10, 4/7, 4/7, and 2/5 patients respectively. Group mean MCD values at Tb, T1, T2, T3 and T4 were 55.7(19.3), 42.9 (11.1), 31.1(7.9), 30.6 (12.9), 36.9 (7.9). Percent decrease in group mean MCD was: T1 -19.8 (15.1); T2 -27.6(25.5); T3 -20.5(18.4); at T4 an increase of 22.1(30.9) was observed. SFEMG became normal in 8 patients (T2 - 4/7, T3 - 5/7, T4 -1/5). Two of the patients with normal SFEMG at T2 had taken steroids for short term/ in suboptimal doses. At T4, SFEMG was still abnormal in 4/5 patients after being normal in 3 of them at T3 - related to poor compliance/ inadequate immunosuppression.

Conclusions

Serial SFEMG studies demonstrated normalisation of jitter parameters 8-20 months after starting treatment - in 43% with “adequate” treatment and in 14% with “inadequate” treatment. Worsening/ persistence of SFEMG abnormalities at 23-35 months, observed in 4 patients, may be due to inadequate immunosuppression/ continued disease activity. Serial SFEMG studies may provide useful information for management of restricted form of MG.
P343
Influence of a single dose of fluoxetine on brain activity during movement observation and execution, muscle activity and motor function in chronic stroke patients

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Question

How does a single dose of fluoxetine influence the cortical activity during movement execution and imagination and how do these changes relate to changes in muscle activation patterns and motor function in chronic stroke patients?

Methods

The study was a double-blind, randomized, placebo-controlled, cross-over design. Ten chronic stroke patients were included and received a single dose of 20 mg fluoxetine or placebo on two different days. Identical measurements were done 4 times: before and after the administration of the placebo and of fluoxetine. To examine changes in cortical activity, 64-channel electroencephalography (EEG) was measured during movement execution and imagination, whereafter the event-related synchronization (ERS) was calculated of the theta, alpha and beta frequency bands. To examine peripheral changes, EMG (electromyography) of the extensor carpi radialis and flexor carpi radialis was measured during maximum voluntary isometric wrist extension and flexion (maximum voluntary force (MVF)), and 20% of MVF. Functional motor outcomes were measured using the Fugl Meyer Motor Assessment.

Preliminary Results (n=5)

When using a MANOVA, no significant effects were found for fluoxetine on motor function (FM), on ERS, or on muscle activation patterns. Significant differences were found between the affected and the healthy arm when the MVF and the root mean square (RMS) of the EMG of the extensor carpi radialis are considered.

Conclusions

In contrast to previous studies, no potential effect of a single dose of fluoxetine on the rehabilitation of motor function after stroke is found.
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Inhibitory theta burst stimulation of affected hemisphere in chronic stroke: a proof of principle, sham-controlled study

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Question
Non-invasive brain stimulation is a potential therapeutic intervention for stroke rehabilitation. Following a model of competitive interactions between the hemispheres, these interventions aim to increase the plasticity of stroke hemisphere by applying either excitatory protocols to the damaged hemisphere or inhibitory protocols to the non-stroke hemisphere. Here we test the safety and feasibility of an inhibitory protocol on the stroke hemisphere to improve the response to conventional therapy via a homeostatic increase in learning capacity.

Methods
12 chronic stroke patients received TBS to stroke hemisphere (6 patients inhibitory and 6 sham TBS) followed by physical therapy daily for 10 working days. Patients and therapists were blinded to the type of TBS. Action Research Arm Test (ARAT), Nine-Hole Pegboard Test (NHPT) and Jepsen-Taylor Test (JTT) were the primary outcome measures, dynamometry was the secondary outcome measure.

Results
All patients improved ARAT and JTT scores for up to 3 months post-treatment. ARAT improved significantly in both real and sham groups, but only patients receiving real TBS significantly improved on the JTT: 3 months post-treatment mean execution time was reduced compared to baseline by 141 s for real group and by 65s for the sham group.

Conclusions
This small exploratory study suggests that ipsilesional inhibitory TBS is safe and that it has the potential to be used in a larger trial to enhance the gain from a late rehabilitation program in chronic stroke patients.


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Effects of cerebral blood flow augmentation by external counterpulsation on corticomotor excitability in subacute stroke patients: preliminary results

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Question

External counterpulsation (ECP) is a novel noninvasive method used to augment cerebral perfusion. The purpose of this study was to determine whether improving cerebral perfusion via ECP can facilitate ipsilesional corticomotor excitability in subacute stroke patients.

Methods

We included in this report the first 19 patients with subacute ischaemic stroke from this randomized, sham-controlled, single-blinded study. The patients were randomly assigned to one of 2 groups: the first group (n=9) received real ECP; the second group (n=10) received sham ECP, one hour daily for 10 days. Modified Rankin scale (mRS), Purdue pegboard test, and cortical excitability measures including resting motor threshold (RMT) and motor evoked potentials (MEPs) at 130% of RMT recorded from the first dorsal interosseous muscle of each hand were made at baseline, post-intervention day 1 (post1), and post-intervention day 30 (post30). Post-intervention data were normalised to baseline (Post-ECP/Pre-ECP).

Results

Compared with the sham ECP group, the real ECP group showed facilitation of ipsilesional MEPs at post1 (real 2.66 (1.78), sham 0.92 (0.21), P <0.001) and post30 (real 2.70 (1.08), sham 1.08 (0.36), P < 0.001), and a decrease in the ipsilesional RMT at post1 (real 0.89 (0.11), sham 0.99 (0.03), P = 0.002) and post30 (real 0.86 (0.12), sham 0.97 (0.02), P = 0.002). No effects were found on contralesional RMT or MEPs. For clinical measurements, the real ECP group improved significantly in mRS and Purdue pegboard test at post1 (mRS: real 0.66 (0.30), sham 1.10 (0.32), P = 0.008; Purdue: real 2.55 (1.89), sham 1.06 (0.41), P = 0.004) and post30 (mRS: real 0.53 (0.23), sham 0.82 (0.20), P = 0.011; Purdue: real 2.71 (2.22), sham 1.41 (0.42), P = 0.049).

Conclusion

Ten daily sessions of ECP can facilitate ipsilesional corticomotor excitability in subacute stroke patients, probably by enhancing cerebral perfusion. This proof-of-principle study indicates a larger trial to explore the effects on recovery of motor function after stroke is warranted.
Automatized error cueing during impaired execution of action sequence in stroke patients with apraxia.

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Question

Stroke frequently causes specific deficits in the execution of action sequences (apraxia). Such symptoms of action disorganisation may affect activities of daily living (ADL) and can therefore prevent independent living after a stroke. An autonomous system is currently under development (EU project CogWatch) that aims to recognize action and detect errors during ADL performance, based on information from various sensors. Here we investigate whether cues that are automatically generated on the basis of the action error information are effective in modifying patients’ behaviour.

Methods

Ten stroke patients with left brain damage participated in the experiment. All patients suffered from apraxia according to clinical testing. The patients’ task was to make a cup of tea of choice. Patients’ actions were identified by the examiner and transmitted to the system. If an error was identified or the patient requested help, an adequate cue was emitted. Cues delivered auditory information accompanied by a video that showed the corrected action.

Results

The majority of patients committed at least one error in the tea making (e.g. did not boil the water in the kettle). Number of errors was correlated with the severity of apraxia. There were however, patients with signs of apraxia in clinical testing but no error in the tea making task. When errors were cued, the patients typically responded in the intended way and performed the missing action or corrected the error. Compliance with the cue was not related with aphasia as no correlation was found between successful responses and score in the Aachen Aphasia Tests. Some patients with severe apraxia used the help option frequently and benefitted from the cue being presented prospectively.

Conclusions

The results showed that automatized cueing could assist patients with apraxia to compensate impairments of the execution of ADL. Multimodal cues were successful in evoking the intended response despite the presence of aphasia in some patients. It is concluded that automatized cueing is a feasible method to support the execution of ADL activities after stroke and as a consequence, to foster independent living in those patients.

This work was funded by the EU STREP Project CogWatch (FP7-ICT- 288912).
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Paired Associative Stimulation-25ms in stroke patients.

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Question
The primary aim of this study was to evaluate the excitability and plasticity of cerebral cortex affected by an acute ischemic event in order to gather prognostic indices for evolution of clinical deficit.

Methods
We recruited 5 healthy subjects and 10 patients affected by ischemic stroke with cortical involvement in the territory of middle cerebral artery and clinical outcomes of motor deficit into the upper limb. All subjects underwent a protocol of Paired Associative Stimulation-25ms (PAS-25). Motor evoked potentials (MEPs) were recorded at Abductor Pollicis Brevis Muscle. Electrical stimulation was performed by stimulating median nerve at the wrist. The amplitudes of MEP before and after PAS-25 protocol was recorded and the difference in terms of mean MEP's amplitude was an index of excitability of motor cortex.

Results
Cortical excitability seemed to be age related

A statistically significant correlation between excitability of motor cortex at T₀ (acute phase) and NIHSS collected at the same time was noticed.

Furthermore at T₀ patients showed a lesser excitability of motor cortex compared to controls, but at T₁ (three months after stroke) the values are similar. Excitability in acute phase was greater in the injured hemisphere; this difference ceased to exist at follow-up.

We observed an important increase in MEPs’ mean amplitude of the healthy hemisphere between T₀ and T₁.

Conclusions
The correlation observed at T₀ between NIHSS and excitability let us to suppose that the latter could be an important index linked to clinical improvement: so it could represents a possible future prognostic index. We are waiting for the data about NIHSS in T₁ to confirm this hypothesis.

The decrease of imbalance between two hemispheres could be related to clinical reduction of deficit together with the gain in excitability from T₀ to T₁ in injured hemisphere.

Also mean MEPs’ amplitude in healthy hemisphere follows clinical improvement, but this correlation isn’t clear enough.
Method for long term RR-alternans quantification from single-lead ECG monitoring

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Problem

ECG alternans, as defined by alternation in the ECG morphology in every second heartbeat, has been linked to electrical instability of the heart[1]. Advancements in signal processing algorithms has allowed detection of alternans that is not visually detectable, such as microvolt T-wave alternans, as a risk-assessment tool for patients with cardiomyopathy[2]. Similar methods for RR-alternans do not exist. As such electric alternans may have significant impact on the prognosis of cardiovascular disease in stroke patients, we wanted to create and evaluate a method for quantification of RR-alternans from long-term ECG monitoring.

Methods

ECG data were collected from 14 patients with acute stroke and 14 control subjects undergoing full night polysomnography. Patients on beta-blockers or with known arrhythmias were excluded. For each patient, 10 segments with 60s of ECG data was extracted at random for analysis. A QRS complex detection algorithm was implemented based on a modified Pan-Tompkins detector, and the heart rate was derived. In each segment, the number of alternating heart rate changes was counted by convoluting the sign of the heart rate change at every heartbeat with an alternans sequence (+1, -1, +1). The result was divided by the number of heartbeats in the segment in order to yield a heart rate normalised alternans index from 0 to 1.

Results

A two-sample t-test of the mean alternans index value for each patient revealed that patients with acute stroke had significant higher alternans indexes than the control group (p<0.001). Eight stroke patients and two controls had mean alternans values above 0.25, while three stroke patients and no controls had mean alternans values above 0.3.

Conclusion

The developed algorithm was able to efficiently identify segments with visually undetectable RR-interval alternans. The alternans index differed significantly in the two groups, and several stroke patients had mean alternans values above the highest observed control level. Further studies are needed to investigate a possible impact of RR-alternans for morbidity and mortality and correlations with other cardiovascular diseases.

[1]: M L. Walker, D S. Rosenbaum; Repolarization alternans: implications for the mechanism and prevention of sudden cardiac death, Cardiovascular Research, 2003;57:599-614
Fatigue after stroke is related to motor cortex ‘restfulness’ and not to physical or cognitive functional ability

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Post stroke fatigue (PSF) is a commonly reported problem, the origin of which is poorly understood. This cross sectional study explores the relationship between fatigue (fatigue severity scale, FSS) and cognitive measures of information processing speed (IP; Symbol Digit Modalities Copy and Coding tests), sustained attention (SAI; Auditory Attention Test of the Birmingham Cognitive Screen) and conventional TMS measures of motor cortex excitability in the first dorsal interosseous muscle (Resting Motor Threshold (RMT), Active Motor Threshold (AMT), Short Interval Intracortical Inhibition (SICI), Long Interval Intracortical Inhibition (LICI) and recruitment curves (RC)) and biceps (voluntary activation (VA) using twitch interpolation methods).

Forty physically well recovered (grip strength $\geq$ 60% unaffected side) first time stroke patients, without depression (HADS-D $\leq$ 11) participated in the study. A Backward Stepwise Regression with FSS as the dependent variable and age, time post stroke, combined functional score, IP speed, SAI, RMT, AMT, AMT/RMT, SICI, LICI, RC and VA as independent variables revealed that FSS was explained by the single variable AMT/RMT ($P=0.030$) and did not depend on other factors in the model. The quotient AMT/RMT is a measure of how excitable the corticospinal system is at rest in comparison with activity. A low value indicates that resting state is less excitable when compared to the active state.

The results might indicate that increasing PSF is associated with a less excitable resting state, suggesting that in those with PSF motor cortex requires a greater increase in excitability than is usual in order to reach an active state.

\textbf{figure 1}

A significant negative correlation is seen between fatigue levels (FSS score - X axis) and the normalised threshold score (AMT/RMT*100 - Y axis) in chronic stroke patients.
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figure 2

Figure 2: MEP sizes as percentage of test response (black bar) in SICI (A) and UCI (B) and raw MEPs (C) from all 46 participants is shown. In A, the white bars show responses where ISI was 2ms, grey where ISI was 3ms and the intensities are the intensities of conditioning pulses. In A and B all conditioned responses were significantly smaller than test response (black bar), p<0.05. In C, on the X axis the stimulus intensities are shown as times Threshold (T).
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Mirror therapy alters beta desynchronization in M1 cortices of stroke patients

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Questions

Mirror therapy is a new form of stroke rehabilitation that uses the mirror reflection of the unaffected hand in place of the affected hand to improve motor learning. Beta oscillations as measured by MEG can tell us about how the primary motor cortices (M1s) process movement. We wanted to investigate whether looking at a mirror reflection of the unaffected hand altered beta power decrease in both M1s when compared to looking directly at the affected hand in stroke patients during movement.

Methods

Stroke patients and healthy controls were recorded in the MEG whilst performing bimanual hand movements. In one block they looked directly at their affected hand (or dominant hand in controls) and in another block they looked at a mirror reflection of their unaffected hand in place of their affected hand. Percentage of beta power decrease during movement was extracted from the MEG data from both M1s. Two sample t-tests were performed in order to compare between groups.

Results

In patients, during the no mirror condition there was a larger decrease in beta power in M1 ipsilateral to the hand being viewed compared to the contralateral M1, with the addition of the mirror reflection, this was significantly altered so that there was a similar decrease in beta power in both M1 cortices, a pattern similar to the control group.

Conclusions

Mirror therapy could potentially aid in stroke rehabilitation by encouraging a pattern of beta power decrease in both M1s that is more similar to healthy controls.
EVEN-T-RELATED BRAIN POTENTIALS IN PATIENTS WITH BRAIN INJURY

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Objective

Evoked potentials are used up 20 years in comatose patients in order to assess brain function and awakening prognosis. Recently Evoked Potentials Related Events (ERP) has been used in coma for identifying patients in minimally conscious state. The main objective of this study is clarify the correlation between the patterns of ERP and levels of physical and cognitive disabilities due to brain injury. We use the classical paradigm of "odd-ball" and assessing the degree of disability by Glasgow Outcome Scale (GOS).

Methods

ERP, a standard "odd-ball" paradigm and auditory evoked potentials, early responses (BERA) were recorded in 23 normal and 46 brain injured patients. The Glasgow Outcome Scale was determined concurrently with the P300 ERP.

Results

GOS: Good Recovery 7/46(15%), Moderate Disability 9/46(20%), Severe Disability 18/46(39%) and Vegetative State 12/46 (26%). P3b to desviant was found in 25/46 patients. P3a to desviant was found in 6 patients. We were observed a higher incidence of absence of the N2 10/12 and alteration of BERA 7/12 in vegetative state. Twenty percent (20%) of the Vegetative State pacients 2/12 had P3a ERP.

Conclusion

The ERP is useful in the evaluation of patients with brain injury in order to investigate the level of awareness. The absent of N2 strongly describe a vegetative state

References


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Bi-hemispheric corticomotor excitability changes after peripheral electrical stimulation to the affected arm in chronic stroke

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Question

Does peripheral nerve electrical stimulation (PNS) to the affected arm induce corticomotor excitability changes in both hemispheres after stroke?

Methods

This was a randomized cross-over study. Twenty-seven subjects with chronic stroke were assessed the impairment and functional ability of the affected arm, and completed the initial measurement of corticomotor excitability in both cerebral hemispheres for the contralateral first dorsal interosseus hand muscle using the transcranial magnetic stimulation (TMS). The parameters measured included (1) resting motor threshold (rMT), (2) motor evoked potential (MEP) at TMS intensities 10%, 30% and 50% above that for rMT, and (3) cortical silent period (CSP). All subjects then attended two other sessions with intervention - PNS or placebo-PNS was applied to the radial and ulnar nerves of the paretic arm in two separate randomized sessions. The stimulation time was 1 hour, using pulse duration of 450 μsec, and at current intensity just above motor threshold for PNS, but minimal current for placebo-PNS. Before and immediately after the intervention, the subjects were evaluated the 3 TMS-induced outcome measurements plus pinch strength of the affected hand using a hand-held digital dynamometer.

Results

PNS but not placebo-PNS resulted in significant increase in MEP amplitudes at TMS intensities of 150% rMT for the lesioned hemisphere (p=0.002), and 130% rMT for the non-lesioned hemisphere (p=0.001). rMT, CSP duration and pinch strength remained unaltered by the interventions (p >0.05).

Conclusions

In chronic stroke, one-hour PNS to the affected arm led to bi-hemispheric increase in corticomotor excitability for the contralateral hand muscle.
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**tDCS to Primary Motor Area Improves Hand Dexterity and Selective Attention in Chronic Stroke**

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**Question**

Does transcranial direct current stimulation (tDCS) to the primary motor hand area modulate cognitive performance after stroke?

**Methods**

This was a double-blind, placebo-controlled, randomized cross-over trial involving 10 subjects with chronic stroke. All subjects had recovered with some pinch strength in the affected hand at baseline. They received 3 different tDCS interventions assigned in random order in separate sessions - anodal tDCS targeting the primary motor area of the lesioned hemisphere (M₁<sub>lesioned</sub>), cathodal tDCS to the contralateral hemisphere (M₁<sub>non-lesioned</sub>), and sham tDCS, each for 20 minutes. Direct current was delivered using 35 cm² sponged electrodes, and intensity at 1mA for anodal and cathodal tDCS but none for the sham condition. The cognitive domains examined were hand dexterity skill using the Purdue Pegboard test and selective attention using a computerized colour-word Stroop test. Pinch strength of the affected hand was the secondary outcome.

**Results**

Compared to baseline, cathodal tDCS to M₁<sub>non-lesioned</sub> significantly improved affected hand dexterity (by 1.1 score higher in the unilateral Purdue Pegboard task, \( p=0.014 \)) and selective attention (by 0.6 seconds faster response time in the Stroop sub-test on response inhibition, \( p=0.017 \)), but not pinch strength. The outcomes were not improved with anodal tDCS to M₁<sub>lesioned</sub> or sham tDCS.

**Conclusion**

Twenty minutes of cathodal tDCS to M₁<sub>non-lesioned</sub> could promote both affected hand dexterity and selective attention in people with chronic stroke.
Changes in cortical reactivity during stroke recovery - A TMS-EEG study

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Question

Following an ischemic brain lesion, the affected hemisphere undergoes structural and functional changes that may lead to changes in cortical reactivity and connectivity. Our aim was to investigate the cortical reactivity in the acute phase of supratentorial stroke and during the recovery using transcranial magnetic stimulation (TMS) effects on simultaneous EEG.

Methods

Nine patients (3 male, age: 58-83 years) participated in this study. The patients had FAC of 0-3 [1] and Scandinavian Stroke Scale of 18-57 [2] after having suffered a supratentorial stroke. Patients were investigated using navigated TMS and EEG in three sessions, 1) within 9 days, 2) after 3 weeks and 3) after 6 months of stroke onset. During each session, the intact and affected hemispheres were mapped for the optimal stimulation site of the thenar muscle of the contralateral arm. 50 stimuli were given at 110% of the motor threshold on both hemispheres and EEG was recorded. ANOVA was utilized to study changes in cortical reactivity during recovery period.

Results

Global-field-power (GFP) varied significantly between the sessions and differed between the intact and affected hemispheres (fig. 1). The early GFP (<100ms) was greater in the affected hemisphere up to 3 weeks compared to the intact hemisphere; the difference disappeared before 6 months. In inter-trial coherence of M1 there was a significant session*hemisphere interaction effect in the later response (~200-400ms). The difference between the intact and affected hemisphere was significant in the acute phase, after which it disappeared. In event-related spectral perturbation there was a significant inter-session and hemisphere effect <100ms, but no interaction.

Conclusions

We observed that cortical reactivity was increased in the affected hemisphere in stroke. Cortical reactivity was modulated by the phase of stroke recovery with highest reactivity to external stimuli in acute phase and on affected side, normalizing already in 6 months follow-up.

References


Fig. 1: GFPs varied between A) sessions and between B) intact and affected hemisphere. The light grey area indicates pre-TMS time. The TMS-artefact was excluded from the analysis.
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Combination of *in vivo* MRI and histology to evaluate stroke-related brain volumetry in rats

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*In vivo* imaging by means of magnetic resonance imaging (MRI) has become a powerful tool for experimental stroke research in rodents, especially when longitudinal studies are intended. On the other hand, tissue fixation and subsequent histological staining have the advantage of high spatial resolution, even though being prone to tissue shrinkage or distortion. To date, most brain studies apply either the one or the other method which poses the challenge to extrapolate data from both types of methods. Hence, our study was aimed at determining the correlation between *in vivo* MRI and one of the standard histological methods used in the field, i.e. cresyl violet. We compared T2-weighted MRI images (3T Magnetom TIM Trio, Siemens) obtained immediately before sacrifice of the animals to cresyl violet stained slices after transcardial perfusion and fixation with 4% paraformaldehyde. We show that healthy brain tissue shrinks by approximately 25% due to histological processing. In addition, we examined brains after a focal ischemic lesion in the forelimb sensorimotor cortex (photothrombosis model; volumetric measurements carried out after a recovery phase of 30 d). Again, the same volume difference between methods was found, irrespective of whether infarct or brain volumes were analyzed. Thus, we identified a consistent correlation factor (approximately 1.3) which can be used to compare volume data from post-mortem histology and *in vivo* MRI in the adult rat brain.

Acknowledgements: We thank I. Krumbein and S. Tausch for excellent technical assistance. The work was supported by the DFG (RTG1715).
Effects of transcranial direct current stimulation (tDCS) on motor skill learning in the chronic phase after stroke

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Anodal tDCS over M1 can lead to significant improvements of fine motor skills in healthy subjects and an improvement of motor function in chronic stroke patients'.

Here we investigate the effects of anodal tDCS on the temporal subcomponents of motor skill learning (acquisition, consolidation and long term retention) as well as generalization in the chronic phase after stroke.

Patients with unilateral, first ever chronic ischemic stroke (>3mo) with a moderate persisting hemiparesis practiced the sequential visual isometric pinch force task (SVIPT, Reis et al., 2009) for 5 days with their paretic hand while receiving tDCS_{anodal} or tDCS_{sham} for 20 minutes over M1 of the affected hemisphere. A skill measure was developed based on movement time and error rate. The Jebsen Taylor Handfunction Test (JTT) and the Grooved Pegboard Test (GPT) were performed to test for generalization of the motor skill.

All patients (n=24) except 2 (sham) became more skilled in the task. Patients receiving anodal tDCS showed a greater improvement of motor skill compared to sham. Subcomponents of motor learning are under investigation. Patients also showed an improvement in the JTT and GPT in both groups indicating generalization.

These preliminary results suggest that tDCS combined with motor training can facilitate motor learning compared to sham in the chronic phase after stroke. These findings may be transferable to neurorehabilitation of patients after acute ischemic stroke.

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Motor learning differences due to training with an emphasis on fast movement or movement accuracy for reaching movements after stroke.

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Question
Fast movements are not commonly incorporated in stroke rehabilitation because of presumed detrimental effects of increasing spasticity. We here compare motor learning when training with either an emphasis on accuracy or high velocity.

Methods
Healthy individuals (n=14) and individuals affected by stroke (n=37) attend respectively for 5 and 6 consecutive days to perform intensive 20cm horizontal reaching training in a robotic manipulandum. We compare the effect of accuracy training with training at fast movement speed by plotting reaching bias at 4 different movement speeds before and after training. Additionally electrophysiological measures of corticospinal connectivity and EMG activation patterns are established.

Results
In healthy individuals training-speed-specific accuracy improvements are observed which generalise to other movement speeds. However the group training at fast speed show the greatest gains (3way rmANOVA MT*TIME*GROUP (F(3:36)=3.379; p=0.029)). In the stroke population we also observe accuracy improvements (3way rmANOVA MT*TIME*GROUP (F(3:99)=2.792; p=0.044)), which generalise to other movement speeds. Despite a correlation (R=-0.40) between functional ability (Fugl-Meyer) and spasticity (Modified Ashworth Scale) these factors are unable to predict the type and amount of learning observed.

Conclusions
Stroke subjects improve reaching accuracy due to fast and accurate training. Spasticity does not prevent learning or increase with fast movements.
P358
Age-specific transcriptional response to stroke

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Question

Increased age is a major risk factor for stroke incidence and post-ischemic mortality. To develop age-adjusted therapeutic interventions, a clear understanding of the complexity of age-related post-ischemic mechanisms is essential.

Methods

Transient occlusion of the middle cerebral artery (MCAO) - a model that closely resembles human stroke - was used to induce cerebral infarction in mice of four different ages (2, 9, 15, 24 months). Gene expression was analyzed by using Illumina cDNA microarrays and quantitative PCR.

Results

We detected a distinct age-dependent response to stroke involving 350 differentially expressed genes (DEGs). Our analyses also identified 327 DEGs that responded to stroke in an age-independent manner. These genes are involved in different aspects of the inflammatory and immune response, oxidative stress, cell cycle activation/DNA repair, apoptosis, cytoskeleton reorganization/astrogliosis, synaptic plasticity/neurotransmission, and depressive disorders/dopamine-, serotonin-, GABA-signalling.

Conclusions

In agreement with our earlier work (Sieber, et al., 2011), aged brains displayed an attenuated inflammatory and immune response and a reduced impairment of post-stroke synaptic plasticity. Our data also revealed a distinct age-related susceptibility for post-ischemic depression, the most common neuropsychiatric consequence of stroke which has a major influence on functional outcome.
P359  
Anti-inflammatory potential of N-Nitro-L-Arginine-Methylester in Cerebral Injury Induced by Transient Ischemia/Reperfusion in rats

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The role of nitric oxide (NO) inhibition in cerebral ischemia/reperfusion (I/R) remains uncertain. The aim of this work was to explore anti-inflammatory effect of N-Nitro-L-Arginine-Methylester (L-NAME) on rats subjected to transient focal cerebral I/R.

Materials and Methods

The study involved 30 adult male Wistar rats divided into three groups: 10 rats in each. First group was sham-operated (control), I/R group of rats infused with 0.9% normal saline intraperitoneally prior to 30 minutes of left common carotid artery occlusion followed by 24-hour of reperfusion and test group infused with L-NAME (15 mg/kg per weight) intraperitoneally 15 minutes prior to the same I/R period. Neurobehavioral assessments were evaluated using six clinical tests[2], Western blotting was used to estimate Nuclear factor kappa b (NF-κB), Tumor necrosis factor-α (TNF-α) using ELISA and NO metabolites (nitrite and nitrate), were measured colorimetrically in both plasma and affected cerebral hemisphere.

Results

Values are means ± S.E.M, compared by ANOVA. The L-NAME group showed a significant improvement in neurological deficit compared to both I/R and control groups. In I/R rats NF-κB was significantly increased (129.2±1.7 RGB unit/mg protein) compared to the control group (53±1.03) and L-NAME pretreatment resulted in a significant decrease in NF-κB (44.4±1.3) compared to I/R group. Serum and tissue level of TNF-α and NO were significantly increased in I/R group; compared to the control group; while L-NAME administration resulted in a significant decrease in TNF-α and NO compared to the I/R group. Rat brains (n=6) were fixed and stained with hematoxylin and eosin, figure 2 showed that L-NAME treatment limited the neuronal degeneration.

Conclusions

These data demonstrated that L-NAME significantly improve neurological deficit and showed a potential neuroprotection through it is anti-inflammatory effect in a rat’s model of transient focal cerebral ischemia reperfusion.

Reference

P360
Neurophysiological aspects of dysfunction in the area of functional asinapsii at an effective neuroprotective therapy in children with acute hemorrhagic stroke

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The aim of the project was to study the effectiveness of neuroprotective therapy in children with acute hemorrhagic stroke based on clinical and neurological and electro-neurophysiological research. A comprehensive clinical and instrumental examination of 390 patients aged 0 to 14 years of life. All the patients were hospitalized in the clinic urgency in the first 24 hours from the time of onset of the disease. The children in the first days of acute stroke in the EEG recorded dominance in the structure of relative spectral power density of the delta and theta rhythms, with emphasis ipsilateral lesion. In the dynamics of EEG pattern on the background of neuroprotective therapy has been a redistribution of the relative proportion of EEG power spectral density in the form of displacement of the center of gravity of slow-wave rhythms in the ranges of alpha and beta, which was confirmed by a significant decrease of the integral index of bioelectrical activity from 5.8 ± 1.2 to 1.6 ± 0.5 (p <0.001) in the affected hemisphere and, to a lesser extent - from 6.3 ± 1.4 to 1.3 ± 0.4 (p <0.001) - in intact. The analysis of the dynamics of the spectral characteristics of alpha activity against the combined neuroprotection confirmed the tendency to normalization of its zonal distribution and reduces the severity of asymmetry. Registered statistically significant dominant and in caudal hemispheres bilaterally with emphasis on the side ischemia increase relative power spectral density alfa to 18.1 ± 2.6 33.1 ± 4.0% (p <0.001) within the affected hemisphere and 19.2 ± 2.8 to 31.4 ± 5.0% (p <0.01), - within the intact mainly due to synergistic change the alpha range preferably in the occipital region: relative power spectral density of alpha-Lo-range increased with up to 12.1 ± 1.5 19.1 ± 1.6% (p <0.05) ipsilateral and up to 12.8 ± 1.6 16.7 ± 1.6% (p <0.05 ) - contralaterally and relative power spectral density of alpha-Hi-band increased from 4.6 ± 0.8 to 10.1 ± 1.7% (p <0.001) and ipsilateral 4.7 ± 0.6 to 9.5 ± 1.5% (p <0.01) - contralateral. The analysis of the dynamics of an electroencephalograph showed a marked positive impact polymodal neuroprotective therapy in focal ischemia in the functional activity of the brain, caused by a reduction of neuronal dysfunction in the area of functional asinapsii, a decrease dysfunction nonspecific systems of the brain stem, the stimulation of synaptogenesis in the structure of the repair mechanisms.
Neuroprotective Effects of Ischemic Preconditioning after Transient Focal Cerebral Ischemia /Reperfusion in Rats

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Background

Ischemic preconditioning (IPC) is a brief episode of ischemia/reperfusion (I/R) that protects the brain from subsequent prolonged ischemia. Preconditioning stimuli may mimic some of the characteristics of transient ischemic attacks (TIAs), which a TIA occurring before a stroke could lead to delayed tolerance[1]; however, the molecular protective mechanisms of IPC are not fully understood. The aim of the present work was to study the neuroprotective potential of IPC.

Materials and Methods

30 adult male Wistar rats (150 - 250 g) were divided into three groups 10 rats in each; the first group was sham-operated and served as a control. I/R group of rats subjected to 30 minutes of left common carotid artery occlusion (CCAO) followed by 24-hour of reperfusion. IPC group were treated with three episodes of 5- minutes of CCAO with 10 minutes of reperfusion in between, followed by 30 minutes of CCAO and then allowed for reperfusion for 24 hours. Neurobehavioral assessments were clinically evaluated[2]; Rho-kinases (ROCK) and nitrite were measured in affected cerebral hemisphere using ELISA and colorimetric methods respectively.

Results

Values are means ± S.E.M, compared by ANOVA. Rats’ neurological deficits were significantly decreased in the I/R compared with the control group (P < 0.001) whereas rats treated by precondition stimuli showed significant improvement in neurological deficit compared to I/R group (P < 0.001). Nitrite level was significantly increased in the IPC rats compared to both control and I/R groups (P < 0.001). In contrast, the ROCK level was significantly higher in I/R group compared to control group and its level significantly decreased in IPC rats when compared to I/R group (P < 0.001). ROCK correlates negatively with the nitrite (CC = −0.695, P = 0.000).

Conclusions

Down-regulation of ROCK level following preconditioning stimuli with the potential involvement of Nitric oxide appear to be one of the neuroprotective mechanisms of IPC protection against subsequent ischemic challenge evidence by improvement in the neurological deficits.

REFERENCES

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Figure 1

![Graph showing neurological deficits among different experimental groups.](image1)

Fig 1: Neurological deficits among different experimental groups. (10 rats in each group, data are expressed as mean ± SEM).

* Significant with controls, † Significant with ischemia reperfusion, ‡ Significant with Ischemic Preconditioning group

Figure 2

![Graph showing Rho Kinase levels in different experimental groups.](image2)

Fig 2: Rho Kinase levels in different experimental groups. (10 rats in each group, data are expressed as mean ± SEM).

* Significant with controls, † Significant with ischemia reperfusion, ‡ Significant with Ischemic Preconditioning group
P362
An evaluation of neuroendocrine dysfunction following acute aneurysmal subarachnoid hemorrhage: a prospective study

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Question
Evidence that aneurysmal subarachnoid hemorrhage (SAH) is associated with neuroendocrine dysfunction comes mainly from case reports or small series of patients. The aim of this study was to investigate the incidence and pattern of neuroendocrine dysfunction in cases of acute aneurysmal SAH.

Method and material
This prospective study was done on the cases of acute SAH treated in our institute. Their detailed clinical and endocrine evaluation was performed.

Results
Total 100 cases (38 males, 62 females; age range from 17 -76 years; mean age-43.6 years) of acute SAH were studied. The aneurysms were located in the anterior circulation (n=95) and posterior circulation (n=5). The commonest hormone deficiency was of growth hormone (n=67) followed by gonadotrophin (n=50), corticotrophin (n=49) and thyrotrophin (n=35). Hyperprolactinemia was noted in 10 cases. One pituitary hormone axis deficiency was noted in 26 cases while 67 cases had two or more pituitary hormone axes deficiency. A total of 93 cases had hormonal deficiency in one or more pituitary hormone axes and 7 cases had no hormonal deficiency.

Conclusions
Endocrine dysfunction occurs in 93% cases of acute SAH and multiple pituitary hormone axes deficiency occurs in 67% cases. It is suggested that hormonal evaluation should be considered as a part of management of acute SAH.
P363
Response to Maintenance Treatment in Children Primary Angiitis of the Central Nervous System (cPACNS).

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PURPOSE
We aimed to assess a maintenance treatment regimen, predictors of disease progression in order to identify high-risk patients and describe long-term neurological outcomes in a cohort of children with subtypes of cPACNS at diagnosis and during follow up.

Study Type: observational and analytic.
Place: The department of the Neurology of the Children’s Hospital Lahore and the Brain Associates Model Town Lahore -Pakistan.

Methods
We did an open-label cohort study in children with childhood primary angiitis of the CNS and its subtypes, who were less than 16 years old at diagnosis. The treatment protocol consisted of intensive induction therapy with steroids and/or immunoglobulins followed by maintenance therapy with either Aspirin or combination of Aspirin and Azathioprine, depending upon the type of cPACNS at presentation. Clinical and neurological assessments, quality of life measures, and laboratory markers were done at baseline, 3, 6, 9, 12, 18, and 24 months and when required thereafter till 60 months since the discharge from the hospital. Brain imaging was done at baseline and later when clinically indicated. The primary outcomes were, relapses, mortality and the pediatric stroke outcome measure (PSOM) score at 60 months after discharge from the hospital.

Results
From January 2008, to July 2013, 84 patients (boys 62%, girls 38%, with mean age of 8.2 years -median age 7.4 ± 3.2 years), were enrolled, 70 of whom were put on maintenance therapy after successful completion of induction therapy. 40 patients(57%) had non-progressive angiography and were put on only Aspirin , 16(23%) patients had progressive angiography positive cPACNS and 14(20%) had angiography negative cPACNS. The latter two groups were started on combination of Aspirin and Azathioprine, as maintenance therapy. After the final follow-up of 60 months, of the total 70 patients was; 34(49%) had relapse/flare, 24 (34%) died, 17(24%) were receiving drugs, 25(36 %) were off any medication and were neurologically sable, 6(9 %) were receiving both Azathioprine and Aspirin, and 4(6 %) were lost in follow-up. The neurological assessment assessed by PSOM-SNE at final 60 months follow up was: normal 8(19%); minimal neurodisability8 (19%) moderate neurodisability10 (24%) and severe neurodisability 16(38%).

Conclusion
Distinct subtypes of childhood PACNS have unique disease activity and response to treatment. The treatment protocol of immunosuppressive and antiplatelet therapy therapy may improve long-term neurological outcome in children with small PACNS.
Movement-related sensorimotor activity in severely-affected stroke survivors depends on preserved thalamo-cortical connectivity

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Question

Human motor system is characterized by oscillatory activity in µ- and β-frequencies. Damage to the motor system on a cortical or subcortical level following stroke is suppressing sensorimotor rhythms (SMR). However, the relation between electroencephalographic (EEG) changes of cortical physiology following stroke, lesion location and the role of cortico-subcortical integrity is unclear.

Methods

Chronic stroke patients underwent multimodal assessment including the Fugl-Meyer Assessment Score (FM), detection of movement-related electroencephalographic (EEG) activity using a Brain-Computer-Interface (BCI) approach, voxel-based lesion mapping (VBLM) and cortical-subcortical connectivity analysis by probabilistic Diffusion-Tensor Imaging (DTI).

Results

Time-frequency analysis of sensorimotor oscillations showed significant reduction of ipsilesional movement-related β- activity in patients with worst recovery after stroke. There was no correlation between EEG activity and overall lesion volume or extend of sensorimotor damage. We hypothesized a relation between SMR activity and preserved connectivity within the motor system. DTI-based connectivity analysis revealed best correlation between number of remaining ipsilesional thalamo-cortical (TC) fibers and SMR. Notably, cortico-muscular coherence in the β-band required TC integrity.

Conclusions

Our results indicate that thalamo-cortical feedback loops are prerequisite for the evolution of sensorimotor rhythms. Hence, further evidence is added for the importance of haptic feedback in stroke rehabilitation.
Premotor cortical stimulation in stroke rehabilitation: Neural mechanisms of recovery

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In recent clinical trials, adjuvant cortical stimulation has shown inconsistent benefit for rehabilitation of paretic hand in stroke. Variable success may be due to damage to typical target- primary motor cortex (M1) and/or its corticospinal output. Targeting higher motor areas, such as premotor cortex (PMC), may be more effective since it can reorganize to assume role of damaged M1 via its significant contribution to corticospinal and inter-hemispheric connections. In a pilot randomized, double-blinded clinical study, we investigate efficacy of stimulating PMC in rehabilitation of paretic hand in chronic stroke. In anticipating variable success, we also study neural mechanisms of recovery. Patients received stim or sham with rehabilitation for 1hr, 3 days/wk for 5 wks. Stimulation involved anodal transcranial direct current to ipsilesional PMC. Patients were tested on function of paretic hand, Diffusion Tensor Imaging (DTI) and Transcranial Magnetic Stimulation (TMS) to define corticospinal integrity and output, and TMS and Functional Magnetic Resonance Imaging (fMRI) to measure inter-hemispheric interactions. Patients improved with stim in rehabilitation, though all perceived they had improved. Patients receiving stim improved inter-hemispheric interactions, mainly for PMC. While at baseline all patients had moderately good corticospinal integrity, output was poor. But, after treatment, all improved on output. Thus, premotor cortex may be an alternative target for stimulation in rehabilitation. Still, success may depend upon corticospinal integrity and output, and the potential of targeted cortex to modulate inter-hemispheric interactions. Variability of cortical stimulation can best be predicted by combining DTI, TMS and fMRI.
Where language meets action: a combined behaviour and lesion analysis of aphasia and apraxia due to left-hemisphere stroke

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Question

Both aphasia and apraxia frequently occur after left-hemispheric stroke and have delirious effects on neuro-rehabilitation. As previous studies mainly focused on either syndrome our knowledge about their relationship remains scarce. Clinically, the co-occurrence as well as the dissociation of both syndromes can be observed. To further elucidate the behavioural patterns and neural substrates of aphasic and apraxic deficits after left-hemispheric stroke, neuropsychological testing and statistical lesion analyses were performed in 50 sub-acute stroke patients.

Methods

Eight neuropsychological tests were administered to detect and characterise aphasic and apraxic deficits. Voxel-based lesion symptom mapping (VLSM) was performed to identify lesion sites associated with aphasic and apraxic deficits as well as combinations thereof.

Results

Behaviourally, half of all patients or two-thirds of the 37 aphasic patients suffered from co-morbid aphasia and apraxia. While 24% (n=12) of the patients exhibited aphasia without apraxia, apraxia without aphasia was rare (n=2, 4%).

As expected, VLSM revealed that aphasic deficits were associated with lesions to left inferior frontal, superior temporal and supramarginal gyrus. Apraxic deficits correlated with lesions to left inferior frontal gyrus, the central region, and parietal lesions for imitation. Lesions to the opercular part of the left inferior frontal gyrus (i.e. Brodmann's area 44 as part of Broca's region) led to combined apraxic and aphasic deficits.

Conclusions

This is the first study which demonstrates the lesion site for comorbidity of aphasia and apraxia. Our findings stress the importance of Brodmann's area 44 (as part of Broca's region) as an interface between language and praxis.
P367
High frequency deep rTMS over the right homologous Broca's region improves naming in chronic post-stroke aphasia: a pilot study.

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Objective

this study aimed to compare the effect of excitatory, inhibitory and sham rTMS delivered with H-coil over the right inferior frontal gyrus (IFG) in chronic post-stroke aphasic patients.

Methods

five right-handed post-stroke aphasic patients underwent a picture naming task before and immediately after each of three sessions of rTMS: excitatory (10 Hz), inhibitory (1 Hz) and sham rTMS, in random sequence and separated by at least one week.

Results

only the excitatory 10 Hz stimulation was associated with a significant improvement in naming performance, (p=0.043) and was significantly more effective than 1Hz rTMS (p=0.043).

Conclusions

a single session of excitatory deep brain rTMS over the right IFG with H-coil significantly improves naming in right-handed chronic post-stroke aphasic patients. This result is in line with the hypothesis of a positive, rather than detrimental role, of the right hemisphere in chronic aphasia due to a left-hemispheric stroke.
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P368
Association between dysphagia and OSAS in acute stroke patients

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Introduction

Co-occurrence of dysphagia and Obstructive sleep apnoea (OSAS) may negatively impact clinical course in stroke.

Objective

The objective of this study is to evaluate the correlation between dysphagia and sleep apnoea in acute stroke patients.

Methods

Inclusion criteria: ischemic or hemorrhagic stroke (≤ 48 hours).

Exclusion criteria: NIH stroke scale < 2, the presence of concurrent neurological diseases, a former diagnosis of OSAS and/or dysphagia. Patients underwent medical examination, evaluation of BMI and neck circumference, neurological assessment according to NIH stroke scale (NIHSS). The presence and the entity of dysphagia through the Gugging Swallowing Screen (GUSS). The extent and location of brain lesion was valued by the Alberta Program Early CT Score (ASPECTS). A polysomnographic recording was performed not later than 48 hours of stroke onset.

Results

The total number of patients enrolled is 69 (56 males, 13 females), mean age 68.9±11.3, BMI 27.6±5.5 Kg/m2; neck circumference 42.7±4.3cm; NIHSS 8.8±7.7; ASPECTS 2.9±2.6; GUSS 11.6±7.7; ODI 21.5±21.5 events/hours.

Polysomnographic recordings suggestive for OSAS were found in 47(8%) patients; dysphagia was assessed in 65.2% of patients; co-occurrence of OSAS and dysphagia was observed in 31.8%. Patients with dysphagia (D+), respect to patients without dysphagia (D-), presented significant differences concerning age (D+=70.8 vs D-=64.7 t-test p=0.037), NIHSS (D+=11.1 vs D-=3.4; t-test p<0.001), ASPECTS score (D+=3.4 vs D-=1.4; t-test p=0.004) and BMI (D+=26.2 vs D-=30.7 Kg/m2; t-test p<0.002). Patients with OSAS, respect to patients without OSAS did not presented any significant differences for none of the analyzed parameters. The correlation analysis through Pearson index showed that ODI had a direct correlation with neck circumference (r(67)=0.388 p<0.05), with BMI (r(67)=0.322 p<0.05) and an inverted correlation with age (r(67)=-0.282 p<0.05). GUSS score presented a direct correlation with BMI (r(67)=0.371 p<0.05) and inverse correlation with NIHSS score (r(67)=-0.721 p<0.01) and ASPECTS (r(67)=-0.679 p<0.01).

Discussion

Considering the enrolment of about half of the sample expected, our data suggest the presence of a significant correlation between dysphagia and OSAS in acute stroke patients.
Cognitive Evoked Potential in Poststroke Patients

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Question

To confirm the regression of poststroke cognitive impairment using cognitive evoked potentials.

Methods

Thirty-one poststroke patients (33-75 years, 15 males and 16 females) were evaluated with a neuropsychological battery and cognitive evoked potentials at one and three months after the first hemispheric ischemic stroke. Neuropsychological examination included MMSE, FAB, Semantic and Phonetic Verbal Fluency test (SVFT and PVFT), attention test (AT). All poststroke patients received ipidacrine during 2 months. Standard values of N200 and P300 latencies for age were calculated using P. Anderer formula. Control group consisted of 35 persons without stroke.

Results

The data differences between patients and control group were fixed in MMSE (p=0.0002), FAB (p=0.0000), SVFT (p=0.0024), PVFT (p=0.0000), AT (p=0.0003) one month after stroke. The N200 and P300 latencies in poststroke patients were significantly longer compared to standard value one month after stroke. The P300 amplitude in poststroke patients didn’t change. Correlations between P300 latency and MMSE, FAB, SVFT, PVFT, AT were revealed one month after stroke. Neuropsychological reinvestigation demonstrated that MMSE (p=0.0000), FAB (p=0.0000), SVFT (p=0.0000), PVFT (p=0.0063) and AT (p=0.0017) significantly improved, differences with control group in MMSE and SVFT disappeared. A statistically significant reduction in P300 latency was observed at the second visit. Correlations between baseline P300 latency and FAB at the second visit were revealed.

Conclusions

Poststroke cognitive impairment reflecting decrease of frontal functions, verbal fluency and attention is identified. Extended latencies of N200 and P300 are recorded in poststroke patients. Extension of P300 latency associate with reduced executive functions.
P370
The use of environmental sounds in the rehabilitation of apraxia in stroke survivors.

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Question
The CogWatch project aims to create an intelligent assistance system to improve activities of daily living (ADL) in stroke survivors, who suffer from impaired ability to use everyday tools (apraxia). This study explores the use of cues, based on ecological sound linked to the action goal, in rehabilitation of those patients by reinforcement of the appropriate motor plan. Recent research suggests that motor networks associated with mirror neurons respond to the action-related sounds [1-2].

Methods
We have tested ten patients with left-brain damage as a result of cardio-vascular accident on pantomimed and actual tool use in three tasks: hammering, sawing, and toothbrushing. In addition, 20 age-matched controls were tested, 10 on the dominant hand and 10 on the non-dominant hand. The experimental design comprises of four different cueing modes: no cue, auditory instruction, pictorial instruction and ecological sounds. The movement data is collected with the use of 5 Qualisys Oqus cameras.

Results
Preliminary results show improved motor performance in terms of movement organisation (see Fig. 1), frequency and amplitude in the patient group when cues with ecological sound for all tasks. Detailed analysis is ongoing and focuses on error occurrence classification [3] and other kinematic variables as movement time, peak velocity and movement path.

Conclusions
The results of this study will feed in the development of the CogWatch system. Use of ecological sounds provides an optimistic outlook for neurorehabilitation of ADL in stroke patients.

References:

Figure 1: Normalised phase planes (velocity over time) for the apraxic patient performing a pantomime of hammering in comparison to control age-matched subject. Deviation from the circular form characterises poor motor control.

This work was funded by the EU STREP Project CogWatch (FP7-ICT-288912).
Selective attention and performance in controlling a P300-based Brain Computer Interface in people with amyotrophic lateral sclerosis

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Question

We investigated the involvement of attentional and memory processes in controlling a P300-based brain-computer interface (BCI) for communication purpose in people with amyotrophic lateral sclerosis (ALS).

Methods

Eight participants with ALS performed a P300-based BCI spelling task and: (i) a rapid serial visual presentation (RSVP) task, screening the temporal filtering capacity and the speed of the update of such attentive filter, in order to detect two targets in a stream of distractors, and (ii) a change detection (CD) task with the simultaneous presentation of target and distractor stimuli, to screen the spatial filtering capacity of attention for visual working memory consolidation. We performed correlation and regression analyses to investigate the relationship between the indexes of selective attention and visual working memory and the amplitude of P300 event related potential (ERP) elicited during a P300-based BCI task as well as of the performance obtained in such task.

Results

Amongst the indexes evaluated, only the temporal filtering capacity was found to significantly correlate with both P300 amplitude ($r=0.84$, p<0.05), and the accuracy achieved during the BCI task ($r=0.79$, p<0.05). We therefore conducted a linear regression analysis with such index as independent factor, revealing that it significantly predicted both P300 amplitude and BCI accuracy (p<0.05).

Conclusion

The overall findings indicate that the capability to selectively filter a stimulus and to keep such filter active in a temporal domain influences the performance in achieving a P300-based BCI control. The present study partly clarifies the cognitive substrates related to BCI control in people with ALS.

Acknowledgment

The work was supported by the Italian Agency for Research on ALS-ARiSLA project “Brindisys”. This paper only reflects the authors’ views and funding agencies are not liable for any use that may be made of the information contained herein.
Scalp-recorded slow potentials during neuro-feedback training well reflects cortical activity?

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Question

Recently, neuro-feedback (NFB) training by self-regulation of slow cortical potentials (SCPs) recorded at scalp vertex has been applied for seizure suppression in patients with refractory epilepsy. However, it is not clear whether the whole cortices or parts of the cortices contribute to the scalp-recorded SCPs. It is also uncertain whether scalp-recorded SCPs may contain slow component of galvanic-skin slow potentials.

Methods

To clarify the two questions, we evaluated the correlation between scalp- and subdural- recorded slow potentials by means of coherence analysis. In 7 patients with refractory partial epilepsy while invasive recording was done before epilepsy surgery, scalp- and subdural SCPs were recorded simultaneously during NFB training by means of DC-EEG machine (IRB#C533). SCPs at C1 or C2 (contralateral to the subdural electrodes) was employed as a reference to the coherence analysis.

Results

Coherence analysis suggested that SCPs recorded at vertex scalp electrodes mainly derived from the cortices of the high lateral convexity, namely in the precentral and postcentral gyri. Statistically, a significant correlation was observed between the linear distance to the scalp electrode and coherence power (Spearman’s rank correlation, ρ = -0.795; P = 0.003) (Fig. 1).

Conclusions

It is most likely that scalp-recorded SCPs from the scalp vertex area exclusively could reflect SCPs from the cortices of the lateral convexity close to the vertex, and thus is unlikely that that scalp-recorded SCPs contain the galvanic skin slow potentials. It suggests that single-trial decoding/neuro-feedback of the slow activity from the high lateral convexity is possible by means of scalp recorded SCPs from the vertex.

\textbf{figure 1}
Abstracts of Poster Presentations – Poster Session 22 – Brain computer interface

P373
Brain-computer interfaces for assessment and communication in patients with disorders of consciousness

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Question

Patients with disorders of consciousness (DOC) usually stay in rehabilitation institutions several months before they are released to professional home-care or to their homes. For that it would be advantageous to have a system that can assess cognitive functions and potentially allows patients to communicate. The aim of this study was to test if locked-in syndrome (LIS) patients and healthy controls could use a vibrotactile brain-computer interface (BCI) system to establish communication.

Methods

We designed an EEG-based system by using (i) auditory evoked potentials (AEP), (ii) vibrotactile (VT) evoked potentials and (iii) motor imagery (MI) experimental protocols. Auditory and vibrotactile experiments were designed to elicit P300 responses whereas the MI experiment allowed to analyze event-related desynchronization/synchronization (ERD/ERS) driven by MI. Six LIS patients and ten controls performed an experimental oddball task to elicit a P300 response by mentally counting deviant stimuli. Then, they had to answer five questions by counting the vibrations on the right wrist for ‘yes’ or the left wrist for ‘no’.

Results

All participants were able to elicit a P300 response using the vibrotactile paradigm. In the counting task, four patients and all controls achieved an accuracy of 100 % and in the question task, one patient and five controls reached 100 % accuracy.

Conclusion

This study shows the feasibility of a vibro-tactile based BCI system for communication in healthy subjects and LIS patients. The combination of P300 and MI based paradigms forms a testing battery that can be used for the detection of consciousness in non-communicating patients.
Detecting Spatial Auditory Attention in Cocktail-Party Situations

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Neurotechnological data analysis methods are capable to extract information from the ongoing electroencephalogram (EEG). Brain-Computer Interfaces (BCIs) exploit this information to create EEG-driven applications for control or monitoring, which may be used for chronically motor-impaired patients, rehabilitation purposes or cognitive assessment. While the challenging SNR of EEG recordings is prohibitive for the extraction of most detailed mental states, event-related responses (ERP) upon external stimuli have been used quite successfully for BCI applications. As ERPs can reveal the attentional state of a listener, spelling applications have been realized, which rely on the detection of spatial attention to spatially distributed, brisk and well-controlled tone stimuli.

Thriving to expand the usefulness of BCI neurotechnology, we go beyond the state of the art by replacing the brisk tone stimuli by massively overlapping human speech streams. In this more natural condition, a listener has to focus his auditory attention in order to solve a cocktail party problem. Six normal hearing, native German speaking subjects (aged 23-25) participated in an EEG recording (32 channels). They listened to three concurrent mono speech streams played from the left, right and middle/front position via headphones. Streams were sampled from three audiobooks, each read by a different human speaker. Including a 15 s break a trial duration was 45 s. The overall 90 trials per subject were split into six blocks. Auditory cues prior to trial start indicated the randomized target stream, and at times participants had to answer questions about the content of the target to ensure endured attention. For offline analysis, speech streams were labeled manually to mark various events. EEG epochs relative [-200 to 800 ms] to events were extracted. Epochs were baseline corrected, filtered [0.5-18 Hz] and cleaned from artifacts.

Observed target/non-target ERP differences were most distinct for sentence onsets. They varied in shape, latency and single-trial classification performance (evaluated by cross-validation of shrinkage-regularized linear discriminant analysis) from ERP responses evoked by brisk tone stimuli or syllables of earlier studies. These first results encourage us to further explore this very natural attention paradigm.
Spatial and Temporal Dynamics of Electrocorticogram related to Visual Stimuli for Signal Decoding and functional mapping

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For careful interpretation of spatial and temporal dynamics of electrocorticogram (ECoG) by semantic paradigms, we visualized high Gamma-band activity (HGA) induced by the tasks on individual brains, comparing functional MRI (fMRI) with similar paradigms. In order to reveal relationship between HGA and fMRI activity, we performed normalization of ECoG and fMRI on a template brain. Furthermore, we applied normalized ECoG patterns for classifiers in development of brain computer interface (BCI). Thirty patients underwent implantation of subdural electrodes bilaterally for diagnostic purpose of intractable epilepsy. Semantic-ECoG was recorded with word, figure, face recognition and memory tasks. The ECoG raw data was processed by averaging and time-frequency analysis and the functional profiles were projected on individual brain surface. Because of different electrode configuration of each patient, we made ECoG-fMRI normalization using SPM8. Time-frequency analysis showed three major spots with increased HGA in the left frontal, posterior left temporal and bilateral temporal base. The basal temporal-occipital cortex was activated within 250 msec after visual object presentations. Face stimulation evoked significantly higher ECoG amplitudes and stronger HGA than other stimuli. We found a positive correlation between HGA and fMRI activity, suggesting that the HGAs could be physiological correlates of fMRI. The time-course analysis revealed that different temporal dynamics of HGAs in the various regions. The frontal lobe showed longer-lasting HGA than the temporal lobe. Prediction rate of ECoG-classification reached 90% using the template, which was sufficient for clinical use. ECoG-fMRI normalization contributes to neurophysiological basic during semantic processing and improvement of decoding accuracy.

Figure 1. HGA dynamics of word reading task.

Figure 2. Temporal dynamics of high gamma activity of noticeable electrode clusters in frontal and temporal lobes. Each line color corresponds to electrode color. X and Y axes indicate latency and high gamma broadband index (HGBI), respectively. HGBI in the frontal lobe lasted longer beyond 1000 ms. On the other hand, rapid decline of HGBI was observed after 500 ms in the temporal lobe.


P376
Wireless EEG with individual channel positions facilitates efficient motor imagery training

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Question

Motor imagery (MI) neurofeedback holds great potential as a rehabilitation approach for patients with severe neuromuscular disabilities. The current study (1) identified the most informative bipolar EEG channels for each individual separately and (2) evaluated the accuracy achieved with a low-density, individualized electrode layout over three consecutive days.

Methods

EEG data were recorded from sixteen naive participants on four consecutive days each. At the first day a high-density recording was conducted and common spatial patterns (CSP) applied for online motor imagery. For the subsequent recordings the total number of channels was reduced to three bipolar channel pairs, consisting of one standard 10-20 channel pair and two individually-selected channel pairs. Since our goal was to improve the practicability of MI, online motor imagery sessions on the days 2 to 4, were conducted outside of the laboratory with the individualized low-density electrode layout and a wireless, mobile EEG system.

Results

Online classification accuracy on the first day was 85.1% on average (range: 64.7 - 97.7 %). Offline, CSP- and independent component analysis (ICA)-informed bipolar channel pairs revealed that CSP (71.3%) significantly outperformed ICA (68.3%) and standard bipolar channel pairs (66.3%). From day 2 to 4 online MI accuracy increased significantly, which was largely caused by less ipsilateral event-related desynchronizantion of sensorimotor rhythms.

Conclusions

We conclude that MI can be transferred out of the laboratory towards a daily life environment, using few EEG electrodes and a wireless, highly portable EEG system requiring very little application time.
LP24
Changes in the resting-state EEG induced by one single SMR-based Brain-Computer Interface session

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Question
Based on neurofeedback principles, the motor imagery task of sensorimotor Brain-Computer Interfaces (SMR-BCIs) has shown to speed up neurorehabilitation in stroke patients. Moreover, the amplitude of Electroencephalography (EEG) at rest over the sensorimotor areas was correlated with BCI performance [1]. A big issue is still how fast and how consistent among users the hypothesized BCI induced brain plasticity is.

Methods
In a recent study (18 users) which combines online algorithm adaptation [2] and a newly developed spatial filter [3], resting-state EEG has been measured before and after one single BCI session. All volunteers except for three novices, were chosen among poor performing BCI users. Here, the EEG at rest before and after the BCI session is analyzed by means of the SMR predictor [2], a measure of the SMR strength and its possible modulation. One SMR representative channel (subject-dependent) has been selected. By modeling its power spectral density (PSD) and the respective background noise, the SMR strength is the difference between the highest peak of the PSD and the noise.

Results
Fig. 1 shows, for each participant, the modeled PSD, noise and the SMR strength before and after the BCI session. In the title, the BCI performance achieved in the last run is indicated. A significant improvement (Fig. 2) of the SMR strength is obtained (p≈0.02). Most of users exhibited or developed the mu-rhythm, whereas beta is chosen as reactive frequency for users with no evident peak in the mu-band. One user with a prominent SMR in beta before the BCI session, developed a prominent mu-peak during the BCI training.

Conclusions
A precise neurofeedback as given by machine-learning BCI training can lead to significant development of SMR rhythms within one single BCI session as visible by EEG.

References


P377
Cortico-pallidal oscillatory connectivity in patients with dystonia


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Question

Deep brain stimulation (DBS) in the internal pallidum (GPI) is an effective treatment for patients with idiopathic dystonia. Therapeutic effects of DBS are hypothesized to originate from modulation of cortico-basal ganglia network activity. Enhanced pallidal low frequency activity (5-12 Hz) has been observed in dystonia that is coherent to involuntary dystonic muscle activity. However, little is known about the organisation of oscillatory network activity in cortico-pallidal circuits. To characterize the oscillatory cortico-basal ganglia network we performed simultaneous magnetencephalographic (MEG) and local field potential (LFP) recordings from the GPI in 10 patients (age: 48.9±0.7 years; 6f/8m) with idiopathic dystonia.

Methods

Simultaneous MEG-LFP recordings were conducted with the patients at rest with eyes open. LFP were recorded bipolarly from adjacent contact pairs of the DBS electrodes. Dynamic imaging of coherent sources (DICS) beamforming was utilized to visualise peaks of frequency specific cortico-pallidal coherence in Montreal Neurological Institute (MNI) space. Significant clusters were identified using Statistical Parametric Mapping (SPM).

Results

Two spatially and spectrally distinct cortico-pallidal networks were identified. Prominent peaks of cortico-pallidal coherence were found in the cerebellum and the ipsilateral temporal cortex for the alpha band (7-13 Hz), whereas significant beta band (12-35 Hz) coherence was more focally distributed in the ipsilateral frontal motor area.

Conclusions

Our results suggest a motor network characterized by beta band coherence between GPI and motor cortex that is in line with previous MEG and EEG studies in patients with Parkinson’s disease. Interestingly, we found alpha band coherence between the GPI and the cerebellum in our patients. The latter could hint at additional cerebellar involvement as abnormalities in cerebellothalamocortical fiber tracts have been described in dystonia.
P378
Right hemispheric dominance of visual phenomena evoked by intracerebral stimulations of the human visual cortex

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Electrical brain stimulation provides important information about the functional organization of the human visual cortex. Here we present an extensive report of visual phenomena evoked by intra-cerebral electrical stimulations performed at low-intensity with depth electrodes implanted in the occipito-parieto-temporal cortex of epileptic patients. Focal electrical stimulation evoked a majority of visual hallucinations with various complexity: simple (spot or blob), intermediary (geometric forms) or complex meaningful shapes (faces). Visual illusions and impairments of visual recognition were more rarely observed. The probability to evoke a visual phenomenon was significantly higher in the right than the left hemisphere (27 % vs. 8%). Intermediary and complex hallucinations, illusions and visual recognition impairment were almost exclusively evoked by stimulation of the right hemisphere. The probability to evoke a visual phenomenon dramatically decreased from the occipital pole to the most anterior sites of the temporal lobe, and this decrease was more pronounced in the left hemisphere. The greater sensitivity of the right occipito-parieto-temporal regions to intracerebral electrical stimulation to evoke visual phenomena supports a predominant role of right hemispheric visual areas from perception to recognition of visual forms, regardless of visuospatial and attentional factors.
Automatically generated STN model based on intraoperative microelectrode recordings assists in postoperative management of DBS settings and clinical research.

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Question

MRI images used for preoperative targeting in STN-DBS surgery, do not always show all STN boundaries clearly. Therefore, intraoperative microelectrode recordings (MER) are often used to fine-tune STN targeting and thereby guide electrode implantation. However, this detailed neurophysiological information is currently not used postoperatively. The current study uses the MER information to create a detailed model of STN size and location which may be of help to delineate the true boundaries of the nucleus in relation to the implanted electrode.

Methods

An elaborate optimization routine, which uses the classifications of MER points as inside/outside the STN together with preoperative planning parameters, is used to fit an atlas-based 3D model of the STN body to the exact stereotactic location of the measured MER ¹ (figure 1). Independently fitted STN models for both hemispheres are exported to DICOM images which include a model of the stereotactic frame as well as AC, PC and midline markers. The model can thus be fused with preoperative MRI and postoperative CT images to verify its position and relate it to the implanted electrode’s position (figure 2).

Results

Initial results show good overlap in STN size and position between calculated STN models and T2 MRI images in which the STN is clearly visible, even when STN position is asymmetrical or deviant from atlas coordinates. With the coordinates of the DBS electrode from the postoperative CT a detailed 3D model of the lead’s path through the STN body can be made.

Conclusions

A detailed representation of the DBS contact points within the true STN body can be provided by a MER based model which delineates STN boundaries, improving on the imaging-based initial STN model by providing functional information. This can be of help in answering clinical research questions on the relation between stimulation sites and effects of DBS.

References


Figure legends

Figure 1: Automated fitting of the atlas-based STN body and its sub-areas to the classifications of the MER points.

Figure 2: Fusion of the fitted STN models and preoperative T2 MRI images in axial and coronal view.
Abstracts of Poster Presentations – Poster Session 23 – Deep brain stimulation

figure 1

<table>
<thead>
<tr>
<th>STN atlas fitting</th>
<th>MER data</th>
<th>MER data + atlas STN</th>
<th>MER data + fitted STN</th>
</tr>
</thead>
<tbody>
<tr>
<td>MER scored inside STN</td>
<td>MER scored outside STN</td>
<td>Sensorimotor STN</td>
<td>Non-sensorimotor STN</td>
</tr>
</tbody>
</table>

figure 2
Abstracts of Poster Presentations – Poster Session 23 – Deep brain stimulation

P380
Single cell firing patterns may guide Anterior Thalamic Nucleus targeting in Deep Brain Stimulation surgery for refractory epilepsy

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QUESTION
Patients with medically refractory epilepsy receiving deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) vary in their response to the stimulation. This may be due to suboptimal targeting based on anatomical landmarks in MR imaging. Here, we have tested the hypothesis that intraoperative micro-electrode recording is an adequate method to identify the ANT and guide DBS electrode implantation.

METHODS
9 patients with medically refractory epilepsy were included. The lead trajectory was planned via an extra ventricular route to the ANT. The ANT was defined as the thalamic area where the mamillothalamic tract projects to, which could be identified and tracked on routine T2W 3T images. (Multi-)electrode microelectrode recordings were performed to identify the (single unit) neuronal signals of the anterior thalamic neurons.

RESULTS
We consistently found neurons firing in high-amplitude bursts, starting at 10 to 4 mm above the pre-defined target. These bursts, sometimes occurring in runs, were found in all 9 patients. See figure for illustrative recordings. In some patients, the amplitude of the bursts was higher in the vicinity of the target, when compared to the levels further away from the target.

CONCLUSIONS
The bursting firing pattern we found might be characteristic to the target area, and perhaps specific to epilepsy patients. This needs further investigation. We experienced that microelectrode recording can facilitate the implantation of DBS electrodes in patients with refractory epilepsy.

Legends to Figure: Bursting firing pattern of neurons in the ANT

figure 1
Abstracts of Poster Presentations – Poster Session 23 – Deep brain stimulation

P382
Cerebello-thalamo-cortical circuits and basal ganglia interactions in Parkinson’s patients with bilaterally implanted deep brain stimulating electrodes into subthalamic nuclei.

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Question

Deep brain stimulation (DBS) into subthalamic nucleus (STN) is an effective treatment for advanced Parkinson disease (PD). However, our knowledge about its effects over cortical activity is still lacking. In a previous study, we demonstrated that levodopa-induced dyskinesia in PD can be reduced by cerebellar continuous theta burst stimulation (cTBS), through the modulation of cerebello-thalamo-cortical (CTC) circuits activity, thus suggesting an interaction between CTC and basal ganglia circuits. Therefore, our aim was to investigate the effects of DBS and cerebellar cTBS over the cortical activity of STN-DBS treated PD patients with a combined Transcranial Magnetic Stimulation (TMS)/EEG approach.

Methods

Six PD patients with DBS were tested in 3 different conditions on distinct days. In the Off-OFF condition first-morning levodopa medication was suspended and DBS turned off. In the Off-ON condition the dopaminergic medication was suspended but DBS was on. In the On-ON condition, patients continued their usual dopaminergic medications and the DBS was on. In each condition before and after cerebellar cTBS, 80 single pulse TMS were delivered over M1, contralateral to the clinically more affected side while acquiring EEG. Event-related desynchronization/synchronization was than calculated for theta (4-7Hz), alpha (8-12Hz) and beta (13-30Hz) band.

Results

During On-ON condition, TMS induced a higher beta synchronization when compared to all other conditions (p=0.006) and Off-OFF condition was associated with lower level of beta. After cTBS there was an increased beta synchronization regardless the condition (p<0.05), boosting the beta level of Off-On and Off-OFF conditions to the On-ON induced level. All effects were restricted to the closest electrode to M1.

Conclusion

In conclusion, the increase of beta level after cerebellar stimulation suggests a possible interaction between CTC and basal ganglia circuits.
Identification of genetic predictors on positive therapeutic outcome in subthalamic stimulation in Parkinson's disease

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Question

Deep brain stimulation of the subthalamic nucleus (STN-DBS) provides an established therapy in idiopathic Parkinson's disease (iPD) complicated by motor fluctuations. However, the therapeutic outcome and disease progression presents with high interindividual variability and may reflect the pathogenic heterogeneity of iPD. Genetic biomarkers on therapeutic outcome and disease progression are highly warranted.

Material and Methods

We analyzed the therapeutic outcome of 59 iPD patients with STN-DBS. Clinical data (UPDRSIII and others) were obtained from the regular clinical follow-up documentation and pooled for consecutive 2-year intervals. Here, we report on the preoperative data and two-year follow-up with STN-DBS. All patients were screened for the SNCA gene (α-synuclein), LRRK2 (leucin-rich kinase) und MAPT (microtubulus-associated gene). We applied a linear regression model to determine disease impairment according to the UPDRS III and introduced SNCA, LRRK2, and MAPT as dependent variables.

Results

Our preliminary exploratory analyses reveal that there were no preoperative differences between the distinct genetic profiles. At two-year follow-up, however, the variance was reduced by 7% in the SNCA group only (coeff = -7.59, S.E = 2.54, P = 0.004). Patients with SNCA risk gene responded better on STN-DBS.

Conclusion

Genetic predictors may indicate favorable therapeutic outcome from STN-DBS in future. Further analyses are planned to evaluate the long-term therapeutic outcome. It is of particular interest to predict the emergence of resistant axial motor symptoms and cognitive impairment and this will be analyzed.
Can low-frequency stimulation of subthalamic region improved self-generated isometric movement in patients with Parkinson's disease?

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**Question**

Growing evidence suggests that oscillatory activity at ~10 Hz in the subthalamic area (STN) may correlate with the speed of gait and ballistic movement. Whether the ~10 Hz stimulation can modulate motor performance in patients with Parkinson's disease (PD) in some particular circumstance remains unclear.

**Methods**

15 PD patients implanted with deep brain stimulation electrodes (DBS) in bilateral STN were stimulated at 5, 10, 20, 50 and 130 Hz and the effects of the DBS on self-initiated isometric movements were compared to performance with stimulation.

**Results**

Peak force was significantly greater during 130 and 10 Hz stimulation when compared to no stimulation. Cumulative sums of the changes in mean rising force and peak force upon stimulation at 10 and 20 Hz demonstrated that patients improved their performance on stimulation, except for those with the best performance off stimulation who deteriorated with 20 Hz stimulation.

**Conclusions**

It is necessary to consider the baseline performance of a subject in a given task when determining the effects of low frequency stimulation in PD. 10 Hz stimulation can improve motor function in subjects with poor baseline function.
Local field potentials in the Parkinsonian STN recorded with a new 32-contact DBS lead can be used to localize the STN and to evaluate the neuronal response to stimulation.

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Question

During STN-DBS stereotactic surgery a new DBS lead is used with a 32 contact array. Since contacts are pointing in different direction, in principle it is capable of directionally steering stimulation and it also can be used to record local field potential (LFPs) from its contact points. Spatial and temporal content of the LFPs, related to the patient’s symptomatology, could be used to determine how to direct the current delivered through a selection of the contact points. In this way microelectrode recordings (MER), conventionally used for fine-tuning of the MRI-based target, but which require additional recording time and may increase the risk for haemorrhage, might be no longer needed.

Methods

Eight patients with Parkinson’s disease are included in the study. After MER the new 32-contact electrode is temporarily inserted during surgery. MER performed successively at different depths are compared with the multidirectional 32 channel LFPs recordings, which are measured simultaneously. After artifact removal, frequency analysis of the LFPs is performed at baseline, just prior to and immediately after the stimulation period. Particularly the frequency band between 10 to 40 Hz has been evaluated.

Results

The distribution of spectral information across the electrode array shows a clear relationship with the morphology and the abnormal oscillatory behavior of the Parkinsonian STN. In addition, recordings after different modes of stimulation, i.e., steering or ring mode, show various effects of stimulation on the spectral distribution in the 10-40 Hz frequency band. In general, stimulation shows a suppression of the oscillatory beta activity of the STN.

Conclusions

Through 32 small contacts of a new DBS lead it is possible to perform simultaneous LFP recordings across the entire STN without moving the electrode, providing multidirectional spatial and temporal information about disease-related electrical activity of the STN and the effect of stimulation. This may potentially be of benefit in predicting how to steer the current in the most effective way.

![Figure 1](image-url)
LP25
Predicting “free” motor-decisions from subcortical brain signals.

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During the last three decades, neuroscience has challenged our belief that we can consciously control our decisions. Brain activity prior to an action is modulated before a conscious decision (Haggard & Eimer 1999; Libet et al. 1983) and even contains information predicting the choice outcome (Libet et al. 1983; Fried et al. 2011; Soon et al. 2008, 2013). However, the majority of these findings is based on cortical activity, whereas the role of subcortical regions still remains largely unexplored. In this study we investigated the role of the Nucleus Subthalamicus (STN) in the formation of free decision. To do so, we recorded local field potentials (LFPs) from the STN of 13 patients that underwent deep brain stimulation for severe Parkinson’s disease. We used a variant of the self-paced Libet task in which patients freely decided which of two buttons they want to press and press it immediately. Patients had also to remember and report the time $W$ at which they believed to have decided (Libet et al. 1983). The time course of choice-related information was computed from LFPs using multivariate pattern classification and compared to the self-reported $W$. Due to poor behavioral performance, only six patients were analyzed. Our group analysis shows that, the STN activity predicts the decision about one second before the action and four times the standard deviation before the average $W$. Consistently with Soon et al. (2008, 2013), accuracy of prediction is moderate, suggesting a potential modulating role of STN in formation of free decisions.
Intraoperative Microelectrode Recording for the Mapping of the Subthalamic Nucleus in Parkinson’s Disease: A Descriptive Analysis of 145 Patients

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QUESTION
The subthalamic nucleus (STN) is the main surgical target in advanced Parkinson’s disease (PD). The deep brain stimulation (DBS) of this nucleus improves the predominant symptoms (akinesia, rigidity, tremor) of the disease making possible the diminution of dopaminergic drugs which also contributes to reduce the dyskinesia. The micro-electrode recording (MER) during surgery is a technique that allows the mapping of the sensorimotor region of the STN, the goal of stereotactic electrode placement in high frequency DBS.

METHODS
The MER of the STN in each track was made with a single high impedance electrode. The following data was collected: presence/absence of thalamus in the MER; millimeters (mm) of STN recorded; presence/absence of movement response units (“driving”); effect to microstimulation; difference in mm between X-Y-Z theoretical coordinates as planned with neuroimaging (CT-MRI fusion) and the final coordinates of the track chosen based on the result of MER.

A detailed analysis is presented corresponding to 914 MER tracks from which 299 were definitive tracks, of 145 PD patients who underwent stereotactic surgery in our hospital from the year 2000 until 2013.

RESULTS
In 30% of the tracks the thalamus was identify; in the remaining 70%, the tracks went directly through the internal capsule.

A mean of 4.5 mm of STN was recorded. “Driving” was present in a 44.5% of the interventions. When the STN is defined in the first track, an average of 2.25 tracks/target were made. A single track was made for the target in a 31.8% of the procedures.

In 53.5% of the final targets the X or Y coordinate was modified in a 1.5-3 mm and in 14.7% >3 mm. The mean deviation is 2.38 mm in the X-axis with discrepancies in 39.5% (118) of the tracks: 24.5% (29) lateral and 75.5% (89) medial. Regarding the average deviation in the Y-axis is 2.51 mm with a mismatch in 41.5% (121): 29.7% (36) anterior and 70.3% (85) posterior.

CONCLUSIONS
The variations of the theoretical coordinates are in regard to the internal capsule adverse effect to the stimulation. The MER technique modifies the X-Y coordinates in more than 1.5 mm in 68.2% of the targets so it represents a useful tool in this functional neurosurgery to improve the accuracy for definition of the sensorimotor region of the STN.

In vivo human microstimulation and microrecording of a sclerotic hippocampus and a cortical dysplasia

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Intracerebral microelectrode recording (MER) and microelectrode stimulation (or microrecording and microstimulation, respectively) involve the application of an electrical stimuli through a microelectrode and simultaneously the recording of the response of one or few neurons in proximity of the stimulation. We applied these techniques in humans with epilepsy with the objective to better understand the mechanism of action of brain stimulation against epilepsy.

MER were recorded simultaneously or not to microstimulation in two patients with epilepsy (one with hippocampal sclerosis; one with cortical dysplasia). Neuronal spikes were extracted from multi-unit recordings with clustering. Multi-unit activities were recorded simultaneously to 1Hz stimulation (biphasic pulses, 60 ms/ph; 500 mA for macrostimulation; 25 mA for microstimulation).

Different patterns were recorded from the hippocampus and from cortical dysplasia. Microstimulation (1 Hz) induced a significant decrease in spike firings in the patient with hippocampal sclerosis (p<0.001), while it induced a significant increase in spike firings in the patient with cortical dysplasia (p < 0.001).

For the first time in humans, we showed that 1 Hz microstimulation induced, in agreement with previous in vitro observations and in vivo animal models, 1) an inhibitory effect in a sclerotic hippocampus at the neuronal level (whereas an epileptogenic effect is usually associated with low frequency macrostimulation); 2) an excitatory effect in a cortical dysplasia, supporting the ability of cortical low frequency stimulation to modulate neuronal activity for seizure prevention. In fact, combined microstimulation and microrecordings in humans, providing measurements at the level of a few neurons only, can bridge the gap with studies conducted in vitro and in vivo, leading to a better understanding of therapeutic electrical brain stimulation.
P387
SEIZURE DETECTION WITH AUTOMATED EEG ANALYSIS: A VALIDATION STUDY FOCUSING ON PERIODIC PATTERNS

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Question
To evaluate an automated seizure detection algorithm in EEGs with periodic and other potentially challenging patterns (artifacts, normal variants).

Methods
Selected EEGs recorded in patients over 1 year, from January 2012 to March 2013, were classified into four groups: A. Periodic lateralized epileptiform discharges (PLEDs) with intermixed electrical seizures (any variation of the PLEDs/PEDs amplitude, together with acceleration of frequency and/or change in field or morphology). B. PLEDs without seizures. C. Electrical seizures and no PLEDs. D. No PLEDs or seizures. Each recording was analyzed separately by Persyst P12 software, and compared to the raw EEG, interpreted by two experienced neurophysiologists, representing the gold standard; 2x2 tables were constructed for A. and C., using B. respectively D as true negatives. Positive percent agreement (PPA) and false-positive rates/hour (FPR) were calculated.

Results
We assessed 98 recordings (Group A= 21 patients; B= 29, C= 17, D= 31). The total duration of all recordings was 82.7 hours (median: 1 hour); these contained 268 seizures (groups A and C). The software detected 204 (=76.1%) seizures; all ictal events were captured in 29/38 (76.3%) patients; in only in 3 (7.7%) no seizures were detected. The median overall PPA was 100%, and the median FPR 0/h; however, lower performances were seen in the groups containing periodic discharges.

Conclusion
This analysis provides data regarding the yield of the automated seizure detection in a particularly difficult subset of EEG recordings, showing that periodic discharges may bias the results. It is likely that ongoing refinements in this technique will enhance its utility and lead to a more extensive application.
**P388**  
Intracranial Metallic Body Artifact in Routine scalp EEG.

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**Background**

EEG artifacts are considered a disturbance in a measured brain signal and can be divided into physiological and extra physiological. Routine scalp EEG recording with an impeded intracranial metallic bullet represent a situation of merge between both types of artifacts in the same instance that is expected to interfere with the signal quality.

**OBJECTIVES**

We searched online for literature on rare EEG artifacts with an emphasis on intracranial metallic body artifacts yet there was no available data. The aim of this report was to create awareness about what to expect during the EEG recording in this situation.

**Case Series**

Two patients were presented one of them for stat EEG and the other for routine EEG. The former was a 19 years old male with a deeply imbedded intracranial bullet near the base of the skull presented with a rapidly progressive disturbed conscious level. The latter was a fully conscious 26 years old male with an imbedded bullet in the right hemisphere presented with focal seizures with secondary generalization.

**Discussion**

Standard EEG recording was done with the high filter set at 70 Hz. Other than an initial generalized interference pattern that disappears with meticulous adjustment of the impedance, the presence of intracranial metallic foreign body in both cases didn't exist a significant effect upon the EEG signal quality. The interpretation of the EEG for both patients was moderate cerebral encephalopathy and right regional epileptiform discharge with secondary bilateral hypersychrony respectively. The second patient's right hemispherical bullet show an additional finding of background asymmetry that was interpreted as a breech rhythm. The EEG record of both patients was very sensitive to any minor change in the impedance.

**Conclusion**

Routine scalp EEG record of patients with an intracranial metallic foreign body was expected to show a difficulty in EEG interpretation, yet a good quality EEG signal can be achieved by proper EEG application with a meticulous concern upon the impedance. Further work is required to identify if the material or the location of the metallic foreign body might represent a different finding than this presented here.
P389
Can event related desynchronization be used as a cognitive marker?

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Aim of the study

The present research aims to show that the occurrence of alpha blocking (or ERD) strongly depends on the amplitude and also on the phase angle of alpha activity at the stimulus onset.

Method

Simple visual stimulation was presented to 17 healthy subjects during EEG recording. An O₂ electrode was used for analysis with a 32 channel EEG sampling system. We used a segmentation of raw data in order to obtain the evoked potential. Prestimulus and poststimulus activities were filtered in the alpha (8-13 Hz) frequency band. Later, four different events (Blocked, Time-locked, Phase-locked, and Eliminated) were separately averaged. Phase-locked sweeps were determined by application of Inter-trial coherence analysis.

Results

The evaluation of the data shows that “time-locked and phase-locked sweeps” were the dominating pattern and not “the blocked pattern”, which occurred only when the prestimulus alpha was high. In the analyses of EEG-EP sweeps, only 22 % of epochs showed (ERD). The ANOVA revealed significant differences between four different alpha responses (F(3,48) = 11.175; p<0.001). Furthermore, alpha oscillations in time-locked responses were significantly higher than blocked (p<0.0001).

Conclusion

The analyses clearly demonstrate that important precaution is needed when using the ERD as a cognitive or pathological marker.
Assessment of the relationship between EEG signals in epileptic patients and cerebral lateralization using nonlinear analyses and MRI

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Physiological functions are considered to be associated with cerebral lateralization; the brain is physiologically and anatomically asymmetric. The nonlinear analysis may assess the normal and pathological condition of these systems. Although it has been shown that the both normal and epileptic Electroencephalography (EEG) signals had chaotic dynamics, the normal EEG signals are strongly chaotic than epileptic EEG signals [1]. This result is considered as there is a variability loss in the brain’s electrical activity with the epilepsy.

Lyapunov exponent is a quantitative indication of the chaotic level of a system. In this study, the Lyapunov exponents of the left frontopolar - the left inferior frontal (FP1-F7) and right frontal - right inferior frontopolar (FP2-F8) channels of the EEG signals recorded from both right-handed patients with the epileptic seizure and seizure-free interval were investigated and it has been shown that the first positive Lyapunov exponents of patient with seizure-free interval were greater than patient with epileptic seizure for all channels.

The chaotic difference for both right-handed patients between the left frontopolar - the left inferior frontal (FP1-F7) channels were stronger than the chaotic difference for both right-handed patients between right frontal - right inferior frontopolar (FP2-F8) channels. The results of nonlinear analyses compared with Magnetic Resonance Imaging (MRI) data. Lyapunov exponent values in the hemisphere with lesions were found to be smaller than the values in the healthy hemisphere.


Keywords
Cerebral Lateralization; Electroencephalography; Epilepsy; Nonlinear Analyses; Magnetic Resonance Imaging
P391  
Electrophysiologically assessment of patients with isolated thalamic infarcts: a large, prospective, case control study  

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Purpose  
The aim of this study was to analyse the EEG changes in patients with isolated thalamic infarcts in relation to their localization within thalamus.  

Methods  
Cranial magnetic resonance imaging (MRI) and EEG features of 42 patients who had thalamic infarcts were evaluated in acute and chronic states with a prospective long term follow-up design. The patients were separated into 4 groups: Anterior, Medial, Lateral, Other involvements (posterior and central) according to the lesion localization in MRI. Control group consisted of healthy matched people.  

Results  
Lateralization of EEG abnormalities was consistent with the infarct side in 83.3% of the patients. EEG abnormalities were detected in all of the Anterior Group. EEG showed a significant abnormality in none of the Central and in half of the Medial Group. Generalized slow wave activities had significantly higher proportion in the Lateral Group which is the group including patients with a prominent involvement of the reticular nucleus. The rate of lateralized EEG findings was significantly higher in the Medial Group when compared with the Control Group. Sharp waves were observed in 5 out of all patients, 2 of them were in the Lateral Group. There was no specific EEG patterns.  

Conclusion  
Lateralizations of EEG and MRI findings correlated well in most of the patients with ischemic lesion limited to thalamus. Further studies with large number of patients and assessment of EEG findings with spectral analysis can give more detailed information about the effect of thalamic nuclei to electrophysiology.
West Syndrome (WS) is an age-related epileptic encephalopathy characterised by seizures called infantile spasms, arrest of psychomotor development and hypsarrhythmia on interictal electroencephalogram (EEG) recordings. It is resulting from multiple and diverse causes divided into prenatal (cerebral dysgenesis, genetic disorders, intrauterine infection), perinatal (anoxic injury, head trauma, infection), and postnatal (metabolic disorders, trauma, infection). No etiology (cryptogenic) can be identified in as many as 40% of cases.

METHODS

We present a descriptive and retrospective study of clinical and electrical characteristics in 46 children (23 boys and 23 girls) diagnosed of WS in our hospital between 2008-2012. We have analysed aetiology, epidemiology, EEG characteristics, treatment and clinical evolution data.

RESULTS

Most of patients revised (85%) are symptomatic WS, while 15% of them are cryptogenic. The clinical debut is spasms in 85%, with a mean age of 5 months, drop head in 6.5% and other seizures in 8.5%. The EEG shows bilateral hypsarrhythmia in 95.7% and unilateral in 4.3%. The treatment used is Vigabatrin in monotherapy in 65% of the patients, Vigabatrin and corticosteroids in 19.5% and Vigabatrin in combination with Valproic Acid in 15 %. The mean time between the appearance of the hypsarrythmia in the EEG and the disappearance of this, once the treatment is administrated is 2 months. 3 patients died during the review. After the onset of treatment, the hypsarrhythmia in EEG disappears completely in 28% of the cases having a normal EEG, while in the other 72% a pathological EEG persists (4 of the patients develop a Lennox-Gastaut syndrome).

CONCLUSIONS

The EEG is a very useful tool for the diagnosis and the follow up of children with WS. The sooner these patients are treated, the better will be the prognosis, although there is a high percentage of patients with a very bad outcome.
P393
Electrocortical activity matched with gait cycle during treadmill walking

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Question
Locomotor disorders represent a major burden after stroke and the walking rehabilitation represents one of the most challenging aspect in the field of stroke treatment. With the aim to better understand the neurophysiopathological mechanism underlying the gait impairment in stroke survivors we developed an approach consisting of simultaneous recording of electrocortical activity and kinematics of gait. We present a feasibility study on healthy subjects.

Methods
Cortical activity was recorded by a 64 channel EEG with actiCAP active electrodes system and a DC-coupled amplifier (Micromed SD MRI, System Plus acquisition software). Participants walked on a treadmill at 2Km/h speed for ten minutes. Gait cycles (epochs between two left heel strikes) were identified with 4 footswitches. The EEG data were high pass filtered (1.5 Hz) and processed with REMOV [1]. After epoching ([0 - 2]s time-locked to the left toe off) the ERSP (Event-Related-Spectral-Perturbation) was computed on two Independent Components localized onto the motor area. Spectra were time-warped so as to align heel strike/toe off events for both legs, and normalized with a whole-trial-wise baseline. Significant ERSP changes were computed with a bootstrapping procedure.

Results
ICA components showed the presence of electrocortical sources active during human walking (Figure 1). Their ERSP shows an alternating spectral power density activity in beta e gamma frequencies which is time-locked to the gait cycle.

Conclusions
The experimental setting described above proved to be appropriate to record gait-related cortical activity in healthy subjects and it may also be used also for stroke patients.


Figure 1. Activation maps with ERSP extracted from the EEG signal of a healthy subject during walking on a treadmill: primary motor area activity respectively on the right (a) and left (b) sides.
P394
EEG PATTERN RELATED WITH THE ADMINISTRATION OF KETAMINE IN THE TREATMENT OF REFRACTORY STATUS EPILEPTICUS MIMICKING EXTREME DELTA BRUSH: A CASE REPORT.

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QUESTION

To describe the presence of an electrographic pattern mimicking ‘extreme delta brush’ (EDB) in a patient with refractory status epilepticus associated to a diffuse leptomeningeal melanocitosis.

METHODS

Patient of 16 y.o. with a diagnosis of diffuse leptomeningeal melanocytosis admitted to our hospital with a partial status epilepticus. Previously, he presented partial complex seizures beginning in the right lower limb and a chronic cephalalgia. The cranial MRI showed at first a cortico-subcortical wide lesion and a chronic subdural collection in frontal left hemisphere with a leptomeningeal infiltration. A brain biopsy confirmed the diagnosis. EEG at the beginning of the disease showed a focal slow activity in fronto-temporal regions without epileptiform abnormalities.

RESULTS

Serial EEG studies were performed in ICU showing initially a pattern of pseudo-periodic delta waves with spikes and sharp waves in left hemisphere and focal ictal discharges in left temporal regions (PLEDs-plus). Pharmacologic coma was induced with pentobarbital obtaining ‘burst-supression’ pattern without epileptiform activity. Three days after pentobarbital was suspended and electrographic seizures reappeared in the left frontal area. A second barbiturate coma was induced for three days more and after that sedation with Midazolam was instaured with the persistence in the EEG of left frontal sharp waves. Thereafter ketamine was administered (dose 2 mcg/kg/d). On the second day the EEG recording showed rhythmic delta activity (1-1.5 Hz) with beta activity (13-14 Hz) superimposed in the negative deflection of the delta wave localized in the frontal left hemisphere regions, unmodified by the external stimuli, but with the persistence of electrographical seizure. Because of the refractoriness of the seizures and the bad prognosis ketamine was stopped three days after. At that moment the EDB-like pattern disappeared.

CONCLUSION

The EDB was described as a unique EEG pattern in anti-NMDAR encephalitis. Ketamine is a NMDAR antagonist producing in animals an enhancement of gamma frequency oscillations and an attenuation of theta activity. We hypothesize that the pattern observed in our patient will be the reflection of the ketamine anti-NMDAR effect.

Figura 1-2: Extreme delta brush - like pattern. Rhythmic delta activity (1-1.5 Hz) with beta activity (13-14 Hz) superimposed in the negative deflection of the delta wave localized in the frontal left hemisphere regions.
P395
Switching from bimanual to unimanual tapping reveals two distinct post-switching beta synchronization processes

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Question

Post-movement beta synchronization is involved in several mechanisms, such as the deactivation of motor execution, the processing of sensory reafferences or the active inhibition preventing movements from other body parts. These phenomena have still not been investigated in relation to the selective inhibition during multi-limb coordination task. In this study, we investigated post-switching beta synchronization (PSBS) during a switching from bimanual to unimanual finger tapping. We computed source estimation to discriminate the implication of PSBS in inhibitory and sensory reafferences processing.

Methods

Participants (n= 17) initiated a 2 Hz auditory-paced bimanual tapping. After a 1500 ms preparatory period, an imperative stimulus required to either selectively stop the left while maintaining the right unimanual tapping (SWIT) or to continue the bimanual tapping (CONT). Paired t-tests were performed between SWIT and CONT conditions on 14-30 Hz time-frequency data from the switching period (epoch duration: 2500 ms).

Results

PSBS significantly increased in SWIT compared to CONT with maximal difference within right central region in 14-30 Hz and within left central region in ~22-26 Hz. Source estimations localized these effects within the right pre-frontal cortex (superior frontal gyrus) and within the left parietal cortex (superior and inferior parietal lobules).

Conclusion

This study shows for the first time simultaneous PSBS with distinct functions in different brain regions and frequency ranges during a switching task. The left parietal PSBS restricted to ~22-26 Hz could reflect the sensory reafferences of the right hand tapping. In contrast, the right frontal PSBS in a large 14-30 Hz frequency band is likely reflecting the active inhibition of the left hand. Switching was revealed to be a suitable paradigm to evidence distinct functional aspects of post-movement beta synchronization.
P396
ANALYSIS OF EVENT RELATED BETA AND GAMMA OSCILLATIONS IN PERCEPTION OF AFFECTIVE PICTURES

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Question

The previous literature showed that unpleasant stimuli of affective pictures (IAPS) elicited higher beta and gamma oscillatory responses than neutral and/or pleasant stimuli. However, it was not clear yet how the stimulation design would affect the oscillatory responses. The present study analyzed event related beta and gamma oscillatory responses upon presentation of unpleasant, neutral, pleasant pictures, which were shown to the subjects in block or random design.

Methods

EEG of 22 healthy subjects were recorded at 32 locations. The participants passively viewed 120 emotional pictures (10X4 unpleasant, 10X4 pleasant, 10X4 neutral) in a block and random design. The phase locking and power of event related beta (15-27 Hz) and gamma (28-48 Hz) oscillations were analyzed in two different time windows (0-200 ms and 200-400 ms).

Results

Statistical analyze showed that in the first time window during the block design unpleasant stimulation elicited higher beta phase locking and beta power than the pleasant and neutral stimulation (p<0.05). In the second time window during the block design over occipital electrodes unpleasant stimulation elicited higher gamma response power than the pleasant stimulation and neutral stimulation (p<0.05). Unpleasant stimulation did not elicited higher beta or gamma responses in random design.

Conclusions

The present study showed that design matters in perception of IAPS pictures. Unpleasant stimulation elicited higher event related beta and gamma phase locking and power only in block design but not in random design. It seems that continuous observation of unpleasant stimuli affects the brain more than random observation.
P397
Fast Automated Detection of Inter-Ictal Epileptiform Discharges Using Smart Templates and Iterative Reviewing

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Question

Automated detection of Inter-ictal epileptiform discharges (IEDs) may assist clinicians in reviewing EEGs faster and more efficiently. Although many algorithms exist, all of them face a similar problem: to achieve high sensitivities, false positive rates remain high, making the manual search for IEDs faster than reviewing all detected events. Our objective was to find a solution that will make automated detection faster and more efficient than conventional methods.

Methods

Using an automated detection algorithm described in Lodder and van Putten (Inter-Ictal Spike Detection using a Database of Smart Templates. Clin Neurophysiol; 2013), IEDs are detected using a database of trained templates each representing an IED waveform. During a detection phase, templates nominate IEDs with high correlations to themselves and pair them with detection certainty values. During the review phase, the ten most likely nominations based on certainty values are presented to the reviewer, which either confirms or rejects them as IEDs. After ten events are reviewed, certainty values of the remaining nominations are updated based on the reviewer feedback, and iteratively another ten nominations are presented for review. Confirmed events are stored and marked as detected IEDs.

Results

Evaluation was performed on a test set of 15 EEGs (306 min, 244 IEDs marked by an experienced reviewer). A total of 8426 events were nominated as epileptiform events, and 241 of the 244 IEDs were detected (25.8 fp/min over all certainty levels). Using the described method, 15 iterations (10 events reviewed per iteration) were performed on each EEG, and the number of confirmed IEDs was counted after each iteration. Results show that 74% of all marked IEDs were found after five iterations, 90% after ten iterations, and 95% after fifteen iterations. The review time for each iteration was on average twenty seconds, resulting in a total review time of five minutes per EEG.

Conclusions

The use of automated IED detection algorithms are limited by their high number of false detections. The proposed method shows how automated detection can be used to find IEDs in a fast and efficient manner, regardless of a high false detection rates. Compared to conventional methods, it can improve review times significantly and make long-term recordings for epilepsy diagnosis more feasible.
Electroencephalographic abnormalities in antisocial personality disorder

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The presence of brain dysfunction in violent offenders has been frequently examined with inconsistent results. The aim of the study was to assess the EEG of 84 violent offenders by visual inspection and frequency-domain quantitative analysis in 84 violent prisoners. Low-resolution electromagnetic tomography (LORETA) was also employed for theta band of the EEG spectra. Antisocial personality disorder (ASPD) was present in 50 of the offenders and it was absent in the remaining 34. The prevalence of EEG abnormalities, by visual inspection, was similar for both the ASPD group (82%) and non-ASPD group (79%). The brain topography of these anomalies also did not differ between groups, in contrast to results of the EEG quantitative analysis (QEEG) and LORETA that showed remarkable regional differences between both groups. QEEG analysis showed a pattern of excess of theta-delta activities and decrease of alpha band on the right fronto-temporal and left temporo-parietal regions in the ASPD group. LORETA signified an increase of theta activity (5.08 Hz) in ASPD group relative to non-ASPD group within left temporal and parietal regions. Findings indicate that QEEG analysis and techniques of source localization may reveal differences in brain electrical activity among offenders with ASPD, which was not obvious to visual inspection.
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P399
EEG Independent Component Analysis and 3D Localization of Brain Pathological Areas

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EEG Independent Component Analysis and 3D Localization of Brain Pathological Areas

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Independent Component Analysis (ICA) is a computational method widely used in practice for EEG artifact removal. ICA can be also used for the improving of 3D dipole localization method. ICA decomposition of an EEG allows to separate independent components containing paroxysmal activity. Independent components without paroxysmal activity are to be excluded from analysis. The target trace processed with ICA contains only fragments with paroxysmal activity. This technique provides clear visualization of paroxysmal events on trace and improves results of 3D dipole localization.

The validity and performance of the approach were confirmed by medical trial. A total of 8 patients aged from 13 to 58 year with clinically proven epilepsy were examined. Long-term EEG was recorded from all the patients. Recorded EEG traces were processed using ICA method. Raw EEG traces and traces obtained after ICA processing were exposed to 3D localization by dipole model using BrainLoc 6.0 software for 3D dipole localization (Neurosoft, Russia).

Research shows that the graphic representation of paroxysmal events on trace is denser for ICA-processed EEG trace than for raw trace. So, the 3D dipole localization of ICA-processed EEG traces is far more efficient than 3D localization of raw EEG traces.

Conclusion: This composite method helps to reduce redundant data for better feature extraction. The efficacy of the combined algorithm was proven during medical trial.
P400
Home Video Telemetry vs Inpatient Telemetry- An Evaluative Comparison

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Abstract

Objective

Evaluation of current attended Home VT practice, looking at video quality.

Is video quality in Home Video Telemetry worse than Inpatient Telemetry?

Method

One of the first studies completed to assess our Home Video Telemetry (HVT) practice, which commenced in 2012, was to retrospectively compare the video quality against Inpatient Video Recording, considering the latter as the gold standard. A pilot study was conducted in 2008 using the Test-Re-Test design on 5 paediatric patients.

Patients (n=28) referred for diagnostic or presurgical evaluation were included in each group over a period of one year.

Data were collected from referral spreadsheets, King's ePR and telemetry archive.

Consensus scoring, by 2 scorers were carried out of the events only. Clusters of events were considered as one event.

Variables compared included- visibility of body part of interest; visibility of eyes; time of event; lighting; contrast; sound quality; quality of picture when amplified to 200%

Data were quantified and statistical evaluation carried out using Shapiro-Wilk and Chi-square tests. P-value of <=0.05 was considered statistically significant.

Results

- Significant differences were demonstrated in- Lighting and Contrast between the two groups (Home VT performed better in both)
- Quality of Picture When Amplified was slightly better on the HVT group.

- Conclusion- HVT is not inferior to IPT; in fact it surpasses IPT in certain aspects like lighting and contrast. Results reconfirmed in a larger sample of patients with more variables.
A NEW APPROACH FOR ANALYSIS OF GAMMA EVENT-RELATED OSCILLATORY RESPONSES IN ALZHEIMER’S DISEASE

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Background

The changes in brain dynamics of Alzheimer’s disease (AD) can be detected by brain event-related oscillations (ERO). Gamma oscillatory responses were explored in many neuropsychiatric conditions and reported to be related to cognition.

Methods

In this preliminary study, we explored ERO target gamma responses of AD subjects (n=12) and healthy elderly controls (HC) (n=13) in four time frames of post-stimulus 0-200, 200-400, 400-600, 600-800 ms and a wide window of 0-800 ms. We calculated event-related spectral power (ERSP) in two frequency bands (28-39 Hz and 40-48 Hz). Repeated measures of ANOVA was performed for 4 x anteriorposterior, 3 x coronal, 2 x frequency bands.

Results

The group difference of gamma ERO responses was not evident, however there was a significant frequency x coronal x group effect (p<0.002) in 0-200 ms time window, showing lower amplitudes at 28-39 Hz over right sided electrodes in AD. In 600-800 ms time interval, anteriorposterior x group effect was significant (p<0.044), indicating late responses over frontal regions in AD. These significant findings disappeared when analysis was done in 0-800 msec time block. Analyses in time intervals of 200-400 ms and 400-600 ms did not show any significant group effect.

Conclusions

It was found that gamma oscillatory responses in AD are almost abolished in early time frame (0-200 ms), but appeared as a delayed response in later time frame (600-800 ms). This delay could be a compensatory mechanism to recover gamma responses. Analysing multiple band intervals of gamma frequency from multiple time frames can depict to understand the underlying pathophysiological brain dynamics in AD.

Acknowledgements: This study was supported by TUBITAK 112S459 grant.
Healthy Controls (n=13) Gamma ERSP Power

Alzheimer's Disease (n=12) Gamma ERSP Power
P402
Does repeated hyperventilation during routine EEG monitoring increase the yield of Absences?

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Question
Hyperventilation (HV) is an activation method used to provoke interictal discharges and absence seizures during routine electroencephalogram (EEG) monitoring. In most EEG departments this is performed once during the routine EEG recording but in some departments it is considered advisable to repeat hyperventilation if the indication of the EEG was to diagnose absence epilepsy. This paper addresses whether there is an increase in yield by repeated HV in terms of capturing absences and whether there is an increase in the diagnostic yield in terms of classifying absences.

Methods
Retrospective data was collected from the children’s and adults EEG departments of patients who have performed repeated HV. Patients found to produce absence seizures or interictal activity as outcomes of HV were included. Patients presenting inadequate HV effort and patients found to be non epileptic were excluded.

Results
11 children and 34 adults found suitable for the study were analysed using the Two Proportion Z-test. The increase in the yield of absence seizures in patients from the first HV to repeated HV was found to be significant in children but insignificant in adults. Diagnostic yield of repeated HV and outcome of breath holding showed a positive outcome in both age groups but slightly higher in children. Epileptiform activity produced was found to increase in duration for children with repeated HV, but no significant change was seen in adults.

Conclusion
Repeated HV was found to increase the yield of absences and the diagnostic yield by helping to define the type of absence epilepsy syndrome in children and adults.

Key references
P403
EEG ANALYSIS OF CHILDREN WITH ATTENTION DEFICIT AND AUTISM

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Question

Autism is accepted as a neuropsychiatric disorder that begins at early ages and causes retarded and deviated communication, social, cognitive and behavioral development. We aim to evaluate the EEG findings of children with attention deficit and autism.

Methods

Retrospective analysis of electroencephalographic (EEG) findings obtained from children diagnosed with autism and attention deficit by Child Psychiatry Clinic was performed. Cases were evaluated according to age, gender, clinical diagnosis and detailed EEG findings.

Results

Total of 20 subjects consisting of 14 males (64.7%) and 6 females (35.2%) between the ages of 2 -15 years were evaluated. EEG findings were normal in 10 (50%) out of 20 patients with autism and/or attention deficit. Focal epileptiform anomaly was found in six cases (30%) which was localized to central area in four, temporoparietal area in one patient. Besides in five cases, one of which has also epileptic anomaly, mild and diffuse slowing was found. None of these cases had epilepsy history.

Conclusions

It was reported that EEG anomaly rates were 10-83% and epilepsy history was 4-32% in patients with autism and attention deficit. We found 30% of epileptic abnormality without any history of epilepsy. Further prospective studies are needed to enlighten these differences and related patho-physiological mechanisms and to understand the prognostic value of the EEG.
P404
Prognostic relevance of EEG lateralized abnormalities and photo-paroxysmal response in a series of 92 patients with juvenile myoclonic epilepsy

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Question

Juvenile myoclonic epilepsy (JME) is a common age-related epileptic syndrome, which makes 5-10% of all epilepsies. Generalized discharges of single or multiple spike and slow wave of > 3.5 Hz or 2.5-3.5 Hz, often with anterior accentuation, are typical EEG features. We analysed the prognostic value of localization-related EEG anomalies and photoparoxysmal response (PPR) in our patients with JME.

Material and methods

The study included 92 patients diagnosed as JME who were treated at the Clinic of neurology and psychiatry for children and youth in Belgrade. Antiepileptic treatment (AET) was discontinued in 32 patients. Lateralized EEG abnormalities included asymmetric sharp waves, focal and unilateral discharges and paroxysms with unilateral onset becoming generalized.

Results

There were 57 females and 35 males, the mean age of seizure onset was 14.7 ± 2.3 years. The PPR was noted in 30.4%, while focal/lateralized EEG abnormalities were recorded in 39.1% patients. Among 40 patients with initially achieved complete seizure control, PPR was observed in 35%, while, the EEG lateralization was noted in 25% patients. No significant association of these EEG parameters with initial seizure freedom was found (p>0.05). The PPR was recorded in 12/32 (37.5%) with AET withdrawal and in 16/50 (32%) patients still on therapy. Focal and lateralized abnormalities were observed in 7/32 (21.8%) patients with AET withdrawal and in 19/50 (38%) patients with continued treatment, without significant difference. In addition, seizure relapse after AET withdrawal was not associated with EEG anomalies investigated.

Conclusion

Focal/lateralized EEG abnormalities and photo-paroxysmal response are found not to have prognostic relevance for therapeutic response, level of seizure control and long-term clinical outcome.
Abstracts of Poster Presentations – Poster Session 24 – EEG 1

P405
Value of the response to Clonazepam in post-anoxic comas

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Introduction

In post-anoxic comas, to make the difference between a "pure" post-anoxic encephalopathy and a post-anoxic status epilepticus is not still obvious on EEG, particularly in case of a paroxystic and flat record (alternation of periodic spikes with periods of electric silence). Our objective was to study the value of the injection of Clonazepam.

Methods

We included the cases of patients presenting a paroxystic and flat record, who received the injection of 1 mg of Clonazepam during the recording. In case of significant modification of EEG after injection on clonazepam, we treated them as a status epilepticus by anaesthesia. Then we looked at the evolution of these patients.

Results

Eight patients were studied. Seven on 8 EEGs were clearly improved after the injection of Clonazepam with the disappearance of paroxysmal abnormalities. An EEG reactivity reappeared even in 3 patients.

Five patients presented with seizures or EEG rhythmic discharges. Among them, one fully recovered, one remains in a vegetative state, two died from complications other than neurological, with the persistence of N20, and another one died after limitation of the cares because of the absence of N20.

Conclusion

The improvement of the EEG after the injection of Clonazepam is frequent in post-anoxic comas. The value of the EEG reactivity after injection of Clonazepam seems to be low. The presence of seizures could be associated with a better prognosis in post-anoxic comas.
Interest of EEG recording during head-up tilt testing

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Question

To make the differential diagnosis between syncopes and seizures is sometimes difficult. Some authors suggested to record EEG during head-up tilt testing to improve the diagnostic value of the test. But the value of this method remains unclear. We evaluated the impact of EEG recording during head-up tilt testing in the diagnostic value for syncopes of unkown origin.

Methods

87 EEG monitoring were performed during head-up tilt testing in our hospital (62 females and 25 males; mean age, 32.6 years) with an history of recurrent syncope of unkown origin. EEG and head-up tilt testing were interpreted independently by cardiologist and neurologist. We determined if the EEG changed the conclusion of the cardiologist. Then, we described the EEG modifications associated with the cardioinhibitory syncopes.

Results

A syncope occurred in 67 patients (77%) during head-up tilt testing and was found to be cardioinhibitory in 26 of 67 (38.8%). The EEG helped the conclusion of the cardiologist in 4 cases (4.59%). All these patients presented convulsions in their medical history. In these patients, a generalized slowing of EEG activity appeared in 21 subjects (81%), on average 7.9 seconds after the start of the bradycardia, with a mean total duration of 36.8 seconds. Twelve patients (46%) presented sharp-waves with a mean duration of 11.5 seconds, on average 6.9 seconds after the start of the slowing of EEG activity. We found focal paroxysmal abnormalities in 3 patients.

Conclusions

EEG monitoring during head-up tilt testing had a low diagnostic value in our population.
Comparison of completely automated and visually controlled pre- and postprocessing of resting state EEG, a pilot-study

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Question

Processing of resting state EEG for quantitative analysis is time consuming. A tool for automated preprocessing of event-related potentials has been proposed (FASTER, Nolan et al. 2012). However, for resting-state EEG tools including automated segmentation and post-processing are lacking. Is reliability of a completely automated analysis (AA) comparable to a visually controlled analysis (VA) by an experienced rater?

Method

35 normal volunteers (Age: 36.9 +/- 7.9) had three 256-channel resting-state EEG at one year intervals. For VA, segments, bad channels and bad activations (independent component analysis) were visually selected. For AA, the same EEG were processed without any user-interaction applying routines developed in Matlab. For VA and AA, epochs for frequency analysis (12x4sec) were automatically generated. Median frequency (MF) and relative band power in 10 different brain regions were compared between AA and VA with correlation coefficients, and reliability over time was assessed with intraclass correlation coefficients (ICC).

Result

Mean correlation coefficients and ICCs (± SD) over all regions are given in the table.

<table>
<thead>
<tr>
<th>Bandpower</th>
<th>correlation coefficient</th>
<th>ICC over time (VA)</th>
<th>ICC over time (AA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>delta</td>
<td>0.86 ± 0.03*</td>
<td>0.79 ± 0.09</td>
<td>0.65 ± 0.09</td>
</tr>
<tr>
<td>theta</td>
<td>0.86 ± 0.01*</td>
<td>0.85 ± 0.02</td>
<td>0.78 ± 0.02</td>
</tr>
<tr>
<td>alpha1</td>
<td>0.94 ± 0.01*</td>
<td>0.92 ± 0.01</td>
<td>0.83 ± 0.03</td>
</tr>
<tr>
<td>alpha2</td>
<td>0.90 ± 0.01*</td>
<td>0.86 ± 0.02</td>
<td>0.83 ± 0.03</td>
</tr>
<tr>
<td>beta</td>
<td>0.94 ± 0.01*</td>
<td>0.92 ± 0.01</td>
<td>0.86 ± 0.02</td>
</tr>
<tr>
<td>MF</td>
<td>0.82 ± 0.03*</td>
<td>0.86 ± 0.02</td>
<td>0.72 ± 0.06</td>
</tr>
</tbody>
</table>

* p < 0.001

Conclusion

While visually controlled analysis produces slightly better results regarding ICC over time, the main advantage of automated analysis is an essential reduction of working time with still good reliability (ICC > 0.75) in normal volunteers. Assessment of validity of automated processing in patients is warranted.
P408
Increasing reliability of EEG frequency analysis by automated rejection of bad EEG

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Question
Results of EEG frequency analysis are increasingly evaluated as biological marker for diagnosis and prognosis of brain disorders. Sufficient reliability of EEG evaluation is a requirement for clinical validity. Currently, rejection of EEG due to high artifact load or to low signal to noise ratio is based on simple visual inspection and, therefore, susceptible to subjective factors of the raters. Is reliability increased by automated rejection of bad EEG as compared to visual rating?

Methods
40 normal volunteers (Age: 36.2 +/- 8.5) had three 256-channel EEG recordings at one year intervals. EEG were processed with visual selection of segments, bad-channels, artifacts and epochs followed by a frequency analysis. For calculation of peak- and median frequency (PF, MF) we use the median of PF/MF determined at single parieto-occipital electrodes. All EEG were classified good/bad by two raters independently twice at 2 months' interval. Disparate individual ratings were decided upon a consensus procedure. For automated classification a random forest model including PF, MF and results of frequency analysis was used to define criteria for rejection. Visual and automated rejections were compared using Kappa coefficients.

Results
Amplitude of PF, ratio PF to minimal power and bandpower (4-14Hz) were defined as criteria for rejection. Kappa coefficient of the first visual ratings was 0.75, of the second 0.91. Kappa between first and second consensus rating was 0.79, between automated and second consensus rating 0.91.

Conclusion
While visual evaluations by two raters are changing over time, automated rejection is stable and may be time sparing.
P409
Automatic MSLT sleep/wake detection using novelty feature scaling

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**Question**

The multiple sleep latency test (MSLT) is a sleep diagnostic day-test, which measures a patient’s sleepiness for diagnosis of central sleepiness including narcolepsy. We aimed to develop an automated method for detection of sleep and wakefulness automatically using the EEG (F4-A1, C4-A1 and O2-A1) combined with novelty feature scaling.

**Methods**

A total of 250 MSLT tests were recorded according to the AASM. They were divided into three sets; training set (100), validation set (75) and test set (75). The detector was designed (cross-validated) using the training and validation set, and the tuned (optimal settings) detector (obtained from the cross-validation) was then tested on the unseen test set. A total of five amplitude features (five clinical bands) were computed from each 30-second epoch, which corresponds to a total of 15 features when including all three EEG channels. Based on the break periods (the periods between the naps opportunities), the features were re-scaled into a range of approximately zero and one using a novelty detector (one-class SVM) combined with a modified min-max scaling scheme. This was conducted on each patient independently. A two-class classifier (linear SVM) was used to separate sleep and wakefulness.

**Results**

It was possible to obtain a validation and test accuracy of 88 % and 86 % respectively. Without the novelty scaling scheme, the test accuracy dropped to 79 %.

**Conclusion**

Supervised method based upon EEG signals has a potential for automated analysis. Classification improvement of automatic detectors can be obtained by discarding noisy samples and proper feature scaling.
P410
Temporal variability in EEG functional connectivity in children with Attention Deficit Hyperactivity Disorder

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Question

In a previous work, our group has demonstrated an increasing in the EEG cortical connectivity in children with Attention Deficit Hyperactivity Disorder (ADHD) when compared with healthy children (González et al., Clin. Neurophysiol. , 124 (6), 1139-1150, 2013). In this work, the temporal variability of EEG functional connectivity in ADHD children is analyzed.

Methods

Signals: digitised EEGs (sampling rate: 256 Hz ) from an ADHD of mixed type (11-males, 10-15 years) and a control (CONT) group (13-males, 10-15 years). EEG recording were from 16 monopolar EEG channels using the international 10/20 system (Fp1-2/F3-4/F7-8/T3-4/T5-6/C3-4/P3-4/O1-2, reference: linked A1-A 2 mastoid). Pairwise interdependence between EEG channels was assessed through two measures: the covariance and the nonlinear synchronization. Thus, EEG functional connectivity was estimated by averaging the corresponding intra&interhemispheric interdependence measures for each electrode. Temporal variability (TVA) of EEG connectivity was assessed through the standard deviation of interdependence measures from 30 EEG artifact-free segments of 5 s each. Conditions were: basal, eyes-closed (EC) and eyes-open. ANOVA test for repeated was used for between-group comparisons.

Results

a) As to covariance measures: TVA of EEG connectivity was greater for ADHD group than for CONT group (p<0.05) and only during EC; this result was clearer for the connectivity of O1 and O2 (p<0.001) and for that of F7, F8, T3, T4 and T6 regions (p<0.01); b) As for the nonlinear synchronization, the TVA was also greater for ADHD than for CONT in EC condition (p<0.001) and this result was true for the connectivity of most channels of the right and left hemisphere (Fp1,T3, T5, C4, T4 with p<0.01 and F7, C3, P3, P4, O1, O2, F4, F8, P4, T6 with p<0.001).

Conclusions

Children with ADHD of mixed type show increased the temporal variability of the EEG functional connectivity of certain cortical regions compared with CONT. This result is evident primarily when the connectivity of each region is estimated through measures of nonlinear synchronization with eyes closed.

Work supported by the Spanish MINEC grant TEC 2012-38453-C04-03 and FIS (ISCIII)&FEDER grant PS09/00856.
**P411**
**ERD/ERS differences between young and older adults during passive ankle movement**

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**Question**

Age-related proprioceptive impairments can lead to serious functional consequences in performing sensorimotor tasks such as posture and gait. The measurement of the response time (RT) to kinesthetic perception is a way to assess the proprioceptive system and represents a sensorimotor task involving receptors and peripheral pathways as well as processing in upper levels of the central nervous system. Electrophysiological correlates of ankle passive movement are little known in older adults, so the aim of the present study was to investigate the electroencephalographic (EEG) oscillatory changes during passive ankle movement in healthy older and young individuals.

**Methods**

Nineteen older (70.3±4.1 years) (OA) and 19 young adults (28.5±2.9 years) (YA) were evaluated in two conditions: with and without motor response to kinesthetic perception. In the first condition, participants had only to feel the ankle movement. In the second condition, participants were instructed to press a button with their right thumb as fast as possible whenever a dorsiflexion movement of the ankle was detected. Passive movement was performed at 22º/s. EEG epochs were aligned with the ankle movement onset and the grand average event-related desynchronization and synchronization (ERD/ERS) in the beta band (14-37 Hz) for each group was analyzed.

**Results**

OA showed an increased RT (286.31±34.44 ms) compared to YA (238.86±23.64ms). In both conditions, OA showed larger ERD and lower ERS than YA. Moreover, both ERD and ERS were longer for OA than YA.

**Conclusions**

Larger ERD in OA might represent higher cognitive efforts to process the proprioceptive information, as a compensatory mechanism for the reduction in the afferent sensory inputs. In addition, the attenuation of beta ERS in OA suggests an alteration of the motor cortical resetting by inhibitory systems. Finally, longer ERD/ERS in OA might reflect a slower central sensorimotor processing with normal aging.
A mouse model for EEG resting state using high-density recordings in the awake animal

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Human neuroimaging studies are increasingly focusing on the behavior of large-scale whole-brain networks during rest. Electrophysiological recordings with EEG/MEG thereby complete the fMRI studies by providing information on the temporal dynamics of networks at timescales that are more closely related to mental activity. In order to better understand the mechanisms underlying the temporal dynamics of resting-state networks we developed a model of high-density EEG recording in awake, head-fixed mice using 32 electrodes equally distributed over the scalp. By looking at the EEG synchronized to a video monitoring of resting mice during recording, we observed that striking differences in spatial EEG patterns (scalp potential maps) appear during periods without significant behavioural output, directly indicating different networks being active at rest. A k-means clustering revealed that four distinct maps dominated the recordings with similar topographies within and among animals. Each topography was dominant for a certain time period and repeatedly appearing across time. These maps were still present in anesthetized animals, but with different durations. The observation is very similar to what has been described in human resting EEG studies and is known as EEG microstates. The animal model now allows us to study the mechanisms underlying these temporally stable network states in more detail.
P413

ANTIRETROVIRAL THERAPY EFFECTS ON SOURCES OF CORTICAL RHYTHMS IN HIV SUBJECTS: RESPONDERS VS. MILD RESPONDERS

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Objective

Naive patients with immunodeficiency virus (HIV) are characterized by diffuse abnormalities of resting state cortical electroencephalographic (EEG) rhythms. Here we tested the hypothesis that the cortical sources of alpha rhythms show some normalization in the HIV subjects who receive a successful cART also after a very short period of therapy.

Methods

Resting state eyes-closed EEG data were recorded in 38 HIV patients (mini mental state evaluation - MMSE- of 27.8±0.4 SEM) in a baseline period and after a cART of 5 months, and in 40 age-matched cognitively normal subjects (MMSE of 29.8±0.1 SEM). Based on the CD4 count, we divided HIV subjects into two sub-groups: those with an increase (ΔCD4) of at least 100 cells/µl (Responders) and those with ΔCD4 < 100 cells/µl (Mild Responders). EEG rhythms of interest were delta (2-4 Hz), theta (4-8 Hz), alpha1 (8-10 Hz), alpha2 (10-12 Hz), beta1 (13-20 Hz), and beta2 (20-30 Hz). Cortical EEG sources were estimated by LORETA software.

Results

Results showed that the amplitude of the posterior alpha sources increased after a cART of 5 months.

Conclusions

The present results suggest that in HIV subjects, cortical sources of resting state alpha rhythms are related to systemic immune activity.

Significance

These results lead support to the notion that in HIV subjects, a successful ART therapy partially restores brain synchronization mechanisms generating the resting state EEG rhythms.
Involvement of different cortico-subcortical circuits in chronic tinnitus: an sLORETA-based study in normoacoustic patients

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QUESTION

Chronic tinnitus is a debilitating disorder that has negative impacts on the quality of life. Treatment is often difficult and the mechanisms responsible for this condition are still not understood. Thus, we aimed at assessing the level of involvement of cortico-subcortical circuits in chronic, normoacoustic tinnitus sufferers using electroencephalography (EEG).

METHODS

Seventeen medication-free normoacoustic patients (6 females, mean age 43.6 ± 9.8 y., mean disease duration 22 ± 35 months) presenting with chronic, unilateral high-pitched tinnitus were included, and compared to 13 controls matched for gender and age. Subjects underwent a 29-channel EEG recording at rest (eyes opened and closed, 5 min each) and auditory event-related potentials-ERPs (N1, P2, P300) to oddball paradigm (counting rare tones: 20%, 2000Hz among a series of 1000 Hz stimuli). ERPs latencies and amplitudes were measured and compared between groups using an ANOVA for repeated measures. Cortical three-dimensional distribution of current source density (CSD) of various EEG frequency bands was computed with sLORETA, and compared between groups using the sLORETA software.

RESULTS

Eyes closed, tinnitus sufferers had significantly decreased CSD of alpha2 (10.5-12Hz) rhythm in the left postcentral and inferior temporal gyri, and of gamma rhythm (30-100Hz) in the left temporal gyrus. Eyes opened, CSD of the alpha2, beta2 (18.5-21Hz), and gamma bands were decreased in the tinnitus group over the inferior parietal lobule. Latency and amplitude of the P300 and P2 did not differ between groups. N1 latency was significantly shorter in tinnitus sufferers.

DISCUSSION

Our results suggest an impairment of the cortico-thalamo-cortical circuits involving the auditory cortex in chronic tinnitus, even in normoacoustic sufferers, although a thalamic or cortical origin could not be defined with this method. Desynchronized alpha is compatible with an increased activity of the postcentral and inferior temporal gyri, and might reflect a maladaptive plasticity in chronic tinnitus.
P415
Getting older: decline or regulation? An EEG study on attention and emotion

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Question

Previous studies on emotion regulation have reported an increasing attentional bias towards positive aspects across the lifespan (“positivity effect”). The present study examined this effect by analysing behavioural and electrophysiological data in young (18-24 yrs.) and elderly adults (50-71 yrs.). It was assumed that a behavioural positivity effect would be reflected in brain oscillations measured by EEG (Schmiedt-Fehr & Basar-Eroglu, 2011, Clinical Neurophysiology).

Methods

Participants (n=40) were presented simultaneously with two faces, one to the left and one to the right of a central fixation cross. The expression of one of the faces was emotional (positive or negative) and the other neutral. Subsequently, a vertical line appeared. Participants were asked to indicate the position of the line with respect to the centrally displayed fixation cross. EEG data were analysed using time frequency wavelet transformation.

Results

Females responded faster than males, when the position of the vertical line co-occurred with a positive face. This effect was not observed in males. Older adults responded faster when the position of the vertical line co-occurred with a neutral face, only if the other face showed a negative expression. These gender and age-related effects were reflected in beta and alpha oscillations.

Conclusions

Irrespective of age, female adults showed an attentional bias towards emotional faces, when the face was of positive valence. The positivity effect could also be confirmed for older adults, as older age was associated with the tendency to shift attention away from negative faces. This attention shift was reflected in alpha and beta oscillations.
Abstracts of Poster Presentations – Poster Session 24 – EEG 1

LP28
Finding brain oscillations with power dependencies in neuroimaging data

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Question

In order to investigate power-to-power cross-frequency interactions, we present a novel source separation approach using spatial filters that maximize the correlation between the power of brain oscillations recorded with electro-/magnetencephalography (EEG/MEG). Our approach, which is called canonical source power correlation analysis (cSPoC), is thereby capable of extracting genuine brain oscillations (within as well as across subjects) solely based on their assumed coupling behavior even when the signal-to-noise ratio is low.

Methods

cSPoC seeks a pair of multivariate spatial filters such that the envelopes of the filter outputs are maximally correlated with each other. This objective is cast into a nonlinear optimization problem and solved using numerical tools. N=7 healthy subjects underwent continuous auditory stimulation in a steady-state auditory evoked potential (SSAEP) paradigm (40 Hz SSAEP frequency). A slowly varying amplitude modulation scaled the perceived loudness of the SSAEP stimulus within a 35 dB range.

The unsupervised method cSPoC is benchmarked against the supervised method SPoC (Daehne et al., 2014). SPoC is the appropriate decomposition method if envelope correlations to a given target signal are of interest. cSPoC assumes that identical stimulation across subjects leads to envelope dynamics that are correlated across subjects, irrespective of the exact relation between stimulus and envelope dynamics.

Results

The correlations obtained by cSPoC are on par with those obtained by SPoC. For all subjects, the spatial patterns of the components extracted by cSPoC are consistent with source analysis of SSAEP responses (Herdman et al. 2002). The high similarity between between SPoC and cSPoC patterns indicates that cSPoC is able to detect the relevant neural sources, without explicit knowledge of the target function.

Conclusions

cSPoC is able to identify brain oscillations with correlated envelopes from high-dimensional and noisy electrophysiological recordings. We believe that the method will be a valuable tool in the quest for understanding the mechanisms and functions of power-to-power coupling within and across subjects.

figure 1

Figure 1: Results of inter-subject envelope correlation in a SSAEP paradigm: correlations. The unsupervised cSPoC method was applied to pairs of subjects with an objective to maximize a correlation between the spectral power (the envelope was used) of corresponding neuronal activities relative to an intensity modulated auditory steady state stimulus. In contrast, the supervised SPoC method was applied to each subject individually, with an objective to maximize a correlation between the power of neural activity and the intensity modulation of the auditory stimulus.

(A) Cross-validated correlations between envelopes of sources estimated by SPoC and cSPoC, averaged across subjects. (B) Pairwise envelope correlations for all subjects as obtained by SPoC and cSPoC, averaged across subject pairs. (C,D) Pairwise envelope correlations for all subjects as obtained by SPoC and cSPoC, averaged across subject pairs. (C) Pairwise envelope correlations for all subjects as obtained by SPoC and cSPoC, averaged across subject pairs. (D) Pairwise envelope correlations for all subjects as obtained by SPoC and cSPoC, averaged across subject pairs.
LP29
Considering transcallosal coherence as a marker of consciousness

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Question
Recent studies revealed differences in interhemispheric connectivity in disorder of consciousness (DOC)-patients. Based on this we investigated transcallosal coherence as a marker of consciousness. We compared Minimally Conscious States(MCS)-patients, Unresponsive Wakefulness Syndrome(UWS)-patients and healthy subjects(h). We assume to find greater coherence in healthy than in DOC-Patients and greater coherence in MCS- than in UWS-patients.

Methods
Rest-EEG was recorded in 66 subjects (24 MCS, 30 UWS, 12 Healthy). The magnitude value of coherence between each electrode of the left hemisphere and each electrode of the right hemisphere was computed (F3, F4, F7, F8, C3, C4, P3, P4, O1, O2). T-tests were calculated for each of the used 12 frequency steps (1-28 Hz) and for each electrode combination between MCS- and UWS-group and between healthy subjects and DOC-patients.

Results
The statistics did not reveal notable differences between MCS- and UWS-patients. The comparison of DOC-patients and healthy subjects revealed statistical trends (p<.05, uncorrected) in about 53.66% of the computed tests. We found an interesting pattern of common differences between DOC-patients and healthy subjects in a frequency of 6Hz.

Conclusions
Transcallosal coherence of MCS- and UWS-patients seems not to differ systematically. Due to the differences of DOC-patients and healthy subjects, one might conclude that the impairment of DOC-patients is based on a common mechanism to a certain extent. The earlier mentioned interesting pattern of common differences might reflect a damage to frontal midline theta coherence which in turn might reflect an impairment of the working memory³.

References
P416
Sensory-Motor Integration After Selective Stimulation of Intraepidermal Aδ Nociceptors: Results From Normal Cases and Patients with Polyneuropathy

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**Question**
Sensory-motor integration (SMI) between the somatosensory afferents and motor responses to transcranial magnetic stimulation (TMS) has previously been studied with electrical stimulation of the nerves. Is it possible to perform SMI studies in normal cases and patients with selective electrical stimulation of intraepidermal Aδ fibers?

**Methods**
Twenty two healthy volunteers and 7 polyneuropathy patients with primarily small fiber involvement were included. Paired stimuli at twice the sensory threshold were applied with custom made intraepidermal stimulation (IES) electrodes placed on the 1st dorsal web space of the dominant hand. A butterfly shaped coil was placed over the cortical hot spot for the first dorsal interosseous muscle adjacent to the IES site. Inter-stimulus intervals (ISI) between the IES and TMS were consisted of 18 steps between 20 and 450 ms. Mean amplitudes and areas of the eight motor responses elicited at each ISI were divided by those evoked by TMS alone and SMI graphs were created.

**Results**
SMI curves of the normal controls showed an afferent inhibition between ISI 80 and 300 ms (Fig 1, solid line:amplitude ratios, dotted line:area ratios, bars:standard deviations). In the patients; afferent inhibition lasted longer, until the end of the studied ISIs.

**Conclusion**
The afferent inhibition of the motor outputs after IES begins later and lasts longer than the inhibition following electrical peripheral nerve stimulation. These findings may provide some contribution to the knowledge on the function of small afferents. Longer duration of the afferent inhibition in the patients may be related to abnormalities in the peripheral conduction and/or central processing of nociception.

**figure 1**
P418

“Dynamic ENMG” using the collision technique. Application to explore activity-dependent conduction block in patients with chronic inflammatory demyelinating polyneuropathy (CIDP).

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Activity-dependent conduction blocks (Ad-CB) are the consequence of hyperpolarization induced by voluntary activity (1-2). Dynamic electroneuromyography using the collision technique (DC-ENMG) before and after a voluntary contraction is appropriate to investigate this phenomenon. The aim of our study was to validate, in two centers, the reliability of this technique in healthy subjects and in patients with CIDP. We recorded compound muscle action potentials (CMAPs) from the abductor pollicis brevis following paired-stimulation of the median nerve at wrist and elbow before and after a 60 second voluntary contraction of the thumb. The delay between the wrist and elbow stimulations was initially 6 ms and was increased by 0.5 ms step until the CMAP reached its maximum value. For each delay we analyzed the difference between the CMAP amplitude before and after contraction, the number of stimulation to reach the maximal CMAP before (ICbe) and after (ICaf) contraction and the ratio IC [(ICbe-ICaf)/ICbe]. 24 healthy subjects and 6 patients were investigated. We described 2 profiles: a mean positive difference for each delay of stimulation in control subjects and a negative difference for each delay in CIDP patients. The difference between the CMAP amplitude before and after the contraction was significantly lower in CIDP patients in comparison to healthy subjects (0.48 versus 4.5 p < 0.05) moreover the ratio IC was smaller in patients (-0.05 versus 0.11). These first results confirm the reliability of the DC-ENMG in healthy subjects and patients with CIDP. Further studies are needed to evaluate its prognostic role.


P419
Benign tumour as a rare cause of tarsal tunnel syndrome - case report

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Question
Tarsal tunnel syndrome is the most frequent entrapment neuropathy of the posterior tibial nerve1. It may involve also its plantar and/or calcaneal branches2. It is a rare and frequently underdiagnosed condition leading to motor, sensory and autonomic complications affecting the sole. Early decompression in the symptomatic cases promotes good recovery2.

Methods
We present the case of a 59-year-old female who was admitted to our Clinic with a 2-month-history of progressive weakness and burning of the right foot. The diagnosis of the symptomatic tarsal tunnel syndrome was made based on electrodiagnostic testing and magnetic resonance imaging of the right foot.

Results
Electroneurography revealed a severe right tibial nerve injury in the tarsal tunnel. MRI showed a polycyclic cystic mass medially to the lower ankle joint distorting the swollen tibial nerve. The postoperative outcome was good.

Conclusions
Tarsal tunnel syndrome can be easily overlooked due to the rarity and nonspecific symptoms of this pathology and a tumour in the tarsal tunnel is an exceptional cause2. Insightful electrodiagnostic testing can help identify the site of injury. When combined with imaging, it constitutes a proper therapeutic regimen.

References

Figures:
1. T-2-weighted magnetic resonance image of the tarsal tunnel - polycyclic tumour and swollen tibial nerve.
2. Magnetic resonance image of the tarsal tunnel showing peripheral post-contrast enhancement of the tumour.
3. Motor and sensory conduction studies of the tibial nerve.
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P420
EMG in Pediatric Population: Was it Worth it?

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Question

Electrodiagnostic evaluation provides an important extension to the neurological examination for the evaluation of pediatric neuromuscular disease. Many pediatric neuromuscular diseases are analogous to those seen in the adult, however, the relative frequency of these illnesses varies greatly when different age populations are compared. The purpose of the present study is to provide analysis of children referred to our electromyography (EMG) laboratory for electrophysiological examinations.

Method

We retrospectively reviewed electrodiagnostic records of patients aged between 0-15 years, attending our electromyography (EMG) laboratory with suspicion of a neuromuscular disease and a referring diagnosis on the referral form between years January 2004 and June 2013. Patients were classified as having plexopathy, nerve root lesions, polynuropathy, myopathy, mononeuropathy, anterior horn cell disease, neuromuscular transmission disorder, facial nerve palsy and other rare disorders.

Results

We reviewed 5563 pediatric records, which was 578 studies per year. It was about 14% of the all EMG examination performed in our laboratory. When we looked at the all procedures, 3271 of the records were including needle EMG, 170 of them were single fiber EMG, 100 of them were repetitive nerve stimulation, and 52 of them were evoked potentials. The results were normal in % 55 of the cases. The common diagnosis were plexopathy (% 28,6), polyneuropathy (PNP) (% 7,4), and myopathy (% 6,6) in patients aged between 0-5 years (% 41,2 of all records). Between 6-10 years (% 28,2 of all records) the common diagnosis were myopathy (% 9,4), PNP (% 8,5), mononeuropathy (% 6,4) and plexopathy (% 5,9) and between 11-15 years (% 30,6 of all records) the common diagnosis were PNP (% 11,3), myopathy (% 6,6), and mononeuropathy (% 5,6).

Conclusion

Nearly half of the examinations were normal. Infants and toddlers were mostly suffered from brachial plexopathy which can be prevented by proper obstetrical management. Nerve conduction studies and EMG yielded diagnostic importance for demyelinating neuropathy and myopathy in patients older than 6 years of age.
P421
Age influences recovery after carpal tunel syndrome surgery

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Question
To determine if parameters of conductive studies are significantly affected by age

Methods
This retrospective study included 258 hands of patients with idiopathic carpal tunnel syndrome subjected to surgical treatment according to the open carpal tunnel release method. We compared differences in distal motor latency (DML), the amplitudes of compound muscle action potential (CMAP) and sensory conduction velocity (SCV) before and 3 months after the surgery. Age dependency of measured parameters were analyzed by the Pearson correlation coefficients. Because preoperative DML significantly depends on age, latency differences were compared using paired t-test for patients with the same preoperative distal motor latency and minimal age difference of 20 years.

Results
There were detected statistically significant difference of the recovery of DML between the younger and older group of patients (1.4 ± 1.5 ms versus 0.8 ± 0.9 ms). No significant difference of the recovery of the amplitude of CMAP and SCV were found. Preoperative DML was significantly increased in older patients while CMAP amplitude and SRV were significantly decreased.

Conclusions
Slower recovery after carpal tunnel syndrome surgery in the elderly is an argument for early diagnosis and therapy to this disease. However, is not an argument against the surgical treatment of the carpal tunnel syndrome in this group of patients.
Prevalence of Martin Gruber anastomosis in healthy subjects

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Background

Martin Gruber anastomosis (MGA) is an anatomical connection on the forearm between the median and ulnar nerves. Some ulnar motor fibers are joining the median nerve in the elbow region. There are 3 types of MGA - motor fibers for ADM (MGA-I), for FDI (MGA-II), and for adductor pollicis (MGA-III). The prevalence of MGA is reported between 15% and 35%.

Methods

To carry out normative conduction study of the ulnar nerve at the elbow, 292 healthy volunteers were investigated in five different EMG laboratories. The group consisted of 166 women (256 arms) and 126 men (201 arms), aged 20-67 years (average 39.4 years). Motor and sensory neurographies of the median and ulnar nerves were performed. The ulnar nerve was examined in 90° flexion in the elbow, 10 cm elbow segment, registration from ADM and FDI. The ulnar nerve was stimulated 4 cm distally of the line connecting middle of olecranon and medial epicondyle, and 6 cm proximally. Motor nerve conduction velocities and CMAP were evaluated in all tested nerve segments. If the amplitude of CMAP below elbow was at least 20% lower than A-CMAP at the wrist, the finding was evaluated as MGA.

Results

In our sample we found MGA in 79 arms. There was the drop of A-CMAP for ADM (MGA-I) in 22 arms, for FDI (MGA-II) in 49 arms, and for both ADM and FDI in 8 arms. In 12 persons we found MGA (always type II) on both sides, including one woman with concurrent MGA-I on the right side. The persons with MGA had to be excluded from further analyses to establish normal conduction values of the ulnar nerve.

Conclusion

In a group of 292 healthy persons (459 evaluated arms) we found MGA-I and/or MGA-II in 79 arms (17.2%). Because we have not investigated adductor pollicis muscle, we could not assess prevalence of MGA-III.
P424

TOXIC EFFECTS OF DEXMEDETOMIDINE PERINEURALLY ADMINISTERED TO THE SCIATIC NERVE OF RATS (AN ELECTROPHYSIOLOGICAL EVALUATION)

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Objectives

To demonstrate the toxic effects of dexmedetomidine which is perineurally administered to the sciatic nerve of rats.

Methods

Fifteen Sprague Dawley rats were divided into three groups: in Group I (n=7), 40 µg (0.2 mL) dexmedetomidine, in Group II (n=6), saline (0.2 mL) was administered to the right sciatic nerve and in Group III (n=2), the right sciatic nerve was only surgically explored in a similar way. Sciatic nerve CAMPs were recorded (10 per each nerve) bilaterally before the surgical procedure and after 15 days by LabChart apparatus and program.

Results

In Group I, the RoRR duration was statistically longer than the other groups (p < 0.001). The PWL values returned to the baseline values in a significantly longer time in Group I (p < 0.001) as well. There was no statistically significant difference between the sides of sciatic nerve CMAP amplitudes before the procedure but after 15 days (p=0.000). The right to left (R/L) side ratios of the pre and post procedure showed statistically significant difference (p=0.000). By ANOVA, Group I had significantly lower values than Group II (p=0.016) in the post-procedure period and also the whole groups (p=0.000) in the pre-procedure period.

Conclusion

The administration of 40 µg dexmedetomidine perineurally in the sciatic nerve of the rat prolongs RoRR duration in rats, causes a delay in PWL durations and causes axonal damage of the sciatic nerve. On the other hand, the damage in sciatic nerve has to be histologically supported, as well.
P425
The Clinical And Neurophysiological Evaluation Of Leprosy

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Objective

The aim of this study is to evaluate neurological and neurophysiological features of leprosy.

Material and Methods

Seventy seven hospitalized leprosy patients (52 male, 25 female) were examined neurologically and neurophysiologically between 2010 and 2012. Standard procedures were performed to evaluate sensory and motor conduction studies to all patients. Motor studies were carried out on median, ulnar, tibial and common peroneal nerves, and sensory studies on median, ulnar and sural nerves. Recordings of sympathetic skin response (SSR) on both hands and feet, and the heart rate (R-R) interval variation (RRIV) on precordial region were done in order to evaluate the autonomic dysfunction.

Results

The mean age was 59.1±14.95 years ranging between 17 and 80 years. The mean duration of disease was 35.6±18.3 years. Clinically, the patients had severe deformity and disability. In neurophysiological examinations, sensory, motor conduction studies of the lower extremities were found to be more severely affected than upper, and sensory impairment predominated over motor. Abnormal SSRs were recorded in 63 (81.8%) cases of leprosy. Abnormal RRIVs were recorded in 41 (53.2%) cases and abnormal RRIVs with hyperventilation were recorded in 55 (71.4%) cases. Significant differences were found between SSR and sensory conduction parameters of median, ulnar nerves as well as motor conduction parameters of median, ulnar and peroneal nerves (p<0.05).

Conclusion

Peripheral nervous system dysfunction is accompanied by autonomic nervous system dysfunction in leprosy patients. Sympathetic involvement may predominate over parasympathetic involvement.
P426
Laryngeal Electromyography: Sensitivity and Specificity in Brazilian Patients with Dysphonia

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Dysphonia is a common symptom found not only in neurologic disorders of the larynx. Laryngeal electromyography (LEMG) is considered a useful technique to identify some neurological diseases that affect the larynx.

QUESTION

Which is the sensitivity and specificity of laryngeal electromyography (LEMG) in patients with dysphonia?

METHODS

Ninety four subjects were prospectively submitted to LEMG: 80 with dysphonia and 14 controls. In dysphonia group, laryngeal endoscopy diagnosed vocal fold immobility in 55 subjects, and movement disorders in 25. We analyzed the following features to define normal and abnormal LEMG: rest activity, insertion activity, spontaneous activity, discharges, motor unit action potential morphology and firing recruitment, interferential pattern at maximum effort.

RESULTS

In dysphonia group LEMG diagnosed neurologic involvement with 89% sensitivity and 100% specificity. Considering only vocal fold immobility subjects this sensitivity increased to 93%, but for the movement disorders patients there were a sensitivity of 80%, both with the same specificity of 100%.

CONCLUSION

LEMG has a high sensitivity diagnostic rate for neurologic involvement in dysphonia, especially for patients with vocal fold immobility.
Laryngeal Electromyography: Are the results reproducible?

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Laryngeal electromyography (LEMG) is an important diagnostic tool to identify neurological diseases that affect the larynx. But there are anecdotal remarks concerning the difficulty of obtaining reproducible results when LEMG is performed repeatedly, even in the same patient.

QUESTION

Are LEMG findings obtained by different approaches of the same laryngeal muscle reproducible?

METHOD

This is a prospective, blind, randomized and controlled study. Forty subjects, 21 male; aged between 21 to 78 years, were submitted to LEMG of the thyroarytenoid muscles by two different techniques totalizing 120 sites of insertions for analysis. The electrophysiological findings were grouped as: 1) Identical LEMG findings; 2) Not identical LEMG findings but complimentary; 3) Completely different LEMG findings.

RESULTS: We find 5% of completely different LEMG findings between the sites analyzed. All the group 3 pairs of findings were obtained in the right-hand side approaches of patients with easy recognizable laryngeal surface references. In all the other patients LEMG findings were identical or complimentary for each site analyzed.

CONCLUSION

In our opinion LEMG is a reproducible technique but caution must be taken to avoid subjective misinterpretation and wrong muscle approach.
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P428
Discret EMG-evaluation of anal reflex.

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Classic anal reflex, first described by GI Rossolimo (1891), implies the presence of spinal reflex connection between the perianal skin and the external anal sphincter. The essence of the reflex is to see a reduction in the anus with a mechanical or electrical stimulation of the perianal skin.

Duration anal reflex also referred to as "latency" - i.e. the time from the perianal skin irritation up to the contraction of anal sphincter.

We conducted a study of the anal reflex in 13 patients (6 women) (mean age 52.9 ± 7.5 years) with the absence of anorectal diseases.

We studied the latency of anal reflex by EMG-recorders "NeuroEMG - Micro" and «Medtronic Keypoint». Stimulation was conducted currents of duration 0.2 ms with an interval of 3-5 seconds, and increasing the power pulse of 0.1 mA until the discomforts the patient (30-40 mA).

In all patients the anal reflex latency was 35-45 ms (T3).

Further, vaginally or rectally we examined the latency of the pudendal nerve (T1).

Then, without changing the position of the index finger, the pudendal nerve stimulation was performed in the «F-wave" study program (T2). It uses a series of 20 pulses of 100 ms each, the size of the stimulation current, at which the minimum obtained in latency and maximum amplitude of M-response.

Next, perform mathematical calculations:

a) Estimation of the time the signal for motor fibers Tmot = T1 + T2 - 1 (ms) / 2.
b) Assessment of the signal times the sensory fibers Tsen = T3 - 1 (ms) - Tmot.

Thus, the proposed method allows to study the discret characteristics of the anal sphincter reflex:
- Distal pudendal nerve;
- Motor fibers from the sacral spine to the anal sphincter;
- Sensory fibers from anal sphincter to the sacral spine.

Clinical example: Patient G., 39 years old:
- Pudendal nerve latency - 2.00 ms;
- F-wave latency - 50.3 ms (standard value 26 - 32 ms);
- Anal reflex latency - 37.2 ms (standard value 35 - 45 ms)

We expect discrete data:
- Tmot = 25.65 ms (normal 14-16 ms);
- Tsen = 10.60 ms (normal, 9-11 ms)

Conclusion

pathology of motor pathways of anal reflex.

Thus, the study of the quantitative parameters of the anal reflex as a whole, as well as a discrete assessment of motor and sensory pathways are fairly simple, but highly informative method for studying the function of the anal sphincter, has no contraindications and can be recommended for use in clinical practice.
Bulbocavernosus Reflex and Pudendal Nerve Somatosensory Evoked Potentials Responses in Female Patients with Acute Cauda Equina Syndrome

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To assess the value of bulbocavernosus reflex (BCR) and pudendal nerve somatosensory evoked potential (SSEP) in the topical diagnosis of acute cauda equina syndrome with or without sphincter dysfunction in female patients. In this prospective study were included 40 healthy adult females (Control Group) and 53 female patient (Case Group) with acute cauda equina syndrome which 24 patients with sphincter dysfunction were included in Group A and 29 patients without sphincter dysfunction in Group B. All the subjects underwent different studies: BCR and SSEP. BCR and SSEP latencies in Case Group were remarkably prolonged than that in Control Group. BCR and SSEP latencies in Group A were remarkably prolonged than that in Group B. Both BCR and SSEP were changed in the patients with acute cauda equina syndrome with or without sphincter dysfunction, and they were especially changed in the patients with sphincter dysfunction. Because acute cauda equina syndrome lack of symptoms in prephase and earlyphase and sphincter dysfunction were accured only in midphase and latephase, so it was difficult to diagnosis CES in prephase and earlyphase. BCR and SSEP are valuable in the diagnosis of cauda equina lesions in females, especially in the early diagnosis of cauda equina lesions. BCR and SSEP are valuable in the objective diagnosis for the severity of acute cauda equina syndrome in females.
A study of F-wave velocity parameters in C7-C8-Th1 radiculopathy

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F-wave study in the diagnosis of demyelinating radiculopathy is one of the complex questions of neurophysiology. The main challenge is the difficulty in determining which are the injured fibers which implies that data may be inconsistent. For the full evaluation of the proximal conduction system, study of F tachodispersion and F chronodispersion were proposed. The research objective was to study F-wave parameters in the presence of radicular disease at C7-C8, C8-Th1 level.

A total of 96 patients with C7, C8, Th1 radiculopathy symptoms were examined. The control group consisted of 30 patients. Velocity parameters of F-wave acquired using peripheral nerve stimulation by 40 stimuli train were studied. Both the affected and the unaffected sides were examined.

Changes of F-wave velocity parameters were found in 63.5% of patients. The increase of median nerve tachodispersion to up to 12 m/s was found in 53% of patients. The minimal velocity was 43.1±1.8 m/s. The study of ulnar nerve showed that tachodispersion increased to up to 12 m/s in 19% of cases. The minimal velocity was 42.7±1.6 m/s. The significant difference between minimal velocities in the affected and in the unaffected sides was observed in both cases.

Conclusion: The decrease in minimal F-wave velocity can lead to the increase in tachodispersion. Decrease in minimal F-wave velocity to below 44.5 m/s in median and ulnar nerves can be considered as one of neurophysiological findings in demyelinating radicular lesion at C7-C8-Th1 level. It can be a sign of radiculopathy.
Subclinical Motor Root Involvement in Guillain-Barré Syndrome: Presentation of Three Cases

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Objective and Method

The routine electrophysiological investigations might be normal in the early stage of Guillain-Barré syndrome. In this study we examined three patients who had clinically suspected Guillain-Barré syndrome who had normal peripheral nerve conduction using lumbar root stimulation.

Lumbar root stimulation was performed with the subject lying in prone position on the examination bed. Teflon coated monopolar needles were used for stimulation. The cathode electrode was inserted between the spinal processes of L2 and L3 vertebra. The anode was placed subcutaneously two or three levels above the cathode. Supramaximal intensity delivered with a duration of 1.0 ms. The responses were recorded from vastus medialis, tibialis anterior and gastrocnemius medialis muscles bilaterally and simultaneously.

First case had diplopia, slurred speech, and loss of balance since the day before admission. The neurological examination disclosed ptosis of left eye lid, vertical and horizontal eye movement restriction, dysarthria, areflexia, broad based ataxic gait. Second case complained numbness of hands and feet and a loss of strength in an ascending fashion for two months before admission then routine nerve conduction studies, needle EMG examinations and cervical spinal MRI were found to be normal. His complaints had persisted even though mild improvement was present. He was mildly quadriparetic. Deep tendon reflexes were absent in the lower extremities and were reduced in the upper extremities. Third case had bilateral facial paralysis following a flu like infection three weeks previously. The neurological examination was normal except facial diplegia.

Results

The lumbar root stimulation revealed increased latencies and decreased amplitudes suggesting conduction block at the lumbar root level.

Conclusion

Lumbar root stimulation should be considered to overcome diagnostic difficulties in acute demyelinating polyradiculoneuropathy with conduction block.

figure 1

![Image of figure 1](image-url)
P433
CLINICAL ELECTROMYOGRAPHY CORRELATION IN PATIENTS ADMITTED TO AN UNIVERSITY HOSPITAL

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INTRODUCTION

Electromyography (EMG) is indicated to neurophysiological assessment of the peripheral nervous system. The interpretation of the results depend on the clinical correlation, but its contribution to the diagnosis and management of inpatients is not often reported in the literature.

The aim of this study was correlate the clinical hypothesis with the results found in EMG, of inpatients at the Hospital de Clinicas, Universidade Federal do Paraná, within one year, to evaluate the contribution of the examination in the diagnosis of patients.

METHODS

A retrospective review of all EMG examination and medical records of patients admitted to HC-UFPR during one year period.

In the medical records was obtained demographic data, specialty who request the exam, indication for the EMG, topography, result of exam and number of exams done in the same patient in the same year.

Clinical hypothesis were grouped in topography.

The results of EMG were correlated with clinical hypothesis as: confirmatory correlation, new diagnosis, incidental diagnosis, inconclusive diagnosis and normal.

RESULTS

We performed 406 EMG in one year period (210 exams in 204 inpatients). There were 123 males and 81 females, with mean aged 38 year (range 4 months - 91 years old).

Five patients were submitted to additional EMG, one of them twice.

DISCUSSION

Confirmatory correlation found was similar to described in literature. However this study had a greater number of normal EMG. It occurred because in myopathy suspicion, the EMG sampling could be normal.

In patients with peripheral neuropathy and normal EMG, the main symptom was pain. Since pain is conducted by small fiber caliber, the routine nerve conduction studies were unable to detect abnormalities of these fibers.

In patients with neuromuscular junction dysfunction, repetitive stimulation test was normal in 47% of cases.
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**P434**

ULTRASONOGRAPHY SUPPORT DURING THE ELECTRICAL EVALUATION OF THE PERIPHERAL RESPIRATORY MUSCLE DISFUNCTION.

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**Question**

Weakness of respiratory muscles has been found to be a frequent symptom in the medical history of patients in Intensive Care, which precede to flaccid paralysis in some severe cases.

Phrenic nerve stimulation, electrical (ES) or from cervical magnetic stimulation (CME), is an uncommon technique, often considered difficult to perform.

We try to improve technique’s reliability by adding ultrasonography assessment during the evaluation of the peripheral respiratory muscle dysfunction at our institution.

**Methods**

We performed 10 hemidiaphragms studies on 5 in-patients with clinical respiratory muscle dysfunction. Each phrenic nerve was stimulated transcutaneously in the neck at the posterior border of the sternocleidomastoid muscles, trying to minimize co-stimulation of the brachial plexus, which could cause activation of the upper limb musculature. Square-wave impulses of 0.1 -ms duration were delivered, using a conventional bipolar electrode. Diaphragmatic muscle action potentials were recorded with surface electrodes placed over the seventh intercostal space (active), at the costochondral juncture, and the xiphoid process (reference). Simultaneously ultrasonography (M-mode traces) of the ipsilateral hemidiaphragm was performed.

**Results**

Of the 10 studies, we obtained 5 normal hemidiaphragm potentials followed by normal motion (represented as a spikelike deflection) at the ultrasonography. In 3 cases, responses were markedly reduced in amplitude with increased latencies and decreased motion. One diaphragmatic response showed mild amplitude reduction but normal motion. We obtained no electrical response, with no motion in one study.

**Conclusion**

Electrical stimulation can be difficult to accomplish as a consequence of morphology of the subject, anatomical variations of the nerve, and lack of uniformity establishing an standard protocol of recording and stimulation.

Furthermore stimulation of many of the muscles of the upper thoracic cage, as well as other external artifacts, could be responsible for contaminating the electrical signal.

We find ultrasonosonography support during electrical stimulation a reliable combination of techniques, that can help to avoid false positive and negative results.
P435
Usefulness of nerve conduction studies and F-responses of the peroneal nerve in L5 radiculopathy and its correlation with the degree of severity assessed electromyographically

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The lumbar radiculopathy refers to a pathological process involving spinal nerve roots, causing radicular symptoms in the lower limbs. F-responses are late waves that come from recurrent discharges of motor neurons depolarized antidromically, which may be useful in evaluating root lesions. The goal of this study is to evaluate the use of nerve conduction studies and F responses of the Peronial nerve in the diagnosis of L5 radiculopathy and its correlation with the degree of severity. We studied 47 subjects suffering from L5 radiculopathy, compared with a control group consisting of 28 healthy individuals. We evaluate the amplitudes of the deep Peroneal nerve CMAP, the superficial Peroneal SNAP, F-responses in terms of minimal, mean, maximum latencies, chronodispersion and persistence. In order to classify the severity of lesion of the root we also performed an electromyographic evaluation. Were noticed significant differences between both groups in the amplitude of the deep Peroneal CMAP (p<0.0001), the minimum, mean and maximum F-waves latencies (p<0.0001), and persistence (p=0.014). All these parameters were significantly correlated with severity of radiculopathy. We found that the F-wave latencies and chronodispersion were progressively larger and persistent and the amplitude of motor conduction studies was lower. The factor that showed higher sensitivity in the diagnosis of this condition was the F-wave maximum latency, 31.25%, and the less sensitive was the persistence, changed only in 9.34% of individuals. Taking into account all the parameters evaluated in the F responses we achieved a global sensitivity of this technique to 42.19%. With this research we concluded that the nerve conduction studies and F-responses may be useful as a supplement in the evaluation of lumbar radiculopathy, presenting a considerable sensitivity to this pathology. One should not limit the study of this technique for the evaluation of minimal F-wave latencies, but always include all other parameters, thereby increasing its sensitivity. These techniques should be included in the L5 radiculopathies studies.

Keywords
L5 Radiculopathy; F-Response; Electromyography; Nerve conduction studies; Peroneal nerve
P436
Assessing motor units with improved MUNIX

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Objective: Improvement and validation of the new non-invasive neurophysiological method MUNIX (motor unit number index). The reliability, practicability and inter-rater-variability of potential improvements to MUNIX were determined and compared to two established Motor Unit Number Estimation (MUNE) methods.

Methods: 40 Healthy subjects and 18 patients with amyotrophic lateral sclerosis (ALS) were studied prospectively at single point or multiple points in time. MUNIX results were compared with incremental stimulation MUNE (IS-MUNE) at abductor digiti minimi muscles (ADM), and with spike-triggered averaging MUNE (STA-MUNE) at trapezius muscles (TRA). In contrast to the original MUNIX method, we recorded a continuous electromyogram during increasing muscle contraction to reduce the influence of both patient’s compliance and investigator bias. Moreover, baseline correction for CMAP was implemented and the influence of the parameter settings (filters, number of data points, rectifying) was systematically studied.

Results: The best parameter setting includes high pass-filter 10Hz, low pass-filter 3000Hz, number of data points 1000, and rectification of the signals. This leads to an improved correlation between MUNE and MUNIX, up to 0.81 for ADM and 0.7 for TRA. The inter-rater-agreement is 90-93 % for data acquisition and 97-99% for data analysis.

Conclusion: The improved MUNIX needs minimum patient cooperation, and provides stable results easily and quickly. Improved MUNIX is suggested as an excellent alternative to the established MUNE methods in distal and as well as in proximal muscles.
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P437
Different types of fibrillation potentials in human needle EMG

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QUESTION

Rhythmic fibrillation potentials are the hallmark of recent axonal damage or muscle injury in striated muscle. Also irregular fibrillation potentials exist and these should be distinguished from end plate spikes of a normal muscle. Fibrillation potentials are generated by three basic mechanisms: oscillations of the membrane potential, fibrillatory origin potentials, and "giant" miniature end plate potentials without depolarization of the nerve terminal. The aim of this presentation is characterization of different types of fibrillation sequences and end plate spikes.

METHODS

94 different sequences of spontaneous activity was collected with concentric needle electrode and classified to 5 categories: rhythmic, slightly irregular with pauses, random, and "myokymic" fibrillations, and end plate spikes.

RESULTS

All different types of fibrillation potentials differed significantly from each other and from end plate spikes by the firing pattern but not by the waveform. Only the initial part of the potential was different when fibrillation potentials were compared to end plate spikes. The most effective variables were the minimum interval, the average proportional consecutive interval difference (APCID), and mean consecutive difference (MCD).

CONCLUSION

A physician performing EMG studies should recognize both rhythmic and irregular types of fibrillation potentials, and distinguish irregular fibrillations from end plate spikes, which is a normal phenomenon. Interval analysis of motor unit potentials show an entirely different discharge pattern, compared to spontaneous potentials. The functionality to calculate variables of the discharge pattern should be included in the future EMG devices. The lack of tools for editing and interval analysis of EMG potential sequences is the major shortcoming in the present EMG machines.

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P438
MUNIX, MUAP analysis, and peak-ratio analysis in the biceps brachii muscle in anterior horn cell disorders

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Question

Individual motor unit action potential (MUAP) analysis and peak-ratio (PR) analysis are well known routine methods used to evaluate reinnervation of muscles in chronic partial denervation. The motor unit number estimation technique MUNIX may provide additional information on number of motor units and their average size (MUSIX).

This study evaluated how these methods complement each other in a large muscle.

Methods

MUAP, PR and MUNIX were prospectively studied in 15 biceps brachii (BB) muscles with MRC force 2-5 in patients with motor neuron disease (MND) and a disease duration of 7-108 months and in 8 BB muscles with MRC force 4-5 in 8 previous polio (PP) patients. MUNIX was performed in 9 healthy controls.

Results

MUNIX showed large inter-subject variation both in MND (9-209) and PP (40-122). Compound motor action potential (CMAP) amplitude was strongly correlated with MUNIX and showed a similar inter-subject variation. MUSIX was rather constant at MUNIX values above 40, at values below 40 MUSIX was increased in 5 MND patients and one PP patient.

In PP patients MUAP duration correlated with PR and with MUSIX, while in MND patients such correlations could not be found. MUNIX did not correlate with MUAP duration or PR in any patient group.

MUAP duration was prolonged in 4/8 PP patients and in 14/15 MND patients and PR was decreased in 6/8 PP patients and in 12/14 MND patients. MUNIX was below 50 in 1/8 PP patients and in 7/15 MND patients. Abnormal MUNIX was not seen in any patient with normal MUAP duration or PR.

MUAP duration was the only parameter that correlated with disease duration in MND patients.

Conclusions

As expected MUAP duration and PR have the highest sensitivity in the biceps brachii muscle of patients with anterior horn cell disorders, emphasising that the strength of MUNIX may be monitoring of disease processes. The lack of correlations between different methods in MND may, in contrast to the correlations found in PP, reflect that MND patients are at different stages in the reinnervation process.
P439
On historical aspects of conduction blocks

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Nowadays, conduction block is defined as a partial or complete loss of the nerve function, usually more marked on the motor fibers. The CB is due to a focal loss of the electrical properties of the nerve fibers. The objective of this study is to highlight historical texts with reference to functional inexcitability of a nerve and to underline to whether the clinical signification has changed over time. An extensive search was conducted in PubMed “Motor conduction block neuropathy”: 422 references between 1977 and 2013, the material of the thesis of Ochsner who described the first two patients with permanent conduction blocks. A comprehensive review of the literature reveals the genesis of the concept of conduction block and its development through time in several historical references. In the 19th century, the anatomo-clinical method emerges; a work on Duchenne and faradic currents concerning the location of the motor points of Hermann von Helmholtz and related early studies on nerve conduction of electrical stimulation of Erb stepped. In 20th century, Seddom defines neurapraxia, Lambert quantifies conduction blocks and Roth delimits the electrophysiological characteristics of persistent conduction block by monopolar stimulation. A body of work that leads to the revision of the pathophysiological basis of demyelinating and axonal neuropathies, as well as the emergence of new clinical entities, such as Lewis-Sumner syndrome, pure motor multifocal neuropathy and hereditary neuropathy with liability to pressure palsies. The contribution of nerve conduction blocks was therefore not exploited until the 1980s. The 21st century is marked by the development and use of novel neurophysiological approaches, such as triple magnetic stimulation, and high-resolution ultrasonography, with the discovery of biological markers permitting to detect and monitor disease course, and new treatment options, notably by immunomodulation drugs. Knowledge of the semiology of electrical conduction block significantly increased the diagnostic capacity of electrophysiological studies allowing the definition and early recognition and detection of new nosological entities. More importantly, it led to a more target-oriented therapeutic approach by conservative measures or drugs like immunotherapy with promising results.
P440
Determining New Features for Diagnosis of Neuromuscular Diseases

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Objective
The aim of this study is to extract new features supporting diagnosis of neuromuscular diseases.

Method
Data groups being constituted by using EMG Simulator v3.6 consists of 5 normal, 5 neurogenic and 5 myopathic cases. Data have been acquired through scanning EMG method using concentric needle electrode. Four new features such as maximum amplitude, phase duration of the maximum amplitude, number of peaks and maximum amplitude times phase duration have been extracted.

Results
For neurogenic cases mean value of maximum amplitude is 571.22±296.51 mV, phase duration of the maximum amplitude 23.33±12.52 sample, number of peaks 4.13±1.31, maximum amplitude times phase duration 12403.25±7066.1. For normal cases mean value of maximum amplitude is 462.59±162.19 mV, phase duration of the maximum amplitude 23.2±5.72 sample, number of peaks 2.4±0.7, maximum amplitude times phase duration 10297.09±3296.2. For myopathic cases mean value of maximum amplitude is 247.31±190.5 mV, phase duration of the maximum amplitude 19.28±8.4 sample, number of peaks 2.87±0.98, maximum amplitude times phase duration 3855±2025.4.

Conclusion
By inspecting the statistical characteristics of these features, prominent features for each case have been determined. The future studies will be focused on building the fibre-density map of the motor unit in which the needle electrode is inserted.

Keywords
Neuromuscular diseases, scanning EMG, feature extraction, fibre-density

References
TEACHING LARYNGEAL ELECTROMYOGRAPHY


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**Question**

Although recognized as a valuable diagnostic tool for more than 60 years, it is unclear why many laryngologists do not routinely use laryngeal electromyography (LEMG). This may be due to a persisting lack of agreement on methodology, interpretation, validity, and clinical application of LEMG. But also the learning-process, requiring practical and theoretical teaching, may be a drawback of LEMG. To achieve progress in these fields, a working group on Neurolaryngology of the European Laryngological Society (ELS) was founded 2010 to evaluate guidelines for LEMG performance, clarify vague or doubtful issues and teach key techniques to interested laryngologists and neurophysiologist.

**Methods**

By screening Medline, existing knowledge and research about LEMG and laryngeal electrostimulation was identified. Additionally evidence-based recommendations for the performance and interpretation of LEMG and also for electrostimulation for functional evaluation were considered, as well as published reports based on expert opinion and single-institution retrospective case series. The working group discussed knowledge about LEMG and laryngeal electrostimulation and performed the techniques together. Consensus was achieved on: minimum technical equipment; best practical implementation; criteria for interpreting.

To disseminate the techniques, several modalities where used: Presentations using slides and videos, publications in scientific journals, hands-on-training on patients, animal models, and anatomic specimens, and a web-blog.

**Results**

Co-registration of the laryngeal EMG, voice, and breathing multiplies the scientific and didactic value of the LEMG-recordings. The advantages and disadvantages of the different teaching-modalities will be presented and discussed during this contribution.

**Conclusion**

Successful learning LEMG benefits from multi-sensory teaching concept.

**Literature**


2 www.lemg.org
P442
The value of SSR recordings in the assessment of autonomic nervous dysfunction in patients with sacral-pudendal impairment.

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Question

Neural control of pelvic structures reveals a complex interaction between central and peripheral nervous pathways and a coordination of somatic and autonomic systems. While it is well known the usefulness of neurophysiological tests to investigate somatic nervous system of pelvic floor (needle electromyography, nerve conduction studies, evoked potentials, sacral reflexes), it is not yet recognized the real efficacy of sympathetic skin response (SSR) in patients with sacral-pudendal dysfunction.

Methods

In the last six years we examined 1745 patients with different pelvic disorders (urinary, anorectal and sexual pathologies), age range 7-85 years. The SSR was recorded from the skin of the sacral area (dorsum of the penis or mons pubis, perineal area, perianal area, in function of clinic), applying random single square pulses at the wrist or supraorbital region. Also SSR and EMG-ENG of legs were performed in all patients.

Latency and amplitude (peak to peak) of SSR were measured and the results were compared by mean age with those of control group.

Results

We observed alterations in latency and amplitude in various diseases: spinal cord injury, sacral plexus pathology, sexual disfunctions, etc. In some cases SSR changes were the only present abnormality (frequently in case of sexual dysfunction and syringomyelia). We have also observed it is important to differentiate anterior from posterior perineal area in SSR recording, mostly in pelvic disorders (traumatic or not).

Conclusion

SSR test may be an useful tool to investigate autonomic sacral involvement, because until now it the only test to explore autonomic system, even if it explore only sympathetic system. In our experience SSR is always present, in absence of pathology, so it could become a standard investigation for clinical routine of patients with sacral disorders.
SWALLOWING DIFFICULTY IN OCULOPHARYNGODISTAL MYOPATHY: Electrophysiological Evaluation

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Introduction

Patients with oculopharyngodistal myopathy (OPDM) present with progressive ocular, pharyngeal, and distal limb muscle involvement. Respiratory and swallowing difficulties occur at or soon after presentation.

The aim of this study was to assess swallowing difficulty in patients with oculopharyngodistal myopathy via electrophysiological measurements to detect the primary site causing swallowing and/or respiratory difficulty, namely pharyngeal or laryngeal involvements.

Methods

Patients diagnosed as having oculopharyngodistal myopathy in the department of neurology of Istanbul Faculty of Medicine underwent electrophysiological examination. For the clinical evaluation of swallowing, a previously described grading system is used. Electrophysiological measurements consisted piecemeal deglutition and dysphagia limit using 3, 5, 10, 15, and 20 ml bouts of water and sequential water swallowing of 100-ml water in 15 patients, swallowing assessment via needle electrodes placed on thyroarytenoid and cricopharyngeal sphincter muscles in 10 patients, percutaneous needle EMG evaluation on thyroarytenoid (TA) and cricopharyngeal (CP) sphincter muscles in 6 patients.

Otolaryngologic examination evaluating the alignment and function of vocal cords, voice, articulation, and swallowing excluded non-neurologic swallowing and respiratory difficulties.

Results

Dysphagia limit was abnormal in 12 patients with grade 2-3 dysphagia but normal in 3 patients with grade 1 dysphagia. Also sequential water swallowing was normal in 7 patients including all patients with grade 1 dysphagia and abnormal in 8. The recording of swallowing on cricopharyngeal sphincter and thyroarytenoid muscles muscles revealed normal swallowing patterns in all patients. Needle EMG of TA and CP sphincter muscles revealed myopathic pattern in thyroarytenoid muscles in 4 of them.

Conclusion

Swallowing difficulty develop in a purely myopathic patern involving first laryngeal muscles in patients with oculopharyngodistal myopathy.
Anatomofunctional mapping of the opercular cortex by intra-cerebral electrical stimulations in epileptic patients explored by means of stereoelectroencephalography (SEEG)

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Background
Operculum is the part of cerebral cortex that covers the insula (Mazzola et al 2012). Although the literature addresses its functions in numerous studies, the vast majority of them consist of inferences made on activation patterns revealed by functional imaging. Few studies have been published using a direct electrical stimulation paradigm, and the ones that have done so, studied subjects with a pathological process involving this area.

Objectives
Our aim is to perform a systematic mapping of this highly relevant cortical structure with different stimulation protocols.

Methods
We elicited clinical responses at various stimulation parameters (mainly 1 Hz for 40 s, 50 Hz for 5s) in a lot comprised of 11 consecutive patients explored for drug resistant focal epilepsy during presurgical work up. Using the SEEG method, a number of depth electrodes ranging from 7-17 were implanted, to map the seizure onset zones (SOZ), propagation pathways and functional cortex that should be avoided during surgery. All the patients had SOZ located outside the opercular cortex and this areas had no particular pathology. Effects obtained on contacts touching the insular cortex, laying in the pericortical white matter, or producing any after-discharges were discarded (Afif Afif & al 2010). The others were projected on a Maximum Intensity Projection (MIP) map with their relative position derived from the 3 D axial coordinates generated by the neuronavigation software.

Results
We have applied about 350 stimulation trains, on 90 bipolar contact pairs situated on 30 different electrodes implanted orthogonally in the frontal, rolandic, parietal and temporal operculum. 18% of the 1 Hz and 50% of the 50 Hz stimulations produced a discernable clinical effect classified as somatosensory 33%, motor 17%, auditory 16%, speech disturbances 14%, oropharyngeal 11%, visceral 8%, gustatory 3%, vertiginous 2% and painful experiences 2%. Clinical effects were distributed both contra and ipsilateral. 20% produced a clinical effect in multiple modalities.

Conclusions
MIPs demonstrate a clear clustering of these effects around constant anatomical areas. The majority of responses were sensory-motor both somatic and visceral distributed in the oro-facio-brachial territories.

figure 1
Idiopathic Generalised Epilepsy, Sleep-Spindles, and the Thalamocortical Network

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**Question**

Coordinated thalamocortical network (TCN) oscillations during sleep process and integrate information acquired during wakefulness. These transient phenomena manifest on the electroencephalograph (EEG) as sleep-spindles (SS), with topographic heterogeneity reflecting different pre-sleep learning domains. The TCN also underlies the pathological spike and wave discharges (SWD) of the idiopathic generalised epilepsies (IGE). This study addressed the question of whether the known TCN dysfunction in IGE disrupts physiological SS phenomena.

**Methods**

Sleep-deprived EEG records of 29 IGE and 27 control subjects were analysed. Mean frequencies were calculated from ≥6 SS over frontal and central EEG derivations during stage 2 non-REM sleep.

**Results**

No significant difference was found between IGE and control subject mean central or frontal SS frequencies (p=0.215 and p=0.448, respectively). Central SS were highly significantly faster than frontal SS in IGE and control subjects (p=0.000, p=0.009, respectively), evidencing the normal rostro-caudal frequency gradient being intact. Additionally, central nervous system medication (necessarily including antiepileptic drugs (AEDs)) conferred no significant effect on mean IGE central or frontal SS frequencies (p=0.688 and p=0.105, respectively).

**Conclusions**

With no SS frequency abnormality between groups, and normal SS topography maintained in IGE subjects, our results suggest purely transient dysfunction of the TCN during SWD. In view of this we infer no disruption by IGE to physiological processes SS are ascribed to. Additionally, AEDs also confer no effect on SS frequency. Taken together these results suggest that with adequate seizure control IGE impacts minimally on patient quality of life.
Correlation between Bispectral Index and the quality of the electrocorticography during epilepsy surgery.

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**Introduction**

The Electroctricography (ECoG) is useful to identify the epileptic zone during epilepsy surgery and the Bispectral Index (BIS) allow the hypnotic anesthesia component monitoring, however, the correlation between the scores of BIS and the ECoG patterns to optimizing the quality and time of the ECoG recordings are unknown.

**Objective**

Analyze the correlation between the BIS scores and the duration of suppressions periods (seconds) in the burst-suppression (BS), background frequency (Hz) and type of patterns (1 [normal] to 5 [ECoG seizure]; Bindra A et al., 2012) of ECoG recordings during epilepsy surgery under intravenous general anesthesia with propofol.

**Material and Methods**

Prospective study that included consequently pharmacoresistant epileptic patients who underwent epilepsy surgery guided by ECoG and BIS (September 2008 to October 2012).

**Results**

We included 28 epileptic patients, 15/28 (53.5%) female, age mean 30.5 (13-56) years old, weight mean 68.32 (42-100) kg who underwent 22/28 (79%) temporal and 6/28 (21%) extra temporal epilepsy surgeries with propofol mean plasmatic concentration 3.2 (0.75-4.4) µg/ml and ECoG duration mean 40 (5-178) min. We found on a non-linear relationship (e.g. polynomial cubic) between the mentioned variables by emphasizing that for a BIS range 40-60 the following characteristics follow: ECoG burst suppression periods below 5 s, background brain frequency ranging between 10-17 Hz and 2 ECoG pattern characterized by lacking of >20 Hz background frequencies.

**Conclusion**

Our findings support that the BIS is a non-linear multidimensional measure which possesses high variability, although a BS increasing tendency with respect to the BIS scale appears when comparing to background frequency and ECoG patterns. Figure 1. Non lineal polynomial cubic regression between the BIS scores and the duration of suppressions periods (seconds) in the BS. Figure 2. Non lineal polynomial cubic regression between the BIS scores and the background frequency in the ECoG during the epilepsy surgeries.
Abstracts of Poster Presentations – Poster Session 26 – Epilepsy 2

figure 1

figure 2
Challenges of Automated Detection of High Frequency Oscillation

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Question

High frequency oscillations (HFOs) in the EEG are distinct oscillations in the 80-500 Hz range. They have been proven biomarkers of epilepsy. Finding HFOs in the EEG is time-intensive and subjective if done visually. Alternatively, automated detection algorithms are employed. As we show, automated detection is afflicted with other pitfalls based on the non-uniformity of HFOs.

Methods

HFOs from one minute of intracranial slow-wave-sleep EEG of six patients with medically refractory epilepsy were marked visually. Three patients had subdural grid electrodes, three had depth electrodes. An automated detector (R. Zelmann et al. Conf. Proc. IEEE Eng. Med. Biol. Soc. 2010; 2329-2333) was trained and tested with respect to the visual HFOs. Within a training phase of 30 sec, a set of parameters was optimized channelwise for each patient (local opt.) and for each patient across channels (global opt.) based on the events visually marked. Within a testing phase of another 30 sec, the performance (Cohen's kappa, false detection rate, and others) of the detector was assessed wrt to the events visually marked.

Results

The performance of the detector varied strongly between, both patients and channels. This variation as well as false detection rate, but also kappa values were lower for global than for local optimization. In channels of high variability of baseline activity the performance was decreased. The detector performed better in depth electrodes than in grids (p

Conclusions

Assumptions of automated detections are stability EEG- and HFO-properties. However, those assumptions are not met, neither within patients nor within channels. This affects the performance of automated detectors in general. We conclude that parameters and performance of a detector obtained from a set of patients is not transferable to another set of patients.

Fig 1: Optimization in deep electrodes performs better than in grids.

Fig 2: Optimization on many events does not imply good performance.
Abstracts of Poster Presentations – Poster Session 26 – Epilepsy 2

figure 1

Global:

Local:

figure 2

Global:

Local:
New onset seizures in elderly: clinical presentation and etiology of first ever seizure.

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Question

To study the possible etiologies and clinical characteristics of seizure in elderly population.

Method

All patients presented to our emergency room (ER) at King Fahad Medical City (KFMC) aged 60 years and above with their first seizure, were recruited. Seizures were classified according to the revised ILAE (International League against Epilepsy)¹ classification into primary generalized, simple partial seizure (SPS) complex, partial seizures (CPS) and secondary generalized (focal onset followed by secondary generalization). Events were identified as single or multiple (two or more episodes). Status epilepticus was defined as a seizure lasting more than 30 minutes or recurrent seizures without full return of consciousness between two episodes.

Results

Hundred and five patients were included in this study; their mean age was 69.75 years (range 60-93), 51(48%) patients were male, 41(39%) patients presented with partial seizures, out of those 14(13.33 %) had SPS, 27(25.7%) had CPS, 3 (2.85%) patients presented with partial seizure with secondary generalization. Generalized tonic-clonic seizures were found in 37(35.24%) of the patients, while 7(6.65%) presented with status epilepticus. Myoclonic seizures were found in only 3 (2.85%) patients. Stroke was the etiology of seizures in 66(62.77%); out of those 9(8.57%) were due to ICH (Intra Cerebral Hemorrhage) and 57(54.2%) were secondary to ischemic stroke. Cortical infarcts were found in 42(40%), 12(11.43%) had acute symptomatic seizures and 30(28.57 %) had remote symptomatic seizures. Sub-cortical strokes were found in 15(14.29%) of the cases, 5(4.76%) with acute and 10(9.52%) with remote injury. Brain Tumors were found in 18(17%), 15 (14.29%) presented acutely, while only three (2.86%) presented remotely. No identifiable etiology was found in 15(14.29%) and hence was labeled as cryptogenic. Acute symptomatic seizure was the commonest presentation with brain tumors followed by cortical strokes, with p-value of <0.0001. EEG abnormalities were found in 81(77.11%) patients, 23(21.9%) had focal epileptogenic abnormalities, 29(27.62%) had generalized slowing, and 23(21.9%) had either localized or lateralized slowing. EEG was normal in 15 (14.29%) patients, while not recorded in 9 (8.57%) patients.

Conclusion

The most common etiology of seizures in elderly was cerebro-vascular disease and most of them presented within two years of stroke. Commonest presentation was focal seizure, either simple or complex partial.
Abstracts of Poster Presentations – Poster Session 26 – Epilepsy 2

P450
Is there any link between head trauma and generalized epilepsy disorder?
Post trauma generalized epilepsy observational case series

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Question
Is there any link between head trauma and generalized epilepsy disorder?

Method
Patients were collected from epilepsy clinic / EMU. We present a series of four patients where a strong temporal relationship between head injury and onset of generalized epilepsy observed.

Results
We found four patients, three of them presented with typical GTC seizures with witness account and one with absence seizure; all of them had history of head trauma and significant TBI, as evident by head CT/MRI, which confirmed the presence of brain injury. We reviewed EEGs of all patients; case one showed frequent generalized spike and wave discharges that appeared more prominent at times over right or left frontal areas. Case two had left temporal spikes followed by generalized spike and wave discharges. Case threeshowedsymmetrical. 3-5Hz spikes & slow waves complex, associated with polyspikes, case four had typical 3 spike and wave discharges.

Conclusion
Understanding the molecular and cellular basis that lead to the development of PTE is key for preventing its development or modifying the disease process in such a way that epilepsy if it develops is milder or easier to treat. Our observation raised the concern that TBI can result in GE disorders, and it differs in terms of response to treatment. Our findings are very interesting and crucial to investigate more insight in PTE, which is very important cause of epilepsy throughout the world and especially in KSA and Middle East. It can challenge the established guidelines regarding epilepsy prophylaxis after TBI as well.
Compensatory mechanisms lead to nonlinear correlations between episodic memory and BOLD activity in temporal lobe epilepsy

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Question


Methods

Fifteen patients with left TLE (23 - 69 years, eight female) underwent a verbal memory fMRI paradigm. Correlations between BOLD activity in the mesial temporal lobe (mTL) and neuropsychological data were calculated.

Results

Analyses revealed cubic (and - with less explained variance - quadratic) correlations between neuropsychological data and activation within mesial temporal regions during recognition of verbal material. Consideration of the right mTL in addition to the left mTL lead to a higher proportion of explained variance compared to the left mTL ROI alone (74 % vs. 60 %) (Figure1).

Conclusions

We suggest that the observed nonlinear correlations result from inefficient compensatory mTL activations during unsuccessful recollection due to marginal memory performance in both healthy individuals and patients with mTLE. Furthermore, we were able to demonstrate that the right mTL contributes to verbal memory performance, although the damaged mTL seems to be dominant, underlining the importance of asymmetry indices in the prediction of memory outcome after mTL surgery.

Figure 1

Scatterplots demonstrating correlations between percentile ranks of verbal learning and memory test and activations in (A) left mTL and (B) right + left mTL during verbal fMRI memory task. Explained variance for both mTL higher compared to left mTL ROI alone.

Dashed line = cubic fit; solid line = quadratic fit; R² values illustrate the explained variance of the fits. White dots = patients with impaired memory; black dots = patients with marginal memory; grey dots = patients with normal memory.
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P452
PureEEG: Automatic artifact removal for long-term EEG monitoring

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Question

An automatic EEG artifact removal algorithm called PureEEG was developed. The algorithm is based on an electrophysiological signal model and utilizes spatio-spectral filtering techniques. The algorithm was evaluated in a validation study investigating the artifact removal performance and the attenuation of true EEG patterns in order to show the added value of PureEEG for EEG review.

Methods

The PureEEG algorithm was evaluated by two independent reviewers on 102 twenty-second epochs from seizure onsets of 48 consecutive epilepsy patients. Each epoch had to be evaluated regarding the amount of artifacts before and after PureEEG processing and the attenuation of true EEG patterns in a multiple-choice questionnaire.

Results

A major improvement due to PureEEG was found in 59% and 49% of the EEG epochs by the reviewers respectively, a minor improvement in 38% and 47% of the epochs. The answer "similar or worse" was chosen in 0% and 4% respectively.

Neither of the reviewers found a “major attenuation”, a significant attenuation of significant EEG patterns. Most EEG epochs were found to be either “mostly preserved” or “all preserved”. A minor attenuation was found in 0% and 17% by the reviewers, respectively.

Conclusions

The PureEEG artifact removal algorithm effectively removes artifacts from EEGs and improves the readability of EEGs impaired by artifacts. Only in rare cases the algorithm attenuates EEG patterns slightly, but the clear visibility of significant patterns was preserved in all cases of this study. PureEEG is a valuable tool for EEG artifact removal, which reliably preserves significant EEG patterns from cerebral sources.
P453
Heart rate variability analysis of seizure leading to sudden unexpected death in a patient with epilepsy indicates increased pre-ictal parasympathetic tonus.

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Evidence for seizure-induced cardiac dysrhythmia leading to sudden unexpected death in epilepsy (SUDEP) has been elusive. We present the case of a patient with focal cortical dysplasia who has had epilepsy for 19 years and was undergoing presurgical evaluation. The patient did not have any cardiologic antecedents. During the long-term video-EEG monitoring, following a secondarily generalised tonic-clonic seizure the patient had prolonged (174 s) postictal generalised EEG suppression and asystole, followed by malignant ventricular arrhythmia, and the patient died in spite of cardiopulmonary resuscitation. Analysis of heart rate variability showed a marked increase in the parasympathetic activity during the 30 minute period preceding the fatal seizure, compared with values measured one day and six month before, and also higher than the pre-ictal values in a group of 10 patients with generalised tonic-clonic seizures. This unfortunate case documented during video-EEG monitoring indicates that seizure-induced cardiac dysrhythmia can lead to SUDEP, and suggests that patients with increased parasympathetic activation in the pre-ictal period might have an increased risk of SUDEP in the period following the seizure.

Figure legend:

A) High Frequency (HF) power of Heart rate variability (HRV) for the case of SUDEP in ½-hour inter-ictal periods (7-months day/night, 1 day day/night before death) and ½-hour pre-ictal the seizures leading to death.

(B) HF-power and RMSSD (root mean square of differences of successive R-R intervals) in ½-hour pre-ictal periods from the case of SUDEP and control seizures from other patients.

![Figure 1](image-url)
P454
Coincidence of non-convulsive epileptic seizures and stimulation-on phases in a patient with deep brain stimulation of thalamic anterior nuclei

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Question

Deep brain stimulation (DBS) of the thalamic anterior nuclei (AN) represents a complimentary option for treatment of drug-resistant epilepsies. The putative induction of epileptic seizures by DBS of thalamic AN has been occasionally reported. However, an exact correlation between thalamic stimulation and the electroclinical onset, duration, and semiology of seizures has not been documented until now. Therefore, it is not known whether this side effect occurs as a result of the syndrome and/or protocol. We report the case of a patient with non-lesional epilepsy, who experienced spontaneous and DBS-induced epileptic seizures. In this patient we performed an accurate analysis of the electroclinical effects of thalamic DBS.

Methods

A 23 year-old female with non-lesional epilepsy with tonic-dyscognitive focal and bilateral convulsive seizures was treated by means of bilateral deep brain stimulation. DBS electrodes were implanted bilaterally in the thalamic anterior nuclei using a stereotactic technique. The following stimulation parameters were used bilaterally and mostly symmetric: amplitudes between 3 and 7.5 V, frequencies between 145 and 180 Hz, pulse widths between 90 and 120 µs, stimulation cycling on/off between 1min / 5min and 20s / 20s, stimulation plots: 3 and 11 (most lateral located plots).

Results

Immediately after initiation of DBS the patient developed almost stupurous mutism. The electroencephalograms (EEGs) showed series of sharp-slow-waves or high amplitude theta-delta discharges that regularly occurred during the on-phases of a stimulation cycle and correlated well with fluctuating neurocognitive impairments. In a long-term EEG recording, regularly occurring periods of sharp-slow-waves or slow-wave discharges, coincident to the thalamic stimulation were also documented. Neuropsychological assessment performed at the end of a stimulation-free period of several months and three days after restarting the thalamic stimulation showed an abrupt impairment of attention and executive functions.

Conclusion

In difficult-to-treat epilepsy patients, DBS of the anterior thalamus may occasionally induce electroclinical worsening.
P455
Enhanced ictal and interictal gamma coherence in children with idiopathic generalised epilepsy

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Background and aim

Cortico-thalamo-cortical circuits play a crucial role in generating oscillations in various frequency bands in association with idiopathic generalized epilepsy (IGE). We here tested the hypothesis that cortical rhythmic EEG activity in the gamma band (40-80 Hz) coincided with and possibly caused spike-wave-discharges (SWD) in patients with idiopathic generalised epilepsy (IGE).

Method

Ictal and interictal EEG recordings of 14 children with IGE (mean age 8.5 +5 years) and age and sex matched controls were evaluated. Network operator functions of high frequency synchronization were assessed in IGE patients during interictal and ictal states with respect to cortical coherence to evaluate cortico-cortical connectivity. Power spectrum density and intra- and inter-hemispheric coherence profiles were estimated using a block autoregressive parametric model.

Results

In the interictal state IGE patients displayed significantly larger number of coherence peaks in the gamma range as compared to controls (p

Conclusions

IGE patients showed abnormal EEG hypersynchrony in the gamma range compared to control patients in the interictal state with preponderance in frontal and frontocentral regions. Different brain rhythms, with both low- and fast-frequency activities, were grouped within complex wave-sequences during SWD associated with absence seizures. Thus, SWD are characterized by coalescence of high and low frequency bands at high power and not one or a few slow frequencies associated with a spike as it is commonly believed.
P456
Comparison of high gamma electrocorticography and fMRI with electrocortical stimulation for localization of somatosensory and language cortex.

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Question
In patients with pharmacoresistant epilepsy, electrocortical stimulation (ECS) has been established as the gold-standard for pre-surgical mapping. Yet, ECS is not suitable for all patients due to lengthy sessions and imperfect collaboration. To overstep the limitations of ECS, we investigate the contribution of time-frequency analysis of electrocorticography (ECoG) and functional magnetic resonance imaging (fMRI) for the localization of primary (somatosensory) and associate (language) cortices.

Methods
23 consecutive patients with subdural electrodes underwent a somatosensory stimulation protocol and/or an auditory semantic decision task. Fourteen patients did the same protocol with fMRI before implantation. We compared functional mapping by induced high gamma (hg) ECoG activity (70-160 Hz) and by fMRI with that suggested by ECS and with respect to the postoperative outcome.

Results
ECS resulted in the identification of somatosensory area sites of the thumb in 12/16 patients. HgECoG revealed somatosensory cortex in all these patients, overlapping with 67% of the positive ECS electrodes (true positive). Positive hgECoG responses were found in 4% of the negative ECS electrodes (false positive). In 3 ECS non responsive patients, hgECoG identified 12 electrodes presumably corresponding to somatosensory cortex. FMRI responses showed 33% of true positive and 5% of false positive electrodes. Language-related sites were identified with ECS in 7/12 patients. In all 7 patients, hgECoG responses demonstrated 50% of true positive and 8% of false positive electrodes. FMRI responses revealed 64% of true positive but 23% of false positive electrodes. Nevertheless, in 3 patients who developed post-surgical language deficits, hgECoG and fMRI sites were inside the resection, consistent with ECS. Moreover, in one patient who suffered from post-surgical language impairments, the resection included hgECoG positive sites that ECS failed to detect.

Conclusions
HgECoG and fMRI are useful tools for pre-surgical mapping and provide additional localization information in patients who cannot sufficiently collaborate for extra-operative ECS sessions. However, hgECoG is significantly more specific than fMRI to identify primary and associate cortical areas.
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P457
Influence of low-frequency Repetitive Transcranial Magnetic Stimulation on the Expressions of KCa1.1, NaV1.6, NMDAR1, GAD65 Proteins in Hippocampus CA3 of SD Rats

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Question

A number of animal and clinical studies have shown that low-frequency repetitive transcranial magnetic stimulation (rTMS) can effectively reduce seizures, but its underlying mechanisms are still unknown. We speculate that ion channels and excitatory/inhibitory transmitter, which are believed to play a key role in the process of epileptic development or seizures, might involve in the antiepileptic mechanism of low-frequency rTMS. Therefore, we aim to investigate whether low-frequency repetitive transcranial magnetic stimulation (rTMS) can affect the expressions of KCa1.1, Nav1.6, NMDAR1 and GAD65 proteins in the rat CA3 region pyramid layer.

Methods

50 rats were randomly divided into the experimental group and the sham group. The former was administered with low-frequency rTMS for 14 consecutive days; the latter was given sham stimulation for also 14 days. After finished the rTMS protocol, each group was further divided into five subgroups according to time point (6h, 24h, 1w, 3w, 6w). The animals were killed at corresponding time points respectively, and the expressions of KCa1.1, Nav1.6, NMDAR1 and GAD65 in the CA3 region of hippocampus were examined by immunohistochemistry. Results: Compared with the sham group, the KCa1.1-positive neuron densities were significantly increased in the period of 6h-3w after rTMS (p<0.01); the GAD65-positive neuron densities were also obviously elevated at 6h(p<0.05), especially in the duration of 24h-3w following rTMS (p<0.01); the Nav1.6-positive neuron density was transiently decreased at 6h after rTMS protocol(p<0.05); similarly, the NMDAR1-positive neuron density was also shortly decreased at 6h following rTMS treatment (p<0.01).

Conclusions

The study shows low-frequency rTMS can upregulate the expressions of KCa1.1 and GAD65 and last for at least 3w; but transiently downregulate the expressions of NaV1.6 and NMDAR1 in the rat hippocampal CA3. These changes might be one of its anti-epileptic mechanisms.
HMGA2 gene allele variants are associated with EEG interictal epileptiform activity in temporal lobe epilepsy

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INTRODUCTION

EEG interictal epileptiform discharges are a hallmark of epilepsy, and they are considered a biomarker for localization of the epileptogenic area, besides to be implicated in disease severity, and in prognosis after a first seizure and after epilepsy surgery. They are influenced by several factors, like dipole localization and orientation, sleep-wake cycle and CNS active drugs. Few authors have studied the influence of genetic variants on the EEG. Recently, some genes or genetic polymorphisms have been associated with brain development and eventually with epilepsies associated with structural brain lesions. Thus, it is plausible that some of these genes might also influence epileptogenicity in patients with epilepsy. Accordingly, genes coding Discoidin Domain Receptor Tyrosine Kinase 2 (DDR2), Tescalcin (TESC), and High Mobility Group A Protein (HMGA2) were associated with brain volume, and might influence epileptogenicity.

OBJECTIVE

Investigate the association between DDR2, TESC and HMGA2 genes and interictal spike activity in temporal lobe epilepsy (TLE).

METHODS

Case-control study of 76 patients with TLE exploring the influence of polymorphisms rs10494373 of DDR2, rs7294919 of TESC and rs10784502 of HGMA2 on the incidence, distribution and lateralization of interictal epileptiform EEG of these patients. All individuals had an awake and asleep standard EEG recordings, and tracings were analyzed by experienced and certified electroencephalographers.

RESULTS

No association between rs10494373 of DDR2, and rs7294919 of TESC polymorphisms with EEG spike rates was found in TLE, regarding the EEG variables studied. However, presence of C allele in homozygosis in rs10784502 variant of HGMA2 was associated with significant less interictal discharges (p = 0.008), in other words, presence of T allele in this specific polymorphism was associated with a doubling of discharges per minute, when compared with C allele in homozygosis (OR: 2.15 ± 2.99 x 1.01 ± 0.65).

CONCLUSION

Our data allow us to hypothesize that variability in the HMGA2 gene might influence EEG interictal epileptiform activity and epileptogenicity in patients with TLE. We believe that further studies will shed some light on molecular mechanisms involved in the generation of EEG epileptiform activity.
Electro-clinical features of focal epilepsy patients with postictal generalized EEG suppression

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Question
Postictal generalized EEG suppression (PGES) may be associated with sudden unexpected death in patients with epilepsy. Generalized tonic-clonic seizure (GTCS) is one of the well-known risk factors for PGES. However, which types of epilepsy are associated with PGES remain unclear. The present study investigated the electro-clinical features of focal epilepsy patients who suffered secondary GTCSs (sGTCSs) with PGES.

Methods
We retrospectively reviewed 32 consecutive patients (13 men) with focal epilepsy aged 13 to 47 years, who presented with sGTCSs during long-term video EEG monitoring. PGES was determined using the previously published criterion of generalized absence of EEG activity of amplitude >10 µV. Patients with at least one sGTCS showing PGES were classified into the PGES (+) group (n = 18, 56%). Electro-clinical findings including localization of epileptic foci and lateralizing signs on semiology were compared between the PGES (+) and (-) groups.

Results
Temporal lobe epilepsy (TLE) was significantly (p < 0.05) more common in the PGES (+) group (56%) than in the PGES (-) group (14%). Preceding "figure 4 sign" was significantly (p < 0.001) less common in the PGES (+) group (33%) than in the PGES (-) group (93%). However, preceding "version" was not associated with PGES occurrence (56% in PGES (+) and 36% in PGES (-) groups).

Conclusions
Diagnosis of TLE and absence of "figure 4 sign" may be potential risk factors for PGES. Localization of both epileptic foci and propagation pathways leading to sGTCSs are important for the occurrence of PGES.
Electroencephalography and clinical findings in a SCN8A epileptic encephalopathy: a case report.

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Background

Epileptic encephalopathies refer to a severe condition where epileptic activity itself may contribute to progressive cognitive, behavioural and motor dysfunction. Several genes have been associated with early infantile epileptic encephalopathy (EIEE).

We report a SCN8A mutation contributing to neonatal epileptic encephalopathy. Previously, mutations in SCN8A have been reported in two patients with EIEE, the first case with epileptic encephalopathy presenting at 6 months of age, and second one at 18 months of age.

Methods and results

The patient was born at term in foetal hypoxia. Seizures were present immediately after birth; were generalized tonic with apnoea and bradycardia or focal tonic, very frequent and refractory to treatment. The patient also had central hypotonia, movement disorders (coarse tremor, myoclonias and voice expression), dysmorphic facial appearance and multiple congenital anomalies. He did not achieve developmental milestones according to his age. Magnetic resonance imaging performed at the ages of 9 days and 1.5 months was normal. At the age of 11 months moderate bilateral frontotemporal atrophy, thinning of the corpus callosum and mild delay in white matter myelination were described. Using whole-exome sequencing we identified a novel pathogenic c.3979A>G missense mutation in SCN8A.

Electroencephalography (EEG) showed slight low-voltage background activity and occasional interictal epileptiform discharges in bilateral temporal areas during the first months. Ictal EEG was characterized by bilateral centrotemporal theta rhythm. Burst-suppression-like pattern in sleep recording was noticed at 11 months of age. He died at the age of 1 year and 5 months due to progressive respiratory failure during respiratory illness.

Conclusion

Mutations in SCN8A can lead to EIEE with a broad spectrum of EEG and clinical features. Detailed phenotypic descriptions are needed to avoid unnecessary investigations and optimize the therapy.
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Vagus nerve stimulation is beneficial in a patient with postural orthostatic tachycardia syndrome: a case report

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Question

Postural orthostatic tachycardia syndrome (POTS) is defined by a heart rate increment of 30 beats/min or more within 10 minutes of standing or head-up tilt (HUT) in the absence of orthostatic hypotension. Vagal nerve stimulation (VNS) is a safe and effective adjunctive treatment for drug-resistant epilepsy when surgery is inadvisable. Limited data suggest that long-term VNS therapy might affect cardiac autonomic function. However, there are no data of the VNS utility in patients with POTS.

Methods

A 29-year-old female patient was implanted with VNS due to pharmacoresistant epilepsy (elementary sensory-motor partial seizures of the left extremities and complex partial seizures of temporal origin with occasional secondary generalization. Couple of years she noticed palpitations and dizziness in standing upright that were relieved by sitting or lying flat. Brain MRI showed bilateral frontoparietal polymicrogyria and right subependimal nodular heterotopia. During the preoperative work-up autonomic nervous system testing revealed POTS that was refractory to life style modification measures.

Results

One weak after implantation, VNS was initiated at 0.25 mA (duty cycle set to a 30-Hz signal frequency, a 500-ms pulse width, 30 sec of on-time, and 3 min of off-time). HUT done at one month and three months after implantation was normal. VNS was gradually increased to 1 mA which led to significant reduction in seizure rate and disappearance of orthostatic intolerance symptoms.

Conclusion

To our knowledge, this is the first reported case of the positive VNS effect in patient with POTS. Further studies with a larger number of patients are needed.

Key words

Postural tachycardia syndrome, Vagus nerve stimulation, Pharmacoresistance, Epilepsy
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Diffuse brain dysfunction in benign adult familial myoclonus epilepsy (BAFME)

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Abstract

Objectives

To clarify the clinical implication of posterior dominant rhythm (PDR) of electroencephalogram (EEG) in benign adult familial myoclonus epilepsy (BAFME).

Methods

Maximum frequency of PDR in EEG was studied in 17 BAFME patients with clinical diagnosis of this condition (8 men and 9 women, mean age of 49.0 ± 17.6 years, 21-76 years). For control subjects, 101 adults (age > 20 years old) diagnosed as “normal” in EEG and 34 age-gender matched subjects (16 men and 18 women, mean age of 48.6 ± 16.3 years, 21-77 years) elaborated from them were also studied. We also investigated the chronological change of 9 BAFME patients whom EEG was recorded more than twice.

Results

Maximum frequency of PDR in BAFME was 9.2±0.7 Hz, and it was significantly smaller in comparison to that of 101 control subjects (10.5±0.9 Hz) and 34 age-gender matched subjects (10.5±08 Hz), respectively (P < 0.05). This finding was also seen regardless of the anticonvulsant intake in control subjects. There was a tendency, but not significant, in slowing PDR with aging in both BAFME and control subjects. There was no significant relationship between myoclonus scale and PDR and no significant chronological change in PDR of 9 BAFME patients.

Conclusions

These findings of PDR in EEG suggested that mild diffuse brain dysfunction was present in BAFME. However, slowing in PDR with aging in BAFME was quite comparable with that of control subjects, which suggest that diffuse brain dysfunction does not have clear progressive pathophysiology in BAFME.
Dysfunction guided neuromodulation with rTMS in severe childhood epilepsy.

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Background

Over recent years, neuromodulation has been reported to be of value for the treatment of different conditions where the pathophysiologic background is believed to be a central nervous dysfunction. One such entity is epilepsy where positive effects have been reported in adults. In children, the experience is extremely scarce. Given that the technique is non-invasive and that there is no reason to believe that it could be harmful, it seems reasonable to try it at least in severe cases that do not respond to conventional therapy.

Methods

Daily one hour sessions of low frequent repetitive TMS (rTMS, 0.5 Hz) were used to treat two children with severe epilepsy.

A two year, eight months old boy with Alper’s disease developed epilepsy partialis continua with rhythmic jerking of the left upper extremity, mainly the hand. Pharmacological therapy was unsuccessful and scalp EEG could not reveal the seizure focus. The hand area of the primary motor cortex was localised using navigated TMS based on the patients structural MR. This position was used for rTMS treatment.

A six year, three months old girl developed a CSWS syndrome due to a cortical malformation. After tapering of corticosteroids her seizure situation worsened. Scalp EEG revealed a number of electrical seizure foci. While waiting for a planned neurosurgical treatment, rTMS was used directed by the EEG localisations.

Results

The treatment sessions were mainly uneventful, in the majority the children slept during the stimulations. (The boy often needed a light procedural sedation though.) During about two weeks of treatment, the number and severity of seizures reported by parents and personnel were reduced for both patients.

Conclusions

rTMS for the treatment of epilepsy can be performed successfully even in small children. The procedure requires a lot of resources. If tried in less severe cases than the two presented, it may be even more efficient.
Electroencephalographic evaluation of mucopolysaccharidosis type II undergoing enzyme replacement therapy

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**Question**

Do electroencephalographic and clinical features of mucopolysaccharidosis type II (MPS II), an X-linked disorder characterized by glycosaminoglycans accumulation due to deficient iduronate 2-sulfatase, change by enzyme replacement therapy (ERT)?

**Methods**

Reported is a male with MPS II, who started showing developmental delay at the age of 3 years, was diagnosed as having deficient iduronate 2-sulfatase enzyme activity at the age of 5 years, became bed-ridden in his childhood, and was introduced ERT at the age of 20 years. We evaluated clinical features and electroencephalographic findings before and after the commencement of ERT.

**Results**

After the introduction of ERT, he improved in alertness and responsiveness to auditory stimuli, however, developed generalized tonic seizures for several seconds needing additional antiepileptic therapy with valproate. Electroencephalography before ERT showed lack of posterior dominant rhythm, very rare fast waves, continuous generalized irregular theta and delta waves maximum in bilateral fronto-central areas, and sharp waves regional left frontal and anterio-temporal areas. After starting ERT, the amount and amplitude of fast waves increased, however, sharp waves became more frequent.

**Conclusions**

In this patient with MPS II, ERT produced an improvement of cortical function but aggravated epileptogenic activities as well.
Clinical and Electrophysiological Profile of Omani Patients with Idiopathic Generalized Epilepsy, Experience of a Tertiary Center in Oman

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Aim

To classify cases of idiopathic generalized epilepsy (IGE) based on the EEG abnormalities, seizure types reported and family history of epilepsy. Gender difference and EEG characteristics in different IGE syndromes were also noted.

Methods

Patients with EEG abnormalities, suggestive of IGE were selected for a consecutive 20 months period. Clinical information was obtained from electronic patient record, EEG requisition and report.

Results

Ninety five patients met our inclusion criteria, 41 males and 54 females (57%). Generalized tonic clonic seizure (GTCS) is the commonest type of seizure reported (61 patients, 64%). In our cohort, Juvenile myoclonic epilepsy (JME) was the most common syndrome which diagnosed in 36 patients (15 male, 21 female), GTCS alone (GTCSA) in 20 (7 male, 13 female), childhood absence epilepsy in 10 (6 males, 4 females), Juvenile absence epilepsy (JAE) in 5 (1 male, 4 female), Jeavon’s syndrome in 2 (1 male) and Doose’ syndrome in 1 patient (male). Photo-paroxysmal response noted in 35 patients (13 male, 22 female). Generalized spike wave discharges (GSWDs) lasting more than 2 secs were well organized in 11 patients (6 CAE, 4 JAE, 1 GTCSA) and poorly organized in 25 patients (17 JME, 6 GTCSA, 1 JAE). Atypical EEG abnormalities were noted in 37 patients.

Conclusions

IGE shows a female preponderance in our cohort. A gender difference was noted in the diagnosis of JME and GTCSA, and PPR. GSWDs are well organized in absence seizures and least in JME. Atypical EEG abnormalities are not uncommon in IGE, particularly in JME.
P466
Home Video-Telemetry (HVT) is superior to inpatient Video-Telemetry (VT)

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Background

HVT is a new service provided at home to investigate seizure and sleep disorders. It has been successfully used over the last four years at King’s College Hospital. Inpatient video-telemetry is not always successful. A previous internal audit showed that only 8% of patients with a repeat inpatient video-telemetry had habitual episodes captured on retesting.

Hypothesis

The diagnostic yield of patients with a repeat HVT is higher than 8%.

Methods

Two hundred and twenty five patients who underwent HVT between August 2010 and October 2013 were identified from our database. Patients with inpatient VT as the first test(s) and subsequent HVT as repeat diagnostic test were identified. The telemetry reports of these patients were reviewed. A test was defined as successful if the patients’ habitual attacks were captured.

Results

Ten patients were identified who had a repeat HVT following unsuccessful inpatient video-telemetry. In 4/10 patients repeat HVT captured their habitual episodes (40%).

Conclusion

Investigation with repeat HVT captured the habitual attacks in 40% of patients compared to 8% with repeat inpatient VTs. These results suggest that if repeat telemetry is required, HVT is the most successful option to capture habitual attacks. Further work is needed to confirm diagnostic accuracy and utility of HVT considering parameters such as age and nature of disease (epileptic v. non-epileptic attacks).
P467
Combined neurophysiological and imaging assessment of motor cortical areas in EPM1A patients

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Question

To assess functional organization of the motor cortex in patients with cortical myoclonus due to Unverricht-Lundborg disease (EPM1A) using multimodal neurophysiologic and imaging approach.

Methods

Seven healthy subjects and nine EPM1A patients were enrolled in the study. TMS-based mapping of primary motor cortex of the hand associated to real-time frameless neuronavigation system was performed. fMRI activation maps related to hand motor task was obtained. Cortical thickness (CTH) analysis were applied on T1-weighted 3D images.

Results

Bilaterally resting motor threshold was significantly higher and mean amplitude of the motor evoked potentials was significantly lower in the patients with respect to healthy subjects. There were no differences between groups in the extension of the cortical representation of the ABP muscle, but bilaterally the centers of gravity (CoGs) of EPM1A patients (Figure 1, filled circles) lied posteriorly than that of healthy subjects (Figure 1, crossed circles). fMRI did not revealed significant differences between groups, although a slightly posterior localization of activated cluster was found in patients (Figure 2.A, red cluster) with respect to healthy subjects (Figure 2.A, blue cluster). CTH analysis revealed significant alterations in both precentral and paracentral areas bilaterally, resulting in a thinning of these areas in EPM1A patients (Figure 2.B).

Conclusions

The multimodal study performed in EPM1A patients highlights a posterior shift of both CoGs and fMRI activation and a thinning of motor areas. The altered motor cortical organization is probably associated with the structural abnormalities of the primary motor cortex in EPM1A patients. We hypothesize that a displacement of the CoGs reflects a functional reorganization of the pool of residual cortical neurons due to neuronal plasticity mechanism.

figure 1
P469
Magnetic resonance imaging (MRI), Electroencephalographic (EEG) and Risk of Recurrence In Developmentally and Neurologically Normal Children with a Newly Diagnosed, Unprovoked Seizure

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Outline in Question

Seizures are symptoms of various neurological conditions. Overall, in untreated individuals, 40-50% can expect a recurrence within 2 years of the initial seizure. EEG and etiology are consistently found to be the best predictors for seizure recurrence and prognosis. This study aimed to find the predictors for seizure recurrence in developmentally and neurologically normal children who had a newly diagnosed, unprovoked seizure.

Methods

The medical record was retrospectively reviewed in children who had a newly diagnosed, unprovoked seizure by using the standardized data collection form at the Pediatric New Onset Seizure Clinic of Emory University. Exclusion criteria include children with (1) absence or myoclonic seizures (2) history of prematurity (3) known history of structural brain lesion, static encephalopathy or autism. A total of 107 children met the inclusion criteria.

Results

Mean age was 6.6 year at the first clinic visit. The first seizure was characterized as generalized tonic or tonic-clonic seizure in 67 cases (63.2%), dyscognitive seizures in 33 cases (31.1%), and focal motor seizures in 6 cases (5.7%). Routine EEG was abnormal in 37 cases (34.9%). Focal epileptiform abnormality was most commonly observed in 23 cases (62.2%) and 8 of them (34.8%) has the characteristics of benign rolandic spikes. Generalized epileptiform abnormality (9 ), focal slow (2) and background slow(3) followed. Brain MRI was done in 57 cases. Brain MRI showed the structural abnormality in 7 cases (12.3 %), focal cortical dysplasia in left frontal region (1), encephalomalacia in left occipital (1) and right occipital regions (1), gliosis in left posterior periventricular white matter (1), periventricular leukomalacia (1), arachnoid cyst (1), and Chiari 1 malformation (1). Fifty-three (51.9%) experienced recurrent seizures over the mean follow-up duration of 13.8 months. Seizure medication included Levetiracetam (37), Oxcarbazepine (9), Valproate (5), Topiramate (2) and Lamotrigine (1). An abnormal EEG had no association with seizure recurrence (p >0.05).

Conclusions

EEG findings poorly predict recurrence after a single unprovoked seizure. Brain MRI was not high-yield for finding the significant structural lesion.
Pre-surgical evaluation of occipital lobe epilepsy in children - a retrospective review

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Introduction

Occipital lobe epilepsy is relatively uncommon and it is well recognised that semiology, interictal and ictal EEG findings can be misleading (Taylor et.al 2002). This is even more challenging in the paediatric population due to the difficulties with children describing their potential auras. The aim of this study is to evaluate the lateralising and localising value of non-invasive video-EEG monitoring in occipital lobe epilepsy in children.

Method

Patients with known or presumed focal symptomatic occipital lobe epilepsy were selected from a video-telemetry database at a tertiary paediatric epilepsy centre between 2003-2013. Idiopathic occipital lobe epilepsies were excluded. The interictal and ictal EEG data was compared with seizure semiology, MRI and where available other pre-surgical investigations (SPECT, PET and MEG).

Results

Twelve patients aged 4-16 years were included in the study. Seizure semiology was lateralising in all 12 twelve patients and localising (visual aura) in 11 patients. Scalp-recorded seizures were concordant with the known MRI lesion in 9 of our 12 patients compared with only 3 which originated from the contralateral occipital lobe. However, in 1 of the 3 discordant patients MEG and SPECT were concordant with the EEG findings despite the contralateral MRI findings.

Conclusion:

In contrast with other studies which have shown scalp EEG in occipital epilepsy to be misleading our data suggests that scalp EEG can be accurately localising and lateralising in the majority of cases.

P471
Effects of anaesthetic agent on intraoperative functional stimulation in Young Children

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Introduction

Electrocorticography (ECoG) is used to guide surgical resection of epileptic foci and map eloquent sensory-motor cortex intraoperatively. However, in younger children success rate of motor stimulation is often poor. The aim of this study was to evaluate the effect of different types of anaesthetic agent on intraoperative functional stimulation in young children.

Methods

ECoG was performed to identify the irritative zone during epilepsy surgery between 2003 and 2013. Sensory stimulation (SSEP) (up to 35mA) was followed direct cortical motor stimulation (up to 25mA). Anaesthesia was performed either with halogenated volatile agents (VA) or with intravenous propofol (IP). Success rates were compared between group 1 (<5 years) and group 2 (5 years and older).

Results

22 patients (group 1: n=11; group 2: n=11) underwent ECoG with sensory (all patients) and motor stimulation (15 patients). For group 1 motor responses were obtained in 17% and sensory responses in 73%. For group 2 motor responses were obtained in 67% and sensory responses in 82%. Motor responses not were found in the 4 patients with VA. Sensory responses were not influenced by the choice of anaesthesia in both age groups.

Conclusions

As reported in previous studies the successful mapping of motor responses was low especially in young children but sensory motor cortex was successfully mapped in most patients irrespective of anaesthetic agent and age.
Abstracts of Poster Presentations – Poster Session 26 – Epilepsy 2

P796
Intrahippocampal Field Potential correlates of Small Sharp Spike discharges

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Background: Small sharp spikes (SSS) are frequently regarded as benign epileptiform potentials. Whereas some studies found a higher incidence in patients with epilepsy, their exact relation to epilepsy has remained controversial. We here report findings from combined surface and intracranial EEG recordings during the appearance of small sharp spiked in the surface EEG.

Methods: Simultaneous surface and intracranial EEG recordings using subdural and depth electrodes from the EPILEPSIAE database and from additional long-term recordings of the Epilepsy Center Freiburg were retrospectively analyzed with regard to the presence of SSS in surface recordings. Criteria for potentials to be classified as SSS were: sharp appearance on conventional visualization, occurrence during sleep stage I/II, duration below 50 ms, and fronto-temporal fields involving at least 2 contacts of a 10-20 montage. At time points of SSS marks, intracranial EEG was analyzed with regard to possible epileptic patterns.

Results: In 8 patients (3 male, age range 8-60 years) with intrahippocampal depth electrode recordings, SSS were found on surface recordings which fulfilled the above visual criteria. In all of them, high amplitude intrahippocampal polyspike or spike-wave discharges simultaneous with SSS were identified (see figure), whereas lateral temporal contacts did not show extended spiking as typically found with spikes or sharp waves on the surface EEG. Amplitudes of intrahippocampal polyspike discharges accompanied with SSS were significantly higher compared to matched samples without surface correlate.

Conclusions: Intrahippocampal depth recordings show ipsilateral high amplitude polyspike- or spike-wave discharges when SSS were visible on the surface EEG. This suggests an epileptic mechanism of SSS generation at least in patients with focal epilepsy. Presence and specific appearance of SSS may reflect a different potential spread from typical sharp waves propagating from the hippocampus to cortical areas.

figure 1
Abstracts of Poster Presentations – Poster Session 26 – Epilepsy 2

P1094
Detailed Video-EEG characterization and clinical aspects in 25 children with neonatal onset epileptic encephalopathy and suppression burst pattern

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Introduction

Suppression-burst pattern associated to seizures in early life is a severe epileptic encephalopathy (EE). Two different syndromes are recognized by the International Classification: EIEE (Early Infantile Epileptic Encephalopathy or Othahara syndrome) and EME (Early Myoclonic Encephalopathy). The etiology is multiple, with cerebral malformations and metabolic diseases. Recently new genes have been described in few patients as mutations in the gene encoding STXBP1 (MUNC18-1), ARX, SLC25A22, KCNQ2 et SCN2A. Phenotype genotype correlation is mainly based on small series and EEG aspects are not well defined for all genotypes.

Patients and Methods

We analyzed Video-EEG recordings of 25 patients presenting EE with SB. We studied the background pattern and the ictal manifestations, as well as etiology and electroclinical evolution.

Results

We identified heterogeneous subgroups:

1) In a familiar case of 2 siblings the younger girl having been closely screened from birth showed initially normal EEGs but later appearance of the suppression burst pattern at the age of 3 weeks.

2) Two children presented surprisingly a persistence of the SB pattern until the the age of 4 and 9 yrs with no change in EEG neither in seizure types compared to neonatal period

3) Two children with a mutation in the gene encoding STXBP1 (MUNC18-1) did not present the same electroclinical pattern.

4) In 7 children, ictal pattern consisted in unclassified serial stereotyped asynchronous complex movements of the whole body including face.

Conclusion: Although EIEE and EME are well defined, the identification of the seizure pattern and of genetic etiology, and the presence of unclassified ictal patterns leave a number of cases difficult to classify.
Abstracts of Poster Presentations – Poster Session 26 – Epilepsy 2

LP30

Electroencephalographic features of temporal lobe epilepsy with myoclonic seizures

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Question: It is thought that temporal lobe epilepsy tends to show three types of seizures: simple partial seizures, complex partial seizures and secondary generalized motor (tonic or tonic-clonic) seizures. We found out very interesting case of temporal lobe epilepsy with myoclonic seizures.

Methods: We investigated female patient 23 years old with multiple bilateral myoclonic seizures that happened hundreds time per day.

Results: At 2 years patient presented paroxysm of febrile convulsions, that repeated 7 times for the next two years. At 4 years patient started presenting afebrile paroxysms of generalized tonic-clonic seizures from 2 to 5 times per month. For 2 years before our first meeting patient had been suffering from multiple bilateral myoclonic seizures that happened during wakefulness hundreds time per day. Patient had been treated with Carbamazepine, Phenobarbital, Fenitoin, Lamotrigine in therapeutic and overtherapeutic doses did not give any result. The treatment with the valproic acid (main medicine against the myoclonic seizures) did not give any result too.

Patient did not have any kind of mental impairment typical for progressive metabolic syndromes or neurodegenerative diseases.

Although the usual EEG pattern of myoclonic epilepsies is generalized symmetric polyspike-wave discharges, on vide-EEG monitoring we found only focal epileptic activity in right and left temporal zones with amplitude up to 130 mcV. Moreover the generalized epileptic activity did not exist. Background activity was consistently normal. On the previous multiple routine EEG (when patient was from 9 to 22 years old) was focal epileptic activity too.

The treatment regimen was changed. As a result remission of epilepsy was reached on Clobazame 30 mg per day. EEG on this treatment did not show any kind of epileptic activity.

Conclusion: according to this case it becomes clear that temporal lobe epilepsy can manifest not only by focal seizures but by myoclonic seizures too. The interictal encephalographic pattern of this kind of epilepsy is focal epileptic activity in temporal lobes without secondary bilateral synchronization.
LP31
EEG and MEG source localization of the epileptogenic foci in tuberous sclerosis complex: a pediatric case report

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Question

Tuberous sclerosis complex (TSC) is a disorder of tissue growth and differentiation, characterized by benign hamartomas in the brain triggering epilepsy in up to 90% of TSC patients. There is an ongoing debate on whether or not the epileptogenic zone is within the tuber itself or in abnormally developed surrounding tissue.

Methods

We examined a four-year old patient with TSC-related refractory epilepsy undergoing magnetoencephalography (MEG) and electroencephalography (EEG) recordings. For MEG, we used a prototype system that offers higher spatial resolution and sensitivity compared to the conventional adult systems. EEG was simultaneously recorded from 32-leads according to the 10-20 international system. The source analysis of interictal activity was performed using both EEG and MEG data. Equivalent current dipoles (ECD) were fitted to the peak of individual interictal spikes. For averaged interictal spike signals, we performed ECD localizations to the spike upslope. Further, we estimated the minimum norm estimates (MNEs) to averaged interictal spike signals.

Results

Multiple cortical tubers were identified in patient's MRI including one prominent calcified tuber in the right parietal-occipital lobe. The simultaneously recorded spikes in EEG and MEG data provided a time shift of 20 ms between peak latencies. ECDs localized to individual and averaged interictal activity in EEG and MEG consistently clustered in the millimeter vicinity of the large calcified cortical tuber. The ECD trace localized to the averaged EEG data located on the posterior side ~5 mm superior to the tuber. The ECD trace localized to the averaged MEG spike located ~4 mm anterior to the tuber. MNE and ECDs indicated epileptiform activity in the same areas.

Conclusion

Our source analysis indicated generators of epileptiform activity in the millimeter vicinity of the tuber margin outside the tuber volume. Separate EEG and MEG source analysis provided distinct source characteristics.
LP32
Scalp EEG in Malformations of Cortical Deveploment (MDC). Analysis by localization

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Objectives: The aim of our study was to describe the EEG findings of the MDC according to the localisation in the MRI. Patients and Methods: We analyze the scalp- EEGs of the patients diagnosed of MDC by RM in the Clínica Universidad de Navarra, and we considerate: the background activity, the presence and regional localisation of focal slow waves, interictal epileptiform discharges and focal fast frequencies. Results: We identified 51 patients with MDC (31 women and 20 men). In 21 patients the MDC was located in the temporal lobe, 12 showed focal slow waves and 13 showed epileptiform discharges. These EEG abnormalities had a high topographic correlation with MRI findings (> 80% for slow waves and > 90% for epileptiform discharges). In 19 patients the lesion was located in the frontal lobe, and the EEG showed focal slow waves in 12 of these patients, and epileptiform discharges in 9; however, these abnormalities coincide with the location in the MRI in less than 50% of the cases. In 8 patients the lesion was located in the parietal lobe, and just in only one case the EEG abnormalities correctly identified the location showed by MRI. Finally in 3 patients the lesion was located in the occipital lobe, and EEG showed slow waves in one case and epileptiform discharges in 2 cases. Only 2 patients had theta-alpha rhythm and were well correlated with the MRI findings (frontal and temporal MDC). One patient with temporal lobe MDC had a no localising continuos beta rhythm. Conclusions: Most of the MDC were located in the temporal and frontal lobes. The slow waves and the epileptiform discharges were highly well localising when the lesion was located in the temporal lobe, but failed in more than 50% of the cases when it was extra temporal. Focal rhythms were rare but have a good correlation with dysplasia. Therefore the presence and locator value of the EEG abnormalities are highly dependent on the location of the focus.
P472
EPILEPTIFORM ACTIVITY IN PATIENTS TREATED WITH THERAPEUTIC HYPOTHERMIA AFTER CARDIAC ARREST

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QUESTION
Since the implementation of therapeutic hypothermia (TH) after cardiac arrest (CA), some researchers have been trying to redefine the value of the parameters traditionally used as predictors of neurologic outcome. In this context, the EEG represents an important tool to improve prognostication in postanoxic coma

METHODS
We retrospectively reviewed the electronic medical records of all patients undergoing TH after CA from January 2011 until October 2013. We identified the patients with any type of epileptiform activity and reviewed their EEGs.

RESULTS
Forty patients were included. Sixteen died (40%). Epileptiform activity was found in 11 patients (27.5%), from whom only 2 (18.2%) had a favorable outcome (CPC 1 or 2). This epileptiform activity appeared in the following patterns; 2 patients had isolated interictal discharges, 2 had 2-2.5 Hz generalized periodic epileptiform discharges (GPEDs) over a continuous, diffusely slowed background, 2 had 2-2.5 Hz GPEDs over a suppressed background and 6 fulfilled non convulsive status epilepticus (NCSE) criteria. In one of the patients with NCSE, the EEG evolved into the pattern of GPEDs at 2-2.5 Hz over a suppressed background. When treating these 3 patients with benzodiazepine trials, even though they remained comatose, the epileptiform discharges stopped, and a continuous theta background appeared. Two of these patients died eventually, and the other one remains in a persistent vegetative state.

CONCLUSIONS
Epileptiform activity is common in comatose patients treated with TH after CA. The presence of epileptiform discharges during the TH or shortly after was associated with a poor outcome.
DEFINING EEG REACTIVITY IN PATIENTS TREATED WITH THERAPEUTIC HYPOTHERMIA AFTER CARDIAC ARREST

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QUESTION

In patients treated with therapeutic hypothermia (TH) after cardiac arrest (CA), the EEG reactivity in the first 24 hours has an important prognostic value. However, it has not been reported yet whether or not there are differences between the type of stimuli required or the reactivity patterns obtained.

METHODS

We prospectively assessed EEG background continuity and reactivity in 16 consecutive patients undergoing TH after CA from August 2012 to October 2013. EEG background reactivity was tested to auditory, tactile and painful stimuli. We analyzed the relation between the continuity of the background, the EEG reactivity patterns, and the neurologic outcome.

RESULTS

All of our patients had the first EEG done within 24 hours after the CA. We established 4 backgrounds categories; continuous, discontinuous, burst-suppression and low voltage, and 2 reactivity patterns; increase of faster frequencies and background attenuation. All survivors (11/16) had different degrees of background reactivity in the first EEG (<24h), and the majority of them (10 /11) had a favorable outcome (CPC 1 or 2). When the EEG was reactive, the response to auditory stimulus was always positive and attenuation of the background was the pattern most frequently seen. All of the non-survivors (5/16) had a low voltage background. Four of the survivors had a discontinuous background.

CONCLUSIONS

Background reactivity in the first 24 hours after CA is strongly associated with neurologic outcome. In patients with a marked response to stimulus, brief periods of attenuation may represent reactivity to environmental auditory stimuli instead of a discontinuous background.
P474
Quantitative EEG reactivity in comatose neurosurgical patients

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Question

EEG reactivity to external stimulation may predict the prognosis in comatose patients. The usual assessment is based on the visual appearance of EEG patterns making it liable to vary between individual interpreters. Quantification of EEG reactivity may improve reliability and sensitivity of the test. In this study we investigate quantitative measurements of EEG reactivity including which frequency bands are most affected and how they correlate with outcome.

Methods

Seven comatose neurosurgical patients undergoing 24 hour EEG recording were subjected to four noxious stimulations of 30 seconds duration separated by at least 2 minutes. Average power at F3 and F4 in the alpha, delta, and theta bands during stimulation was divided by average power of the 30 seconds period prior to stimulation yielding reactivity ratios (RR) of the three frequency bands. Quantitative reactivity in a frequency band was defined as a RR different from 1. A preliminary 3-8 weeks evaluation of outcome was done by the Cerebral Performance Category (CPC) Scale.

Results

Mean RR of the alpha, theta, and delta band varied between 0.865-1.494, 0.824-2.357, and 0.831-1.437, respectively. Four patients had quantitative reactivity in one or more bands. RR in the alpha band was increased in one patient (CPC 2-3), in the theta band in two patients (CPC 1-2 and 2-3), and in the delta band in one patient (CPC 3-4). One patient had a decrease in RR in the delta band and had a CPC of 5. Of the three patients who showed no reactivity one had a CPC of 3 and two had a CPC of 5. Five patients were partly sedated, one of which had a CPC of 5.

Conclusion

It seems possible to achieve a quantitative measure of reactivity. In this study we found no obvious systematic correlation with outcome but larger studies are required.
P475
Face validity of IDOS, an ICU depth of sleep index from a single channel of EEG

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Question

The measurement and analysis of sleep in the intensive care unit (ICU) is notoriously complex and time-consuming. This is reflected by the variable and often poor interrater agreement between R&K raters in previous studies (Ambrogio, Koebnick, Quan, Ranieri, & Parthasarathy, 2008; Elliott, McKinley, Cistulli, & Fien, 2013).

To evaluate the face validity of a new index for depth of sleep in ICU patients, we compared it to manual scoring by R&K criteria in outpatient and ICU polysomnographic (PSG) recordings.

Methods

The ICU depth of sleep index (IDOS index) was constructed from the ratio of gamma and delta band power spectral density (PSD) of a single channel of EEG. PSG recordings of five ICU patients (24-72 hours each) and 15 healthy outpatient recordings (18 hours each) were analyzed with both methods. Manual selection of thresholds was used to classify the IDOS index as either wake, sleep or slow wave sleep (SWS). This classification was compared to manual scoring by R&K criteria.

Results

When reduced to 3 classes, the obtained overall agreement between R&K and the IDOS index, as quantified by Cohen’s kappa statistic, was 0.82 for the outpatient recordings. Sensitivity and specificity were highest for the wake state (91% and 97%, respectively) and lowest for SWS (91% and 67%, respectively). For ICU recordings, the average agreement was good, with kappa=0.68, but varied between individual recordings.

Conclusions

The IDOS index shows striking resemblance with manually scored outpatient recordings, with excellent agreement. With the established face-validity, the IDOS index could be useful in real-time, automated, single channel visualization of depth of sleep in ICU patients.

Figure 1: Hypnogram of ICU sleep recording (1A) versus IDOS index, calculated from a single channel of EEG (1B). To facilitate calculation of agreement between both methods, 30 second epochs were classified into three possible classes; wake (blue), sleep (red) and slow wave sleep (SWS, green). Average agreement for outpatient recordings was excellent, with Cohen’s Kappa = 0.82 (n=15). For ICU recordings the average agreement was good, with Kappa = 0.68 (n=5).
Sleep and Biorhythm in the ICU

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Question

Sleep deprivation is among the most common stressors experienced during critical illness (Watson, 2007), and there are strong indications that delirium and sleep deprivation are closely intertwined (Bellapart & Boots, 2012; Boyko et al., 2012). Sleep is important to the recovery of the critically ill, but may be hampered by disturbances in biorhythm (Mundigler et al., 2002; Paul & Lemmer, 2007; Figueroa-Ramos et al., 2009).

Recent findings contradict the assumption that biorhythm is disturbed in all ICU patients, warranting further investigation (Gehlbach et al., 2012). ICU patients could potentially benefit from interventions to optimize biorhythm and consequently sleep. To this end, a protocol to monitor sleep and biorhythm was designed, and tested in the ICU.

Methods

Critically ill patients (n=5) were subjected to 24-72 hour polysomnographic (PSG) recording followed by R&K analysis. Bihourly serum-melatonin samples were analyzed with tandem mass-spectrometry.

Results

Of the 5 included critically ill patients, three showed severe fragmentation of sleep. Melatonin secretion was lower for patients with worse sleep, although biorhythm was visible in all but one patient. PSG with R&K analysis proved to be time-consuming and cumbersome, while the use of tandem mass spectrometry resulted in high throughput with excellent accuracy.

Conclusions

Taking the limited scope of this pilot into account, worsening characteristics of sleep seem to coincide with loss of circadian rhythm.

Currently, the availability of materials and the time-consuming analysis of PSG recordings are the main limiting factors of the study of sleep in the ICU. Automated, objective measures of quality and quantity of sleep are currently being validated in ICU and non-ICU patients, using only single channel EEG data.

figure 1 Hypnogram after R&K classification of ICU patients' PSG recording. Of the shown 8 days of PSG, only 1 day could be classified as 'normal'; the second day of patient A. Patient B and C experience severely fragmented sleep, with little to no contrast between day and night.

figure 2 Melatonin secretion and best fit curves of ICU patients. Severe fragmentation of sleep in patient B seems to coincide with low contrast in melatonin secretion between day and night. During intubation (day 3) there is no melatonin peak. Other patients (A, C and D) show remarkably robust biorhythms, with increasing phase-delay and lower peaks as quality of sleep worsens.
Abstracts of Poster Presentations – Poster Session 27 – ICU monitoring

**figure 1**

Hypnogram

A

B

C

D

Time of day (hours:minutes)

**figure 2**

Biorhythm

A

B

C

D

Melatonin secretion (pmol/L)

Time of day (hours:minutes)
Abstracts of Poster Presentations – Poster Session 27 – ICU monitoring

P477
Continuous EEG monitoring in Critical Care

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Introduction

Continuous electroencephalographic monitoring (cEEGm) is the main tool for diagnosis in subclinical seizures and non-convulsive status epilepticus (NCSE), in the intensive care units (ICU).

Methods

We prospectively evaluated the cEEGm conducted between April 2012 and October 2013 in the Adult and Pediatric ICU of Hospital Clínico Pontificia Universidad Católica de Chile.

Results

We analyzed 88 cEEGm, corresponding to 76 patients (36 men). Mean age was 51 years (range 1 month to 102 years). The most common indication for monitoring was impaired consciousness (53%), seconded by, the presence of seizures observed by an ICU staff (42%). Total reading time was 6.557 h (between 12-936 h per patient). We found NCSE in 26 patients (34%) and subclinical seizures in 20 (26%). The mean duration of NCSE was 79 hours (range 11 to 400 hours). 16 patients met criteria for super-refractory NCSE (62% of all NCSE). The treatment of choice was the association antiepileptic drugs (3 on average and range from 1 to 10 drugs) and then the use of anesthetics. In 85% of the patients, cEEGm motivated a change in the treatment plan. Overall mortality was 18%, and severe neurological sequelae were observed in 40% of patients.

Conclusions

The cEEGm is a fundamental tool in the management of ICU patients; it allows accurate diagnosis of NCSE and subclinical epileptic activity, especially in patients with impaired consciousness and no clear evidence of seizures. These findings are associated with significant mortality and neurologic sequelae.
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Prediction of good and poor outcome in comatose patients after cardiac arrest: the utility of early EEG/SEP recordings during therapeutic hypothermia

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Question
Somatosensory evoked potentials (SEPs) are a reliable predictor of poor outcome in comatose patients after cardiac arrest (CA) treated with therapeutic hypothermia (TH). The role of EEG has been recently emphasized during early phase after CA.

Our aim is to evaluate the prognostic value of EEG and SEPs in post-anoxic comatose patients within 12hs and 24hs from cardiac arrest (CA).

Methods
Comatose patients after CA treated with TH were included. EEG and SEPs were recorded within 12hs and 24hs after CA. EEG was classified into discontinous (low voltage, isoelectric, burst suppression) and continuous (other patterns except epileptiform). SEPs were dicotomized into “bilaterally absent” (BA) and “present”. Neurologic outcome was evaluated at 6 months by GOS: “awakening” (GOS 3-5) was considered good outcome.

Results
EEG and SEPs were recorded in 72 patients: 25 of these were studied within 12hs from CA.

All patients with a continuous EEG pattern at 12hs awakened. The same EEG pattern recorded at 24 hs was not always predictive of awakening. BA SEPs at 12hs predicted poor outcome and were associated to discontinuous EEG patterns. Continuous EEG pattern was always associated with present SEPs.

Conclusion
Combined early EEG / SEPs recordings are a useful tool for reliable prognostication both of good and poor outcome in comatose patients treated with TH.
Continuous EEG monitoring in neurointensive care. Organisation and assessment of impact

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Background

Continuous EEG (cEEG) is an emerging discipline for assessment of acute changes in cerebral function in the intensive care unit (ICU). A number of publications demonstrate that non-convulsive status epilepticus is a common complication in both neurological and non-neurological ICU patients and that cEEG is superior to conventional 30 minute standard EEG in capturing these patients. Yet establishing cEEG as part of daily routine is resource demanding and raises a number of treatment-related issues. Furthermore cEEG as a daily routine must be carefully introduced to assure that the most relevant patients are monitored, and that neurophysiologists and clinicians communicate in an efficient way.

Methods

At Rigshospitalet, cEEG for suspected non-convulsive status epilepticus has been offered as a 24/7 service since april 2013. Recordings are assessed by senior clinical neurophysiologists at no more than eight hours interval, and a report is written directly into the patients electronic records. Clinicians may phone the neurophysiologist around the clock for discussion or referral. After six month, a total of 67 patients had been monitored with cEEG. At this time, an anonymous web-based survey was performed addressing 168 clinicians within paediatrics, neurology, neurosurgery and neuroanaesthesiology.

Results

We obtained 51 responses. Of these 74% were senior /consultants and 26% trainees/researchers.

48 (94 %) found that cEEG was an important investigation in neurocritical care.

50% of the clinicians had been involved in patients monitored with cEEG. Of those, 88 % found that the logistics and communication with the neurophysiologist worked optimally or quite well in the best case, and 76-80% on average.

cEEG had an impact on clinical decision-making that was optimal in 76 % (best) and 44 % (average) of cases and quite good in 20 % (best) and 52 % (average) of cases. Only one clinician found cEEG suboptimal for clinical decision-making in the actual case.

When additional indications for cEEG were asked for, monitoring of patients with subarachnoid hemorrhage for delayed ischemia was the most prevalent suggestion.

Conclusion: In this survey cEEG is highly demanded and supports clinical decision-making in the vast majority of cases where non-convulsive status epilepticus is suspected.
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Treatment of electroencephalographic status epilepticus after cardiac arrest - retrospective analysis and notification of a multicenter randomized controlled trial

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Question

Electroencephalographic seizures, including status epilepticus, occur in 9-35% of comatose patients after cardiac arrest. Mortality is 90-100%. It is unclear whether (some) seizure patterns represent a condition in which treatment improves outcome, or severe ischemic damage, in which treatment is futile.

Methods

In two teaching hospitals, we retrospectively identified patients that were treated with anti-epileptic drugs from our prospective cohort study on the prognostic value of continuous EEG monitoring in comatose patients after cardiac arrest. Outcome at six months after cardiac arrest was dichotomized between “good” (CPC 1 or 2) and “poor” (CPC 3, 4, or 5). EEG analyses were done at 24 hours after cardiac arrest and during anti-epileptic treatment, blinded for outcome.

Results

Thirty-one (22%) of 139 patients were treated with anti-epileptic drugs (fenytoin, levetiracetam, valproate, clonazepam, propofol, midazolam): two with one, nine with two, thirteen with three, five with four, one with five, and one with six different drugs. This treatment improved epileptic EEG patterns temporarily (Cloostermans 2012)

Conclusion

In comatose patients after cardiac arrest with electroencephalographic status epilepticus, the general practice of treatment with conventional anti-epileptic drugs does not improve patients’ outcome. A multicenter randomized controlled trial to estimate the effect of early and aggressive treatment, directed at complete suppression of epileptiform activity during at least 24 hours, is in preparation.
P481
cEEG monitoring in patients with traumatic brain injury in the ICU

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Motivation

Traumatic brain injury (TBI) is one of the leading causes of death and invalidity in young people. ICU patients with TBI are often sedated and ventilated, which makes clinical evaluation unreliable. In addition, after the initial event, various processes may result in secondary brain injury, caused by e.g. cell swelling.

Continuous EEG (cEEG) recordings may detect these processes and may be useful in prognostication or guide interventions to limit secondary injury. For clinical application, quantitative analysis is necessary to reduce time-consuming visual analysis and to allow evaluation by non-trained personnel.

Question

What is the value of cEEG in outcome prediction in patients with TBI?

Methods

All TBI patients admitted to a 20 bed ICU will be included in this observational, explorative study. cEEG is recorded up to seven days, using a full-band 21-channel amplifier (TMSi, Netherlands). EEGs will be analysed visually. Quantitative features will be calculated including Brain Symmetry Index (BSI) and Alpha Delta Ratio (ADR). Previous research shows that single features are not specific enough, therefore combinations of features will be correlated with functional outcome and clinical parameters. Clinical outcome is scored using the GOSE.

Results

Currently, thirteen patients have been included. Visual analysis of the EEG appears correlated with outcome. Quantitative analysis shows that single features are not sufficient to predict outcome or detect deterioration. Currently, we are studying combinations of features.

Conclusion

cEEG monitoring in TBI is feasible and shows correlations with patients’ outcome. Quantitative analysis needs to be based on a combination of features.

Figure 1. Recording and results of one patient over 8 days. Top row: CT scans from day 1 and 5. The lesion in the right frontal lobe increased in size but the temporal resolution is low. Second row: cEEG fragments of 5 seconds from each day. During day 3 the amplitude of the signal declines (red arrow) and the frequency follows in day 4 (green arrow). Third row: Alpha Delta Ratio. When the ratio shift towards -1 the EEG becomes more pathological, when it shift towards 1 it becomes more physiological. This qEEG feature shows deterioration before it can be seen in the cEEG. Bottom row: Topographical representation of the ADR.
Reliable Monitoring of Respiration Rate with Reflectance-Mode Photoplethysmography

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Problem

Recent innovations in embedded, networked sensors have enabled ubiquitous recording of selected vital signs, but widespread monitoring is still hindered by the intrusiveness of the available methods.

Methods

In this study, we describe a signal processing method for respiration monitoring based on reflectance-mode photoplethysmographic (PPG) sensors placed on the sternum. The method was applied with two PPG sensors on 6 healthy subjects under controlled conditions with known respiration rate showing prominent respiration signals with dominant frequencies corresponding to the respiration rate. Subsequently the method was applied in a clinical validation study including 27 consecutive patients (age 26 to 78 years, BMI from 21.5 to 50.4) admitted for the evaluation of obstructive sleep apnea (OSA) with polysomnography (PSG) during sleep. A digital signal processing framework and implementation for assessment of sensor stability and respiration rate was developed using band pass filtering, multi-modal feature derivation and probabilistic classification that dynamically qualifies segments for reliable detection of respiration.

Results

The method was compared to expert validated respiration rates from nasal flow cannula and thoracic/abdominal belts showing a mean absolute error of 0.9+/-0.2 resp/min (RMS accuracy 1.5+/-0.4 resp/min) for a respiration estimate reported every 5 seconds.

Conclusion

The method was found to be accurate and reliable for continuous respiration monitoring during sleep as compared to more intrusive methods available today, and show potential for clinical implementation. Further validation including accuracy during physical motion and the sensitivity to pathological respiratory disturbances is warranted.
Abstracts of Poster Presentations – Poster Session 27 – ICU monitoring

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Burst Suppression with identical bursts: a distinct pathological EEG pattern in post anoxic coma

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Question
Recently, we reported on “burst suppression with identical bursts” [1]: a distinct EEG pattern that is exclusively observed in patients with postanoxic coma and invariably associated with a poor outcome. Here we present additional quantified characteristics and confirm the prognostic significance in a larger cohort. Additionally, we discuss potential pathophysiological mechanisms.

Methods
Burst-suppression EEGs with and without identical bursts were visually identified from a cohort of comatose patients after cardiac arrest. Patients’ outcome was assessed at three and six months. Identical and non-identical burst-suppression patterns were compared for quantified EEG characteristics, including cross-correlation of burst shapes, and clinical outcome. Results of a bifurcation analysis of the signal will be associated with potential underlying mechanisms.

Results
Of 179 patients, 34 had bursts suppression with identical bursts. Kappa was 0.8 and disagreement resulted from sampling error. Burst-suppression with identical bursts was always bilateral synchronous, amplitudes were higher and correlation coefficients of burst shapes were higher than in burst-suppression without identical bursts. All patients with identical bursts had a poor outcome. Bifurcation analysis is ongoing.

Discussion
We confirm that “burst-suppression with identical bursts” is a distinct pathological EEG pattern after diffuse cerebral ischemia. It represents a low dimensional state of which potentially underlying mechanisms are currently explored and will be presented at the conference.

References

Figure: EEG of a comatose patient after cardiac arrest showing “burst-suppression with identical bursts”.

figure 1
Guillain Barré syndrome (GBS) is an acute immune-mediated peripheral neuropathy with a high variable clinical course and outcome. Despite immunotherapy up to 20% of patients remain severely disabled and mortality in the first year is approximately 4%. Aim of this study is to perform an epidemiological analysis of clinical and electrophysiological features of patients admitted in our ward for GBS in last ten years; to test the incidence of different GBS subtypes and their clinical and electrophysiological evolution; to test on our sample the prognostic value of variables known in literature and we suggested integration with new prognostic markers.

We collected data prospectively from 89 patients regarding: demographic features, previous infections, clinical manifestations, kind of therapy received, motor deficit and disability (evaluated respectively with MRC sumscore and GBS disability score (GBSDS)). We measured dosage of protein in the cerebrospinal fluid (CSF). Serial nerve conduction studies (NCS) were performed. Differences between groups were compared by Fisher’s exact test. Potential prognostic factors were tested in uni and multivariable logistic analysis and was estimated by regression analysis.

19% of GBS were acute motor axonal neuropathy (AMAN) and showed more severe prognosis. High age was predictive of poor prognosis in acute inflammatory demyelinating neuropathy (AIDP) but not in AMAN. High GBSDS at nadir and cranial nerves involvement were predictive of being able to run at 1 year. Conduction block did not have a significant distribution in GBS subtypes and showed no correlation with clinical outcome. In NCS performed between 30 and 90 days from the clinical onset, a pathological distal cMAP duration (DcMAPD) represented a distinctive marker of primary demyelinating pathophysiological mechanism, in our sample of GBS. The endurance of pathological DcMAPD showed a predictive value on long term disability in AIDP.

This study confirms the key-role of serial NCS for a proper diagnosis of GBS subtypes. Further clinical-electrophysiological studies are necessary to define more inclusive work-up in GBS enabling forecasting of the patients with poorest long term outcome.

Yuki (2012); Hughes (1997); Van Doorn(2005); Rajabally (2012); Walgaard (2011) ; Asbury(1990); Uncini (2012).
Abstracts of Poster Presentations – Poster Session 28 – Inflammatory diseases of CNS and PNS

**Figure 1**

| Subtypes analysis | Outcome analysis of clinical features | Age 

| DEMOGRAPHIC FEATURES | | 
|---------------------|--------------|--------------|--------------|
|                      | n %          | n %          | n %          | p VALUE (MEN/PATIENTS) |
| Total                | 89 (22.9%)   | 17 (20.9%)   | 20.9%        | 0.56          |
| Age (years) Mean age 57.9 (30.8) | | | | |
| ≤ 40                 | 22 (25.8%)   | 4 (24.5%)    | 17.2%        | 0.77          |
| 41-60                | 25 (28.1%)   | 7 (41.2%)    | 17.2%        | 0.93          |
| > 60                 | 41 (47.5%)   | 6 (34.3%)    | 64.7%        | 0.02          |
| GENDER               | 31 (35%)     | 18 (32%)     | 15 (30%)     | 0.56          |
| Male                 | 31 (35%)     | 18 (32%)     | 15 (30%)     | 0.56          |
| Female               | 58 (65%)     | 9 (18%)      | 15 (30%)     | 0.56          |

<table>
<thead>
<tr>
<th>INTELLIGENT FUNCTIONS</th>
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<tbody>
<tr>
<td>dexterity</td>
<td>29 (33%)</td>
<td>6 (36%)</td>
<td>18 (36%)</td>
</tr>
<tr>
<td>left/30</td>
<td>20 (23%)</td>
<td>5 (30%)</td>
<td>10 (20%)</td>
</tr>
</tbody>
</table>

| CLINICAL DATA | | |  |
| weaknes            | 47 (53%)     | 14 (82%)     | 61 (31%)     | 0.05          |
| ataxia             | 52 (59%)     | 1 (7%)       | 1 (2%)       | 0.05          |
| Oculogy             | 10 (11%)     | 4 (24%)      | 6 (12%)      | 0.05          |
| dysarthria          | 8 (9%)       | 0 (0%)       | 8 (12%)      | 0.05          |
| dysphasia/dysphagia | 29 (33%)     | 9 (50%)      | 10 (20%)     | 0.05          |
| facial              | 4 (4%)       | 0 (0%)       | 4 (8%)       | 0.05          |
| PATTERN LEVEL IN THE EP | 13 (15%)     | 15 (90%)     | 5 (10%)      | 0.05          |

| TOXICITY | | |  |
| hla      | 59 (67%)     | 22 (11%)     | 22 (11%)     | 0.05          |
| Plasma exchange | 9 (10%)     | 2 (10%)     | 7 (14%)      | 0.05          |
| Steroids | 1 (1%)       | 0 (0%)       | 1 (2%)       | 0.05          |

**Figure 2**

**Electrophysiological results**

- **Conduction blocks (CB):**
- **Distal CNAP duration (DCNAPD):**
- **DCNAPD predictive marker of poor outcome:**

*Pathological DCMAPD at 50-90 days, from clinical onset represents distinctive marker of primary demyelinating pathophysiological mechanism.*

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Event-related potentials in patients with primary Sjogren’s syndrome

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Question

Primary Sjogren's syndrome (pSS) is an autoimmune inflammatory disorder characterized by infiltration of exocrine glands, especially the salivary and lacrimal glands. Our aim was to investigate the event-related potentials (ERP) as the electrophysiological measure of cognitive performance in patients with pSS without evident cognitive decline.

Methods

The study group consisted of 30 individuals with diagnosed primary Sjogren’s syndrome (29 women and 1 man, mean age 51.3 years) and 30 healthy, age- and gender-related controls. Mini Mental State Examination (MMSE) and auditory ERP were performed in both groups, with the analysis of P300 and N200 response parameters.

Results

Twenty five patients (83.3%) scored above 27 points in MMSE. P300 latencies and N200 latencies in all the references were significantly longer (p=0.015; p<0.0001, respectively) in pSS patients than in the controls. P300 and N200 amplitudes were higher (but not significantly) in the patients than in the controls.

Conclusions

Abnormal parameters of ERP in pSS patients without overt cognitive decline may indicate subclinical central nervous system involvement with possible affection of cognitive functions.
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Immune-modulating therapies for encephalitis of unknown origin - Importance of early application for improving clinical outcomes.
2 cases of encephalitis of unknown origin who had similar clinical findings and with serial electrocencephalogram(EEG) follow up, who had considerably different outcome according to whether immune-modulating therapy was applied or not.

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Introduction
Encephalitis is associated with high morbidity and the major portion of it is of unknown etiology. So there is tendency to delay prompt management, which would lead to poor disease outcome.

Case 1 : A 21 year-old previously healthy man suffered from confusion preceded by fever and headache from 3 days ago. In CSF analysis, there was prominent pleocytosis with predominate lymphocytes. Initial diagnosis was viral encephalitis, so we started acyclovir 10mg/kg three times a day. Initial MRI image showed subtle cortical swelling.

During first three days, he gradually got comatose. EEG showed generalized continuous slow waves. We started potent antibiotics and added antiepileptic drugs in the suspicion of non-convulsive status epilepticus(NCSE). Full work up to find causative etiology including viruses, bacteria, rickettsia, fungus, auto-antibodies was done, but none of them was positive.

After 10 days, he remained comatose and quadriplegic despite full dose of antimicrobial treatment. 2 weeks after admission, intravenous immunoglobulin was given in 0.4g/kg for 5 days, but there was no neurologic improvement. Follow up EEG showed no change.

Case 2 : A 16 year old previously healthy man suffered from drowsiness preceded by fever and headache from 5 days ago. CSF analysis showed pleocytosis with predominate lymphocytes. Initial MRI image was normal. We started acyclovir 10mg/kg three times a day.

After two days, his gradually got comatose and quadriparetic. EEG showed generalized continuous slow waves. We added antibiotics and antiepileptic drugs, and checked up for possible etiologies, but nothing was positive. Follow up MRI image showed T2 high signal in bilateral thalamus, basal ganglia, and brainstem. At the fifth day of admission, we started intravenous steroid 1g for 5 days and intravenous immunoglobulin 0.4g/kg for 5 days, successively. After administration of steroid, the patient got alert and oriented, and general weakness gradually diminished. Follow up EEG also returned to normal.

Discussion
High proportion of etiology-unidentified encephalitis is due to incomplete study or late seroconversion. We suggest that most of encephalitis classified as by unknown cause are undiagnosed cases of major etiologies, such as HSV encephalitis, or ADEM. So we should consider inducing immune-modulation simultaneously with the antimicrobial therapy, if neurologic status deteriorates despite improvement of CSF profile. And the response can be followed up by EEG.
Abstracts of Poster Presentations – Poster Session 28 – Inflammatory diseases of CNS and PNS

figure 1

Figure 1. Initial MR Brain images of Case 1.
(A) FLAIR MR image of the day of admission shows no T2 signal change, or cortical swelling. (B,C,D) Images taken at the fourth day of admission. FLAIR image (B) shows generalized cortical swelling and high signal intensity on bilateral basal ganglia, thalamus, midbrain, and insular cortex. DWI shows subtle diffusion restriction at the same area. T1 enhance image shows diffuse meningeal enhancement.

Figure 2. Delayed MR Brain images of Case 1.
Images taken at the fourteenth day of admission. FLAIR image (A,B) shows increased extent of high signal intensity on bilateral basal ganglia, thalamus, midbrain, pons, insular and basal frontal, temporal cortices. DWI shows subtle diffusion restriction at the same area. T1 enhance image shows no focal enhancement.

figure 3

Figure 3. Initial MR Brain images of Case 2.
DWI (A) shows diffusion restriction at posterior corpus callosum splenium. FLAIR (B,C) shows high signal intensity on bilateral basal ganglia, thalamus, midbrain, and insular cortex. T1 enhance (D) image shows no focal enhancement.

Figure 4. Delayed MR Brain images of Case 2.
FLAIR (B,C,D) shows decreased high signal intensity on bilateral basal ganglia, thalamus, midbrain, but new high signal intensity lesions at bilateral subcortical white matter. T1 enhance (D) image shows no focal enhancement.
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#### figure 2

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Mar/21</th>
<th>Mar/16</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General sign &amp; symptoms</strong></td>
<td>Fever (39.5°C), headache, poor oral intake</td>
<td>Fever (39.5°C), headache, nausea</td>
</tr>
<tr>
<td><strong>Neurologic sign &amp; symptoms</strong></td>
<td>Confusion, stupor, stiff neck, irregular breath, hiccup, weakness</td>
<td>Confusion, stupor, stiff neck, irregular breath, hiccup, down beat nystagmus, ataxia, weakness</td>
</tr>
<tr>
<td><strong>Initial EEG</strong></td>
<td>Generalized continuous slow waves</td>
<td>Generalized continuous slow waves</td>
</tr>
<tr>
<td><strong>Initial CSF profile</strong></td>
<td>Opening pressure: 25cmH2O WBC 0/4 (Poly 6% Lympho 80%, Others 14%) Protein 114 (Poly 6% Lympho 80%, Others 11%)</td>
<td>Opening pressure: 20cmH2O W 640 (Poly 3% Lympho 86%, Others 11%) Protein 243 glucose 47/122</td>
</tr>
<tr>
<td><strong>MRI finding</strong></td>
<td>Diffusion restriction + T2 high signal intensity Insula, medial temporal and frontal cortex, thalamus, basal ganglia, midbrain and and pons with no focal enhancement</td>
<td>Diffusion restriction + T2 high signal intensity: corpus striatum splenium, thalamus, basal ganglia, posterior portion of medulla oblongata and pons with no focal enhancement</td>
</tr>
<tr>
<td><strong>Antimicrobial therapy</strong></td>
<td>Acyclovir 10mg/kg three times a day Vancomycin 4000mg a day Ceftriaxone 2g a day Clarithromycin 1000mg per day and Doxycycline 200mg per day</td>
<td>Acyclovir 10mg/kg three times a day Vancomycin 4000mg a day Ampicillin 2g a day</td>
</tr>
<tr>
<td><strong>Immune-modulating therapy</strong></td>
<td>From the 6th day of admission IV steroid 1g for 5 days IV immunoglobulin 0.4g/kg for 5 days, successively</td>
<td>From the 14th day of admission IV immunoglobulin 0.4g/kg for 5 days</td>
</tr>
<tr>
<td><strong>Follow up EEG</strong></td>
<td>Generalized continuous slow waves (no change)</td>
<td>Within normal limit</td>
</tr>
<tr>
<td><strong>Follow up CSF profile</strong></td>
<td>Opening pressure: 30cmH2O WBC 21 (Poly 6% Lympho 95%, Others 3%) Protein 70 glucose 54/110</td>
<td>Opening pressure: 25cmH2O W 290 (Poly 1% Lympho 52%, Others 47%) Protein 182 glucose 58/95</td>
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<tr>
<td><strong>Neurologic outcome</strong></td>
<td>Comatose, quadriplegic, impaired brain stem reflex, hopeless discharge</td>
<td>Alert, oriented, able to walk without assistance, transferred to rehabilitation dep.</td>
</tr>
</tbody>
</table>
Clinical and Electrophysiological Features of Guillain-Barré Syndrome in Northeast China

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Question

Neurophysiological features are still unclear in the early stage of Guillain-Barré syndrome (GBS), especially within seven days of GBS onset. Intravenous immunoglobulin (IVIg) has been proven to be an effective management for GBS. However, the efficacy of IVIg beyond two weeks of symptom onset, as well its benefit for mildly affected patients who can still walk, remains uncertain.

Methods

The clinical and electrophysiological data were collected and reviewed retrospectively in 138 patients hospitalized for GBS during the period between 2006 and 2010.

Results

Analysis of age distribution revealed a high incidence among young adult patients. Gastroenteritis was the predominant previous infection. The initial and main symptom was hypotonic muscle weakness of the lower extremities, particularly, weakness in all four limbs simultaneously. Acute inflammatory demyelinating polyneuropathy (AIDP) was the main subtype of GBS in Northeast China. Intravenous immunoglobulin (IVIg) was effective for patients beyond two weeks of symptom onset and for mildly affected patients. Low compound muscle action potential (CMAP) amplitudes, abnormal H reflexes, and F waves were the main features of neurophysiological studies. In addition, no statistical differences in electrophysiological features were found between patients within seven days of onset, as well as 8-14 days and 14 days after GBS onset.

Conclusions

GBS in Northeast China has characteristic clinical and electrophysiological features. Early neurophysiological studies are helpful for diagnosis of GBS.
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ACUTE BRACHIAL PLEXUS NEUROPATHY WITH INVOLVEMENT OF CRANIAL NERVES IX, X, XI AND XII: DIAGNOSTIC VALUE OF MRI

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Introduction
Which is the value of MRI in the diagnosis of acute brachial plexus neuropathy? This is an entity that affects primarily nerves of the upper trunk of the brachial plexus, and cranial nerve involvement is an infrequent association, and implies a diagnostic challenge.

Case report
We report a 56 year-old woman who developed acute dysphonia, dysphagia and left shoulder pain, followed, six days later, by left arm weakness. She suffered from ankylosing spondylitis, treated with Adalimumab; a month and a half earlier she had developed a left dorsal herpes zoster with good response to acyclovir. On examination she presented weakness of the left soft palate with reduced gag reflex, left vocal cord paralysis, confirmed by laryngoscopy, and tongue deviation to the left. Left arm muscle weakness included proximal and distal muscles, with no fasciculations. Left biceps and triceps reflexes were reduced. Needle examination showed only fibrillation potentials and positive sharp waves in the left deltoid muscle. MRI of the brachial plexus shows enlargement of the trunks, cords and terminal branches, with mild gadolinium enhancement and no muscle denervation (Figure A and B). The patient was treated with IV methylprednisolone and Adalimumab was suspended; she had a good response to treatment, with a complete recovery within 30 days. Adalimumab was restarted with no recurrence.

Conclusion
This case illustrates a unique presentation of unilateral involvement of the IX, X, XI and XII cranial nerves in neuralgic amyotrophy, and highlights the importance of MRI for diagnosis and localization, in the absence or with mild electrophysiologic involvement.

figure 1

figure 2
P490
Electrooculogram and trigeminal nerve evoked potentials during neurosurgical operations

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Question
During neurosurgical operations, it is important to identify cranial nerves and to monitor their functions. To date, the cranial nerves have been identified by recording responses in its innervated muscle. However, it is difficult to set the recording electrodes in extraocular muscles and the trigeminal sensory evoked potentials are also difficult to be record due to their short latency. Are the electrooculogram (EOG) useful for identifying the nerves? An action potential of the trigeminal nerve can be used for its monitoring?

Methods
The EOG responses were elicited by the monopolar stimulation on active electrodes on the outside or the upper side of the eyeball and on reference electrodes on the inside or the lower side of the eyeball (horizontal and vertical recording, respectively). The trigeminal nerve evoked potentials were elicited by the supraorbital, infraorbital and mental nerve stimulation on the skull base of the operative filed. Results: The negative monophasic responses were elicited by the stimulation of the oculomotor nerve (onset-latency, 1.59+-0.04 ms), the polyphasic responses were by the trachlear nerve (onset-latency, 3.2+-0.5 ms) and the positive monophasic responses were by the abducens nerve (onset-latency, 1.5ms). The trigeminal nerve evoked potentials were elicited by the stimulation of the supraorbital nerve (peak-latency, 2.81+-0.22 ms) the infraorbital nerve (peak-latency, 2.6 ms) and the mental nerve (peak-latency, 3.9+-0.6 ms).

Conclusions
The EOG responses were useful to identify the extraocular muscle-innervating nerves and to monitor its functions. The trigeminal nerve evoked potentials can be recorded on the trigeminal nerve by the supraorbital, infraorbital and mental nerves.
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P491
Reversible Intraoperative Neurophysiologic Monitoring Changes Associated with Surgical Retraction

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Question

Inadvertent retraction-related injuries are a known risk of intracranial surgical procedures. Retraction in the vicinity of critical neural tissue and vascular structures may result in compression, stretch, or stenocclusive ischemic injuries that are unexpected, and may not be recognized until the postoperative period. The critical role of multimodality intraoperative neurophysiologic monitoring (IONM) in helping to prevent retraction-related injuries is highlighted.

Methods

We present a series of ten intracranial surgical cases where IONM changes occurred in association with retractor placement and positioning, procedures that include resection of tumor (4) and vascular malformations (2), and aneurysm clipping (4). Multimodality IONM monitoring was employed in all cases, including transcranial motor evoked potentials (tcMEPs), somatosensory evoked potentials (SSEPs), and electroencephalography (EEG).

Results

In the four aneurysm cases, critical IONM changes occurred following retractor placement, but prior to any planned intervention. In all remaining cases changes occurred during the interventional period that also coincided with the placement or positioning of retractors. Most commonly transcranial motor evoked potentials were primarily affected. In all cases prompt identification of these IONM changes led to rapid surgical assessment and eventual removal or repositioning of retractors, which resolved neurophysiologic changes and correlated with no new sustained postoperative deficits.

Conclusions

This case series highlights the importance of IONM in the early identification of potentially reversible changes that may correlate with impending retraction-related injuries. In particular, the pattern of IONM changes represented in the majority of these cases emphasizes the critical and distinct role of tcMEPs in identifying early signs of evolving cerebral injury. This further illustrates the utility and necessity of multimodality intraoperative neurophysiologic monitoring in a diversity of intracranial surgical cases for the entire duration of the procedure, including presumably non-interventional periods.
Critical Intraoperative Neurophysiologic Monitoring (IONM) Changes Associated with Patient Positioning Maneuvers

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Question

Positioning maneuvers during surgical cases can place the patient at risk for spinal cord and/or peripheral nerve injury. Initial transition of the patient from the supine to prone position, as well as passive neck flexion or extension, are potentially high risk portions of the procedure, especially during spine surgeries. In addition, sudden or gradual shifts in head, neck, shoulder, and/or arm position may occur unexpectedly during the course of the surgical procedure, which can also result in central or peripheral nervous system injury. The role of IONM in helping to prevent such injuries is emphasized.

Methods

We present a series of six cases where critical IONM changes were identified and resolved following modification of patient positioning in cervical spine procedures. Multimodality IONM monitoring was employed in all cases, including transcranial motor evoked potentials (tcMEPs), somatosensory evoked potentials (SSEPs), and electromyography (EMG).

Results

Critical IONM changes were observed during the initial prone positioning onto the surgical table in three spine cases, while in one case changes occurred with passive neck extension while supine. In the remaining two cases, significant IONM changes occurred during exposure or the interventional period, findings which correlated with unexpected shifts in body or limb position over the course of the surgical procedure. In all cases prompt identification of IONM changes enabled rapid assessment and repositioning of the patient, which largely resolved all neurophysiologic changes and correlated with no new sustained postoperative deficits.

Conclusions

This series highlights the importance of appropriately instituting IONM early, prior to initial patient positioning, to facilitate prompt identification of potentially reversible changes that may indicate impending positioning-related injuries.
P493
Retrospective Waveform Analysis of Transcranial Motor Evoked Potentials (MEP) to Identify Early Predictors of Impending Motor Deficits in Spinal Surgeries

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OBJECTIVE This study aims to identify neurophysiologic parameters of motor evoked potentials (MEPs) that predict early compromise during spinal surgeries with the ultimate goal of providing real-time intraoperative neurophysiologic monitoring (IONM) feedback to surgeons to prevent irreversible post-operative neurologic motor deficits.

BACKGROUND Although a 50% amplitude decrease in SSEPs correlates with potentially reversible physiologic ischemia, there are no corresponding standard warning criteria for MEPs [1]. Surgeons are not alerted until MEPs are no longer obtainable, by which time irreversible motor injury may have already occurred.

METHODS From 2011-2013 at Stanford University and Lucile Packard Children's Hospitals, we retrospectively identified 15 true positive cases of intraoperative loss of MEPs and post-operative motor deficits. The following MEP parameters were measured: latency, amplitude, duration, turns, phases, area under the curve (AUC) and an intraoperative spinal cord index (ISCI) [2] was calculated for each involved muscle group and for 5 traces prior to the complete MEP loss.

RESULTS Out of 26 muscle groups in 15 cases, latency increased or had no change in 23 MEPs, duration decreased in 16 MEPs, amplitude decrease in 15 MEPs, AUC decreased in 14 MEPs, and ISCI decreased in 16 MEPs. In 12/15 cases (80%), there was more than > 50% drop in ISCI in at least one monitored muscle group before the MEPs were completely lost. In 14 cases with concurrent SSEPs monitoring, 9 cases had > 50% decrease in SSEPs: 2/9 changed before MEPs, 5/9 changed simultaneously with MEPs, and 2/9 changed after MEPs.

CONCLUSIONS In cases of impending irreversible motor injury, there is a trend toward smaller and simpler waveforms detected by IONM before complete MEP loss occurs. A 50% drop in ISCI could potentially be used an early warning parameter for motor compromise. In the future, MEPs need to be obtained more frequently to increase the sensitivity of impending injury. We hope further research will help identify a reliable index to alert surgeons before motor injury becomes irreversible.

References

Figure Legends
[1] Amplitude vs Time
[2] Latency vs Time
[3] AUC vs Time
[4] ISCI vs Time
Usefulness of Intraoperative Neuromonitoring (IONM) in the surgical management of spinal cord neurofibromas in patients with neurofibromatosis type 1 (NF1)

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Question

Is IONM useful to achieve a favourable functional outcome after tumour removing surgery in neurofibromatosis type 1 (NF1) patients?

Methods

Description of a case series. Eight NF1 patients underwent interventions in order to remove spinal roots neurofibromas causing cervical spinal cord compression. A second intervention at the lumbosacral spine was necessary to remove neurofibromas located at the cauda equina in 2 cases. In all cases, IONM by means of motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs, epidural SSEPs), D-Wave monitoring and Bulbocavernosus Reflex (BCR) was performed. Additionally, in order to identify motor nerve roots and to preserve their function during surgery, neural tissues mapping was performed by direct electrical stimulation of the structures with a bipolar probe.

Results

A total of 54 neurofibromas at the cervical and lumbosacral spine were removed. Motor nerve roots were identified and subtotally resected, sparing rootlets with small tumour nodules. Tumours on sensitive nerve roots were fully resected. When tumours were located at the cauda equina, nerve roots were also monitored using a train of stimulus to determine if these sensitive roots were critically involved in BCR. BCR was successfully elicited in both patients with tumours involving cauda equina and were preserved after tumour removing. No significant changes occurred in MEPs, SSEPs or D-Wave monitoring during surgeries.

Conclusions

IONM provides continuous, real-time information about the function of neural pathways at risk during surgery and helps the surgeon to identify motor neural structures. The importance of BCR for the clinical outcome of the patients requires the use of special techniques intended to intraoperatively maintain the reflex. As opposed to schwannomas, neurofibromas grow encasing neural fibres from motor and sensory nerve roots. Subtotal resection should be performed in motor roots in order to preserve motor function.
Selective loss of the D - wave evoked by contralateral hemispheric transcranial electric stimulation (TES)

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Question

D - waves correspond to descending action potentials initiated by direct axonal activation of cortical motor neurons. TES technique consists of electrical stimulation applied with scalp electrodes. Coronal TES montages are generally more effective than posterior - anterior electrode arrays. Moreover, inter-hemispheric C1 / C2 simulating array produce stable D - waves with low threshold stimulation. Since anodal stimulus is more efficient for cortical stimulation D - wave predominantly originates from one hemisphere when coronal TES is used. However, D - wave lateralized impairment has been not often reported.

Methods

We report three cases of intraoperative neurophysiological monitoring during resection of intramedullary cervical spinal - cord tumors. D wave and bilateral muscle MEPs were elicited by TES delivered through cork screw electrodes applied over the scalp at C1/C2.

Results

In all cases D - wave deterioration during tumor removal was only present after an hemisphere stimulation with preservation of D - wave elicited by contralateral stimuli. Deterioration of simultaneous MEPs recordings was ipsilateral to pathological D - wave.

Conclusion

Lateralized deterioration of D - waves suggests that switching between left and right anodal hemisphere stimulation can improve the intraoperative assessment of corticospinal tract.
Multimodality monitoring of Somatosensory (SSEPs) and transcranial electric Motor evoked potentials (tce-MEPs) during surgical correction of neuromuscular scoliosis in patients with central or peripheral nervous system diseases

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BACKGROUND

During corrective spinal surgery for neuromuscular scoliosis, intraoperative multimodality spinal cord monitoring is recommended. Literature data regarding the reliability of spinal cord monitoring in patients with neuromuscular scoliosis are conflicting.

MATERIALS AND METHODS

12 patients with central nervous system disease (perinatal encephalopathy in 5, syndromic hydrocephalus in 3, paraparesis due to syringomielia in 2, paraparesis in neurofibromatosis in 2) and 9 patients with peripheral nervous system disease (spinal muscular atrophy in 3, Duchenne muscular dystrophy in 1, congenital myopathy in 3, poliomyelitis in 1, sensorymotor demyelinating neuropathy in 1) underwent surgical correction of spinal deformity under multimodalitary intraoperative monitoring (IOM) of spinal cord function in our institution between 2008 and 2013. Cortical SSEPs were recorded after stimulation of the median and posterior tibial nerves.

TceMEPs were recorded from the abductor pollicis brevis (ABP) and from multiple muscles at lower limbs and from the external sphincteric muscle. EMG spontaneous activity was also recorded from the same muscles to detect radicular sufference.

RESULTS

All patients presented mild to severe motor deficits before surgical treatment. Preoperative SSEPs were pathologic in 5/20 patients and tceMEPs amplitudes were reduced in 10/20 patients.

Three patients demonstrated significant SSEP and tceMEP amplitude changes at lower limbs during surgery: only one patient presented postoperative reversible motor impairment at the right lower limb. No patients presented postoperative sensory or sphincteric deficits.

CONCLUSIONS

The reliability of IOM techniques may be reduced in presence of preoperative pathologic motor evoked responses. However, multimodalitary IOM should be recommended in patients with neuromuscular scoliosis to ensure intraoperative monitoring of functionally intact nerve pathways, even in presence of severe motor deficits.
P497
Saphenous Nerve Somatosensory Evoked Potentials (SSEP) monitoring during Lateral Interbody Fusion (LIF) in preventing femoral nerve injury

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Question
Can the saphenous SSEP monitoring prevent femoral nerve (L2-4) injury?

BACKGROUND
Lateral lumbar trans-psoas interbody fusion is a novel minimally invasive technique reducing the risks related to traditional anterior and posterior approach surgeries. Despite advantages, trans-psoas exposure carries up to 30 % risk of lumbar plexus injury. The multimodality intraoperative neuromonitoring (IONM) is utilized to prevent postoperative deficits, but to date there is no reliable technique to evaluate the upper lumbar plexus.

Methods
Saphenous nerve SSEPs were obtained by stimulation of the inferior medial thigh with needle electrodes and recording from the scalp. Primary outcome was measured by testing reproducibility of SSEPs at baseline, changes from the baseline during the procedure and relevance to standard IONM modalities. Intraoperative changes were identified and correlated to primary outcome.

Results
Twenty-nine patients were included in the study. Reliable saphenous SSEP were recorded bilaterally in 26/29 patients. Reduction of the amplitude > 50 % from baseline in 2 cases was observed during expansion of the tubular retractor in the psoas muscle. Posterior tibial SSEP remained unchanged. Saphenous waveforms returned to baseline after collapsing the retractor.

Conclusions
Saphenous SSEPs can be used to detect electrophysiological changes to prevent femoral nerve injury during LIF. A larger sampling size is underway as to validate whether addition of this technique offers increased sensitivity and/or specificity, and correlates with the postoperative outcomes.
Reliability of Different Amplitude-Related Warning Criteria for Facial Motor Evoked Potential Monitoring During Vestibular Schwannoma Surgery

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Introduction

Transcranial corticobulbar motor evoked potentials for the facial nerve (facial MEPs) have been used over the past decade as an alternative to free running electromyography to monitor the functional integrity of the facial nerve during surgery for vestibular schwannomas. Yet, warning criteria for facial MEP monitoring are not consistent across the literature and the specificity and sensitivity of different criteria remain undetermined. Our goal was to establish the most reliable criteria to interpret facial MEP changes in the light of clinical outcome.

Materials and Methods

In the past four years 100 consecutive patients were monitored with facial MEP (transcranial electrical stimulation at C3/Cz and C4/Cz, train of 4 stimuli, 0.5 ms duration, intensity up to 150 mA) during surgery for vestibular schwannomas. Differences in facial MEP amplitude at the end of the surgery, as compared to the opening baselines, where analyzed. Three different cut-offs were selected: 30%, 50% and 80% amplitude drop. The clinical outcome was assessed using the change in the House-Brackmann (HB) grade at discharge from hospital, 6 months and 1 year after surgery, in comparison to the pre-operative grade. It was considered a good outcome a HB worsening of no more than one grade.

Results

Data were available for the analyses in 89 patients at discharge from hospital, 74 patients at 6 months, and 64 patients at the one year follow-up. The 30% amplitude drop criteria yielded a 51% sensitivity and 82% specificity at discharge from hospital, 58% and 73% at 6 months and 63% and 71% at 1 year. The 50% amplitude drop criteria yielded a sensitivity of 39% and specificity of 94% at discharge, 58% and 87% at 6 months, and 63% and 83% at 1 year. Finally, the 80% amplitude drop criteria yielded 21% sensitivity and 96% specificity at discharge, 29% and 94% at 6 months, and 36% and 90% at 1 year.

Discussion and Conclusion

While a 80% drop criteria appears too little sensitive, we observed no changes in sensitivity using a 50% and 30% drop criteria at the long-term follow-up. Vice versa, specificity was significantly higher in the long term using a 50% drop than a 30% drop criteria. Therefore, we suggest to consider a 50% drop in facial MEP amplitude as the best criteria to interpret intraoperative changes.
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P499
Value of neurophysiological Intraoperative monitoring (IOM) of carotid endarterectomy. Our serie.

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QUESTION
The carotid endarterectomy (CEA) is an effective surgical technique but during this act could appear several neurological deficits in order to cross clamping or the insertion of an arterio-arterial shunt (AAS). The IOM has improved the cerebral functions control in these patients.

mETHODS
We present our serie of patients undergoing CEA under general anesthesia, from February 2012 to October 2013, with monitoring of somatosensory evoked potentials after stimulation of bilateral median and tibial nerves (SSEPs) and motor evoked potentials elicited by transcranial electrical stimulation (tcMEPs). Criteria used for decision to insert and AAS were the reproducible decrement (>50%) of SSEPs amplitudes and/or the loss of tcMEPs. It is also evaluated the stump pressure (previous technique used to indicate the inserting of an AAS), using as criteria to insert the AAS a value <50 mmHg. We evaluate in our serie if setting of AAS is necessary comparing IOM with stump pressure.

RESULTS
We reviewed 45 patients. In 10 of them (22.2%) the stump pressure was <50 mmHg but in 7 of these patients (70%) there were no significative changes in IOM techniques and no shunt was placed. The remaining 3 patients (30%) had significative changes in SSEPs, so it was necessary to insert AAS. In the other 35 patients (77.78%) the stump pressure was >50 mmHg and just in 1 case (1.28%) there were significative changes in SSEPs, inserting AAS. None of the patients showed postoperative neurological deficits.

CONCLUSION
In our serie we show utility of IOM in CEA to indicate properly the insertion of AAS, being better method than older techniques as stump pressure, avoiding new neurological deficits.
P500
Efficacy of intra-operative electrocorticography in terms of seizure outcomes in focal epilepsy.

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Purpose

Intra-operative electrocorticography (ECoG) is a useful tool to guide surgical resection of both the lesion and epileptogenic zone (EZ). The success of surgery in respect of seizure control depends on accurate localisation and complete removal of the EZ. Although the outcome of epilepsy surgery becomes clear only after serial follow up, it has generally been accepted that incomplete removal of EZ as a main cause for early relapses, which occurs in first 6 to 12 months after the operation. In this study, we evaluated the efficacy of ECoG on post-operative seizure outcomes in patients with focal epilepsy.

Methods and Results

Fifty-five focal epilepsy patients with various etiologies (mesial temporal sclerosis, cortical dysplasia, tumors, tuberculomas, cavernomas, non-specific changes) who had been surgically treated, were assessed. The recordings of ECoG were performed before and after the resections and repeated if needed. In terms of functional (eloquent) cortical areas some resections were not completed even if the existence of residual spiking. The relationship between the guided resection and seizure outcome was analysed. Additionally, the residual spikes after resection were assessed.

In this observational study, we found the main determinant of seizure freedom is underlying etiology. Although the numbers are small in respect to meaningful comparison between the groups, the seizure recurrence mainly occurred in grade-II or higher grade glial tumor patients. Especially in the cavernomas and cortical dysplasia group we had very high seizure free rates.

Conclusions

Sequential ECoG recordings guided surgical resections has an additional beneficial effect on good seizure outcomes.
P501
Value of stimulus-triggered EMG of track vs screw for the detection of lumbar radiculopathy in scoliosis surgery

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Question
One of the complications in scoliosis surgery are radiculopathies due to pedicular screw malposition. Our aim is to analyze our cases of lumbar radiculopathies after scoliosis surgery, in which screw malposition was not detected by the usual neurophysiologic techniques.

Methods
We have studied 294 surgeries (6765 screws, 30% lumbar). Intraoperative monitoring (IOM) was performed with muscular MEPs after rTES, SEP and t-EMG of the screws. 8 patients presented lumbar radiculopathy after surgery, despite t-EMG values were normal, and screw malposition was confirmed by CT-scans. In the surgery to withdraw these screws, t-EMG was determined after stimulation of the depth and the middle part of the track.

Results
All of the malpositioned screws showed normal t-EMG thresholds after stimulating the screw. When stimulating the depth of the track, values were also normal, but stimulation in the middle of the track showed very low thresholds in most of the cases. All of the patients improved with the screws withdrawal.

Conclusion
Malpositioned lumbar screws are infrequent, but very symptomatic. t-EMG of the track improves the detection of these cases
Motor evoked potential monitoring in very young patients

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Question

Motor evoked potential monitoring is a standard technique applied in spinal surgery of adult patients. The application of motor evoked potentials in patients under the age of one year is rarely reported and the feasibility of the method is a matter of debate. We have assessed the feasibility of monitoring muscle motor evoked potentials in infants undergoing spinal surgery.

Method

Intraoperative neurophysiological monitoring was applied in eleven infants using somatosensory and motor evoked potentials. Muscle motor evoked potentials were elicited using transcranial electrical stimulation applied via needle electrode placed in the scalp. Short trains of five to nine stimuli using an interstimulus interval of 4 milliseconds were used to generate limb muscle responses. Those responses were recorded without averaging from needle electrodes placed in the limb muscles.

Results

Muscle motor evoked potential could be elicited in all patients. In eight out of eleven patients muscle motor evoked potentials could be recorded from upper and lower extremities. The youngest patient with preserved muscle motor evoked potentials from upper and lower extremities throughout the surgery was 116 days old.

Conclusion

Muscle motor evoked potentials are a feasible method of monitoring spinal cord function that can be safely applied in pediatric neurosurgery for patients under the age of one year.
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P503
Intraoperative language network monitoring by means of cortico-cortical evoked potentials

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Objective

In order to establish a new intraoperative monitoring for preservation of subcortical language pathways, we applied technique of cortico-cortical evoked potentials (CCEP) during brain surgery.

Methods

Subjects were 17 patients with brain tumors located close to the arcuate fasciculus (AF) in the language-dominant left hemisphere. After craniotomy, electrodes were placed over frontal and parieto-temporal perisylvian areas. Single-pulse stimuli were applied to several pairs of electrodes in the frontal area to record CCEP from the parieto-temporal area. Under general anesthesia, the anterior perisylvian language area (AL) was first defined by CCEP connectivity patterns, and also by presurgical neuroimaging findings. We then monitored the integrity of the language network by stimulating AL and recording CCEPs from the posterior perisylvian language area (PL) consecutively during both general anesthesia and awake condition. In the awake condition, language assessment with batteries was also sequentially performed throughout surgical procedures. To confirm language function in AL, high-frequency electrical stimulation (ES) was performed during awake craniotomy in nine patients, who had neither cognitive impairment nor aphasia preoperatively.

Results

In all, the CCEP connectivity pattern delineated perisylvian language network between AL and PL even under general anesthesia. CCEP amplitude declined in two patients (≤32%) during surgical procedures. Two patients had transient language impairment postoperatively. One patient who showed 32% decrease of CCEP amplitude presented phonemic paraphasia during and after operation. Another patient who did not showed decrease of CCEP amplitude developed language impairment immediately after surgery because of brain edema. Language function recovered within a few months in both patients. In all, CCEP monitoring successfully prevented persistent language impairment. In all nine patients who were awakened fully, high-frequency ES confirmed language impairment at AL.

Conclusions

Although further accumulated cases will be warranted for establishing the sensitivity and specificity, intraoperative CCEP delineated the perisylvian or dorsal language network and would be useful for online monitoring of subcortical language pathways.
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P504
NON-INVASIVE NERVE ROOT HIGH VOLTAGE ELECTRICAL STIMULATION IN LUMBOSACRAL SURGERY: A METHODOLOGICAL AND CLINICAL UPDATE.

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Question
Non-invasive, High Voltage Electrical Stimulation (HVES; Troni et al., 2011) has been recently proposed for intraoperative monitoring (IOM) of nerve root function during lumbosacral (LS) surgery (Troni et al, 2013). Supramaximal LS motor root activation at a level rostral to surgery represents the methodological rationale of the technique.

Objective
To report the results of extensive clinical application of this IOM technique and to describe recent methodological improvements of the technique.

Methods
Nerve root IOM was performed in 73 patients (41 male and 32 females; mean age 57 ys ±12) undergoing surgery for various degenerative lumbosacral spinal diseases. Instead of the original pre-operatory neurophysiological approach, the optimal stimulation site (OSS) on the vertebral column was located by reproducing in the subject in prone position the distance between coccyx and the lower third of the lumbar enlargement of the spinal cord directly measured on MRI images. Maximal CMAPs were bilaterally recorded from muscles targeting L3 to S2 root territories.

Results
The IOM procedure was safely accomplished in all patients. Neuroimaging location of the OSS proved to be a simple and effective approach to achieve a complete and balanced maximal stimulation of LS motor roots. Harmful effects on cardiac rhythm or on blood pressure were never observed. HVES-induced muscle jerk never caused detrimental mechanical effects on operatory field at any surgical step. No post-surgical collateral effects were reported. In 7 patients, the technique was able to detect acute distress of manipulates roots, rapidly reversible in most cases, promptly revealed by a significant area reduction of CMAPs targeting the involved radicular territory. L4/L5 roots were found to be by far the most vulnerable to surgical stress.

Conclusions
Non-invasive HVES is a safe and sensitive tool to early detect motor nerve root conduction failure in lumbosacral surgery.

References
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**P505**

**Intraoperative neurophysiological monitoring of the catheter assisted endovascular closure of patent foramen ovale in adults.**

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**Questions:** Catheter assisted, endovascular closure (CAEC) is a non surgical technique to treat atrium septum defects. However, brain embolism could occur during it. Our goals are to describe and assess an intraoperative neurophysiological monitoring (IONM) protocol to prevent stroke during CAEC.

**Methods:** Eighteen (N=18) consecutive patients in whom this procedure was performed between January of 2009 and August of 2012, to close a patent foramen ovale (PFO), were retrospectively reviewed. Somatosensory evoked potentials of upper and lower extremities, as well as, bi-hemispheric electroencephalography were monitored.

**Results:** There were no statistically significant differences on any parameter between groups of patients whether or not a device was successfully deployed (88.9%) or not. Mean age was 52.4 years (SD:±19.3), with 33.3% females. Average constant current stimulation intensities were 35.56 mA (SD:±7.65) for upper, and 48.06 mA (SD:±7.1) for lower extremities. Mean duration of procedure was 80.33 minutes (SD:±32.55). Two cases (11.1%) were aborted because of technical difficulties to deploy a device. No patient had signal changes or needed surgery.

**Conclusions:** Our study comprised a small sample, and because no patient showed signal changes or neurological status change, specificity, sensibility, or false/positive rates could not be determined. However, IONM is a safe way to prevent morbi-mortality during CAEC for PFO, therefore, more studies need to be done.
**LP33**  
**Intraoperative monitoring of facial nerve motor evoked potentials in children**

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**Objective**

Facial nerve function can be continuously monitored by transcranial facial nerve motor evoked potentials (FNMEPs) during neurosurgical interventions. Despite their advantages, FNMEPs are not yet widely used. While there are several publications of FNMEP in adults, the feasibility and safety of FNMEP in children has not yet been documented.

**Methods**

We included 10 consecutive procedures involving 10 patients (median age 2.5 y, range 1-15 y, 7 male) that were operated by the senior author in 2013 and in whom FNMEPs were monitored. While most authors use a 50% reduction of FNMEP response amplitudes as a warning criterion, our approach was to keep the response amplitude constant by increasing the stimulation intensity and to establish a warning criterion based on the “threshold-level” method. A threshold increase greater than 20 mA for eliciting FNMEPs in the most reliable facial nerve target muscle was considered a prediction of reduced postoperative facial nerve function, and subsequently a warning was issued to the surgeon. Preoperative and early postoperative function was documented using the House-Brackmann (HB) grading system.

**Results**

Monitoring of FNMEPs was feasible in all 10 surgeries in at least one facial nerve target muscle. The mentalis muscle yielded the best result (89% of trials), followed by orbicularis oris (85%) and orbicularis oculi muscles (80%). The median stimulation threshold was initially 69 mA (range 40-100 mA) for FNMEP and 60 mA (15-95 mA) for MEP of the thenar muscles. The initial FNMEP threshold exceeded the MEP threshold in 5/10 patients (median difference 5 mA). FNMEP deterioration showed specificity for HB deterioration of 88% CI [47-100%].

**Conclusions**

Intraoperative FNMEP monitoring is feasible and safe also in young children. We found no evidence that procedures and thresholds should differ from FNMEP in adults.
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LP34
Intraoperative direct cortical stimulation motor evoked potentials: Preliminary stimulus parameter recommendations based on rheobase and chronaxie

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Question

Although direct cortical stimulation (DCS) pulse train motor evoked potentials (MEPs) are an established practice option for intraoperative motor cortex mapping and monitoring, there are no published strength-duration data to provide a scientific basis for stimulus parameter selection (MacDonald et al., 2013). The objective of this study is to estimate what the mean rheobase and chronaxie are at four different interstimulus intervals (ISIs) from a sample of patients undergoing DCS MEP monitoring and form recommendations based on the results. An ISI with minimal rheobase should be optimal as it would minimize the stimulus strength required to evoke responses; pulse duration (D) at the chronaxie should be optimal as it would minimize pulse energy (Prutchi and Norris, 2005).

Methods

After identifying hand motor cortex, 5-pulse DCS thenar MEP rheobase and chronaxie were derived from current threshold measurements at 1, 0.5, 0.2, 0.1 and 0.05-ms D for 2, 3, 4 and 5-ms ISI in seven patients under propofol / opioid anesthesia.

Results

Mean rheobase varied with ISI and was minimal with a 3-4 ms ISI (Fig. 1). Mean chronaxie was 0.18-0.19 ms with a 3-4 ms ISI (Fig. 2).

Conclusion

This report presents an approach to base DCS MEP stimulus parameters on rheobase and chronaxie. Preliminary results in seven of a planed n of twenty patients suggest that 3-4 ms ISI and 0.18-0.19 ms D might be generally optimal DCS MEP stimulus parameters.

References


Figure Legends

Fig. 1. Mean DCS thenar MEP rheobase (n=7) by interstimulus interval (ISI). Mean rheobase was significantly lower (P<0.05) at 3 or 4 than at 2 or 5-ms ISI. While mean values were slightly lower with a 4-ms than 3-ms ISI, the difference was not statistically significant; minimal rheobase occurred with a 4-ms ISI in four patients and with a 3-ms ISI in three.

Fig. 2. Mean DCS MEP chronaxie (n=7) by interstimulus interval (ISI). These values were not significantly different except for between 2 and 4-ms ISI (p<0.05).
P506
MEG is influenced by skull defects

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**Question**

While the influence of skull defects on the electroencephalogram (EEG) has been reported, the magnetoencephalogram (MEG) had previously been hypothesized to have a negligible sensitivity to skull defects. The objective is to experimentally investigate the influence of conducting skull defects on the MEG and EEG.

**Methods**

A miniaturized electrical dipole was implanted in the brain of rabbits in vivo. Simultaneously, a 64-channel EEG and a 16-channel MEG were recorded first above intact skull and then above a skull defect. Skull defects were filled with agar gel of tissue-like conductivities. The dipole was moved beneath the skull defect and measurements were taken at regular steps. A computer tomography (0.4 mm³ voxels) provided the geometry of the defect and the position of the dipole.

**Results**

The EEG amplitude increase reached factors of 2-10, while the MEG amplitude reduction reached -20% (Figure 1 and 2). The EEG amplitude deviation is larger if the source is under the edge while the MEG amplitude deviation is larger if the source is centrally under the defect. The MEG topography change (RDM* = 0.15) was geometrically related to the skull defect edge. The conductivity of the skull defect modulated the strength of change in the MEG & EEG. Dense spatial sampling revealed high spatial frequencies in MEG and EEG due to skull defects that are not detectable with current human helmet-type MEG devices and standard EEG setups.

**Conclusions**

MEG and EEG changes due to a skull defect can be substantial and depend on the defect geometry and the relative orientation and position of the source. MEG forward modelling requires realistic volume conductor head model incorporating skull defects. This effect should be investigated further in humans.

Figure 1: (A) EEG and MEG of a source at different locations relative to defect 1. Dipolar source shown as black bar with two poles, outline of the inner; middle and outer skull defect edges drawn in black; Sensor positions marked with grey dots; Minimum and maximum value and isoline difference displayed above each map. (B) Finite element model of the rabbit head showing the implanted source, skull defects, EEG and MEG.

Figure 2: MEG magnitude change (MAGrel) due to a skull defect for a series of locations of a tangential source beneath the defect in four animals (color-coded).
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Figure 1

Figure 2

MEG amplitude deviation (MAGre)

Source depth:
- 4.7mm
- 3.7mm
- 1.8mm
- 2.2mm

Source position beneath skull defect
Predicting neurodevelopmental outcome of infants born < 28 gestational weeks with magnetoencephalography and somatosensory evoked fields

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Question

Despite great advances in neonatal intensive care, many extremely preterm infants still develop with neuromotor impairments. Neonatal neurological examination, serial cranial ultrasonography and term-age magnetic resonance imaging (MRI) are used to predict outcome, but fail to find some of the infants with neurodevelopmental impairments. We tested whether somatosensory evoked fields (SEFs) recorded with magnetoencephalography from the primary (SI) or secondary somatosensory areas (SII) could complement clinical and neuroimaging methods in predicting outcome of extremely preterm infants.

Methods

We recorded SEFs to tactile stimulation of the index finger at term age in 39 infants born <28th gestational weeks and 46 fullterm control infants. Of the preterm infants 29 also underwent MRI, and neonatal neurological examination at term age, serial cranial ultrasonography in preterm era and clinical follow-up at 2-years corrected age.

Results

Responses from SI were present in all infants without significant differences between preterm and fullterm infants. SII responses were absent significantly more often in preterm than fullterm infants (right hemisphere p=0.01; left hemisphere p=0.04). The preterm infants with absent SII response in either hemisphere had significantly worse developmental quotients and locomotor subscales (Griffiths Mental Developmental Scales) at 2-years follow-up than preterm infants with SII responses present (p<0.01). Of the 7 infants with unilaterally absent SII response 5 developed with complex minor neurological dysfunction or CP. Of these five, two were missed by neuroimaging and neonatal neurological examination.

Conclusions

Evaluating SII responses at term age complements neonatal neurological examination and neuroimaging in predicting neurodevelopmental outcome of extremely preterm infants.
P508
MEG aids in differentiating continuous epileptiform activity from EEG breach rhythm, a case report

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Question

Breach rhythm may be reminiscent of epileptiform activity in EEG: how to differentiate between them?

Patient and Methods: A 40 years old male was referred to hospital because of flu and dizziness. Due to mild confusional state and fever, encephalitis was suspected and an EEG recording was performed. The EEG showed mild general slowing and continuous epileptiform spiking in the right occipital area, interpreted as a focal status epilepticus. The patient received antiepileptic drugs and several follow-up EEGs were obtained, all of which showed a similar finding.

The patient was known to have symptomatic epilepsy since childhood and focal gliosis in the right occipital lobe, as verified by stereotactic biopsy in 2011. The biopsy had caused a circular bone defect with a diameter of 8 mm, visible in MRI.

The symptoms (confusional state and fever) disappeared in a few days, and since there were no visuospatial symptoms, the EEG interpretation was doubted. Bone defect is known to cause breach rhythm in EEG, which can be reminiscent of epileptiform activity. In our patient, the continuous epileptiform activity seemed to arise from the site where the brain biopsy had been taken. Thus, misreading of EEG might have been a plausible explanation for the finding, since a completely symptom-free focal status epilepticus seemed unlikely.

Magnetoencephalography (MEG) signal is practically unaffected by the intervening tissues. Therefore we performed a MEG recording to verify the EEG finding of epileptiform activity.

Results

The MEG showed continuous epileptiform activity in the right occipital area, and with equivalent current dipole modeling the sources of this activity were localized in the right occipital lobe at the area of gliosis seen in MRI. This finding was in accordance with previous EEG findings, confirming the existence of real continuous epileptiform activity.

Conclusions

MEG can be a useful tool in verifying epileptiform activity in cases with potential intermingling breach rhythm, which is helpful especially if the EEG finding is in conflict with the clinical picture.
P509
Genetic influence is still maintaining on cerebral language function in elderly monozygotic twin: A MEG study.

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Aim
A genetic influence has been suggested for many cerebral functions, but little is known about language function. To estimate the genetic influence on the cerebral function during a language task, we used MEG to investigate the similarity of the cerebral oscillatory changes in elderly monozygotic twins.

Methods
This study evaluated 55 native Japanese speakers, including 19 monozygotic twin pairs. We measured the brain activity during a verb generation task using a 160-channel whole-head MEG system. In the verb generation task, a Japanese semantic word was presented visually after the presentation of a fixation point. Subjects were instructed to silently read each presented word, then to generate one verb related to the word immediately after word presentation.

We investigated the spatio-temporal distribution of task-related cerebral oscillatory changes (ERS/ERD) using adaptive spatial filtering and a group statistical analysis. The control period was defined as the time period between 200 and 0 ms before stimulus onset, and the periods of interest were defined as continuously moving 200 ms windows from 0 ms to 1600 ms after stimulus onset. The windows were moved in steps of 100 ms.

After detecting the peak coordinates of the ERD at 25-50 Hz, we estimated the power of the ERD in the peak coordinates using a time-frequency analysis. To compare the similarities in the power of the ERD within twin pairs, the correlation coefficient between the powers of the members of each twin pairs was determined. To compare twin pairs to unrelated subjects, we determined the correlation coefficient for 19 pairs of randomly drawn unrelated subjects.

Results
The peak of the ERD at 25-50 Hz was estimated in the left frontal area based on the group statistical analysis. The ERD first appeared in the 200-400 ms post-stimulus window and was sustained until 1600-1800 ms. In the peak coordinate, the power of the ERD showed a high correlation among twin pairs. The correlation coefficient was 0.54 in the 800-1000 ms period at the maximum. On the other hand, unrelated subjects had a lower correlation in all time windows.

Conclusion
We found that there was high similarity of the ERD of the left frontal area in elderly monozygotic twins. This finding suggested that the cerebral activity in left frontal area during a language task is under genetic influence.
P510
Inhibition of somatosensory evoked cortical responses by a weak leading stimulus

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Question
In previous studies, we demonstrated that auditory change-related cortical responses were inhibited by a weak leading stimulus in a similar manner to prepulse inhibition (PPI) of startle responses (Inui et al., BMC Neuroscience 2012). The aim of this study was to investigate whether a similar phenomenon is present in the somatosensory system.

Methods
Eleven healthy subjects (3 females and 8 males) participated. They were instructed to focus on a silent movie. We recorded somatosensory evoked fields (SEFs) elicited by electrical stimulation of the left median nerve. The intensity of the test stimulus was 2.5 times the sensory threshold (2.5 ST). A leading stimulus was presented 100 ms before the test stimulus. The intensity of the leading stimulus was 2.5, 1.5, 1.1, or 0.9 ST. In addition to the test stimulus-alone and test + leading stimulus conditions, four leading stimulus-alone conditions were recorded. These stimuli were presented in a random order with a trial-trial interval of 2.5-3.0 s. We evaluated the effects of the intensity of the leading stimulus on cortical responses to the test stimulus by subtracting the responses of the leading stimulus-alone condition. At least 100 artifact-free responses were averaged for each condition. SEFs were subjected to multi-dipole analysis, and activities from the primary (SI) and secondary (SII) somatosensory cortex were obtained.

Results
Primary SI responses (N20m-P35m) were significantly inhibited by the leading stimulus with 2.5 and 1.5 ST intensities (20.7 and 19.1%, respectively, p<0.05), but not 1.1 and 0.9 ST (15.2 and 6.8%, respectively). In addition to 2.5 ST (P60m:53.8%, SII:50.7%, p<0.01) and 1.5 ST (P60m:35.1%, SII:42.7%, p<0.05), an S1 component at 60 ms (P60m) and SII were significantly inhibited by the 1.1 ST leading stimulus (P60m:21.5%, SII:30.4%, p<0.05).

Conclusion
Even a weak somatosensory stimulus (1.1 ST) could affect late SI and SII activities. These results suggest that the somatosensory system has an inhibitory mechanism similar to PPI, and that each evoked component has different sensitivities to a prepulse.
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P511
Effect of changes in stimulation sites on activation of posterior parietal cortex

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Question
A previous fMRI study elucidated the specific activity of the inferior parietal lobe (IPL) in a two-point discrimination task in comparison to an intensity discrimination task (Akatsuka et al., 2008). If the posterior parietal cortex (PPC), including the IPL, is responsible for detecting changes in stimulation sites, the activity of PPC depends on the level of change in stimulation sites. The aim of this study was to clarify, using oddball paradigm, whether a particular site exists that can detect changes in stimulation sites.

Methods
Somatosensory-evoked magnetic fields were recorded in nine right-handed subjects. Three oddball conditions were performed for all subjects, with the probability of deviant and standard stimuli being 20% and 80%, respectively, under all three conditions. Deviant stimuli were always presented to the second digit of hand and standard stimuli were presented to the first digit (small deviance: SD), fifth digit (medium deviance: MD) of hand and first digit of the toe (large deviance: LD).

Results
Brain Electrical Source Analysis (BESA) showed that the amplitudes of 3b and area1 elicited by the deviant stimuli were not significantly different among the three conditions. In contrast, the amplitude of PPC was significantly greater for LD than for SD and MD.

Conclusion
The activity of PPC tended to increase with greater deviance in stimulation sites, but the activity of 3b and area1 did not differ with greater deviance. These findings suggest that PPC may have a functional role in automatic change detection systems in regard to deviance of stimulation sites.
P512
A magnetoencephalographic study on face processing with morphing human face into monkey face

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Objective
Humans are better at recognizing human faces than the face of other species like monkeys. N170 is a well-known face specific component in event-related potentials and M170 in magnetoencephalography (MEG) is a counterpart of N170. In order to further elucidate the species-specific face processing, we recorded MEG using morphing faces between human and monkey.

Methods
We used three types of morphing faces with different ratio of human (H)/monkey (M) (H/M: 9/1 (H9), H/M: 5/5 (H5), H/M: 1/9 (H1)). The mean luminance, contrast and spatial frequency were adjusted to avoid inter-stimulus physical variances among the stimuli. The MEG signals in response to either upright or inverted faces were recorded in 9 healthy subjects using a whole-head 306-channel system.

Results
In both upright and inverted face conditions, M170 was clearly obtained by all stimuli in the right fusiform face area (FFA). M170 latencies were significantly modulated by the human ratio of stimuli. With the reduction of human face ratio, M170 latencies became longer. In comparison with upright and inverted face conditions, M170 latencies were delayed in all inverted faces. Unlike M170 latencies, M170 activation strengths were not significantly modulated among the stimuli.

Conclusions
These findings suggest that M170 latency reflects species-specific face processing with the face inversion effect. Our results provide further evidence that M170 latency is more sensitive to species-specific face processing than M170 activation strengths.
P513
Influence of times of interfering stimulation on the somatosensory evoked magnetic fields

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Question

Recent studies have reported that somatosensory evoked magnetic fields (SEFs) are modulated by previous interfering stimuli (IS). This study aimed to investigate whether SEFs are modulated by times of IS.

Methods

SEFs were evoked by electrical stimulation applied to the right median nerve in 14 participants and were recorded using a 306-channel whole-head magnetoencephalograph system (Vectorview, Elekta). Stimulus intensity was set at 100% of the motor threshold. Stimulus condition was set with the continuation six pulse trains in interstimulus interval (ISI) of 500 ms. The first, second, third, and sixth stimulation each was used as a trigger for analyzing SEFs. ISI was set at 5000 ms from the first stimulation to the next first stimulation (Fig 1). All participants provided written informed consent, and the study was approved by the ethics committee at our institute.

Results

Compared with the first stimulation, the dipole strengths for the P35m and P60m decreased in second, third, and sixth stimulation (Fig 2), but there were not significantly different among second, third, and sixth stimulation. The latencies of N20m, P35m, and P60m were not significantly different among all stimulation.

Conclusion

The present study showed that somatosensory cortical activation in the S1 (P35m, and P60m) was not affected by IS after the second stimulation.
NeuroElectric Tomography (NET): Very High Resolution Functional Brain Imaging


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Magnetoencephalographic (MEG) recordings were obtained from 14 volunteers (7 healthy controls and 7 patients with chronic concussion symptoms) during performance of a visual language choice task. A new method was devised for reliably extracting neurophysiologic information from the raw single trial data, referee consensus optimization. Electrical current tracings (1 msec resolution) were identified from ≈2,000,000 locations within the brain as if from direct recording electrodes (p < 10^{-12} for each accepted source).

- Spatial resolving power less than 2 mm was demonstrated: Average correlation between simultaneous 80 msec traces was ≈0.2 from locations 1 mm apart.
- fMRI-like differential activation under differing task conditions was found for each individual with very high reliability (2mm^3 voxels): The source count for different task conditions was different ($\chi^2 > 32.8$; $p < 3 \times 10^{-8}$) for at least 400 of ≈200,000 voxels (joint $p < 0.006^{400}$).
- The size of a functional brain unit was found to be as small as 2mm^3 with upper limit of 6mm^3: Almost no voxels showed a significant difference in the number of sources found under different task conditions for 8mm^3 - 24mm^3 voxels. But numerous voxels showed significance for 6mm^3 or less with peak near 3mm^3. When the data were divided per stimulus characteristics, many more voxels were seen with significant count differences than when the data were divided at random. The random division demonstrated indistinguishable overlap replication.
- Neuroelectric tomograms show adjacent voxels with opposite functionality, further demonstrating 3 mm resolving power and ≈3mm^3 functional units.

### Comparison: Functional MR Imaging and Neuroelectric Tomography

<table>
<thead>
<tr>
<th></th>
<th>fMRI: NeuroVascular</th>
<th>NET: NeuroElectric</th>
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</table>
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Fig. Neuroelectric tomograms show gray/white differentiation. 3mm\(^3\) voxels are shown with larger than expected source counts (p<3x10\(^{-8}\)). 1 slices is shown from NET’s from 2 different subjects.

figure 1
**P515**  
A DARK SIDE OF PORTABLE MUSIC PLAYER: A MAGNETOENCEPHALOGRAPHIC STUDY

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**Question**

Nowadays, many people use portable music players everywhere. However, the volume is often set to very high levels in noisy environments. Extensive usage of portable music players might cause damages in the auditory system, which are not detectable by means of pure tone audiometry.

**Methods**

Using complex stimuli consisting of a test tone superimposed on different band-eliminated noises, we objectively measured population-level frequency tuning in the human auditory cortex by means of magnetoencephalography (Figure 1). We compared two young people groups: one group had listened to music with portable music players intensively for a long period of time, while the other group had not.

**Results**

Both groups performed equally in behavioral examinations (pure tone audiometry, speech test, hearing in noise test, etc). However, the obtained auditory evoked responses showed that the population-level frequency tuning in the auditory cortex of the portable music player users was significantly broadened compared to the non-users.

**Conclusions**

Our results suggest that extensive and inappropriate usage of portable music players could worsen population-level frequency tuning in the human auditory cortex, which standard behavioral audiometric measures cannot detect. These damages could lead to irreversible and behaviorally relevant hearing disorders in future.
Modulation of somatosensory evoked magnetic fields by the inter-stimulus interval of interfering stimuli

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**Question**

Somatosensory evoked magnetic fields (SEFs) are modulated by previous interfering stimuli. Here we investigated the modulatory effects of interfering stimuli applied with different inter-stimulus intervals (ISIs) on SEFs recorded from the primary somatosensory cortex (S1).

**Methods**

SEFs were evoked by electrical stimulation applied to the right median nerve in 14 subjects and were recorded with a 306-channel whole-head MEG system (Vectorview, Elekta). The test stimulus (TS) and 3 interfering stimuli (ISs) were set with intensities of 100% and 70% of the motor threshold, respectively. The ISI of TS was 5 s. Five types of pulse trains were delivered in a pseudo-random order. The ISIs between 3 ISs and between the last IS and TS were (a) 250 ms and 500 ms, (b) 500 ms and 500 ms, (c) 1000 ms and 500 ms, (d) 500 ms and 1000 ms, and (e) TS only (control) (Fig 1). All subjects provided written informed consent; the study was approved by the ethics committee at our institute.

**Results**

We observed a cortical response to TS in the contralateral S1. The dipole strengths for N20m, P35m, and P60m for condition (a) were significantly smaller than those for the control (e). The source strengths for N20m and P60m for condition (b) and (c) were significantly smaller than those for control (e) (Fig 2).

**Conclusions**

Our findings indicated that SEFs recorded from S1 following median nerve stimulation were modulated by the ISI of ISs, and the ISI between the last IS and TS.

![Fig. 1.](image1.png)

Schema of the experimental paradigm.

![Fig. 2.](image2.png)

Mean source activities for N20m, P35m, P60m, and N150m elicited by median nerve stimulation.
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figure 1

(a) 250
(b) 500 500 500 (ms)
(c) 1000 1000 500 (ms)
(d) 500 500 1000 (ms)
(e) Conditioning刺激 70% MT Test刺激 100% MT

figure 2

(nAm)

N20m  P35m  P60m  N150m

* : p < 0.05
** : p < 0.01
Intermittent photic stimulation (IPS) leads to a phenomenon in the human cortex called photic driving: The neural network of the visual system synchronizes with the frequency of the IPS. Two measureable phenomena in electroencephalography (EEG) and magnetoencephalography (MEG) characterize this synchronization: resonance and entrainment. We hypothesized that a rod excitation in the retina is a driving input for photic driving. We tested our hypothesis of a rod driven alpha entrainment and resonance by stimulating 12 healthy volunteers with low intensity light flashes at 20 stimulation frequencies. The frequencies were multiples of the individual alpha frequency ($\alpha$) of each volunteer in the range from 0.40 to 2.30*$\alpha$. 306-channel whole head magnetoencephalography recordings were analyzed in the time, frequency, and space domain with the topographic matching pursuit algorithm. We found alpha entrainment and resonance for stimulations at or close to the individual alpha frequency (0.95-1.10*$\alpha$) and half of the alpha frequency (0.50-0.55*$\alpha$). No signs of a resonance or entrainment phenomenon were revealed for stimulation frequencies around 2.00*$\alpha$. Instead, on-responses at the beginning and off-responses at the end of each stimulation train were observed at frequencies 1.30-2.30*$\alpha$, indicating that the flicker fusion frequency was reached. We conclude that the oscillator network in the visual cortex responsible for the photic driving effect receives two different inputs: a cone and a rod driven input of the human eye.
**P518**

**Frequency characteristics of neuromagnetic auditory steady-state response to sinusoidally amplitude modulated sweep tones**

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Auditory steady-state response (ASSR) is a neuronal electrical activity phase-locked to periodic modulations (fm) of a sound. The ASSR is specifically characterized by its sensitivity to carrier frequencies (fc), providing a useful measure in clinical audiometric application. However, the frequency characteristics of the ASSR at the supra-threshold levels remain unclear, despite its potential application, e.g., an objective and automatic adjustment of hearing aids. This study therefore aimed to capture the frequency characteristics of the neuromagnetic ASSR at the supra-threshold levels. Sinusoidally amplitude-modulated tones, with fc sweeping between 0.1?12.5 kHz, were presented as stimulus sounds. The acoustic parameters were varied in fm, sound intensity, fc sweep direction and fc sweep rate/tone duration. The sound intensity was calibrated to be flat with accuracy of +/- 0.5 dB SPL by applying inverse filtering and real-ear measurement techniques. The instantaneous strength of the ECD (equivalent current dipole) moment at fc sweeping through the frequency/time axes was captured. Loudness for 0.1?12.5 kHz at 70 dB SPL was simulated by substituting the detected individual hearing threshold into a formula defining the relationship between loudness and SPL (ISO226:2003(E)). The ASSR moment showed a peak at 0.5 kHz and decreases in the lower and higher frequencies, irrespectively of the stimulus acoustic parameters whereas the loudness was mostly plateau between 0.5?4 kHz. The apparent inconsistency between the neuronal and perceptual frequency characteristics, indexed by the ASSR and loudness, indicates that the loudness perception is not encoded in the ASSR alone, but reflects an interactive function with other neuronal information processing activities. Consequently, the ASSR is unlikely to be an optimal index to evaluate the perceptual hearing characteristics at the supra-threshold level, unless a neuronal-perceptual transformation model is developed and applied.
P519
Localization and propagation of physiological vertex sleep transients (VST) with EEG & MEG using realistic head model.

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Objective

To study the localization of origin and propagation of physiological vertex sleep transients (VSTs) using simultaneous EEG Source Imaging (ESI) and Magnetic Source Imaging (MSI).

Methodology

Simultaneous MEG (306 channels) and EEG (64 channels) in 5 patients (M: F = 3:2; age = 19±12) using NEUROMAG-TRIUX system was performed. Physiological VSTs during stage 1 sleep was analysed individually (10/patient) and then averaged. Source localization was performed using realistic boundary element model and moving dipole source analytical technique with linear least square estimation for both MEG and EEG over the entire epoch at every single time point. Source localization of independent and averaged VSTs was performed individually.

Results

The VSTs noted in MEG were lower in amplitude relative to baseline than in EEG. There was consistency between individual and averaged VSTs in all patients. With MSI, at onset of VSTs, the activities were noted in thalami (100%) and the propagation occurred to a) medial parietal and frontal regions - 80%; b) medial and then to lateral parietal regions - 20%. With ESI, at onset of VSTs, the activities were also noted in thalami (100%) which propagated to a) medial frontal regions - 40%; b) medial fronto-parietal and then to lateral surface of the cortex - 40%; and c) suboccipital and then to medial parietal region - 20%.

Conclusions

Physiological VSTs might originate in thalamus which propagated to medial and parasagittal regions, and then spread to entire hemisphere, confirming the physiological hypothesis. Thus, integrating EEG-MEG and MRI provides a new window to study the normal brain oscillatory activity.
P520
High gamma oscillatory changes of magnetic fields in hippocampus detected by memory task using magnetoencephalography.

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Background
It is controversial that magnetoencephalography (MEG) can detect magnetic fields oscillatory changes in the deep brain structures such as hippocampus. So we evaluated the ability to detect hippocampal signals using our new MEG.

Methods
Ten healthy right handed volunteer were participated in this study. We measured the brain magnetic fields activity during three types of memory task using a 160-channel whole-head MEG system (MEG vision NEO; YOKOGAWA Inc, JAPAN). In the memory task, we use files of fifty presentations each of human face recognition, word reading, and evaluation of visual pattern arts. Subjects were instructed to watch each three seconds of serial images on the screen, and five minutes later, to answer yes or no the question ‘Is this image shown?’ while watching the images mixed among half of the presented files.

We investigated the spatio-temporal distribution of task-related cerebral oscillatory changes (event-related synchronization: ERS/event-related desynchronization: ERD) using adaptive spatial filtering and a group statistical analysis. Time frequency analyses were also evaluated. The control was defined as the time interval from 1000msec before stimulus onset, and the periods of interest were defined as 1000msec after stimulus onset.

Results
Intense theta range ERS were detected in right hippocampus by face memory task. Theta ERS were also elicited by pattern arts memory task in bilateral hippocampus, and were noted by word task in right hippocampus. On the other hand, high gamma ERS were detected by face task and pattern arts in bilateral hippocampus, and by words task in left hippocampus.

Conclusions
Our study showed hippocampal magnetic oscillatory changes using MEG, and especially high gamma range activities were also clearly recorded. These results might be able to evaluate theta-gamma coupling.
P521
Functional motor cortex mapping using fusion technique of corticokinematic coherence (CKC) in magnetoencephalography (MEG) and navigated transcranial magnetic stimulation (nTMS) in stroke patients.

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Bourguignon reported functional motor cortex mapping method using CKC in MEG. We used fusion technique combined with CKC and nTMS to identify functional motor cortex in the stroke patients. [Method] Five healthy subjects and four stroke patients entered this study. CKC for functional mapping of the motor cortex by computing coherence between cortical MEG signals and the kinematics of voluntary movements. Subjects performed self-paced flexion-extensions of the right-hand fingers, with a three-axis accelerometer attached to the index finger. Cross-correlogram and coherence spectra were computed between 306 MEG channels (Electa) and the accelerometer signals. The coherence was statistically significant in all healthy subjects, with sources at the hand area of the primary motor cortex contralateral to the movement. Hotspot of the functional motor cortex was also determined from the nTMS (Nextim) oriented by photo-tracking system. Area of the strongest evoked response from the APB muscle with single pulse stimulation applied by the eight shaped coil, was determined as the hot spot. The mapping data from CKC method in MEG converted from DICOM format to NifTI format outputted to nTMS system, were overlapped to the hot spot from the nTMS method. [Result] Functional motor cortex conducted from the CKC method and nTMS method were determined almost same place located anatomical motor cortex(M1) in the healthy subjects. In the stroke patients, several abnormalities were detected. Some cases show no response with nTMS method whereas normal CKC in MEG in the affected side. Other findings with splitting location elicited by nTMS and CKC method or no response shown by both methods in the affected side, were observed. [Discussion] Central processing of motor system was speculated to be involved various pathways. CKC method in MEG was composed of afferent and efferent motor pathway, but nTMS elicits only efferent pathway. These difference mainly reflects the result from each method.
P522
MEG study of interictal epileptic spikes in patients with Rasmussen's encephalitis assessed by magnetic source imaging

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Question
To assess localization of the MEG interictal spikes in patients with Rasmussen's encephalitis (RE) by means of magnetic source imaging.

Methods
Five patients (mean age: 8±2.9 years, 1 male) with RE underwent MEG recordings in rest condition using a 306-channel helmet-shaped neuromagnetometer (Neuromag Triux, Elekta Oy, Finland) with simultaneous 64-channels EEG recording. A second examination was performed after 8.0 ± 1.4 months. Epileptic discharges were identified by visually examining the MEG recordings and cross-referencing them with the simultaneous EEG recording. The sources of the pathological activities were localized using both equivalent current dipoles and distributed models. The source locations were displayed on individual co-registered MR-images.

Results
Interictal EEG and MEG spikes were detected in all patients. Source analysis identified multiple spike generators within the affected hemisphere. These multiple locations could vary between the two subsequent recordings suggesting an evolving multifocal involvement of the hemisphere thought pathophysiological progress in RE.

Conclusions
MEG was able to detect the presence of multiple sources associated to interictal spikes in patients with RE; therefore, it can be considered a useful tool in the pre-surgical evaluation and follow-up of patients with this intractable progressive hemispheric epilepsy.
P523
Changes in corticomuscular coherence after acute stroke

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Question
Motor cortex activity and electromyographic (EMG) signals from contracting contralateral muscle show coherence in the 15-30-Hz range in healthy subjects. This corticomuscular coherence (CMC) is considered as a sign of functional coupling between muscle and brain. Prior studies have shown that CMC is altered in chronic stroke, but functional significance of the alterations has remained unclear. We examined CMC in acute stroke patients (<7 days from stroke onset) and correlated the results with clinical signs.

Methods
Magnetoencephalographic oscillatory signals and EMG signals were recorded from 21 patients with paresis of the upper extremity due to ischemic stroke and 22 control subjects during isometric contraction of the extensor carpi radialis muscle. CMC amplitudes and peak frequencies at 5-50 Hz were compared between the two groups and between patients with subcortical and cortical stroke.

Results
CMC was reliably identified in 20 patients with peak frequency at 17 ± 1 Hz. CMC amplitude was significantly ($p<0.05$) smaller in patients than in control subjects in the frequency range of 19-30 Hz. CMC peak frequency was lower in subcortical stroke patients than in control subjects (14 ± 1 Hz vs. 21 ± 1 Hz, $p<0.001$), whereas such difference was not observed between cortical stroke patients and control subjects.

Conclusions
The results indicate that CMC is altered in acute stroke. Its alterations vary according to the lesion site, suggesting that cortical and subcortical stroke interfere differently with the control of hand movements.
Magnetoencephalography brain connectivity patterns in traumatic brain injury.

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Background

Neuroimaging techniques have the potential to reveal patterns of neural activation after brain damage and, perhaps more importantly, to identify the rehabilitation interventions that will stimulate the restoration of brain activation patterns. We test the hypothesis that TBI patients exhibit functional connectivity alteration as compared to the control subjects.

Methods

Using magnetic source imaging (MSI) our study aimed to explore this phenomenon in the magnetoencephalogram (MEG), the distribution of its sources, and associations between symptom profiles and decrease of functional connectivity in the brain.

Whole-head MEG recordings were obtained from 25 TBI patients and 25 healthy control subjects during a resting condition. Analysis of the connectivity measures in the frequency domain has been applied to TBI patients and control group.

Results

Brain networks connectivity analysis showed: overall significant reduction of MEG connectivity activity in TBI patients compared with control subjects, significant decrease in the long-distance connectivity and significant increase in the short-distance connectivity as a result of TBI. Extent of functional disconnection was associated with injury severity.

Conclusions

This study demonstrates that TBI disturbances in cortical functional connectivity are associated with network-specific neurological deficits.

This study was supported by grant from the Fundacio Marató de TV3 (111010).
Electrophysiological study to reveal brain mechanism of will for voluntary action

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Question

Since the introduction of clock study by Libet et al in 1983, our knowledge about the neurophysiological mechanism of human will has been advanced but not yet reached enough understanding. The goal of this study is to find cortical area related to the perception of will for voluntary movement and to clarify their relationship.

Methods

Nineteen right-handed healthy volunteers performed self-paced motor task (button press) while listening to the randomly presented tone stimuli. They ignored the tones if they were not aware of the motor intention at the moment when they heard the tone, but pressed another button if they were aware of their intention at the time of the tone. Movement related brain activity was measured by whole-head MEG recording during the task and correlation was evaluated with the time of thought (T) and the point of no return (P) estimated from the tone distribution relative to the button press.

Results

The average T time was 1.4 second and the average P time was 0.25 second before the button press. Permutation test revealed clusters of brain area with significant positive correlation to T time in left orbitofrontal area and left insula at early latency (-2.0 -- -1.6 sec), and left ventral premotor area and posterior cingulate area later (-1.5 -- -1.0 sec.) No significant correlation was found with P time.

Conclusions

This result indicates involvement of fronto-parietal network in the perception and execution of will for voluntary action.

References

P526
Study of binaural interaction using synchronous/asynchronous averaging for dichotic sounds

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Objective

In the clinical examination of auditory function, it is desirable to observe the evoked responses separately to the right- and left-ear inputs during binaural stimulation. However, responses to the contralateral and ipsilateral sounds are mixed in the auditory cortex, which are difficult to discriminate. In this work, we aimed to develop a novel method for the separation of the auditory evoked responses that were evoked by the right and left ear sounds and to study binaural interaction in the central nervous system.

Method

We prepared two sets of time series of onset-triggers of stimulus sounds for dichotic stimulus sounds. The two trigger sets had no temporal correlation with each other. Transient phasic evoked responses were much attenuated in amplitude after repeated averaging of the response-epochs using triggers that were asynchronous to the sound onsets, while original waveform of the response was reserved by synchronous averaging time-locked to the sounds.

Results

In the measurements of evoked magnetic fields, we obtained separated responses to a speech sound /a/ and a 600 Hz pure tone delivered to the right and left ears by using two sets of triggers that were time-locked to the right and left stimuli with random intervals but uncorrelated with each other. Results showed difference between dichotic and monaural stimulation in the auditory evoked MEG response of N1m in a way that depended on the characteristics of the sounds. Contralateral response was dominant over ipsilateral response in dichotic stimulation even it was not the case in monaural stimulation.

Significance

Synchronous and asynchronous averaging has been proved to be an effective method to differentiate long-latency responses (N1m) generating from binaural inputs. The present method would be applicable to dichotic listening tests for individuals with deficits such as Auditory Processing Disorder to study electro-physiological responses.
P527
DETECTION OF INTERICTAL EPILEPTIC DISCHARGES BY MAGNETOENCEPHALOGRAPHY IN THE DANISH PRESURGICAL EPILEPSY EVALUATION

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**Question**

Magnetoencephalography (MEG) is increasingly used in the non-invasive evaluation of patients with refractory focal epilepsy. MEG records the changes in magnetic fields generated by the activity of the neural networks in the brain. EEG and MEG supplement each other in localizing the epileptic focus because MEG detects epileptic sources tangential to the skull and EEG detects both tangential and radial sources. The magnetic field recorded by MEG is not distorted by the brain, tissue, skull or scalp. We investigated which modality was able to identify epileptic discharges in epilepsy surgery patients?

**Method**

MEG (Elekta Neuromag® TRIUX™) 306 channels and simultaneous EEG (60-70 channels) were recorded in 26 consecutive patients with focal epilepsy, referred for epilepsy surgery. Recording duration was one hour in resting conditions, with closed eyes. MEG and simultaneous EEG were manually viewed by skilled personal using CURRY Scan 7 Neuroimaging Suite.

**Results**

MEG has revealed epileptiform discharges in 57% of the patients. Fifteen % had focal discharges seen only in MEG. In 75% of these patients, earlier conventional EEG had not been able to localize a focus. Focal discharges were seen in both MEG and in the simultaneous EEG in 42% (Fig. 1).

**Conclusion**

MEG detects interictal focal epileptic discharges not captured by conventional EEG. This can lead to a better hypothesis on where to operate. Although the number of patients is low, since this is an ongoing project, we argue that MEG should be considered for epilepsy surgery candidates.

**Reference**


**figure 1**

Interictal Focal Epileptic Discharges in MEG and Simultaneous EEG in Epilepsy Surgery Candidates
P528
Modulation of the 20-Hz motor cortex rhythm to passive movement and tactile stimulation

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Question

Modulation of the 20-Hz rolandic rhythm to somatosensory input has been proposed to reflect alterations in the motor cortex excitability. In stroke patients, the strength of this modulation is associated with recovery of hand function. In this study we compared the suppression and rebound amplitudes of the 20-Hz (15-25 Hz) rhythm to tactile stimulation and passive movement.

Methods

We recorded rhythmic brain activity in 22 healthy subjects (11 males, mean 59 years) with a 306-channel MEG system during tactile stimulation and passive movement. Tactile stimuli were delivered using pneumatic diaphragms to both index fingers alternately with an interstimulus interval of 1.5 s. For passive movements, the subjects’ index fingers were lifted by a nurse every 3 s. Suppression and rebound of the 20-Hz rhythm were analyzed using Temporal Spectral Evolution (TSE) and their amplitudes were quantified from the MEG channel displaying the strongest rebound/suppression.

Results

The peak amplitudes of the rebound in both ipsi- and contralateral hemispheres were significantly ($p < 0.05$) stronger after passive movement than after tactile stimulation. In contrast, the peak amplitudes of the suppression did not significantly differ between the stimuli.

Conclusions

According to our results, passive movements are strong modulators of the motor cortex excitability. Thus, passive movement might be a more robust and feasible tool than tactile stimulation to study motor cortex alterations in stroke patients.
Our previous magnetoencephalographic study (Kikuchi et al., NeuroImage 2011) demonstrated that people who stutter (PWS) had both functional and structural reorganization of right auditory cortex with impaired left auditory cortex function. However, it is unclear how right and left auditory cortices interact to compensate stuttering. We re-analyzed previous MEG data in healthy controls and PWS through N100m responses of auditory cortex to pure tone. Their latencies and related hemispheric local and inter-hemispheric phase synchronizations were further evaluated. The results showed that left N100m latency was significantly longer than that of right in PWS while controls did not show such difference. Phase locking factors (PLFs) for local phase synchronization in the right hemisphere in PWS were significantly higher than those of left hemisphere, and greater than those of controls. In addition, the right PLFs in PWS were positively correlated with stuttering severity. Phase locking values (PLVs) representing the synchronizations between right and left auditory cortices were significantly higher in PWS than in controls. Increased right hemispheric local phase synchronization with increased inter-hemispheric phase synchronization could underlie the impaired function of left auditory cortex in PWS. Therefore, we suggest that one of compensatory mechanisms in PWS is abnormal synchronization even in basic auditory processing.
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P530
Functional and directed coherence on simultaneous recorded EEG and MEG data during resting state

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Question

In the last years, more and more attempts have been done to increase validity and sensitivity of different methods of neuroimaging using a combination/fusion of methods. This study focuses on the combination of EEG and MEG and tries to describe advantages of each particular method and their fusion.

Methods

Ten healthy adults were investigated using simultaneous recordings of EEG (60 channels, VSM MedTech system) and MEG (256 channel, VSM MedTech) in two resting state condition: with 5 min eyes closed (EC) and 5 min eyes open (EO). Each recording was segmented into a number of 1s-long epochs. The data were analyzed across the following frequency bands: delta (1-3 Hz), theta (4-7 Hz), alpha (8-13 Hz), and beta (14-30 Hz) for each condition. Analysis of power spectrum, Dynamic Imaging of Coherent Sources (DICS) for source analysis, Renormalized Partial Directed Coherence (RPDC) for information flow between sources, and the signal-to-noise ratio (SNR) analysis were performed using FIELDTRIP. All analyses were carried out for EEG and MEG separately and for combined EEG-MEG data sets.

Results

1) Spectral mean power was significantly higher in EEG than in MEG data for all frequency bands; 2) For the source absolute mean power the combined approach had significantly higher power compared to EEG and MEG alone; 3) For comparison between EEG and MEG for both the cortical and sub-cortical sources, there was no significant difference for the number of voxels in sources (p=0.45). However, the combined approach (EEG+MEG) had significantly lower number of voxels activated for both cortical and sub-cortical sources (EEG vs. MEG+EEG: p=0.006; MEG vs. MEG+EEG: p=0.009); 4) During both conditions with EO and EC the direction of information flow for EEG and MEG was not different between the sources. However, the combined approach detected some additional interactions in each of the frequency bands. The RPDC values in all the four frequency bands showed a similar pattern (p=0.004; MEG+EEG>EEG>MEG); 5) On the scalp and source levels, the relative SNR showed significant difference between the three modalities. In all frequency bands the pattern remained similar (p=0.006; MEG+EEG > EEG > MEG).

Conclusion

The combined approach of EEG and MEG fusion may increase validity of results leading to the more focused source reconstruction, better modeling of information flow and higher SNR.
Correlation between impulsivity and auditory sustained field strength measured by magnetoencephalography

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QUESTION

How is impulsivity reflected in brain activities? This question is important for establishing neurotechnological diagnosis of addiction and ADHD. In this study, we examined the relationship between impulsivity (operationalized as "temporal discount rate (k)", the degree of preference for smaller sooner reward over larger later one, with larger k indicating higher impulsivity) and brain activity in sensory cortices by using magnetoencephalography. We found that impulsivity seems to be associated with strength of sustained brain activity when listening to sounds.

METHODS

Twelve healthy adults participated in this study. A behavioral task of time discounting was used to measure individual impulsivity beforehand. Auditory evoked magnetic fields were then recorded with a whole-scalp MEG device from the same participants who were listening to CEG chords with durations of 0.8 and 1.6 s binaurally. Clear sustained fields were recorded from both auditory cortices when the participants listened to the chords. To normalize the amplitude of the sustained fields, the amplitude time-averaged over 0.4–0.8 s from the sound onset (0.8 s in duration) or 0.4–1.6 s (1.6 s in duration) was divided by peak amplitude of evoked responses of N100m.

RESULTS

In group level analysis, time discount rate was positively correlated with normalized amplitude of auditory sustained field (r(10)=0.63, p=0.027 for 0.8 s in duration and r(10)=0.67, p=0.016 for 1.6 s in duration). Significant correlations were found only in the left hemisphere.

DISCUSSION

We previously reported that temporal cognition is related to impulsivity in temporal discounting. Combined with this previous finding, the present results suggest that a sustained field reflects auditory temporal cognition and that their strength are therefore associated with impulsivity.

Acknowledgement

We thank Prof. Riitta Hari and Dr. Elina Pihko of Aalto University for their helpful suggestions in the experimental design and analysis.

Figure caption

Scatter plot showing correlation between time discount rate (k) and normalized amplitude of auditory sustained field.
Abstracts of Poster Presentations – Poster Session 30 – MEG

figure 1

<table>
<thead>
<tr>
<th>Normalized sustained field</th>
<th>Impulsivity (Logged k)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.8</td>
<td>-10</td>
</tr>
<tr>
<td>0.6</td>
<td>-9</td>
</tr>
<tr>
<td>0.4</td>
<td>-8</td>
</tr>
<tr>
<td>0.2</td>
<td>-7</td>
</tr>
<tr>
<td>0.0</td>
<td>-6</td>
</tr>
</tbody>
</table>

Duration: 1.6 s
r=0.67
p=0.016
Task relevant high frequency neuroelectric oscillations in humans

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Question
The objective was to test for the presence of task specific information in high frequency neuroelectric oscillations.

Methods
Magnetoencephalographic (MEG) recordings were obtained from 32 volunteers (13 healthy controls and 19 patients with HIV disease) during performance of a verbal recognition memory task (Fig. 2). Each identified virtual recording was 80 msec in duration (see Fig. 1). Canonical variate time series analysis was used to identify up to 5 resonant oscillations in each. For each oscillation we obtained (1) a well-defined frequency estimate and (2) a measure of synchronicity that ranges from 0.0 (asynchronous) to 1.0 (noiseless sine wave). Only frequency estimates with synchronicity ≥ 0.7 were used for histograms.

Results
- The histograms are highly consistent between subjects and sessions.
- The portions of the histograms from 0 - 150 Hz are similar to those for scalp EEG recordings during simple and choice reaction time tasks and similar in shape to those for the rabbit olfactory bulb during performance of a go/no go olfactory task.
- Comparisons of individuals’ histograms from different cognitive states show significant differences: (a) resting vs task periods and (b) stimulus processing vs motor preparation and response (Fig. 2).

Conclusion
These results demonstrate that high frequency neuroelectric oscillations (i.e. > 80 Hz) are common and are related to cognitive demands. Localization of differential activation and network analysis may provide clues to functions mediated by resonant oscillations.

Literature

Fig 1. These typical waveforms occurred simultaneously at locations 5.5 mm apart. The resonant frequencies are indicated Fig 2 in red/black for the corresponding waveforms. Time scale is 80 msec. Correlation between these 2 waveforms is 0.156.
Fig 2. Typical results from a single volunteer. Blue/magenta indicate processed time segments (left) and corresponding histograms (right). Black/red dots indicate the resonant frequencies for the corresponding waveforms shown in Fig 1.
P532
Pectoralis major and pectoral reflex in patients with amyotrophic lateral sclerosis

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Question

Some ALS patients’ pectoral reflex is active with the biceps reflex and triceps reflex decreased, and the pectoral reflex center is C5-T1, wider than the biceps and triceps reflex. So is the pectoralis major appeared neurogenic damage lately or does the amplitude of the pectoral reflex can indicate the UMND damage?

Methods

1. Choose ALS patients whose pectoral reflex is active and the biceps, triceps reflex are decreased and agreed to do EMG examination. 2. Performed EMG examination in the clavicular part and sternal part of P. major, biceps, triceps and abductor digiti minim respectively, and compared their neurogenic damage; 3. Stimulate Erb dot antidromically and record the amplitude of the pectoral reflex in the clavicular part and sternal part respectively, and standardize data.

Results

1. two parts of P. major are neurogenic damaged but mismatch with the muscles that innervated by the same cervical root. 2. The amplitude of pectoral reflex is increased significantly in the ALS patients.

Conclusions

1. The pectoral major appeared neurogenic damage lately. 2. The increased amplitude of pectoral reflex indicate the UMND damage in the ALS patients with significant upper limb atrophy.
P533

Repeater F-waves are early signs of motor unit pathology in polio survivors

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Question

The characteristics of F-waves in polio survivors remain to be clarified.

Methods

The subjects included 43 polio survivors (polio group), 20 of whom were diagnosed with post-polio syndrome (PPS) and 20 healthy volunteers (control group) who underwent motor conduction studies of the bilateral median and tibial nerves including F-waves elicited by 100 stimuli, and motor unit number estimate (MUNE). F-wave frequency (FF) and the occupancy rate of repeater F-waves (ORF) [total number of repeater F-waves/total number of F-waves × 100 (%)] were calculated. Polio group were classified into four categories based on FF and ORF in the control group: Group A (normal FF and ORF), Group B (normal FF and abnormal ORF), Group C (abnormal FF and normal ORF) and Group D (abnormal FF and ORF). The National Rehabilitation Hospital Classification (NRH) was used to evaluate the severity of flaccid paralysis.

Results

The polio group showed significantly less FF and more ORF in both the median and tibial nerves than the control group (p < 0.0001). The subjects in Groups A and D exhibited milder and more severe classes of NRH, respectively. Few are in Group C. ORF had a negative correlation with MUNE and increased in number followed by the reduction of FF and MUNE with progression of PPS.

Conclusions

F-wave measurement is useful for evaluating severity of PPS. The presence of repeater F-waves is the most characteristic finding and a possible early sign of motor unit pathology in polio survivors.
P534
Motor Unit Number Index (MUNIX) in Amyotrophic Lateral Sclerosis:
a prospective cohort study

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Objective
Assess the clinical value of the novel motor unit number estimation technique MUNIX in quantifying ALS disease progression.

Methods
Fourteen patients (10 men; mean age 63.8 ± 9.8 years), who fulfill ALS diagnostic criteria (8 limb- and 4 bulbar-onset), were prospectively evaluated for 15 months, at 3 months intervals.

In 6 muscles - 3 from upper limbs, 3 from lower limbs - we determined the compound muscle action potential (CMAP), degree of muscular strength (MRC) and MUNIX. For analysis of these variables we considered the sum obtained in the 6 muscles (Megascore). A validated Multiple Point Stimulation Motor Unit Number Estimation (MUNE) technique was applied to the Abductor Digiti Minimi (ADM). The strongest side was selected. ALS Functional Rating Scale (ALSFRS-R) was evaluated in each visit.

Results were compared using Repeated Measures ANOVA and by calculating the rate of progression through time.

Results
All variables showed a significant decrease through time (p≤0.001). Comparing the MUNIX with other variables that assess the global status of the patient (CMAP, MRC and ASLFRS-R), the MUNIX showed the greatest progression (28% at 15 months). Comparing the two MUNE techniques in ADM, the MUNIX showed comparable decay (35% vs. 32% at 15 months).

Conclusion
MUNIX is a fast and reproducible technique that can be easily applied in most proximal and distal muscles. Our results suggest that MUNIX is a sensitive method to quantify disease progression in ALS and a promising biomarker for ALS clinical trials.

figure 1
P535
Cellular therapy in amyotrophic lateral sclerosis. Preliminary results of a phase I/II clinical trial.

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Introduction
Amyotrophic lateral sclerosis (ALS) is an incurable neurodegenerative disease without effective treatment. Murcia team biomedical research institute have shown that cell therapy has neurotrophic effects in ALS animal models. Therefore we designed a clinical trial to test the feasibility and safety of intraspinal and intrathecal infusion of autologous bone marrow mononuclear cells (aBMNCs). Here we present preliminary results of the study for those patients that have reached one-year follow-up.

Material and methods
This is a prospective, randomized, stratified, double blind study that is intended to include 63 patients. In this preliminary report we analyze 26 patients. Inclusion criteria are age between 18-70 years old, diagnosis of definite ALS according to El Escorial criteria, spinal onset and disease duration between 6-36 months, FVC≥50%, and 5% of the total time with oxygen saturation level lower than 90%. Eligible patients were stratified by Sniff nasal and randomized between 3 arms: (A) Infusion of aBMNCs into the spinal cord at T3-T4 level. (B) Intrathecal infusion of aBMNCs. (C) Intrathecal infusion of saline, as control group. We perform a baseline electromyogram, and pretend to do another one year and two years after the start of the treatment. Parameters to be studied are: CMAP of the Intercostal T7, median, ulnar, peroneal and posterior tibial nerves, MCV of the median, ulnar, peroneal and posterior tibial nerves, F Wave latency and persistence of the each nerve studied, presence of fasciculations in first dorsal interosseous muscle, biceps, quadriceps and anterior tibial muscles, recruitment pattern of these muscles. The primary endpoint is the absence of severe treatment-related adverse events (AE) that were graded according to the CTCAE.

Statistical analysis
Qualitative variables are analyzed using test based on the chi-square distribution homogeneity expected to do so when possible and by Fisher exact test values otherwise. To compare quantitative variables ANOVA is performed, for repeated measures with 2 studied factors: intrasubject factor- (starting time and ending time) and intersubject factor-type of treatment: placebo vs intrathecal infusion and intraspinal implant.

Results
26 patients have reached one-year follow-up (11 A, 8 B, 7 C). Parameters like CMAP amplitude and motor nerve conduction velocity of the nerves studied of each arm decrease with the time. There is a trend close statistical significance of similar behavior between the arms that receive aBMNCs. There is no difference between these two arms. Emphasizes the increased incidence of fasciculations in the biceps muscle.

Conclusions
- Intraspinal implant and intrathecal infusion of aBMNCs in patients diagnosed with ALS are safe and feasible.
- No major complications or significant morbidity is observed.
- Stem cells could modify the characteristics of the F response and the incidence of fasciculations.
- None of the other parameters were influence by cell implant.
- We do not have conclusive statistical evidence that cell therapy alter the natural course of the disease.
- Is necessary another analysis once the study has progressed, to confirm or reject the trends we have found nowadays.

Acknowledgement
This work has been supported by EC10-023 and EC11-288 grants from the Department of Pharmacy and Health Products of the Ministry of Health, Social Services and Equality and RD12/0019/0001 grant from Carlos iii Institute of Health. Spain.
P537
Spreading of amyotrophic lateral sclerosis lesions—multifocal hits and local propagation?

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Objective

To investigate whether or not the lesions in sporadic amyotrophic lateral sclerosis (ALS) originate from a single focal onset site and spread contiguously by prion-like cell-to-cell propagation in the rostrocaudal direction along the spinal cord, as has been hypothesised (the ‘single seed and simple propagation’ hypothesis).

Methods

Subjects included 36 patients with sporadic ALS and initial symptoms in the bulbar, respiratory or upper limb regions. Patients with complicating lumbar spinal disease and any other neuropathies were excluded by MRI and nerve conduction studies. Abnormal spontaneous activities in needle electromyography (nEMG)—that is, fibrillation potentials, positive sharp waves (Fib/PSWs) or fasciculation potentials (FPs)—were compared among the unilateral muscles innervated by different spinal segments, especially between the T10 and L5 paraspinal muscles, and between the vastus medialis and biceps femoris. Axon length and the proportion of muscle fibre types, which are both related to motoneuronal vulnerability in ALS, are similar in the paired muscles.

Results

Fourteen of 36 patients showed a non-contiguous distribution of nEMG abnormalities from the onset site, with skipping of intermediate segments. In eight of them, the non-contiguous pattern was evident between paired muscles with the same motoneuronal vulnerability. FPs, known to precede Fib/PSWs, were shown more frequently than Fib/PSWs in all the lumbosacral segments but L5.

Conclusions

In sporadic ALS, the distribution of lower motoneuron involvement cannot be explained by the ‘single seed and simple propagation’ hypothesis alone. We propose a ‘multifocal hits and local propagation’ hypothesis instead. The 2nd hit seems to occur at L5 and then spread to neighbouring lumbosacral segments.
Amyotrophic lateral sclerosis affects cortical and subcortical activity underlying movement execution and inhibition

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Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by loss of upper and lower motor neurons. Evidence suggests that ALS additionally affects other brain areas including premotor cortex and supplementary motor area. We studied movement execution and inhibition in ALS patients using a stop-signal paradigm and functional magnetic resonance imaging (fMRI).

Methods

Seventeen ALS patients and 17 age-matched healthy controls were included. Participants performed in a stop-signal task that required responding with button press to a right- or left-pointing black arrow (go-stimuli). In stop-trials, a red arrow (stop-stimulus) was presented shortly after the black arrow indicating to withhold the prepared movement. A total of 512 trials were presented (25% stop-trials). Magnetic-resonance images were acquired on a 3-T Siemens Magnetom Scanner.

Results

Patients had marginally higher reaction times in go-trials, but did not differ significantly in their inhibition performance. ALS patients showed however stronger inhibition-related activity in inferior, superior and middle frontal gyrus as well as in putamen and pallidum. Error-related activity on the other hand was found to be stronger in healthy controls, particularly in the insula bilaterally. In go task we found execution related increase of the activated area in contralateral sensorimotor cortex in ALS patients.

Conclusions

ALS patients and controls showed specific differences in neural networks underlying motor execution, motor inhibition and error monitoring. The results provide further evidence for altered prefrontal functions in ALS.
P539
An original method to investigate the origin of the fasciculation potentials

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Question

The origin of fasciculation potentials (FPs) in amyotrophic lateral sclerosis (ALS) and in benign fasciculation syndrome (BFS) remains controversial. We used a novel technique to investigate the origin of the FPs in benign fasciculation syndrome and in patients with ALS.

Methods

We studied 52 patients (29 men and 23 women) aged 36-75 years (mean 59.6, SD 10.1y) clinically suspected as suffering from ALS, referred for diagnostic testing. All patients progressed to ALS. We also included 11 patients with BFS, aged 38-70 years (mean 58.5, SD 11.7y), these patients had normal strength and their EMG showed normal MUP analysis, there was no progression to other disorders in the following two years. All ALS patients included had normal muscle strength of at least one tibialis anterior muscle; they were classified according MUP analysis of the investigated tibialis anterior. We recorded FPs in tibialis anterior using two separate concentric needle electrodes, ensuring by slight voluntary contraction and by electrical nerve stimulation that each electrode recorded motor unit potentials innervated by different axons. The relative number of time-locked versus independent FPs was recorded.

Results

Thirty-two of the 52 ALS patients showed neurogenic change in the TA muscle. In these patients 5-146/patient (mean 34.3+32.5) FPs were recorded - total 1096. In the 20 TA muscles without neurogenic change 5-97/patient (mean 28.1+25.4) FPs were recorded - total 544. In patients with BFS, 5-43 FPs/patient (mean 21.3+13.0) were recorded - total of 234. Time-locked FPs recorded by both electrodes were most frequent in benign fasciculation syndrome (44%) and ALS without reinnervation (27%), but reinnervation (abnormal MUP analysis) in ALS was associated with fewer time-locked FPs (14%).

Conclusions

These observations suggest that in chronic partial denervation FPs are more likely to arise distally and that FPs in benign fasciculation syndrome more frequently arise proximally. The origin of FPs, so characteristic of ALS, is relevant in defining the physiological abnormality in motor units in ALS, as distinct from other disorders.
**P540**

TRANSCRANIAL MAGNETIC STIMULATION IN AMYOTROPHIC LATERAL SCLEROSIS. PREDICTIVE DIAGNOSTIC VALUE

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**Question**

Amyotrophic lateral sclerosis (ALS) is a disease characterized by upper and lower motor neuron involvement. While lower motor neuron may be assessed by electrophysiological examination, upper motor neuron is required to be demonstrated clinically. Despite the recognized difficulty to evaluate upper motor neuron signs in patients with lower motor neuron involvement, transcranial magnetic stimulation (TMS) has not still been included in recent diagnostic criteria of ALS. We analyze the results of TMS in a group of ALS patients, and evaluate their sensitivity and predictive value.

**Methods**

We retrospectively review patients with ALS studied in our laboratory during last 5 years. We selected those patients with transcranial magnetic stimulation performed during electrophysiological study. We evaluated amplitude of motor evoked potentials and central motor conduction time (CMCT) abnormalities.

**Results**

Thirty patients with ALS were included in the study (range ages between 35 and 78 years), including sporadic and familial forms. Mild increase of CMCT was the most frequent abnormality in sporadic ALS patients, while severe increase was detected in familial ALS ones. Abnormalities of TMS preceded clinical pyramidal signs in some cases. Sensitivity and predictive diagnostic value were calculated.

**Conclusions**

Transcranial magnetic stimulation is a useful method to assess upper motor neuron, and its implementation in the diagnosis of ALS can increase diagnostic sensitivity and proves to be a good predictor of corticospinal involvement.
P541
The impact of Spinal Muscular Atrophies with regard to patients’ quality of life: A socio-economic analysis of a German patient cohort

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Objective

Spinal Muscular Atrophies (SMA) represent a group of incurable fatal inherited motor neuron disorders. Disease progression and severity differs according to SMA subtype. Infantile forms significantly reduce life expectancy whereas others lead to progressive disablement with reduced working capacity and high health care utilization. Socio-economic analyzes for SMA are missing but urgently needed regarding innovative therapies and current mandatory health care evaluations. In this study, we evaluate the disease-related consumption of resources (CoR) from a health economic perspective to assess the impact of different types of disease severity on patients’ quality of life (QoL).

Methods

Subtype-specific questionnaires were sent to patients using an established German patient registry. In order to determine the CoR we followed a dualistic approach by applying a micro-costing method to retrospectively examine the direct and indirect cost as well as socio-demographic factors to evaluate the burden of SMA on patients, relatives and society. The current QoL was analyzed using a disease-specific questionnaire.

Results

265 patients aged 0 to 65 years were included into our study comprising SMA subtypes 1 to 3. Our survey resulted in a response rate of 71,7%. Based on current care standards the CoR of patients and their relatives was analyzed and referred to the patients’ QoL. Results suggest a strong connection between CoR and QoL implying options for reducing cost of illness as well as improving both quality of therapy and patients’ QoL.

Conclusion

This study is a first step to evaluate SMA from a health economic perspective. It reveals the demanding character of SMA to patients, families and caregivers. Concerning emerging innovative therapies, an interdisciplinary assessment of both the clinical and health economic situation may support translation of clinical research results to clinical practice. Furthermore, the project contributes to a more comprehensive understanding of health care delivery issues related to neuromuscular diseases in general.
P542
Electrophysiological Evaluation of Respiration-Swallowing Relationship in Amyotrophic Lateral Sclerosis Patients

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Question
Could electrophysiology evaluate respiration-swallowing incoordination in ALS patients with bulbar involvement?

Methods
93 ALS patients and 31 normal controls were included. ALS patients were subgrouped as; bulbar normal (N), bulbar upper motor neuron involvement (UMN), both bulbar upper and lower motor neuron involvement (Mixed). ‘Single Bolus Analysis’, ‘Dysphagia Limit’, Sequential Water Swallowing’, ‘Simultaneous SWS-Respiration Recording’, ‘Spontaneous Respiration and Apnea with Command’ were applied. Vertical laryngeal movement was recorded via piezoelectric sensor, submental EMG via surface electrodes, nasal air flow via nasal sensor. Signals were filtered, rectified. Delay-line technique was used.

Results
Mean age of ALS patients (36F, 57M) was 58,2±1,0±10,6(27-78); mean age of normal controls (18F, 13M) was 52,6±1,6±9,0(34-74). There were 12bulbarN, 40UMN, 41Mixed patients. DL was abnormal in %58,3 of bulbarN, %87,5 of UMN. Absolute apnea during swallowing was defined as ‘preserved respiration-swallowing relationship’. Apnea of controls and 59ALS cases were absolute. Of the apneae with 3 or more cessations, %82 were Mixed. Two groups due to cessation of apnea were defined; absolute vs interrupted. The most significant difference was in Mixed group; in swallowing rate (p<0,01) and swallowing time (p<0,01). There were no statistically significant difference inbetween respiratory parameters (p>0,05).

Conclusions
The study detected subclinical dysphagia in bulbarN and UMN patients even without clinical signs/symptoms. It emphasized the role of dysphagia more than dyspnea in cessation of apnea during swallowing, so called as respiration-swallowing incoordination. Cause apnea was frequently interrupted in Mixed group, ‘bulbar’ swallowing center should be underlined. In conclusion, electrophysiological studies, not only give important clues about pathophysiology but also help early diagnosis of respiration-swallowing incoordination and aspiration risk in ALS patients.
Corticospinal excitability in amyotrophic lateral sclerosis and frontotemporal dementia patients

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Question

Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) tend to overlap. Transcranial magnetic stimulation (TMS) in ALS indicates hyperexcitability of motor cortex in early disease stage, followed by reduced excitability later in the disease course. So far there have been only few studies considering neurophysiological assessment of motor system in FTD.

The aim of the study was to evaluate corticospinal excitability in ALS and FTD patients.

Methods

33 ALS patients, 18 FTD patients and 27 controls were subjected to single pulse TMS study. In 18 ALS patients and 11 FTD patients the study was repeated after several months.

Results

Motor evoked potential (MEP) amplitude was reduced in both patient groups as compared to controls (p<0.001 ALS vs. controls, p<0.05 FTD vs. controls). Contralateral silent period was significantly shorter in ALS patients than in controls and FTD patients (p<0.05). Central motor conduction time was prolonged in FTD patients compared to controls (p<0.05). Within ALS group, motor cortex excitability was substantially reduced in patients with more severe clinical signs. In FTD group, there was a negative correlation between duration of the disease and MEP amplitude (R=-0.53, p<0.05). Repeated evaluation demonstrated increased resting motor threshold (RMT) and reduced MEP amplitude in ALS patients (p<0.01) and increased RMT in FTD patients (p<0.05).

Conclusions

The study revealed impairment of corticospinal excitability in ALS advancing along with disease progression. It also demonstrated subclinical involvement of corticospinal pathways in FTD patients and a tendency towards reduction of corticospinal excitability in FTD over time.
P544
Cortical Hyperexcitability of the Thenar Group of Intrinsic Hand Muscles may contribute to the Split-Hand Sign in ALS

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Objective

Preferential wasting of the thenar group of intrinsic hand muscles including the abductor pollicis brevis (APB) and first dorsal interosseous (FDI) termed the split-hand sign, has been described as a specific feature of Amyotrophic Lateral Sclerosis (ALS). Greater corticomotoneuronal input to the thenar intrinsic hand muscles has been proposed as one of the pathophysiological mechanisms underlying the split hand sign and consequently difference in cortical excitability between the thenar and hypothenar intrinsic hand muscles was assessed in the present study, in a group of ALS patients and age matched healthy controls.

Methods

Cortical excitability was recorded using the threshold tracking transcranial magnetic stimulation (TMS) technique from the APB, FDI and abductor digiti minimi (ADM) muscles in 26 Awaji Criteria possible/probable ALS patients (17 male; 9 female; mean age 58.6 ±1.9 years. Results were compared with 21 age matched healthy controls.

Results

Short interval intracortical inhibition (SICI) was globally reduced (P<0.005) in ALS patients along with significant reduction in the cortical silent period (CSP) specifically over the APB and FDI (P<0.05) muscles. Preferential hyperexcitability of the thenar group of muscles in ALS was further evidenced by greater reduction in normalised values for SICI recorded over the APB (98.1%) and FDI (81.8%) in comparison with the ADM (73.2%).

Conclusion

Global increase in cortical excitability in ALS with is further characterised by a preferential increase in cortical excitability of the APB and FDI muscles which may underlie the clinical split-hand sign.
P545
Selective membrane potential abnormality as a potentially useful early biomarker in ALS.

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Introduction

In ALS patients, peripheral ion channel abnormality and membrane potential changes often exist. A recent study suggests selective membrane depolarization in some ALS patients. We performed the threshold tracking test in patients with upper motor neuron dysfunction.

Patients

Patient 1 is a 52-year-old man, whose chief complaint was gait disturbance for four years. He had no muscle weakness or fasciculations. Deep tendon reflexes (DTR) were exaggerated. The median CMAP amplitude was decreased (2.89mV). EMG was normal except for multiplet of the quadriceps femoris.

Patient 2 is a 69-year-old woman, whose chief complaint was dysarthria for two years. She had no muscle weakness or fasciculations. DTRs were exaggerated and jaw reflex was positive. Needle EMG showed chronic denervation only in the tongue.

Patient 3 is a 52-year-old woman, whose chief complaint was dysarthria for four months. Her strength was normal. DTRs were exaggerated and jaw reflex was positive. Needle EMG showed fasciculations in TA and biceps brachii with mild chronic neurogenic changes. She had no fibrillation and positive sharp waves.

Result

Three patients did not fulfill the diagnostic criteria of ALS. We did threshold tracking in the median motor nerve. Target threshold CMAP amplitudes were set at 10, 20, 40 and 60% of the maximum CMAP. Three patients showed normal TE (threshold electrotonus) at 40%. The threshold changes by the hyperpolarizing current was small at the low target levels that suggests membrane depolarization.

Conclusion

Selective membrane abnormality may precede overt clinical and routine electrophysiological findings in motor neuron disease.
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P546
Comparison of motor unit number index(MUNIX) between abductor digiti minimi and tibialis anterior muscles in ALS patients and control subjects

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Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by progressive loss of motor neuron. Motor unit number index (MUNIX) is a novel diagnostic technique developed to quantify the axonal loss in nerve of the ALS patients. There are some reports that showed reproducibility and feasibility of MUNIX in ALS patients. However, the muscles tested were limited to a few small sized muscles such as abductor digiti minimi (ADM). The objective of this study was to establish the usefulness of the MUNIX of the large muscle in lower extremities using tibialis anterior (TA) muscle compared to ADM muscle in ALS patients and normal controls.

Methods

MUNIX was performed on bilateral ADM and TA muscles in 30 ALS patients and 27 normal controls. MUNIX, compound muscle action potential (CMAP), Medical Research Council (MRC) sum score, and ALS functional rating scale (ALSFRS) were evaluated and their correlation was calculated using Pearson correlation analysis.

Results

There was a significant correlation between MUNIX and CMAP amplitude in both ADM ($r = 0.918$, $P < 0.01$) and TA ($r = 0.850$, $P < 0.01$) muscles in ALS patients. In normal controls, there was also significant correlation between MUNIX and CMAP amplitude in both ADM ($r = 0.629$, $P < 0.01$) and TA ($r = 0.894$, $P < 0.01$) muscles. In ALS patients, MUNIX was significantly correlated with the ALSFRS in ADM ($r = 0.439$, $P = 0.015$), but not in TA ($r = 0.357$, $p = 0.053$). There was a significant correlation between MUNIX and MRC sum score in both ADM ($r = 0.349$, $P = 0.058$) and TA ($r = 0.474$, $P < 0.01$).

Conclusions

This study has shown that MUNIX of TA muscle can be used to evaluate the degree of axonal loss. The pattern of correlation from MUNIX of TA muscles was not much different from that of ADM muscle. Therefore, MUNIX technique could be performed in large muscles in lower extremities. Further prospective, follow-up study with more patients will be needed to confirm the result of this study.
Clustering of discharges in the firing of fasciculation potentials

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**Question**

Fasciculation potentials (FPs) have been considered to be a characteristic feature of amyotrophic lateral sclerosis (ALS) that is useful for its diagnosis. Correct identification of FPs depends on the recognition of their characteristic firing pattern. The authors have argued that the clustering of discharges, lasting around 1 second, is a characteristic marker of FPs, which had not been verified so far.

**Objectives**

To investigate whether there is a clustering of discharges in the firing pattern of FPs in ALS patients.

**Methods**

Subjects were 11 ALS patients in whom needle electromyography revealed profuse FPs in investigated muscles. Evaluated activities were 17 records of spontaneous activities, 5 from triceps brachii, 4 from trapezius and biceps brachii, 3 from vastus medialis, and 1 from tibialis anterior muscles. Signals stored using data recorder were restored and the timing of the FP firing was read off. For each firing, the time elapsed from the just previous firing (t) was used as a primary parameter. FPs having different shapes were not discriminated and were considered all together in this study. Breakpoint (T) was variously postulated for t, and the instantaneous firing probability of FPs was calculated for the period before T and after T, respectively, using the maximum-likelihood method for estimating the exponential distribution. The firing probabilities before T and after T were compared and the t-value was calculated. When the firing probability before T was significantly higher than that after T, it was judged that a clustering of FPs occurred.

**Results**

Among 17 records investigated, eight records showed significantly higher firing probability for the period before T than that after T when T was set at certain lengths from 0.2 to 2.0 s, indicating the clustering of FP firing during this period. Mean firing interval of FPs for investigated records were 2.6±2.2 s (range 0.3-7.8). All 8 records with significant clustering of FPs had mean firing interval shorter than 2.6 s, indicating that this phenomenon occurs for activities with higher firing frequency.

**Conclusion**

FPs with higher firing frequency tend to show clustering of discharges. This clustering phenomenon might be caused by membrane instability of distal motor axons in ALS.
P548
SMA I. Review of sensory involvement in neurophysiological studies in our cohort.

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Question
To review sensory and motor conduction abnormalities in 11 patients with homozygous deletion of SMN 1, who were diagnosed of spinal muscular atrophy, during the first year of life, in our hospital in the last 17 years: 9 with SMA I and 2 with SMA II.

Methods
Motor conduction velocities were obtained in all patients at median or ulnar nerve and at posterior tibial nerve. The sensory nerve conduction studies were performed at median or ulnar nerve by orthodromic technique and at the medial plantar nerve stimulating the mixed nerve at the plantar level, or stimulating the sural nerve antidromically. Patients were compared to age-matched controls for motor and sensory conduction.

Results
Only one patient had abnormal sensory evoked potentials in all nerves, with amplitude decrease at median and ulnar sensory nerves but with normal conduction velocities and absence of mixed plantar nerve response. 5 patients showed isolated motor nerves with slowed conduction velocities, but not a clear demyelinating neuropathy. And CMAP amplitude was reduced in the majority of nerves examined.

Conclusions
The incidence of sensory abnormalities in SMA I is low, and in our cohort represented the 11% of patients.

The existence of a severe sensory-motor axonal neuropathy in neurophysiological studies does not exclude the diagnosis of spinal muscular atrophy and is described in infants with severe SMA who are symptomatic at birth.
**P915**

**Longitudinal motor unit number estimation in a spinal muscular atrophy cohort**


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**OBJECTIVE**

To assess motor unit number estimates (MUNE) over time in a cohort of children with Spinal Muscular Atrophy (SMA).

**METHODS**

We conducted a prospective cohort study of 62 children with SMA type 2 and 3 (SMA 2/3) with follow-up for up to 42 months. We collected longitudinal neurophysiological data including compound motor action potential (CMAP) and MUNE recorded from the abductor digiti minimi (ADM) using the multiple point stimulation method to ascertain the single motor unit potential (SMUP) amplitudes. Clinically, we evaluated motor function, pulmonary function and muscle strength. Data were analyzed for associations between neurophysiological and clinical characteristics, and for change over time.

**RESULTS**

In cross-sectional analyses at baseline, MUNE and CMAP were associated with motor function, i.e. they were lower in SMA 2, intermediate in non-ambulatory SMA 3, and highest in ambulatory SMA 3 participants. SMUP was higher in non-ambulatory, and lower in ambulatory participants. In longitudinal analyses, there was a significant mean increase in MUNE over time (4.92 units/year, CI 1.26-8.57, p100, and SMUP amplitudes were higher (>100 to 400µV range) in those with lower MUNE (≤100).

**DISCUSSION**

As expected, SMA 2 compared to SMA 3 participants had lower motor and pulmonary function, weaker muscle strength, and lower mean MUNE and CMAP amplitudes. There was a moderate association between MUNE and functional outcomes. The greater SMUP amplitude size in those with lower MUNE indicates collateral re-innervation or myofiber hypertrophy. The longitudinal finding of decrease in mean SMUP amplitude and increase in MUNE over time, especially in 5-10 year olds, is unexpected and differs from a previous observation of decline in MUNE over time. It suggests the possibility that young SMA subjects may still be in a growth phase when motor units continue to develop. It is hoped that our data can help further the understanding of disease biology in SMA, and can be useful in evaluating MUNE as potential biomarker in clinical trials.
P549
Diagnostic value of the Bereitschaftspotential in hyperkinetic movement disorders

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Question

What is the diagnostic value of the Bereitschaftspotential (BP) in hyperkinetic jerky movement disorders? In addition, the value attributed to the BP by an expert panel during clinical decision making is assessed.

Methods

A cross-sectional case series of 48 patients with psychogenic jerks, Gilles de la Tourette (GTS) or myoclonus was investigated. We measured the BP prior to the spontaneous jerk and a voluntary wrist extension task. In addition, the various jerky movements were imitated by 25 healthy subjects.

Results

In patients with psychogenic jerks, we observed significantly more BPs, however the BP was absent prior to self paced wrist extensions. In contrast, none of the patients with the clinical diagnosis of myoclonus had a BP prior to jerks but did have a BP prior to intentional wrist extension. In GTS in a minority of cases we demonstrated a BP preceding motor tics with a shorter duration in comparison to patients with psychogenic jerks. In healthy control subjects a BP was found preceding all movements in all cases. The absence of a BP prior to intended wrist extension had a sensitivity of 0.59, specificity of 0.98 and a positive likelihood ratio of 25 for the diagnosis of psychogenic jerks. Preliminary results of the attributed value of the expert panel to the BP will be presented at the congress.

Conclusions

Patients with psychogenic jerks significantly more frequent have a BP prior to the jerks and with a significantly earlier onset compared to GTS patients. An additional finding is the absence of a BP prior to intentional movements in patients with psychogenic jerks.

Part of this data was published as Van der Salm et al. JNPP 2012 83(12):1162-7
P550
Pathophysiology of an unusual hemi-dystonia hemi-parkinsonism syndrome: a longitudinal follow-up study

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Question
Different from genetic dystonia-parkinsonism that usually presents parkinsonism and dystonia symptoms simultaneously, a 44-year-old woman presented insidious onset of progressive parkinsonism in the left limbs and torsion dystonia in the right limbs and neck. Levodopa did not improve parkinsonism, but worsened dystonia and induced dyskinesia. We aimed to answer the pathophysiology of the unusual hemi-dystonia hemi-Parkinsonism syndrome.

Methods
We studied the motor cortical excitation and inhibition, LTD-like plasticity, depotentiation and premotor-motor connectivity with transcranial magnetic stimulation, the brainstem blink reflex recovery cycle (BR) and the spinal reciprocal inhibition (RI) at four time points between 2009 and 2013.

Results
Initially, dystonia pathophysiology was found in the left cortex and right forearm: excessive plasticity, delayed depotentiation, reduced premotor-motor connectivity and short-interval intracortical inhibition (SICI) and reduced 2nd and 3rd RI phases. In contrast, parkisonian pathophysiology was seen in the right cortex and left forearm: reduced plasticity, normal SICI and premotor-motor connectivity and reduced 3rd RI phases. BR was normal in either left or right supra-orbital stimulation. As parkinsonism spreading from left to right in 2013, both hemispheres showed decreased plasticity and SICI while both forearms presented reduced 2nd and 3rd RI phases.

Conclusion
The results suggest different pathogeneses for hemi-dystonia in one side of the body and hemi-parkinsonism in the other. As the disease evolved, the physiology transformed to present cortical parkinsonism phenomena and spinal dystonic disinhibition. These clinically matched findings are helpful for understanding the underlying pathophysiology of the disease and for monitoring the disease progress.
Brain Nervous development and Neurorestoratology of Children with Cerebral Palsy by Acupuncture

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**Aim**

To investigate action and value of acupuncture in Cerebral Palsy rehabilitation.

**Methods**

200 spasm Cerebral Palsy patients from 1 to 7 years old were randomly divided into two groups. Acupuncture group: 100 patients were treated with head acupuncture and body acupuncture; Rehabilitation-training group: 100 patients were treated with physical therapy of Bobath methods.

**Results**

The total effective rate acupuncture and rehabilitation-training group were obvious higher than that of rehabilitation-training group. After treatment the DQ value of rehabilitation-training + acupuncture group were higher than that of rehabilitation group (p<0.01). In acupuncture and rehabilitation-training group, improvement rate of brain dysphasia, brain atrophy in skull CT and recovery normal rate of skull.

**Conclusions**

Acupuncture can obviously increase cerebral blood flow and improve cerebral cell metabolism, promote partial or complete compensation of cerebral function and the restoration and function of plasticity of cerebral tissue in children with cerebral palsy.
Mirror Movements associated with partial agenesis of the Corpus Callosum: the role of ipsilateral motor cortical control

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Mirror movements are involuntary movements executed by homologous muscles during voluntary movements of one side of the body which are mirror reversals with respect to the intended contra lateral movements. This is a case report evaluated a 14 years old right handed Danish boy with mirror movements noticed by his mother since the age of 2 years.

Neurological examination confirms the presence of these involuntary movements on upper limbs muscles more than the lower limbs muscles.

Surface EMG of both right and left Thenar muscles were recorded simultaneously. Interference EMG pattern were studied during maximum voluntary contraction and sub maximal voluntary contraction of the dominant side and the non-dominant side of the body. Mirror movements were seen more with increasing efforts of contraction. It has been noticed that more motor units were recruited with increasing contraction force bilaterally indicating the role of ipsilateral motor control in the initiation and execution of the mirror movements.

The MRI of the brain has proved Corpus Callosum congenital partial agenesis.

The role of ipsilateral motor cortical control of muscular movements has been discussed and the possible neural mechanism inducing these mirror movements has been suggested in respect to the MRI and surface EMG results.

References


figure 1

figure 2
P554  
Propranolol and essential tremor: a central mechanism of action?

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Question

Essential tremor (ET) is the most common tremor disorder and effectively treated with propranolol in 50% of the cases. It has been hypothesized that tremorolytic action is mediated by beta-adrenoceptors located in the deep peripheral muscle compartments, possibly in the muscle spindles (1). Another postulated mechanism is through receptors in the central nervous system. We hypothesize that if there is a peripheral cause, stretch reflexes would be altered in patients taking propranolol. A central mechanism of action would alter the suprasegmental control of muscle tone and long-loop reflexes in these patients. By applying continuous perturbations and ramp-and-hold stretches with a wrist manipulator, we set out to test these hypotheses.

Methods

Propranolol-sensitive ET patients were tested on and off propranolol medication. Continuous perturbations during active (‘resist’, AC) and passive (‘do not intervene’, PC) conditions were applied by a wrist manipulator to assess control of tone of the lower arm extensor and flexor muscles and analyzed by comparison of effective stiffness determined from the low-frequency responses (0.4 - 0.67 Hz, N=12)(2). To assess the stretch reflex, the wrist manipulator applied nine ramp-and-hold muscle stretches (N=22). The two elicited EMG responses, M1 and M2, in the lower arm flexor muscles were averaged.

Results

Preliminary comparison of the effective stiffness during continuous perturbations suggests a trend towards higher gain during PC, and a lower gain during AC in patients on propranolol treatment compared to off treatment (fig. 1). No significant effect of treatment on mean background averaged M1 and M2 reflex responses was observed (mean on/off propranolol: M1: 30.2/31.4 (SD 6.5/6.9), M2: 44.6/41.8 (SD 8.8/9.1).

Conclusions

Preliminary results show a trend towards improvement of central modulatory control of muscle tone in ET patients using propranolol, by means of a decreased muscle tone in the passive condition and an increased muscle tone during the active condition. The absence of an effect on muscle stretches supports the hypothesis that the mechanism of action is not located in the peripheral muscle compartments. Further understanding of the mechanism of action of propranolol will help future development of more specifically targeted drugs.

References:

P555
The role of primary motor cortices in awareness of intention to move studied by repetitive TMS

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Introduction
Libet (1983) found that the awareness of wanting to move appears 200 ms before the movement onset by using the fast-rotating clock task (Libet's clock task). Previous lesion and neuroimaging studies showed that the fronto-parietal network including the medial frontal and parietal cortices play a key role in awareness of motor intentions. However, it is not known whether primary motor cortex (M1) is essential for generating a conscious intention to move.

Objective
To elucidate the functional role of M1 the awareness of motor intention, we used transient suppression of focal neural processing induced by low-frequency rTMS.

Method
Ten right-handed healthy volunteers participated in the study. The experimental paradigm was based on that of Libet (1983). Subjects were asked to report the position of the clock's hand at the time they pushed the button (M-judgment) or at the time they first became aware of their intention to move (W-judgment). We applied 0.9 Hz rTMS (1200 total pulses) over individually determined bilateral M1 to suppress cortical activity and measured subsequent task performance before, immediately after and 15 minutes after rTMS. Sham TMS was also used for the control condition.

Result
In W-judgment task, rTMS over the left M1 significantly prolonged the duration immediately after rTMS and recovered to baseline 15 minutes after rTMS. On the other hand, rTMS over the right M1 or sham TMS did not show any significant effect.

In M-judgment task, rTMS over the bilateral M1 and sham TMS had no effect on task performance.

Conclusion
Our results suggest the functional relevance of the left M1 for the awareness of the intention to move using the right hand. It is likely that the longer duration might be required for the motor intention to reach the threshold of awareness due to the suppression of M1 function. Another possibility is that the rTMS over the left M1 might induce the delay in the feedback processing which might disturb the conscious confirmation of motor execution.
Event-Related Potentials Elicited in a Motor Imagery Task in Children with Unilateral CP Reveal Motor Imagery Capacity with respect to the Unaffected, but not the Affected Hand

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Evidence indicates that motor deficits in Cerebral Palsy (CP) are not only related to problems with movement execution, but also to impaired motor planning. Motor Imagery (MI) is a cognitive process in which the representation of a movement sequence is internally reproduced and is thus closely related to motor planning.

In the current Event-Related Potential (ERP) study, the MI ability of children with unilateral CP and a control group were investigated by means of the Parson’s Hand Laterality Judgment (HLJ) task, a commonly employed task to study MI.

ERPs elicited by rotated hand stimuli contained the classic Rotation Related Negativity (RRN). The RRN was more marked for laterally rotated hand stimuli than for medially rotated stimuli, indicating that an MI strategy was used to solve the task. In the control group this effect was found for stimuli depicting both hands. For CP children, however, this effect was only found with stimuli depicting the non-affected hand. Behavioral data revealed a different speed-accuracy trade-off for children with CP compared to the control group. Children with CP tended for higher accuracy and decreased response speed with respect to the affected hand whereas control children tended to lower accuracy and increased RTs for the non-preferred hand.

Together, these results indicate that in CP children MI capacity is not an abstract, unified cognitive capacity but relies on the specific motor capacities of the body parts involved in the imagined movements at hand. This finding emphasizes the strong embodiment of the cognitive operations involved in MI.
Cardiovascular autonomic functions in idiopathic Parkinson's disease- pre and post bilateral STN-DBS

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Background

Cardiovascular autonomic abnormalities, especially orthostatic hypotension are the major cause of morbidity in late stages of idiopathic Parkinson's disease (IPD) and can be worsened with dopaminergic drugs. The effect of deep brain stimulation of bilateral subthalamic nuclei (STN-DBS) on autonomic functions is not clearly known with different studies showing varying results.

Objective

To evaluate the effect of STN-DBS on cardiovascular autonomic functions in patients with IPD at 1 year follow up.

Methods

It is a longitudinal observational study from 2009-2011. 20 patients with IPD who underwent bilateral STN-DBS were evaluated prior and 12 months after operation. Autonomic function testing was done after stopping anti parkinsonian medication for at least 6 hours and in patients who had undergone STN-DBS, the stimulator was also switched off for half an hour prior to testing. All patients were evaluated with the following tests using WR works software - heart rate variation to deep breathing, BP response to standing, heart rate variation to Valsalva, heart rate response to standing and diastolic blood pressure to hand grip. Patients were graded as per Ewing's criteria into normal, early, definite and severe autonomic dysfunction.

Results

20 patients with mean age (year) of 51.3+8.8, disease duration of 8.9+ 4.4 years and M:F ratio of 60:40 were included. Mean UPDRS in ‘off’ state was 50.7+9.2 and in ‘on’ state was 12+2.8. On autonomic function evaluation, the number of patients with normal, mild, definite and severe abnormalities prior to stimulator implantation were 30%, 45%, 10% and 15% and at 1 year after implantation were 10%, 25%, 40% and 25% respectively which was not statistically significant.

Conclusions

There was no worsening in cardiovascular autonomic functions at 1 year follow up in patients with bilateral STN-DBS. STN DBS may have a beneficial role by reducing dopaminergic dosage.
P559
Elucidating brain networks involved in essential tremor by EMG-fMRI

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Question
Essential tremor (ET) is the most common tremor characterized by an isolated postural tremor of the upper extremities. Despite its commonness, surprisingly little is known about the specific tremor generators in ET. We investigated the brain network involved in tremor generation in a homogeneous group of ET patients using simultaneously recorded electromyography and functional Magnetic Resonance Imaging (EMG-fMRI).

Methods
In total, 38 propranolol-sensitive ET patients with familial upper limb tremor, were included. Only patients with a proven effect of propranolol and tremor present in the EMG spectrum during scanning (without medication), were included in the final analysis (N=23). fMRI tasks consisted of alternating 30 second periods of rest and hand and arm extension with the right arm. EMG was recorded from five (right) fore arm muscles and three (left) fore arm muscles (to verify the absence of left arm movement). EMG power variability of the three most tremulous muscles of the right arm was averaged around the individual tremor frequency and, after MR artifact correction, used as regressor, orthogonalized with respect to the motor task (van Rootselaar et al., 2007), in SPM 8.

Results
We found that unfiltered, unrectified corrected EMG is the most sensitive representation of power variability during scanning. A preliminary fixed-effects analysis of 8 patients showed widespread activation, primarily in the bilateral primary motor cortex, supplementary motor area, superior temporal cortex, bilateral thalamus and right cerebellum (Fig. 1, T=4.7, p<0.05 (FWE), k=100). The final group analysis will be presented at the conference.

Conclusions
Postural tremor in ET is associated with activation in the motor circuit, including bilateral cerebellar activations. In contrast, arm and hand extension correlates with ipsilateral cerebellar activations. These preliminary findings reconfirm earlier findings that the bilateral cerebellum is involved in ET (Bucher et al., 1997).

References

figure 1
Gait analysis after subthalamic stimulation in patients with Parkinson disease

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**Question**

Gait disturbances are a frequent cause of disability in the patients with advanced idiopathic Parkinson’s disease (IPD). Regardless of the improvement of the symptoms after treatment with subthalamic deep brain stimulation (STN DBS), there is some controversy about its effects on instability and gait disturbances.

**Methods**

We have studied 26 IPD patients in advanced stage without axial disability, whose main symptoms were bradikynesia, rigidity and tremor, with good response to L-dopa, with refractory fluctuations and medication- induces dyskinesias. A statistical gait analysis was performed before and 3-6 months after surgery. Balance and postural instability were evaluate by means of clinical scales (Tinetti and Timed Up and Go).

**Results**

Post- surgery short-term analysis showed a statistically significative improvement on most of the gait parameters analyzed. Moreover, clinical evaluation also showed a statistically significant effect on the inmediant improvement on both Tinetti and Timed Up and Go.

**Conclusion**

STN DBS improves gait disturbances, as well as balance and postural instability. These results must be taken into consideration for the selection of those patients who are candidates to surgery. Further investigation would be necessary in order to elucidate long term outcome.
Central integration of dual somatosensory input to the orofacial representation in adults who stutter

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Question

Is stuttering a focal dystonia?

Methods

Persistent developmental stuttering disrupts speech fluency in about 1% of adults, predominantly males. Here we investigated a clinical analogy to task specific dystonias, using a method from Tinazzi and colleagues (Brain 2000; 123:42-50) who observed abnormal central integration of dual somatosensory input (“sensory overflow”) in patients with dystonia. In 15 adults who stutter and 14 matched fluent speaking adults, we recorded somatosensory evoked potentials (SEPs) at C5’ and C6’ induced by stimulating separately or simultaneously the tongue or the cheek at the corner of the mouth. We determined latencies (N13, P19, and N27) and peak-to-peak amplitudes (N13-P19, P19-N27). We divided amplitudes from simultaneous stimulation by the sum of those from separate stimulation.

Results

Amplitude ratios did not differ between groups, suggesting that excessive sensory overflow does not play a major role in persistent stuttering. Unexpectedly, SEP latencies were significantly shorter in stuttering subjects than in fluent speaking participants, particularly after separate tongue stimulation and simultaneous stimulation. Stimulus intensities were significantly weaker in the stuttering than in the control group.

Conclusions

The data do not support the clinical analogy between focal dystonia and persistent stuttering. Evidence of shorter SEP latencies accompanying tongue stimulation, together with lower stimulus intensities, suggest a central sensitization of the tongue sensory representation in adults afflicted with persistent stuttering.
P562
The contribution of intraoperative neurophysiological monitoring to the surgical treatment of hemifacial spasm (literature review and case series)

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Introduction
There is a lot of evidence in the literature concerning microvascular decompressive surgery as a causal treatment for hemifacial spasm. A number of studies have described the predictive value of intraoperative neurophysiological monitoring regarding postoperative outcome.

Methods
We studied a consecutive series of surgical interventions between September 2011 and March 2013. The abnormal muscle response, electromyography of facial muscles and brainstem auditory potentials were monitored. Intraoperative findings were correlated with postoperative outcome. Patient records were analyzed retrospectively and we assessed outcome in all patients via a telephone interview. We performed a literature review and a meta-analysis of the published case series.

Results
Eleven interventions were studied in 10 patients (8 female; 6 right sided). Two of the interventions were reinterventions. In 5 patients the incomplete disappearance of the abnormal muscle response lead to decompression of an additional vessel. In 7 patients the abnormal muscle response was absent at the end of surgery. All of these patients remained spasm free. Four patients had an incomplete disappearance of the abnormal muscle response. Two of them were not spasm free at last follow up. In two patients hearing loss occurred (1 partial) predicted by changes in the auditory evoked potentials. These changes were not reversible. In two patients a partial facial nerve palsy developed (1 transient), not predicted by the electromyogram. Overall patient satisfaction was high. A meta-analysis showed an odds ratio of 7.77 (95% confidence interval 5.69-10.61) for being spasm free when the abnormal muscle response is absent at the end of surgery.

Conclusion
Literature review supports the predictive value of the disappearance of the abnormal muscle response regarding a favorable postoperative outcome. Likewise, the disappearance of the abnormal muscle response was correlated to the outcome in our case series. Changes in the abnormal muscle response are an indication the surgeon is manipulating the correct region. In these cases where the abnormal muscle response does not disappear completely, further exploration is warranted.
P563

Pathophysiologies of simple and complex tics in Tourette syndrome are different -evaluation of pre-movement gating of somatosensory evoked potentials (SEPs)

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Question

Tourette syndrome (TS) is a neurobehavioral disorder characterized by motor and vocal tics lasting more than one year. Simple tics (TS-S) are purposeless involuntary movements and usually resolve spontaneously before adolescence. While, complex tics (TS-C) are in some case apparently purposive involuntary movements with “urge”, which sometimes become intractable associated with obsessive-compulsive disorder (OCD). We studied pre-movement gating of SEPs to evaluate whether there are the pathophysiological differences between simple and complex tics. Methods: Thirty-five patients (6-48y; male 28, female 7) were studied and compared with 18 normal subjects (11-51y). We divided patients into two groups younger (16 patients) and older (19 patients) than 15 years of age, because the prognosis of TS depends on OCD, which develops after adolescence. Fifteen patients showed TS-S and 20 patients were associated with TS-C. Regarding the comorbidity, attention deficit hyperkinetic disorder (ADHD) was seen in 9 and OCD was in 14 patients, all of them demonstrated TS-C over 13 years of age. A pair of warning (auditory) and imperative electric stimuli was presented with a 1 second interstimulus interval. In the pre-movement condition, subjects responded by thumb extension with the ipsilateral hand to the electric stimulation, which also elicited SEPs before movement. In the rest condition, the subjects were instructed not to perform any movement and just listen to auditory stimuli. The amplitude of the frontal N30 (FrN30) in pre-movement state was compared with that at rest and the pre-movement/rest ratio was evaluated.

Results

1) At rest, the amplitude of FrN30 was larger than that of age matched normal subjects before their thirties.
2) The pre-movement/ rest ratio in TS-C was significantly higher than that of TS-S before (P< 0.05) and after adolescence (P<0.01). The ratios were not correlated with ADHD but were correlated with OCD.

Conclusions

Sensory-motor integration is impaired in TS-C but is preserved in TS-S. Furthermore, the involvement of the non-motor basal ganglia thalamo-cortical circuit is suggested in the former after adolescence.

figure 1
P313
Facial pain and multiple sclerosis - a blink reflex study

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Question

Do MS patients with facial pain differ from patients with facial pain but no MS or healthy controls when the blink reflex is tested?

Methods

Due to the nature of the conditions and the painful element of the blink reflex test recruitment was devastating with only 7 healthy controls, 6 patients with only facial pain and 7 patients with MS and facial pain included. The blink reflex response times were recorded after stimulating the first branch of the trigeminal nerve. Progressing through the trigeminal nerve, pontine and spinal centers and finally the facial nerve the stimulus results in 3 distinct responses. The response times and delays relate to the integrity of the pathways. The data was statistically tested through Kruskal-Wallis equality-of-populations rank test and the Mann-Whitney two-sample statistic/Wilcoxon ranksum test post-hoc.

Results

As seen in earlier literature the MS patients differed from the healthy controls in their R1 responses on both the pain afflicted (p=0.018) and non-afflicted side (p=0.006). An expected delay in the contralateral R2 response (p=0.013) and normal ipsilateral response (p=0.076) was seen indicating a delay in the central neural pathways correlating with the pathophysiology of MS with multiple plaques. Surprisingly the patients with facial pain but no MS were delayed in their R1 response (p=0.027) but not in their ipsilateral R2 response (p=0.076) suggesting that the genesis of the pain is a central defect rather than peripheral trigeminal nerve affliction. A larger study is needed to validate the findings and reinforce the statistical methods.
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P564
Evaluation of brainstem involvement in multiple sclerosis

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Objectives

The aim of the present study was to determine the optimum method to detect brainstem lesions in patients with MS.

Patients and methods

72 patients with the diagnosis of relapsing-remitting MS according to the revised McDonald’s criteria were prospectively included in the study. Expanded Disability Status Scale (EDSS) score and brainstem functional system score (BSFS) (part of the EDSS evaluating brainstem symptomatology) were calculated. MRI was performed on 1.5T and T1, T2, PD and FLAIR sequences were analyzed for presence of brainstem lesions. Auditory evoked potentials (AEP) and ocular and cervical vestibular evoked myogenic potentials (oVEMP and cVEMP) were performed according to the standardized protocol.

Results

From 72 patients, 18 (25%) had clinical involvement of the brainstem. MRI showed brainstem involvement in 29 (40%) patients. Of the neurophysiological tests, AEP showed pathological result in 16 (22%) patients, oVEMP in 36 (50%) patients, cVEMP in 18 (25%) patients, and VEMP (combination of oVEMP and cVEMP) in 45 (63%) patients. VEMP detected brainstem lesions in higher percentage than clinical examination, MRI and AEP, which was statistically significant (< 0.0001, 0.012 and < 0.0001, respectively).

Conclusions

Results of the present study have shown that VEMPs are optimal method to detect brainstem lesions in multiple sclerosis and that they detect them significantly better than clinical examination, AEP or MRI.
Tremor in multiple sclerosis: the intriguing role of the cerebellum

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Background

The pathophysiology of tremor occurring in multiple sclerosis (MS) remains poorly characterized. Lesion of protuberential structures, the cerebellum or its efferent pathways are thought to play a role in the generation of tremor in MS.

Objective

To determine the presence of tremor in MS patients having functional disability in one or both upper limbs and to determine the existence of cerebellar or protuberential dysfunction associated with tremor.

Methods

In 32 MS patients, tremor was searched by performing multi-channel electromyographic and accelerometric recordings with FFT and EMD signal analyses. Cerebellothalamocortical inhibitory pathways were investigated by a paired-pulse TMS paradigm. Protuberential function was evaluated by recording the masseter inhibitory and blink reflexes, including prepulse inhibition paradigm.

Results

Clinically, tremor was present in 18 patients and absent in 14 patients. Among the 18 tremulous patients, electromyographic and accelerometric recordings confirmed the presence of a real tremor only in four patients, tremor frequency being around 4 Hz. Clinical presentation with tremor was associated with the presence of clinical signs of cerebellar dysfunction, but not with changes in cerebellothalamocortical inhibition or protuberential reflexes.

Conclusion

A real tremor in MS patients is much less frequent than what previously reported the literature. In a majority of tremulous MS patients, multi-channel neurophysiological recordings revealed in fact a pseudo-rhythmic activity. Only a minority of patients presented a really rhythmic activity in favor of a low-frequency tremor. Although dysfunction of cerebellothalamocortical inhibition is likely involved in the generation of this type of tremor, it may be not the only mechanism. Our data further less support the involvement of any change in protuberential circuits.
Factors Associated With the Time to Next Attack in Neuromyelitis Optica: Accelerated Failure Time Models With Random Effects

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Background and objective

Neuromyelitis optica (NMO) is an inflammatory demyelinating disorder of the central nervous system with a relapsing and remitting course. We aimed to identify factors associated with the time to next attack, including the effect of the natural disease course and the diverse treatment regimens, by applying a longitudinal statistical analysis to the individual attacks of each patient.

Methods

In total, 184 acute attacks among 58 patients with either NMO or NMO spectrum disorder with anti-aquaporin-4 antibody were assessed retrospectively. Patient demographics, clinical characteristics at each attack, and type of treatment during inter-attack periods were assessed. The dependent variable was defined as the time from each attack to the next attack (inter-attack interval). An exponential accelerated failure time model with shared gamma frailty was adapted for statistical analysis.

Results

A multivariable analysis revealed that the time from each attack to the next attack in NMO increased independently by 1.31 times (95% confidence interval (CI), 1.02-1.67; \( p = 0.035 \)) with each additional cumulative attack experienced, by 5.34 times (95% CI, 1.57-18.13; \( p = 0.007 \)) with combined azathioprine treatment and continued oral prednisolone, and by 4.26 times (95% CI, 1.09-16.61; \( p = 0.037 \)) with rituximab treatment.

Conclusion

The time to next attack in NMO can increase naturally in the later stages of the disease as the number of cumulative attacks increases. Nevertheless, both combined azathioprine treatment with continued oral prednisolone and rituximab treatment were also associated with a longer time to next attack, independently of the natural disease course of NMO.
27-hydroxycholesterols in the cerebrospinal fluid of patients with neuromyelitis optica: increased levels and association with disability at acute attack.

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Background and objective

Neuromyelitis optica (NMO) is an inflammatory demyelinating disorder of the central nervous system (CNS). Polymorphism of the CYP7A1 gene, involving in the metabolism of the cholesterol and its side chain oxidation derivatives, hydrocholesterol (OHC), has been known to be associated with risk of developing NMO. These OHCs has been supposed to be actively involved in modulating the receptors for inflammation and demyelination, recruiting the eosinophil and natural killer cell, releasing cytokines, glutamate excitotoxicity, and selective modulating of estrogen receptors , all of which have been proposed to be associated with the pathomechanisms of NMO.

Methods

Twenty six patients with NMO spectrum disorder with autoantibody to aquaporin4 and 23 age- sex-matched controls were included. The levels of 24-, 25-, and 27-hydroxycholesterol were measured with an alkaline hydrolysis, solid-phase extraction, derivatization and detection by ultra fast liquid chromatography-electrospray tandem mass spectrometry (UFLC-MS/MS) with multiple reaction monitoring (MRM) mode in positive ionization.

Results

The levels of 24-ycholesterol (2.35 ± 1.60 ng/mL vs 1.51 ± 0.48 ng/mL, p=0.021), 25-ycholesterol (0.54 ± 0.96 ng/mL vs 0.09 ± 0.04 ng/mL, p=0.032), and 27-hydroxycholesterol (2.68 ± 3.18 ng/mL vs 0.68 ± 0.25 ng/mL, p=0.005) were increased in the CSF of patients with NMO compared with those in controls. The level of OHCs did not differ significantly between these two groups. The level 27-OHC in the CSF were also significantly associated with the disability at acute attacks of patients with NMO by both univariable analysis and multivariable analysis controlling the effect of BBB disruption. Moreover, the CNS-derived 27-OHC, measure by OHC index, was also significantly associated with the disability at acute attack of these patients (0.723; 95% CI -0.181, 0.620; p = 0.002).

Conclusions

The 27-OHC, an endogenous selective estrogen receptor modulator, might be associated with the pathomechanism of NMO, because its level in the CSF of patients with NMO was increased and associated with their disability at acute attack, independently of the BBB disruption. Further studies with experimental design will be needed to determine the exact causal relationship of this phenomenon.
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P568
Multimodal Evoked potentials in predicting response to immunomodulating treatment in multiple sclerosis
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Introduction
While early diagnosis of multiple sclerosis (MS) is now granted, the possibility of early treatment raises the need for biomarkers for response monitoring and prediction. With this respect, evoked potentials (EPs) could be good candidates by providing functional measurements of eloquent pathways.

Methods
Disability (EDSS) and multimodal EPs were assessed in patients with RRMS (96) before immunomodulating treatment and after 2.5 +/- 0.8 years follow-up (75), when patients were classified as non-responders (<50% relapse rate reduction, or > 2MRI enhancing lesions, or >4 new lesions), full responders (no MRI/clinical activity), or partial responders. The severity of all EPs abnormalities was scored using a 0-3 conventional scale from normal to absent and summed to obtain a global EPs score.

Results
EPs score and EDSS at baseline was significantly correlated with EDSS at baseline (r=0.511, p<0.001) and even more at follow-up (r=0.686 p<0.001), and was significantly higher in non-responders subgroup vs the other subgroups. At follow-up, the EPs score significantly increased in the whole group, more significantly in the non-responders vs other subgroups, while EDSS significantly increased in non-responders. Moreover, 34% of full responders had a global EPs score increase >2. Patients with baseline global EPs score >6 had increased risk (OR=5.82) of worsened follow-up EDSS (positive predictive value 78%, negative predictive value 67.5%, chi square p=0.001).

Conclusions
EPs, performed before start of immunomodulatory treatment, may help predicting and monitoring response better than clinical assessment or MRI alone, suggesting their validation as surrogate biomarker in MS.
Corticospinal reserve predicts the effect of deep repetitive brain stimulation with h-coil and neurorehabilitation on walking impairment in progressive multiple sclerosis: results from two randomized, double blind studies

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Introduction

Walking impairment affect up to 85% of subjects with multiple sclerosis - MS - with a major impact on their quality of life. Transcranial repetitive magnetic stimulation - rTMS at high frequency enhances corticospinal and plasticity, potentially favouring the effects of neurorehabilitation. The H-coil allows deeper magnetic fields compared with traditional stimulators, reducing the limit to stimulating lower limb representation, deeply located under the skull. In a preliminary study, we found that improvement in walking speed and endurance after intensive neurorehabilitation was significantly enhanced by the association with deep rTMS. We aimed at replicating the study and at combining results with those of the previous study in order to explore correlations with baseline features.

Methods

We randomized 20 patients with progressive MS into real (n=10) and sham-placebo rTMS (n=10), who underwent 11 stimulation sessions (20 Hz, 90% resting motor threshold or 80% of maximal stimulator output in case of absent motor evoked responses at rest). Walking speed (10 meters test) and endurance (2 and 6 minutes Test) were assessed at baseline and at the end of treatment, as well as modified Ashworth Scale (MAS), visual analog scale-VAS for spasticity and pain, Fatigue Severity Scale, expanded disability score, MS walking scale-12, PASAT and nine hole peg test.

Results

Compared with sham, real rTMS group had a significant improvement in 10MWT and Ashworth, confirming data from a previous pilot study on 21 patients. When pooling data with the latter study, a strong correlation with clinical improvement in walking tests was found exclusively in the real rTMS group.

Conclusion

Resting motor threshold results from the combination of corticospinal excitability and of the amount of corticomotor fibers available for conduction. While rTMS mainly acts on the former mechanism, both at the cortical and spinal level, the latter is a limiting factor in the presence of corticospinal damage, as in the case of progressive MS with lower limb motor involvement. In this condition, resting motor threshold could be considered an rTMS specific therapeutic reserve index, being predictive of therapeutic response to corticospinal neuromodulation.
Abstracts of Poster Presentations – Poster Session 33 – Multiple sclerosis

P570
Intermittent theta burst stimulation in treatment of pharmacoresistant spasticity

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Question

Spasticity appears to be the most common feature of upper motoneuron syndrome that causes a long-term disability in patients with disorders of central nervous system. Our aim is to assess the efficacy of intermittent theta burst stimulation (iTBS), special type of repetitive transcranial magnetic stimulation (rTMS), in modulating lower limb spasticity.

Methods

Ten patients (9 males, 1 female, mean age 45.8±9.1 years) with secondary progressive multiply sclerosis and lower spastic paraparesis were assessed by the Modified Ashworth Scale (MAS), MFIS2, EDSS, KFS and Spasticity Subjective Evaluation Scale (SSES), before and at the end of iTBS session, 2 and 12 weeks after. All included patients have severe disability and spasticity (mean EDSS score 6.5±0.7, mean MAS score in knee joint 3±0). rTMS was performed with eXimia NBS Nexstim device (for motor cortical areas mapping and choosing the stimulation point) and Magstim Rapid2 (for repetitive stimulation). Patients received 10 sessions of iTBS over the motor hotspot of the tibialis anterior muscle in the primary motor cortex with 80% of motor threshold, frequency 30 Hz, burst frequency 5 Hz, number of pulses - 3, number of bursts - 10, total number of pulses - 30. Wilcoxon test was performed for the data analysis.

Result

Patients showed a significant reduction after the stimulations of MAS (3,0 [3.0; 3.0] before; 2,0 [1.0; 2.0] after; p=0.01); MFIS2 (25,11 [31] before; 21,5 [14; 34] after; p=0.02); and SSES (4.0 [4.0; 5.0] before; 3.0 [3.0; 4.0]; p=0.03) scores (fig.1). These effects were persisting for 2 weeks after the end of the stimulation protocol in all patients and remained at the same level in a half of them in 3 months. Some patients had increased weakness in the legs further to reduced spasticity.

Conclusions

Our results indicate evident efficacy of intermittent theta burst stimulation in treatment of severe spasticity. We currently move forward and include more patients with spasticity caused by variable range of disorders.

Figure 1

![Fig.1. Dynamics of spasticity](image-url)
Intermittent theta-burst transcranial magnetic stimulation for spasticity in relapsing-remitting multiple sclerosis.

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**Question**

The aim of the study was to re-evaluate the effect of high-frequency repetitive transcranial magnetic stimulation-intermittent theta burst (rTMS-iTB) on leg spasticity in relapsing remitting multiple sclerosis (RRMS) patients.

**Methods**

12 patients (34-65 years; mean age: 51.9 ± 10.9) in the remitting phase of the disease were selected for the trial. Patients were randomly allocated to sham or magnetic therapy (real-rTMS group) and underwent rTMS-iTB once a day for two weeks. Each session consisted of 10 bursts of three 50-Hz pulses repeated at 200 ms intervals every 10 s for a total of 600 stimuli over the leg motor cortex area. The stimulation effect was assessed by using clinical (modified Ashworth scale for spasticity - MAS) and neurophysiological (H/M ratio and cortical silent period - CSP) parameters. The study was designed as a double blind sham-controlled trial. Baseline (preS1) was compared with post-rTMS values (postS1, postS5, postS10, day-19 and day-26) to check the effects of rTMS-iTB.

**Results**

While rTMS-iTB produced a significant decrease in the contralateral-leg H/M ratio of the real-rTMS group when compared to baseline: (preS1 = 0.39 ± 0.10) vs postS1 (0.32 ± 0.09), postS5 (0.32 ± 0.10), postS10 (0.30 ± 0.10) and day-19 (0.31 ± 0.08), no difference was found between the real-rTMS and the sham group. Besides, the same protocol did not produce any effect on leg spasticity.

**Conclusion**

In conclusion, the rTMS-iTB protocol used in this study does not have therapeutic effect. Therefore, we do not recommend the use of rTMS-iTB for the treatment of spasticity in patients with RRMS.
P572
Treadmill walking until exhaustion reduces isometric maximal voluntary contractions but not electrically evoked muscle twitches in MS patients with fatigue syndrome

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Question

Does peripheral fatigue contribute to disease-related fatigue after exhaustive walking in multiple sclerosis (MS) patients?

Methods

Ten MS patients (9w/1m, 47±11 y, EDSS 3.5±0.9) with reduced walking distance participated in the present study. All participants had a progressive MS fatigue-related motor disabilities affecting the lower limbs during prolonged gait. Before (PRE) and after (POST) exhaustive treadmill walking, we measured isometric maximal voluntary contractions (MVC) of the ankle plantar flexor muscles, maximal soleus M-wave responses (M_max) via peripheral nerve stimulation and EMG measurement as well as single and double resting twitches (sRT, dRT) of the m. triceps surae. Ankle torque was recorded during MVC, sRT and dRT. Paired t-tests were calculated to test for significant differences between the PRE and POST measurements.

Results

Subjects' mean walking distance was 2543m (±1096m). The MVC of the plantar flexors decreased by 33% after exhaustive walking from PRE (98±31 Nm) to POST (65±25 Nm; p < 0.05). M_max, sRT and dRT showed no significant reduction.

Conclusion

We demonstrated fatigue during voluntary ankle plantar flexion after exhaustive walking on the treadmill. The lack in significant changes in the sRT, dRT and M_max indicated that central fatigue rather than peripheral fatigue plays a major role in MS related fatigue after walking.
Optical Coherence Tomography and Visual Evoked Potentials in monitoring neural damage in Multiple Sclerosis.

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**Background**

In the assessment of visual pathway involvement in Multiple Sclerosis (MS), optical coherence tomography (OCT) is used to measure retinal nerve fiber layer (RNFL) thickness as a marker of axonal loss and visual evoked potentials (VEPs) as an indicator of demyelination. However, no clear indications are available on their combined use in MS monitoring. We evaluated cross-sectional and longitudinal correlations and sensitivity of OCT and VEPs and their correlates with clinical and magnetic resonance imaging (MRI) evidence of disease activity in a real-world clinical setting.

**Methods**

80 MS patients (13 clinically isolated syndrome (CIS), 55 relapsing-remitting (RR), 9 secondary progressive (SP), 3 primary progressive (PP)), age 36.7 ± 9.7 years, disease duration 6.0 ± 6.6 years, underwent neurological and neurophysiological evaluation with OCT and VEPs, with routine clinical and MRI monitoring for a mean period of 1 year. Additional OCT-VEPs follow-up was obtained in 50 patients.

**Results**

While VEPs were more sensitive than OCT in eyes with recent (<3 months) optic neuritis (ON) at baseline (80.0% vs 6.7%, p = 0.001), the two sensitivities were similar in chronic ON eyes (78.4%). Comparing eyes with and without previous ON, VEP latency and RNFL thickness were respectively significantly higher (131.2 ms vs 118.8 ms, p = 0.008) and lower (78.15 μm vs 90.00 μm, p < 0.001) in the first subgroup. No significant differences were found between the two subgroups when analyzing VEP latency and RNFL thickness evolution during the follow-up period. However, eyes with baseline recent ON had significant reduction in VEP latency (-15.3 ms) and RNFL thickness (-7.7 μm) at follow-up. No significant correlation was found between OCT-VEPs parameters and disease activity. Similar results were found when considering only RR and CIS patients.

**Conclusions**

These results would exclude recommending OCT and VEPs as surrogate biomarkers in MS phase II clinical trials evaluating disease modifying drugs, even when focusing on relapsing form of MS. The main role for OCT and VEPs in short-to-medium term follow-up programs would consist in monitoring neural damage after acute ON. However, these findings cannot exclude the usefulness of these techniques for longer follow-ups and/or large phase III studies.
P574
Computerized Static Posturography: modified Clinical Test of Sensory Interaction on Balance and Limits of Stability in Multiple Sclerosis patients

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QUESTION

In Multiple Sclerosis (MS) patients the impaired balance control causes increased sway of Centre of Gravity (COG) in quiet stance; muscle weakness and spasticity contribute to reduce the ability to translate the COG towards the limits of stability (LOS). MS patients often complain about unbalance, undetectable in routine clinical examination, already in the early stages of the disease. We investigated the use of computerized static posturography to measure balance impairment in MS patients.

METHODS

Seventy-three recently diagnosed MS patients and 51 healthy controls underwent the modified Clinical Test of Sensory Interaction on Balance (mCTSIB); among MS patients 64 underwent also the LOS test.

mCTSIB was performed with the subject standing for 10 seconds with eyes opened (EO) and then 10 seconds with eyes closed (EC) on a firm surface (NeuroCom Basic Balance Master static platform); each trial was performed 3 times and the best one was selected for subsequent analysis.

LOS test measured the maximum excursion (MxE) and directional control (DCL) of COG toward 3 target directions (Forward, F, Right, R, Left, L). The trial was repeated 4 times and the best one was selected; the LOS composite score (LOScs) was calculated as sum of both parameters (MxE and DCL) obtained from displacement toward all targets; each direction was further analysed separately.

The whole procedure took about 15 minutes.

RESULTS

Normative values of mCTSIB analysis were 0.2 ± 0.06 deg/sec (EO), 0.3 ± 0.08 deg/sec (EC), 599% ± 27.3 (LOScs). Cutoff values (mean +2SD) for mCTSIB were >0.32 deg/sec for EO and >0.46 for EC; for LOS were <504% (LOScs), <167%, <160% and 160% for the three target direction F, R, L respectively.

Mann Whitney test showed significant differences between the 2 groups for mCTSIB (EO p= 0.037, EC p=0.0004), not for LOS measures.

Twenty-seven MS patients (36%) showed an abnormal mCTSIB and 12 (18%) an abnormal LOS test. At least one posturographic abnormality was detected in 48% of patients, despite they had been recently diagnosed with MS.

CONCLUSIONS

This posturography protocol is easy to perform, fast to be administered, not operator-dependent. The obtained data can be stored for further analysis and allow an objective assessment of balance impairment.

The narrow range of normative data is promising, making this approach suitable to measure disability progression in MS patients follow-up.
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P576
Orthostatic intolerance is frequent in patients with clinically isolated syndrome

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Background

The aim of this study was to determine the prevalence of pathologic response to orthostatic challenge in patients with clinically isolated syndrome (CIS) suggestive of multiple sclerosis (MS) and to correlate autonomic dysfunction with clinical and MRI findings and serum catecholamine levels.

Patients and methods

We included 40 CIS patients, 18 males and 22 females, aged 16 to 53 years. The pain-provoked head up tilt table test (PP-HUTT) was used to provoke an orthostatic reaction.

Results

Altogether 32 patients (80%) had a pathological response: orthostatic hypotension (OH) (N=13, 32.5%), vasovagal syncope (N=10, 25%) and postural orthostatic tachycardia (POTS) (N=9, 22.5%). There was no significant difference (p=0.177) between type of CIS and type of response to orthostatic provocation (OH, POTS or syncope). There was no significant correlation between presence of autonomic dysfunction and presence of lesions in the brain hemispheres (Spearman coefficient -0.136, p= 0.403), brainstem (Spearman coefficient 0.025, p= 0.878), cerebellum (Spearman coefficient 0.153, p= 0.346) or the spinal cord (Spearman coefficient 0.048, p= 0.784). Pathological response to orthostatic provocation correlated with difference in norepinephrine levels (standing - supine) (Pearson coefficient -0.419, p=0.012), indicating that MS patients with pathological response to orthostatic provocation have higher increase in norepinephrine upon standing. This increase is mainly due to high percentage of patients with postural orthostatic tachycardia who had statistically higher difference in norepinephrine levels (standing - supine) compared to patients with normal response to orthostatic provocation (p=0.03).

Conclusion

This study has shown that orthostatic intolerance is frequent in the initial phases of MS.
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P577
Tongue somatosensory evoked potentials: evaluation of the brainstem involvement in patients with early multiple sclerosis

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Objective

The aim of this study was to determine the efficacy of tongue somatosensory evoked potentials (tSSEP) in evaluation of brainstem involvement in patients with early multiple sclerosis (MS).

Methods

tSSEP was performed on ten healthy volunteers and 29 patients with first clinical episode of a demyelinating event suggestive of MS. Obtained data were compared between two groups, and tSSEP findings of MS patients were correlated with clinical and MRI data.

Results

MS patients had statistically significant prolongation of N1, P1 and N2 latencies on the left side compared with healthy controls (17.8+-3.5 vrs 15.2+-1.3, p=0.004; 23.9+-3.3 vrs. 20.8+-1.0, p=0; 29.9+-4.2 vrs. 26.7+-2, p=0.01, respectively) and P1 and N2 on the right side (23.8+-3.5 vrs. 20.8+-1.3, p=0.04; 30.3+-3.8 vrs. 27.3+-1.9, p=0.01, respectively).

Out of the 29 MS patients eight (28%) had clinically evident involvement of the brainstem and nineteen (66%) had brainstem lesions demonstrated on brain MRI. There were 20 MS patients with prolonged latencies of tSSEP on either side with no clinical signs of brainstem dysfunction and this difference was statistically significant (p< 0.0001). As well, tSSEP detected brainstem lesions in higher percentage than MR, reaching statistical significance (p< 0.039).

Conclusions

tSSEP is an efficient method for evaluating the afferent trigeminal pathway in patients with early multiple sclerosis, more sensitive than clinical evaluation and radiological imaging in the detection of brainstem lesion.
Clinical and electrophysiological assessment of autonomic function in multiple sclerosis patients with and without fatigue.

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Question

Fatigue is a common complaint in patients with multiple sclerosis (MS). The origin of fatigue remains unclear; the autonomic dysfunction is one of the mechanisms supposed to contribute to its background.

The aim of the study was to evaluate clinical and electrophysiological parameters of autonomic functions in MS patients with regard to level of fatigue.

Methods

The study comprised 86 MS patients (24 men, 62 women, aged 19-60 years) and 40 age- and gender-matched controls. Fatigue was assessed using Fatigue Severity Scale (FSS) and Modified Fatigued Impact Scale (MFIS). Clinical symptoms of dysautonomia were evaluated using Low’s questionnaire. Electrophysiological tests included: heart rate variability (HRV) analysis at rest and during deep breathing, and sympathetic skin response (SSR). Relationships were searched between autonomic function parameters and fatigue measures.

Results

Fatigued MS patients presented with higher Low’s questionnaire score than non-fatigued ones. HRV percentage at rest and coefficient of respiratory HRV were significantly lower in fatigued MS patients than in the controls. MS patients with absent SSR to sensory and/or auditory stimulation showed greater severity of fatigue.

Conclusions

In MS patients with fatigue, clinical and electrophysiological features of dysautonomia can be found, with especially disturbed sympathetic activity.
P579

TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) FOR DYSPHAGIA ASSOCIATED TO MULTIPLE SCLEROSIS

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Background and aims: Treatment options for MS-associated dysphagia are currently limited. In a previous pilot study, we demonstrated that intraluminal pharyngeal electrical stimulation can improving swallowing functions in dysphagic MS patients (Restivo et al., 2013). However, a number of patients do not tolerate intraluminal stimulation. Transcranial Direct Current Stimulation (tDCS) has demonstrated to be able to modulate swallowing motor cortex excitability (anodal stimulation) in healthy subjects (Jefferson et al., 2009). Recently, it has been demonstrated that tDCS over swallowing motor cortex of the unaffected hemisphere, may improve stroke-related dysphagia (Kumar et al., 2011). We therefore postulated that anodal tDCS over the swallowing motor cortex may improve dysphagia in MS. Thus, we assessed the effects of anodal tDCS on swallowing in a sample of dysphagic MS patients, measured by videofluoroscopic, electrophysiological, and clinical evaluations and compare them to the effects induced by intraluminal pharyngeal electrical stimulation. Patients and methods: Eighteen dysphagic MS patients were enrolled. Patients were randomized to receive 5 Hz pharyngeal electrical stimulation for 10 min (6 patients), anodal tDCS 2mA (6 patients), or sham tDCS (6 patients) over the pharyngeal motor cortex for 20 min, for 5 consecutive days. Videofluoroscopic, electrophysiological, and clinical examinations were performed at baseline (T₀), at day 5 (T₁), immediately after the last session of electrical stimulation, and then again two (T₂) and four (T₃) weeks after the last stimulation session. Primary outcome: Variations in the Penetration/Aspiration Scale (PAS) and in the Dysphagia Severity Scale. Secondary outcomes: Variation in the electrophysiological measures; Variation in the clinical scales: VAS, CGI. Results: Patients receiving “real” anodal tDCS and pharyngeal stimulation showed a significant improvement in all the outcome measures as compared to patients who received “sham” tDCS. No significant differences were observed between pharyngeal stimulation and tDCS. tDCS was better tolerated than pharyngeal stimulation. Conclusions: tDCS over swallowing motor cortex may have a potential benefit for the treatment of MS-associated dysphagia.
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P580
The anti-inflammatory effect of progesterone is dissociated from re-myelination: a look at the maturation of oligodendrocyte progenitor cells.

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Background

De-myelinating diseases, such as multiple sclerosis, are characterized by a loss of myelin wrapping around axons of the nervous system and consequently a reduced axonal neurotransmission. These de-myelinating lesions were also associated with enhanced inflammatory response driven largely by resident microglia. Clinical strategies have been developed to dampen brain inflammatory response to promote re-myelination. Re-myelination requires induction of oligodendrocytes progenitor cells (OPC) and their differentiation into mature myelinating oligodendrocytes. In the present study we investigated the role of progesterone on re-myelination process as this steroid hormone is a known for its anti-inflammatory effect and thus has the potential to create conducive environment for re-myelination.

Methods

Aided by a rat stereotaxic apparatus, 2 µl of either sterile saline or the gliotoxin ethidium bromide (EB, 0.04%) solutions were injected into the corpus callosum of adult male rats. The corpus callosum is a white matter tract which conveys a large amount of neuronal signals between the two brain hemispheres. Each of these rat groups received daily injections of either oil or progesterone (5mg/kg). Rats were trans-cardially perfused with phosphate buffered saline at 2 (maximal de-myelination), 7 (peak of de-myelination) or 14 days (start of re-myelination) days post- EB injection. The myelin integrity and the lesion size were assessed using luxol fast blue staining. Immunofluorescent staining was used to explore the impact of progesterone on the recruitment of OPC (NG2), mature oligodendrocytes (CC-1) and the microglia (Iba-1) to the site of the myelin lesion.

Results

Progesterone promoted a significant increase in the number of OPC recruited to the site of the lesion and reduced inflammatory response (number of activated microglia). However, these cellular effects were not associated with maturation of OPC as neither mature oligodendrocytes (CC1), nor the size of the de-myelinated lesion were significantly affected by progesterone treatment 14 days after the de-myelinating insult.

Conclusion

The present data suggest that progesterone promoted the recruitment of OPC to the de-myelination site likely via its anti-inflammatory effect. However, the blunting of brain inflammatory response was dissociated from the process of maturation of oligodendrocyte.
Dysfunction of the immunologic mechanisms is a primary characteristic of experimental autoimmune encephalomyelitis (EAE), which is a classical experimental model of multiple sclerosis (MS). Matrine (MAT), which derived from the herb Radix Sophorae Flave is a quinolizidine alkaloid, has been used for hepatitis B in clinical. Previous reports have suggested that MAT could ameliorate the clinical symptoms of EAE rats, but haven't clarified the mechanism of action until now. Our present study showed that MAT reduced the neurological scores of EAE rats, suppressed infiltration of inflammatory cells and demyelination in the CNS significantly. Furthermore, we studied the possible immunologic mechanism underlying the treatment of MAT for EAE by measuring the expression of system and molecules related with immunoregulation mechanism. In our study, an administration of MAT significantly increased the expression and production in the CNS of Nrf2 and HO-1, the correlation factors of oxidative stress that confront inflammatory cells into the CNS. Furthermore, the expressions of IL-4, IL-5, IL-10, TGF-b1 and Foxp3, which play an important role in the balance between Th1 and Th2 cells in EAE, were also significantly increased. Our findings reveal that MAT could promote the expressions of factors for inhibiting the inflammation. In conclusion, our study clarifies the possible mechanisms underlying the treatment of MAT for EAE, implies that MAT may be a novel therapeutic option for MS.

figure 1
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P582
SHORT TERM FOLLOW UP OF CENTRAL MOTOR CONDUCTION FAILURE IN RELAPSING MULTIPLE SCLEROSIS PATIENTS UNDERGOING HIGH DOSE STEROIDS TREATMENT

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Question
To measure acute changes of central motor conduction failure (CMCF) in Multiple Sclerosis (MS) patients after a full course of high dose steroids therapy.

Objective
Random variability of MEP area limits CMCF quantification in follow-up studies. We have recently developed a method, described in the companion paper¹ to restrain inter-trial MEP variability, mainly based on the combined use of averaged and objectively facilitated MEPs and of unchanged stimulation and recording sites.

Methods
In 10 MS patients, presenting an asymmetrical lower limbs pyramidal relapse, MEPs to TMS using the double-cone coil² and maximal CMAPs to High Voltage Electrical Stimulation of lumbosacral root³ were recorded from Vastus Medialis and Lateralis, Tibialis Anterior, Peroneus Longus and Flexor Hallucis Brevis of both sides. The procedure was repeated at the end of therapy (750-1000 mg of methylprednisolone/day for 5 - 10 days) and 30-40 days later. The distance between nasion and the anterior coil edge defined coil position. The stimulation and the recording sites were marked with small tattoos, to allow a long term follow up. The different sets of MEP Area/CMAP area ratios (ARs) were compared using the coefficient of variation (CV-AR).

Results
In affected sides, pooled data analysis (Wilcoxon test) showed a highly significant AR improvement in the last determination (p=0.008). In 4 of the 10 patients AR increased (p

Conclusions
The described method proved to be suitable to quantify short-term changes in CMCF in agreement with clinical outcome.

1. Troni et al, ICCN 2014
Excitability-decreasing motor plasticity may be reversed in an acute relapse of multiple sclerosis

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Question

Neuroplastic changes may contribute to functional compensation of demyelination and axonal injury associated with multiple sclerosis (MS). Rapid-onset central motor plasticity is likely preserved during the remitting phase of moderate MS. Here, we assessed excitability-decreasing (LTD-like) motor plasticity during an acute relapse of MS.

Methods

Motor plasticity was examined using paired associative stimulation (PAS-10), which combines repetitive electric nerve stimulation with transcranial magnetic stimulation (TMS) of the contralateral motor cortex to model long-term synaptic depression. PAS-10 was performed in 20 MS patients (age 34±12 years) during (t1) and after (+12 weeks, t2) an acute relapse. PAS-10 effects were indexed by baseline normalized amplitudes of motor evoked potential recorded from abductor pollicis brevis muscle. All MS patients received i.v. corticosteroids at t1. To control for corticosteroid effects on PAS-10 effects patients with chronic inflammatory neuropathy were assessed during (t1) and after (+12 weeks, t2) scheduled corticosteroid infusions.

Results

During the acute relapse (t1), MS patients did not exhibit the canonical excitability-decreasing effect of PAS-10, but rather showed an increase (n=20; 119±32% of baseline; vs. baseline, p=0.018) of excitability. This effect tended to normalize after 12 weeks (t2; n=15; 94±29%; vs. t1, p=0.100). No such pattern was observed in the control group.

Conclusions

Our preliminary results indicate a polarity shift of PAS-induced synaptic plasticity during an acute relapse of MS. Although interference by corticosteroids cannot be completely ruled out, the data may be in line with potential metaplastic effects of inflammatory agents on the motor cortex.
P584
The visual evoked potentials (VEP) in the course of multiple sclerosis (MS)

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Question

how do the VEP parameters change in the course of MS?

Materials and methods

The comparison of the results of two VEP examinations performed in different timepoints in each patient. We performed VEP examinations in 63 patients (40 female); mean age 35.7 ± 11.4 years; mean disease duration at the time of the first examination 3.4 ± 5.8 years; mean interval between VEP examinations 69.9 ± 48.9 months. Ten patients were diagnosed at baseline as clinically isolated syndrome (CIS) and in 53 patients clinically definite MS could be diagnosed according to revised McDonald’s criteria: 38 - relapsing-remitting MS, 11 - relapsing-progressive and 4 with secondary progressive course of MS. Mean EDSS score at baseline was 1.76 ± 0.93 and at follow up 3.23 ± 1.83. VEP recordings were performed according to the standard protocol. The VEP score was calculated by quantifying VEP abnormalities for each side separately according to a six-graded scale (Jung et al., 2008).

Results

VEP were abnormal at baseline in 50/63 patients (79.4%), whereas at the follow up examination in 55/63 patients (87.3%). In 32 patients (50.8%) we observed deterioration in VEP’s parameters. In 10 patients (15.9%) VEP score was lower at the follow up and in 21 patients (33.3%) the VEP score remained unchanged during the observation period. We noticed a correlation between the VEP score changes and an increase in EDSS score.

Conclusion

VEP are a useful tool in evaluation of disease progression.
Probing the impact of prefrontal anodal transcranial direct current stimulation on fatigue in multiple sclerosis

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Question

Fatigue frequently affects patients with multiple sclerosis (MS), has a profound negative impact on quality of life and is difficult to treat. Fatigue has been associated with functional and structural abnormalities of the frontal cortex. The aim of this study was to assess whether fatigue symptoms can be reduced by anodal transcranial direct current stimulation (tDCS).

Methods

Excitability-enhancing tDCS (sham-controlled, double-blind) was applied for five consecutive days over the left prefrontal cortex of MS patients with fatigue. Symptoms were tracked for 1 month with known fatigue scales. Lesion load was calculated for each patient and correlated with fatigue levels and responsiveness to stimulation.

Results

In the whole group analysis the scores of the fatigue scales were not altered by tDCS (Fig. 1). However, in an exploratory analysis we found a correlation between response to the stimulation regarding subjectively perceived fatigue and lesion load: patients responding positively to anodal tDCS had higher lesion load in the left frontal cortex, compared to non-responding patients (Fig. 2).

Conclusion

We conclude that tDCS may be a tool for MS fatigue management in patient subgroups discernible by certain morphological alterations.

Figure 1. Changes in fatigue scales compared to baseline for the whole patient group. There was no significant main effect of stimulation. There was a main effect of day on the MFIS, MFISpsych and MFIScog. Scores of the MFIS and MFISpsych were significantly reduced after anodal tDCS.

Figure 2. A. Lesion distribution for the whole patient group (N=12), overlaid on the standard T1-weighted MNI brain template. Lesions were marked on T2-FLAIR-weighted images in native space before registration to standard space. B. Lesion load in the left frontal cortex correlated with the response index (Pearson's r=0.703; p=0.011). C. Responders show higher lesion load in the left frontal cortex (t(10)=3.617; p=0.012).
Is motor cortical excitability altered at early stages of Multiple Sclerosis?

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Question

Transcranial magnetic stimulation (TMS) has revealed to be a useful tool to explore cortical excitability and movement-related cortical plasticity in different diseases. The aim of this study was to compare motor cortical excitability in MS subjects at early stages of the disease versus healthy controls.

Methods

Seventeen patients newly diagnosed with MS in clinical remission and seventeen healthy subjects were studied with TMS. MS patients were drug free. Single-pulse TMS of the non-dominant hemisphere was used to define motor evoked potential (MEP) amplitude, motor threshold (MT) and silent period. Subjects also performed 3 sets (30-s, 60-s, and 90-s duration) of a bimanual repetitive non-fatiguing motor task. Amplitude of MEPs elicited after each period and after 15 min of rest were compared with baseline. Paired-pulse TMS at different interstimulus intervals (ISI) was also delivered.

Results

Single-pulse TMS revealed prolonged central motor conduction time, increased MEP latency and MT in MS subjects compared to controls. Compared with baseline, controls had larger MEP amplitudes after 30 and 60 s of exercise (post-exercise facilitation) and also after 15 min of rest (delayed facilitation). MEP amplitudes in MS patients were not significantly different from baseline after all exercise conditions or after rest. Paired-pulse TMS at 1, 2 and 3 ms ISI in MS subjects revealed a normal intracortical inhibition.

Conclusions

The most important finding of this study is the absence of the normal changes of motor cortex excitability in MS patients compared to controls during and after a non-fatiguing bimanual motor task, indicating the absence of postexercise facilitation and delayed facilitation in MS. Abnormal motor excitability is present also at early stages of the disease, when motor performance is not significantly compromised, suggesting an early modification in the central circuits with a reduction/alteration in the central plasticity that mediates functions such as learning and memory. As in chronic fatigue patients and maybe in the majority of patients affected by central fatigue, impaired motor cortex plasticity may affect recovery of function in the motor system. Further studies are needed to define whether and how disease-modifying therapies influence brain plasticity in MS.

References


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**figure 1**

Single-pulse TMS. MEP amplitudes elicited from the first dorsal interosseous muscle from subjects tested at different times following a bimanual motor task. Note that post-exercise facilitation and delayed facilitation are not present in MS subjects.

**figure 2**

Paired-pulse TMS. At each ISI, the amplitude of the conditioned MEP is expressed as a percentage of the amplitude of the unconditioned MEP. We found no difference in intracortical inhibition between patients and healthy controls.
P586
Mi-2 antibody-positive polymyositis in metastatic rectal carcinoma - paraneoplastic or idiopathic?

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Introduction

There are many causes as infections or drugs which may lead to myositis. Some of the chronic myositis may be autoimmune related, e.g. polymyositis (PM), dermatomyositis (DM) and inclusion body myositis. Autoantibodies can be found in most of these patients. There are myositis-specific antibodies (e.g., anti-Jo1, anti-Mi2) or myositis-associated antibodies (e.g., anti-PM-Scl, anti-Ro 52 kDa). Paraneoplastic DM is associated in Europe with ovary, pancreas, stomach and colon cancer, whereas PM often occurs in patients with non-Hodgkin's lymphoma, lung and bladder carcinomas.

In the following we report about a patient with colorectal cancer and polymyositis, were detected in the Mi-2 antibodies.

Case report

A 79-year-old female patient presented 4 weeks after Liver Resection with curative intent in metastatic rectal carcinoma due to increasing proximal muscle weakness and dysphagia with muscle and joint pain. The diagnosis of polymyositis was made clinically and electromyography with evidence of acute muscle loss and typical myopathic changes, with much increased creatine kinase. In addition, Mi-2 autoantibodies were detected. Under the high-dose administration of corticosteroids unfortunately the patient didn’t improve. Another treatment of metastatic carcinoma and intensive medical therapy were rejected by the patient so that she died 16 days after the diagnosis because of respiratory insufficiency.

Summary

First presentation of a patient with polymyositis with colorectal carcinoma in association with Mi-2 antibodies.
P587
Electrical myotonia in children with suspected muscle disorders

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Question
Myotonic discharges are characteristic spontaneous electrical discharges but rarely encountered in pediatric electromyography (EMG). In this study we shared our experience with electrical myotonia in children with suspected muscle diseases.

Methods
Retrospective chart review of patients less than 18 years, who underwent EMG at the electrophysiology laboratory of the Mayo Clinic, Rochester, MN, USA over 5 years (2009-2013). EMG was performed under conscious sedation in most of the children. Nerve conduction studies were performed in at least 2 nerves (one motor and sensory) and EMG performed in at least 2 muscles in ipsilateral upper and lower limb. 224 patients with the following referral diagnoses (myopathy, muscle weakness, neuromuscular disorders, myositis, myalgia, myoglobinuria, myasthenia, myotonia, cramps, periodic paralysis, hypotonia, and developmental delay) were reviewed. Myotonic discharges were defined as train of spontaneous myofiber action potentials, with waxing and waning amplitudes and frequencies. Myopathic EMG was defined as short duration, low amplitude motor unit potentials with rapid recruitment.

Results
Eight children were identified with myotonic discharges during the study period (less than 0.5%). The age range was 3 to 16 years; 6 were males. Two children had isolated myotonic discharges without myopathic changes on EMG while the rest had myopathic EMG in addition to the myotonic discharges. The final diagnoses were: myotonia congenita in 2 (autosomal dominant inheritance in 1 and lack of definite family history in another), congenital myopathy in 3 (centronuclear myopathy-1, congenital fiber type disproportion-1 and congenital myopathy, indeterminate type -1), muscular dystrophy in 2 (facioscapulohumeral muscular dystrophy -1 and muscular dystrophy of indeterminate type-1), and inflammatory myopathy in 1. Two patients with myotonia congenita had clinical myotonia while the rest had only electrical myotonia. Myotonic discharges were diffuse in patients with myotonia congenita while patchy in other patients.

Conclusions
Electrical myotonia is a rare electrophysiological finding encountered in our study similar to that reported in the published literature. Though rare, identification of myotonic discharges help to narrow the differential in children with suspected muscle disorders. Diffuse myotonic discharges without myopathic EMG are characteristic of non-dystrophic myotonic disorders.
Are the electrophysiological tests helpful in differentiating diagnosis between myotonic dystrophies (DM1 and DM2)?

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The standard EMG is useful in diagnosis of myotonic dystrophy type 1 (DM1) and type 2 (DM2), but it doesn't differentiate between the two.

**The aim of our study** was to estimate the utility of the short exercise test (SET) and short exercise test with cooling (SETC) in differentiating between DM1 and DM2.

**Material & Method**

SET and SETC were performed in 32 patients with DM1, (mean age 35.8 ±12.7yrs) and in 28 patients with DM2 (mean age 44.5±12.5 yrs)

**Results**

We observed a significant decline of compound motor action potential (CMAP) amplitude in DM1 with both SET and SETC immediately after effort. In DM2 there was no marked change of CMAP amplitude with either SET or SETC.

**Conclusions**

SET and SETC may serve as useful tools for clinical differentiation between DM1 and DM2, and they may be used as a guide for molecular testing.
P589

Characteristic EMG features in myotonic dystrophy type 2 (DM2)

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Genetic testing is considered as the only reliable diagnostic criterion in myotonic dystrophy. However it was recently described that a considerable number of patients with genetically proven type of the disease have unusual phenotypic presentation.

The aim of our study was to analyze motor unit reorganization reflected by EMG in myotonic dystrophy type 2(DM2) and compare EMG findings between DM2 and DM1.

Methods

EMG recordings in 63 patients (30 with DM2, 33 with DM1) from biceps brachii (BB), rectus femoris (RF), first interosseus dorsal (FiD) and tibial anterior (TA) muscles were analyzed.

Results

The mean values of amplitude and size index (SI) of MUAPs recorded in TA and RF muscles, mean duration in TA , mean Size Index and number of outliers with amplitude above normal range in BB muscles were significantly increased in DM2 comparing to DM1.

Conclusion

EMG recordings significantly differs DM2 and DM1. The presence of high potentials in lower limb muscles of DM2 patients, atypical for myogenic muscle lesion, could be explained by slow muscle regeneration observed in muscle biopsies findings, further studies are needed in this area.
P590
Distinguishing slow- versus fast-twitch muscle via electrical impedance measurements

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Question

Slow-twitch (Type 1) skeletal muscle fibers have a markedly greater number of mitochondria than fast-twitch (Type 2) fibers. We sought to determine whether electrical impedance methods could be used to assess these differences, ultimately providing a novel tool for non-invasive muscle composition assessment.

Methods

Freshly excised rat soleus (a predominantly Type 1 muscle) and rat gastrocnemius (a predominantly Type 2 muscle) (n = 15 for both) were measured at 1 kHz - 10 MHz frequency range in a custom-designed four-electrode impedance measuring cell in both the longitudinal and transverse directions. Corrections for the inherent electrical properties of the impedance measuring cell and measuring circuit were achieved by performing identical measurements on saline. Data were fitted to the complex resistivity version of the Cole-Cole expression with a weighted complex nonlinear least square method.

Results

Substantial differences in the modeled complex resistivity spectra for the two muscle types were observed in both the longitudinal and transverse directions, as shown in Figure 1. Specifically, the gastrocnemius muscle (Type 2), showed narrow-width, high frequency arcs, clearly displaced from the low frequency arcs produced by the muscle’s sarcolemma. In the soleus muscle (Type 1), in contrast, the second high peak arcs overlapped the low-frequency arcs and were broader in width. These differences in the appearance of this high frequency arc are consistent with larger, more numerous intracellular membranes in the soleus as compared to the gastrocnemius.

Conclusions

Electrical impedance methods can be used to differentiate Type 1 from Type 2 muscle fibers by evaluating the high-frequency components of the complex resistivity. Whereas this work was performed on excised tissue for proof of concept, a modified version of this technique may allow for the assessment of muscle composition using non-invasive surface electrodes. Such a tool may be valuable for assessment of neuromuscular disease status and to assist with athletic training and rehabilitation.

Figure 1 Legend

Fitted complex resistivity plots for rat soleus (A) and gastrocnemius (B) in both transverse (blue and red arcs) and longitudinal (green and gray arcs). Mean +/- standard error of data provided.
Abstracts of Poster Presentations – Poster Session 34 – Myopathies

Figure 1
P591
Late onset myopathy and hyperkinetic movement disorder

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A 72 years-old man complained of slowly progressive walking difficulties over the last five years and “tics” in both hands. Clinical examination revealed generalized symmetric muscle atrophy and proximal muscle weakness in arms, trunk and legs. He had bilateral ptosis, myopathic face, hyperlordosis, and a waddling gait. Trendelenburg and Gowers’ signs were positive. There were discontinuous bilateral choreatic movements involving both hands and feet. Stereotypic myoclonic jerks of his thighs resulting in adduction/abduction movements occurred irregularly. No cognitive or mnestic deficits suggestive of dementia and no cerebellar signs could be noted. Creatine kinase was minimally elevated, no acanthocytes were detected. Needle electromyography showed characteristic myopathic changes with low amplitude short potentials and early recruitment predominantly in proximal muscles, without signs of denervation. Muscle biopsy revealed a mitochondriopathy with ragged red fibers, COX- negative/SDH- positive fibers, and typical abnormalities of cristae like e.g. ‘parking lots’ on electron microscopy. The mitochondriopathies are a heterogeneous group of disorders usually involving several organ systems, and with many different clinical manifestations. They usually become clinically apparent in the first decades of life. The manifestation of a mitochondrial myopathy in the seventh decade is unusual, and chorea as a main clinical feature has only been reported in very few cases in the literature. This case illustrates the broad spectrum of clinical manifestations in mitochondrial disorders and underlines the importance of performing muscle biopsy in elderly patients with myopathies.

figure 1       figure 2
P592
Value of EMG in myopathy

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Question

Many neurologists rely on genetic testing, clinical chemistry and biopsy results and do not refer patients to electromyography (EMG) on suspicion of myopathy. The aim of this study was to address whether EMG makes a difference in the diagnosing of myopathies.

Methods

In a prospective study, 208 myopathy cases were reviewed electronically and discussed in plenum by 8 experienced neurophysiologists in the European multicentre project, ESTEEM¹. By consensus each case was given 3 different blinded diagnoses, each with a probability graded as definite, probable, or possible: 1) the pure clinical diagnosis based on clinical findings solely without considering EMG, 2) the EMG diagnosis based on electromyographic data solely, and 3) the final diagnosis based on all available information. A total of 190 cases obtained a final diagnosis of definite (139), probable (34) or possible (17) myopathy. Of these, 56 were acquired, 47 were inherited, and 87 were of unknown etiology.

Results

The distribution of diagnostic probabilities differed between the pure clinical and final diagnoses, with the probabilities being higher in the final diagnosis (P = 0.000). A total of 49 cases (26%) increased in diagnostic probability by adding EMG information, as 18 and 31 cases changed from possible and probable pure clinical diagnosis, respectively, to definite final diagnosis. The cases changing from possible to definite, was of unknown (94%) or acquired (6%) etiology, while the cases changing from probable to definite was acquired (45%), unknown (39%), and inherited (16%). In only 9 cases (5%) the EMG information decreased the diagnostic probability.

Conclusions

EMG adds significantly in the diagnosis of myopathies of unknown etiology and supports the diagnosis in genetically or biopsy proven myopathies.

P593
fnIRS evaluation during a phonemic verbal task reveals prefrontal hypometabolism in patients affected by Myotonic Dystrophy type 1

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Objective

Myotonic dystrophy type 1 (DM1), the most common muscular dystrophy in adults, is characterized by a multisystem involvement. Cognitive involvement predominantly affecting fronto-temporal functions is an established clinical feature in this disorder. Brain imaging and metabolic studies showed a predominant involvement of fronto-temporal regions in DM1 patients, yet correlation studies among these findings and neuropsychological data gave contrasting results. In order to contribute to clarify the relationship between the metabolic changes documented in the frontal cortex of DM1 patients and a related cognitive task, we applied the functional near-infrared spectroscopy (fNIRS) during the execution of a phonemic verbal fluency task (pVFT).

Methods

We enrolled 29 consecutive right-handed DM1 patients and 30 controls. A 2-channel fNIRS imaging system was used to investigate changes in oxygenated [O2Hb] and deoxygenated [HHb] hemoglobin concentrations in the prefrontal cortex (PFC) during a pVFT. [O2Hb] and [HHb] baseline-corrected activation values were calculated (respectively [O2Hb]c and [HHb]c).

Results

In the control group [O2Hb] significantly increased and [HHb] significantly decreased during the pVFT, in the DM1 group no significant variation was found for both parameters revealing no activation of both PFCs during the task. On the other hand, in the DM1 sample, statistical analysis revealed a direct correlation between [O2Hb]c of the left PFC and the pVFT score, while no correlation was observed in the control group.

Conclusions

Our study reveals that DM1 patients show prefrontal hypometabolism during a specific frontal cognitive task compared to controls. Moreover the rapid temporal discrimination of fNIRS allows revealing the correlation between the PFC hypometabolism and the cognitive performance in DM1 patients.

Significance

fNIRS can be helpful to understand the functional correlates of the frontal cognitive impairment in DM1.
Peripheral nerves involvement in type 1 and type 2 myotonic dystrophy

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The multisystem manifestation in myotonic dystrophies type 1 and 2 is well known, but the peripheral nerves involvement in their clinical picture is still uncertain.

**Question**

are peripheral nerves involved in both types of myotonic dystrophies?

**Material and methods**

We prospectively studied, using nerve conduction studies, patients with genetically confirmed myotonic dystrophy type 1 (32 patients, 10 female) and type 2 (31 patients, 16 female). The mean age was 35.9 ± 12.0 years in the DM1 group whereas in the DM2 group 46.1 ± 12.3 years. The mean estimated disease duration was 9.8 ± 7.75 years in the DM1 group and 12.31 ± 8.74 years in the DM2 group.

**Results**

Abnormal results in electrophysiological studies were found in 28.13% patients with DM1 and in 25.81% patients with DM2, however only in 4 patients in each group (12.5% in DM1 and 12.9% in DM2) abnormalities fulfilled the electrophysiological diagnostic criteria of polyneuropathy. The polyneuropathy was subclinical and mostly sensory axonal, however no correlation between the presence of polyneuropathy and patients age or disease duration was detected.

**Conclusion**

Peripheral nerves are quite frequently involved in both types of myotonic dystrophy, but abnormalities meeting the electrophysiological criteria of polyneuropathy are rarely found. When symptoms of a marked sensory or sensorimotor polyneuropathy can be found in neurological or electrophysiological assessment in patients with myotonic dystrophies other causes of the peripheral nerves involvement should be considered in the differential diagnosis.
Rippling Muscle Disease in Patient with Hypothyroidism and Inflammatory myopathy

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Objective. Rippling muscle disease (RMD) is a benign myopathy with symptoms and signs of muscular hyperirritability. Some cases are associated with hereditary myopathy (caveolin deficiency) and autoimmune disorders, like thyromyoma and myasthenia gravis, suggesting autoimmune pathogenesis. Methods. We describe a case with rippling phenomenon associated with hypothyroidism. Results. A 17 year old girl being treated for hypothyroidism for 10 years and in the last two years started with muscle contractions for five minutes followed by intense muscle pain in the legs and later in the upper limbs, abdomen and back. Symptoms appeared at rest, during exercise and during sleep. Clinical features included muscle rippling and percussion-induced rapid muscle contractions. The needle electromyography showed an electrical silence during rippling phenomenon. The anti-AChR antibody was negative. The muscle biopsy was compatible with inflammatory myopathy. Immunofluorescence studies in muscle revealed a mosaic-like staining pattern of caveolin-3 and dysferlin. There was a significant improvement in symptoms as well as reducing the inflammatory process in muscle biopsy performed 6 months after initiation of treatment with corticosteroids. Discussion. The patient had all clinical, laboratory and EMG features of RMD. We consider this patient to have an autoimmune-mediated RMD.
Magnetic Resonance Imaging (MRI) and ultrasound (US) techniques are increasingly used to support the diagnostic procedure in muscle diseases in order to identify the optimal location of a biopsy. Furthermore, it is well known that MRI is useful in characterizing the pattern of muscle involvement, which might support the classification of the muscle disease. Ultrasound (US) -MRI-fusion imaging is a novel technique which allows US analysis of muscles in freely selectable section planes exactly corresponding to preregistered MRI or CT images. But what is the benefit of using this technique in the diagnostic process of muscle diseases? Here we report about the first clinical applications in a series of patients with muscle diseases.

**Methods**

Muscle MRI included spin echo T1-, T2 and STIR images in sagital, coronar and transversal slices of upper arms or legs. Muscle US was performed with the Esaote Mylab Twice (Italien, Padua) with the commercially available software “Virtual Navigator”.

**Results**

We demonstrate that a matching between muscle US and MRI is possible. We present a series of patients to illustrate the usefulness of this technique in the interpretation of MRI findings in muscle diseases and in the identification of the optimal location of a muscle biopsy.

**Conclusions**

US-MRI-fusion imaging is a promising technique, which should be further evaluated in the diagnostic of muscle diseases.
Electromyographic and histological characteristics of Postpartum Hypernatremic Rhabdomyolysis

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Question

Published literature on the incidence and pattern of electromyographic abnormalities in rhabdomyolysis are diverse. Rhabdomyolysis results from many causes including inflammation, trauma, drugs, inherited metabolic conditions and dyselectolytic states. We planned to evaluate the electromyographic findings in the recently described postpartum hypernatremic rhabdomyolysis with osmotic cerebral demyelination.

Methods

Concentric needle electromyography was performed in five women with postpartum hypernatremia among whom one underwent muscle biopsy.

Results

At admission, all the five patients had varying degrees of encephalopathy. Proximally dominant quadripareisis was present in four patients and one had no weakness. Serum sodium at admission ranged from 154 to 192 mEq per litre. Serum creatine kinase levels ranged from 5,484 to 58,587 units per litre and declined to normal level within one month from onset of symptoms. Nerve conductions were normal. Concentric needle electromyography revealed fibrillations and positive sharp waves in all the five patients. Myotonic discharges were present in three patients. Serial electromyographic study in one patient revealed appearance of transient fibrillations, positive sharp waves and myotonic discharges at two weeks from onset of symptoms which disappeareed five days later. Four patients had small amplitude motor unit potentials. Muscle biopsy was performed in one patient at second week of illness and revealed extensive rhabdomyolysis. All patients recovered completely after gradual correction of hypernatremia.

Conclusions

Patients with postpartum hypernatremic rhabdomyolysis had fibrillations, positive sharp waves and myotonic discharges along with myopathic potentials. Electromyographic findings in acute rhabdomyolysis may be transient and their detection depends on the severity of rhabdomyolysis and the interval of the electromyographic study from onset.
Abstracts of Poster Presentations – Poster Session 34 – Myopathies

P598
McArdle’s disease: electromyographic findings in a patient

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Introduction

McArdle’s disease or Type V glycogen storage disease is a rare condition that is caused by myophosphorylase deficiency; has autosomal recessive inheritance and is located on chromosome 11q13. It produces an alteration in the metabolism of glycogen which accumulates in skeletal muscle, leading to decreased exercise capacity, muscle weakness and cramps. Is diagnosed by the elevation of glycogen content and reduced phosphorylase activity in muscle biopsy.

Case Report

We report the case of 64 years-old woman who, since childhood, has had exercise intolerance, early fatigability, proximal weakness feeling, prolonged duration cramps that worsened with exercise. Additional tests evidence elevated CPK and myoglobinuria, ischemia test with intolerance and the electromyography shows a decrease in the recruitment of motor unit potentials, increase in the polifasia index, decrease in amplitude and mean duration preferably in proximal muscles. Muscle biopsy shows muscle disease pattern of deposit, compatible with McArdle’s disease.

Conclusion

The fluctuating elevation of CPK and its relation to the exercise and myopathic findings on the electromyography, orient towards muscle pathology. The ischemia test is made to detect defects in glycogenolysis, which will subsequently be confirmed by muscle biopsy. It is important to know and diagnose this disease to offer dietary measures and appropriate exercise that can improve the quality of life of these patients.

KEYWORDS: McArdle's disease. Type V glycogen storage disease.
Abstracts of Poster Presentations – Poster Session 34 – Myopathies

P599
McArdle Disease: clinical features, electrophysiological studies, muscle biopsy and molecular genetics

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OBJECTIVES

McArdle disease (MD), or glycogenosis type V, is a metabolic myopathy with symptoms of exercise intolerance caused by deficiency of the enzyme myophosphorylase. Molecular analyses have revealed extensive allelic heterogeneity with different mutations identified in PYGM gene. Since its first description, few patients with this disease have been identified in Brazil. The aim of the study was to analyze a series of Brazilian patients suffering from MD.

METHODS

Ten patients with MD were studied with correlation between clinical findings, laboratorial data, electromyography studies, histochemical and molecular features.

RESULTS

The sample consisted of 10 patients (3 female and 7 male), from different families, aged 23 to 57 years. Exercise intolerance was present in all cases; other symptoms reported included "second wind" phenomenon, myoglobinuria, rhabdomyolysis, myalgia, weakness, muscular fatigue, cramps and seizures. Serum creatine kinase levels were increased in all patients. Forearm ischemic exercise testing in five patients revealed no increase in venous lactate. Needle electromyography presented "myopathic pattern" in 7 patients. Muscle biopsy showed sub-sarcolemal and central accumulation of glycogen (vacuolar myopathy) in all patients. Myophosphorylase stain analysis indicated deficient activity in all patients. The molecular analysis of PYGM gene by PCR/RLFP and direct sequencing showed the R50X was the most common mutation (found in 8 alleles).

CONCLUSIONS

Clinical and laboratory manifestations frequently suggest the MD diagnosis. The muscle biopsy often confirmed the MD diagnosis by presence of vacuolar myopathy and myophosphorylase deficiency. Molecular analysis of PYGM gene could be an important diagnostic criterion for MD. The R50X mutation in PYGM gene is also frequent in Brazil.
P600
ULTRASOUND AND NEUROPHYSIOLOGICAL CORRELATION IN COMMON PERONEAL NERVE CONDUCTION BLOCK AT FIBULAR HEAD

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Objective

Ultrasound (US) and neurophysiological examination are useful tools in the evaluation of common peroneal mononeuropathy. There is only a report comparing US and electrophysiological parameters in patients with common peroneal nerve (CPN) conduction block at fibular head. We investigated the correlation between US and neurophysiologic findings in this condition.

Methods

We retrospectively reviewed patients with CPN assessed in our lab during last two years. Each patient underwent to clinical, neurophysiological and ultrasound evaluations. Cross sectional area (CSA) of CPN at fibular head was assessed.

Results

Twenty-four patients were included. Motor nerve conduction study showed a reduction of distal compound muscle action potential (CMAP) amplitude in 10 patients (mean 1.3 mV). US showed an increased CSA in 10 patients. Statistical analysis revealed a strong correlation between the increased CSA and the CMAP reduction of CPN.

Conclusion

Our data suggest that usually US examination is normal in CPN conduction block at fibular head. However the association with axonal damage is frequently accompanied by an increase of CSA.

Significance

Ultrasound evaluation may represent a powerful diagnostic/prognostic tool in cases with CPN conduction block at fibular head because it usually shows normal pattern in pure conduction block and increase of CSA in associated axonal damage.
A health technology assessment protocol: pediatric neuro-muscular ultrasound normative data

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**Question**

Neuromuscular diseases, mainly the pediatric ones, are clinically heterogeneous, progressive and disabling, often requiring invasive, uncomfortable and expensive investigations. The ultrasonographic evaluation of neuromuscular diseases is a highly specific and sensitive first level screening-tool. It is non-invasive, painless, safe, inexpensive, easy and quickly to perform, characterized by high spatial and temporal resolution. The knowledge of physiological maturation ultrasound neuromuscular modifications is essential to correctly interpret pathological changes, to direct the differential diagnosis and guide focused II level diagnostic choices. Up to now, mainly on pediatric population, only few data are reported. We collected both quantitative and qualitative pediatric normative data, by a neuromuscular ultrasound (NMUS) Health-Technology-Assessment (HTA) study, approved by Local Ethic Committee.

**Methods**

In 120 healthy children shared in 5 age-groups (I)2-5;II)6-8;III)9-11;IV)12-14;V)15-16 years; M65-F55) we have performed a NMUS wide protocol for the first time including bilaterally distal and proximal muscles of upper (Forearm Flexors, Biceps brachii, Flexor carpi radialis) and lower limbs (Anterior Tibial, Long Toe Extensor, Soleus, Medial and Lateral Gastrocnemius, Rectus Femoris, Vastus Intermedius) and nerves (Median, Ulnar, Sural) evaluating muscular thickness, echogenicity and pennation and nerves' perimeter and area.

**Results**

The muscular echogenicity of I-II groups was lower than III-IV-V ones. Muscular thickness increased with age and BMI, especially between IV and V groups. No significative differences were found between males and females.

**Conclusions**

In clinically heterogeneous pediatric neuromuscular diseases, neuromuscular ultrasound (NMUS) is an informative, easy, non invasive screening tool that, predicting presence-absence of neuromuscular disease, can help prioritise subsequent invasive investigations, guide the therapeutic rehabilitation path with restrained cost and with a minor management-duty for the care-giver.
Usefulness of nerve ultrasound in an atypical case of multifocal motor neuropathy

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Background

Ultrasound is a valuable and accessible technique for the diagnosis of neuropathy including multifocal motor neuropathy (MMN).

Case report

A 65 years old male presented with a four months history of progressive weakness in right hand and cervicobrachialgia. The examination revealed a severe global distal paresis in the upper right limb, most in forearm flexors, ulnar areflexia and predominant denervation signs in the electrophysiology. Both examination and motor nerve conductions were normal in the rest limbs, as well as the sensitive study. Magnetic resonance imaging showed a back center C7 disc herniation. The patient was diagnosed of C7 radiculopathy and he underwent cervical disc surgery. One month later, he developed progressive weakness in the right forearm and the contralateral hand, showing signs of moderate subacute denervation with a remarkable proximal demyelination of the median, ulnar and radial nerves. By HRNS (high resolution ultrasonography) (Sonosite, 6-13Mhz), suggestive signs of intense inflammation were demonstrated in non-compressible segments of nerves, thickened with a poorly defined edge and hyperechoic epineural and clear structural alteration. After a 5-day course of intravenous immunoglobulin, the patient had a good result with adequate recovery of motor deficits.

Discussion

MMN is a slow progressive dysimmune multineuritis with a established criteria. although the electrophysiological findings are the gold standart for the diagnosis, ultrasonographic diagnosis of peripheral nerves is a reliable, fast and secure tecnique to support it. We report a case of atypical presentation with rapid and agressive evolution. The initial denervation signs were probably due to intense and sudden demyelinization which altered the electrical findings. Our case highlights that high resolution sonography of the nerve is a useful tool in the evaluation of neuropathies as MMN and it should be included in the clinical practice.
Abstracts of Poster Presentations – Poster Session 35 – Nerve and muscle ultrasound

P603
Contrasting echogenicity in FDP-FCU: a diagnostic ultrasound pattern in sporadic inclusion body myositis

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Question
Over the past few decades, high-frequency US of muscles and peripheral nerves has emerged as a non-invasive and simple tool to assist in the diagnosis of neuromuscular disorders. We aimed to clarify whether muscle ultrasound (US) of the forearm can be used to differentiate between patients with sporadic inclusion body myositis (s-IBM) and those with s-IBM-mimicking diseases.

Methods
We compared the echo intensity (EI) of the flexor digitorum profundus (FDP) muscle and the flexor carpi ulnaris (FCU) muscles in patients with s-IBM (n = 6), polymyositis/dermatomyositis (PM/DM) (n = 6), and amyotrophic lateral sclerosis (ALS) (n = 6) by visual and quantitative assessments. The transducer was placed at 5 cm distal to the right olecranon, as shown in Figure 1.

Results
On visual assessment by using the Heckmatt rating scale, we identified EI abnormalities in 100% of patients with s-IBM, 33% of those with PM/DM, and 33% of those with ALS. An “FDP-FCU echogenicity contrast”, a US pattern involving a higher EI in the FDP than in the FCU, was observed in all patients with s-IBM (arrow in Figure 2), but in none of those with PM/DM or ALS (Figure 2). Quantitative analysis using gray scale analysis also showed that the FDP/FCU EI ratio was significantly higher in patients with s-IBM than those in PM/DM or ALS (P <0.01 and P <0.01, respectively).

Conclusions
“FDP-FCU echogenicity contrast” in muscle US is a sensitive diagnostic indicator of s-IBM.

figure 1
Abstracts of Poster Presentations – Poster Session 35 – Nerve and muscle ultrasound

Figure 2
Abstracts of Poster Presentations – Poster Session 35 – Nerve and muscle ultrasound

P604
A controlled prospective study of ultrasound in carpal tunnel syndrome.

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Question

Does Ultrasound (US) of median nerve at the carpal tunnel add in the diagnosis of carpal tunnel syndrome (CTS) and how reliable is this method compared to nerve conduction studies (NCS)?

Methods

We included 232 (337 arms) consecutive patients referred to our department with symptoms suggesting CTS. All patients underwent routine NCS just prior to US. High-resolution US was performed with a “small parts” broadband linear array transducer (frequency band, 13-6 MHz) and was done bilaterally and blinded to the clinical symptoms and to the findings of NCS. The cross sectional area (CSA) at the level of carpal tunnel (CT) inlet, outlet and in the distal forearm (9 cm proximal to the pisiforme bone) was measured by the free-hand technique. Ratio between the CSA at the CT inlet and the distal forearm was calculated. The patients were re-examined with US one year after the first examination. A subgroup of the patients that were operated were re-examined with NCS. As a control group we investigated 50 healthy subjects (HS). All HS underwent both NCS and US the same day and in a randomised manner.

Results

We considered US examination as abnormal if the CSA at the CT inlet was larger than our cut-off values, which were determined using a regression analysis of the data from the HS group. US was abnormal in 187 arms and NCS in 206 arms, diagnosing respectively 55% and 61% of the cases. US was abnormal in 29 % of arms with normal NCS. When both examinations were considered, then 72 % of the cases were diagnosed. The sensitivity and specificity of US compared to NCS were 72% and 71% respectively. The area under the ROC curve for predicting abnormal NCS was 0.82 with a cut-off value that was influenced by age, but not by weight, height or BMI.

Conclusions

US is an important supplement in diagnosing CTS in patients with symptoms suggesting CTS. The sensitivity and specificity compared to NCS is moderate and thus US should be performed in combination with NCS.
Peroneal nerve damage after knee dislocation. Clinic, neurophysiology and ultrasound in diagnosis, prognosis, treatment and rehabilitation.

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Question
Peroneal nerve palsy may occur after a close traumatic knee dislocation. Ultrasound shows its usefulness in traumatic nerve injuries.

Methods
We present 5 patients with a history of knee dislocation associated with peroneal nerve damage, evaluated by clinical, neurophysiologic and ultrasonographic (US) examination. All the patients were examined in follow-up. At the first evaluation, the patients presented a severe clinic and neurophysiologic damage of peroneal nerve. US showed an increase of the cross sectional area (CSA) of the involved peroneal nerve, between popliteal fossa and fibular head.

Results
Among these, 4 subjects presented a CSA four-seven times larger than normal, while one subject had the damaged nerve CSA only double compared to the other side. The first 4 patients did not present improvement in clinical, neurophysiologic and ultrasonographic follow-up. The latter one showed a general improvement in the later evaluations.

Conclusions
This observation let us consider that larger is the CSA of the involved peroneal nerve and worse is the prognosis for the patient. Associating neurophysiology to US evaluation, we can obtain a guide for diagnosis, treatment and rehabilitation. In fact this combined evaluation gives data about the specific details and the changes over the time of the condition. This allow us to perform the best management for every individual case.
P606
Ultrasonic evaluation as a method for determining diagnosis underlying clinical symptoms of carpal tunnel syndrome

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Background

High resolution ultrasound (HRUS) was used to differentiate carpal tunnel syndrome (CTS) from other pathologies in the media nerve.

Materials and methods

Forty-one patients, referred for diagnosis of CTS, were examined with HRUS supplemental to electrodiagnostic (EDX) evaluation when the medical history gave suspicion of polyneuropathy, cervical root affection on MRI scans, trauma or EDX changes not typical for CTS.

Results

Twelve patients showed CTS in both EDX (29 %) and HRUS, two patients had a bifid median nerve, one was supplemental investigated for HNPP.

Seventeen patients had normal EDX (42 %). Eight had normal findings by HRUS, five had CTS in HRUS, whereas four patients showed other pathologies including neurovascular contacts, bifid median nerve, partial nerve compression under the flexor retinaculum, palmaris muscle contacts and arthritis.

Twelve patients showed atypical changes in EDX (29 %). In this group, eight patients showed CTS in HRUS, four patients showed other pathologies including fibrolipomatous harmatoma, intraneural venous congestion, partial traumatic neuroma and flexor muscle compression under the flexor retinaculum.

Conclusion

HRUS is not only relevant in confirming the diagnosis of CTS but also to reveal other clinical relevant pathologies when electrodiagnostic evaluation is normal or atypical.
Intraneural collateral circulation in the median nerve after radiocephalic fistula

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Introduction

Carpaltunnel Syndrome (CTS) is a known complication to chronic renal failure and radiocephalic fistula for hemodialysis, but the cause of median nerve affection is unknown.

Case Report

A 61 year old male with chronic renal failure, hemodialysis and radiocephalic fistula in the left forearm was referred for CTS, because of pain in the left thumb, progressive in flexion of the wrist and parestesia in finger 1 + 2.

Electrodiagnostic (EDX) evaluation showed normal distal motor latency and motor velocity in the forearm, but reduced motor amplitude from the elbow. Normal sensory velocity from finger 2 and palm to wrist, with reduced sensory amplitudes.

High resolution ultrasound (HRUS) (Esaote MyLab Twice, 6-18 MHz) revealed intraneural arterial blood flow, presumably located in the intraneural venous plexus of the left median nerve at the level of the radiocephalic fistula, as well as hypo-eccogenic changes in the nerve fascicles.

Discussion

Clinically, CTS may be mimicked by proximal nerve damage followed by intraneural collateral circulation in patients with radiocephalic fistula. This condition can easily and non-invasively be visualized using HRUS of the median nerve.
P608
Ultrasound as a novel instrument for tremor evaluation and intervention

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Question
Tremor is a common movement disorder, as which a varied neurological disorders can be presented and pharmacological treatment was firstly tried. Botulinum toxin type A (BoNT-A) has been adopted as another treatment method, and recently ultrasonography-guided injection has been emphasized for accuracy. We hypothesized ultrasonography could takes another role as an objective indicator for tremor.

Methods
We report two case studies in which tremor were the chief complaint.

Case 1. A 29-year-old male patient with a postural and rest tremor of right hand consistent with Holmes tremor secondary to left pontine hemorrhage visited. His tremor gradually spread to wrist and elbow with the characteristics of 1.4-2 Hz, irregular flexion-extension oscillation being present at rest. Ultrasonography-guided BoNT-A injections were administered at extensor pollicis longus (40 U) muscles, and flexor digitorum superficialis 2nd, 3rd and 4th digits (20 U, each), which showed plainest contraction in real time ultrasonography. Ultrasonography revealed the frequency of tremor decreased from 1.4-2 Hz (baseline) to 0-0.5 Hz (2 weeks after injection), as calculated by each muscle contraction.

Case 2. A 30-year-old female patient with bilateral tremor secondary to hypoxic brain damage visited. Her muscle contraction was 0.2-0.4 Hz at her left extensor carpi radialis, extensor pollicis longus, flexor carpi ulnaris muscles with the help of ultrasonography. BoNT-A injections were administered at extensor carpi radialis (20 U), extensor pollicis longus (15 U), and flexor carpi ulnaris (20 U) muscles with ultrasonography. The frequency of muscle contraction decreased to 0.1-0.2 Hz at 2 weeks after injection.

Conclusion
Ultrasoundography has an advantage of objective evaluation of tremor as well as selecting the target muscles. We regard ultrasonography as a novel tool in increasing the accuracy of evaluation and intervention.
LP36
Intraoperative high-resolution ultrasound in the management of traumatic nerve lesions: a new technique

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Introduction

Surgical treatment of nerve lesion in continuity remains difficult even in the most experienced hands. Their regenerative potential is evaluated either by intraoperative electrophysiology and/or intraneural dissection. The values of preoperative ultrasound is often hampered due to low tissue penetration and trauma related artifacts. Therefore the present study for the first time examines feasibility and value of intraoperative high-frequency ultrasound as an imaging tool in the management of traumatic nerve lesions in continuity.

Material and Methods

After development of intraoperative application of high-frequency ultrasound we examined 19 traumatic or iatrogenic nerve lesions of different extent. The information obtained was correlated to intraoperative electrophysiology, the findings of microsurgical intraneural dissection and histopathology of the resected nerve segments.

Results

The intraoperative application of high-frequency ultrasound enabled morphological ultrastructural examination of traumatic nerve lesions with excellent imaging quality. The assessment of the severity of the underlying nerve lesion matched perfectly with the judgement obtained from intraoperative electrophysiology. Both, intraneural nerve dissection and neuropathological examination of the nerve segment resected confirmed the sonographic findings. Based on these findings an ultrasound classification scheme could be developed.

Conclusion

With intraoperative ultrasound for the first time intraoperative morphological ultrastructure examination of nerve lesion became possible. It is a promising method that seems to assess the type (intraneural/perineural) and grade of nerve fibrosis. Therefore on synopsis with intraoperative neurophysiology high-frequency ultrasound may represent a major tool for non-invasive assessment of the regenerative potential of a nerve lesion.
P609
MULTIFOCAL MOTOR NEUROPATHY PROGRESSING TO CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY AND RESPONSE TO AZATHIOPURINE

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Question

Acute onset multifocal motor neuropathy shifting to CIDP?

Acute generalized multifocal motor neuropathy (MMN) presents with weakness and electrophysiological findings of persistent conduction blocks at sites not exposed to entrapment or compression and normal sensory conduction studies.

Case report

A 24 years-old male patient, was followed-up at our clinic since nine years. He admitted first in 2004, with weakness in both legs and left hand, which progressed to a tetraparesis over two weeks. His electrophysiological findings revealed multiple conduction blocks in four extremities, and normal sensory conduction studies. CSF examination revealed mild protein increase. Anti-GM1 IgM was positive. He was diagnosed for MMN and treated with IVIG without any response. Prednisolone (PRD) was started and he improved in 2,5 months. When he stopped his treatment three months later his weakness relapsed. PRD was restarted, with benefit. He relapsed four times over three years due to poor drug compliance. In 2009, sensory nerve conductions showed the first abnormalities on mixed nerve investigations. During PRD tapering, his weakness worsened. Azathiopurine (AZT) was added and PRD was tapered. His compliance is now better and he has no weakness since the last one year.

Conclusion

Our patient had initially been diagnosed as acute generalized MMN, unresponsive to IVIG, who achieved remission following PRD treatment. Later, he became unresponsive to PRD leading to new relapses. At last AZT was added with a good outcome. This case suggested that AZT is a useful potential immunosuppressing agent in relapsing CIDP patients.
**P610**

**Trismus and neuropathic pain caused by a lesion of the mandibular branch of the trigeminal nerve after local anesthesia**

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**Purpose**

What is the utility of neurophysiologic tests after trigeminal injury and neuropathic orofacial pain?

**Material and Methods**

We present a case of a 55-year-old woman referred for pain, hypoesthesia and paresthesias within the left hemifacial region and trismus (mouth opening <7 mm) after tooth extraction (37; lower left jaw) 14 weeks previously. The condition was unresponsive to medical treatment (nsaids, antibiotics, and botulinum toxin). Orthopantomography, cranial and temporomandibular joint CT and MRI were normal. Neurophysiologic study: blink reflex (supraorbital, infraorbital and mental nerves), sensory neurography of the inferior alveolar nerve (IAN; orthodromic recording at the oval foramen), motor neurography of facial nerve (frontal, zygomatic, buccal and marginal mandibular branches) and EMG of facial and neck muscles.

**Results**

The motor neurography of facial nerve was normal on both sides. SCV was slow and amplitude of the left IAN was decreased. The blink reflex study showed an afferent abnormal response with stimulation of the left mental nerve, being otherwise normal. EMG showed subacute neurogenic involvement of the pterygoid and masseter muscles on the left. Recordings were repeated one year later, showing significant improvement.

**Conclusions**

The patient had a severe partial lesion of the mandibular branch of the left trigeminal nerve probably caused by misdirected, intraneural local infiltration anesthesia. The neurophysiologic study provided good diagnostic, prognostic, and treatment orienting assessment of the clinically obscure condition. Although there are many reported cases of isolated injury of lingual or inferior alveolar nerves after local anaesthesia, such iatrogenic lesion of the mandibular branch of trigeminal nerve is extremely rare.
P611
CHRONIC INFLAMMATORY Demyelinating Polyneuropathy: 15 YEARS OF CLINICAL EXPERIENCE

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Chronic inflammatory demyelinating polyneuropathy (CIDP) is a potentially disabling immune mediated disorder of peripheral nervous system. Response to immunomodulatory therapy in CIDP differs by the clinical and electrophysiological characteristics. We present the clinical, electrophysiological, laboratory findings and response to therapy in 81 patients with CIDP.

Methods

Medical records of patients presenting to our neuromuscular diseases outpatients clinic between 1988-2013 were reviewed retrospectively. CIDP was diagnosed according to EFNS/PNS criteria.

Results

A total of 81 patients (27F, 54M) consisting of 65 classical CIDP, 9 MADSAM, 6 MMN, and one DADS, were included in the study (mean age 44.89±14.05). Motor response could not be obtained in one of 141 median, two of 143 ulnar, 29 of 143 tibial and 24 of 130 peroneal nerves. Conduction block was determined in 61 of 141 median, 53 of 144 ulnar, 49 of 118 tibial and 25 of 110 peroneal nerves. F responses could not be obtained in 20 of 75 median, 18 of 66 ulnar and 26 of 56 tibial nerves. Response to treatment could be obtained in 42 of 61 patients treated with prednisolone, four of 5 patients treated with azathiopurine, 10 of 18 patients treated with prednisolone plus azathiopurine, and 23 of 40 patients treated with IVIG. Full or almost complete recovery was attained in 36 patients, moderate improvement in 14 patients, minimal or no improvement in 31 patients.

CONCLUSION

Although criteria for the diagnosis and treatment of CIDP has been well established, clinicians should note that treatment of this disease particularly in cases refractory to all interventions might prove a challenge.

figure 1
P612
Small and large fibre neuropathy in patients with diabetes type 1 compared with type 2: A follow-up study

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2University Hospital of North Norway, Department of Clinical Neurophysiology, Tromsø, Norway
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4University Hospital of North Norway, Department of Pathology, Tromsø, Norway
5University Hospital of North Norway, Department of Internal Medicine, Tromsø, Norway
6University Hospital of North Norway, Department of Neurology, Tromsø, Norway

Question

Are there differences in the spectrum of large and small fibre involvement in patients with diabetes type 1 versus those with type 2?

Methods

Fifty-nine patients (35 type 1 and 24 type 2 diabetes) were included in a follow-up study after 5 years. Nerve conduction studies (NCS), quantitative sensory testing (QST) at the distal calf and skin biopsy for quantification of intraepidermal nerve fibre density (IENFD) in addition to symptom scoring and clinical evaluations were performed. Z-scores were calculated to adjust for the physiologic effects of age, height and gender.

Results

Patients with type 1 diabetes were younger with longer disease duration; they had higher HbA1c and lower BMI. Neuropathic symptoms tended to be more frequent in type 2 (54% versus 37%; ns). Comparing data to the baseline study, the overall NCS score was more abnormal after 5 years in both type 1 (p=0.006) and type 2 diabetes (p=0.02). IENFD became significantly lower only in those with type 2 (reduction from 7.9±4.8 to 4.3±2.8 fibres/mm, p=0.006). Cold perception threshold was higher in type 2 at follow-up compared to baseline (p=0.049). Between the two types of diabetes the difference of progression of abnormalities was only significant for the IENFD (more progression in type 2, p= 0.048).

Conclusions

A 5 year follow-up study in diabetics showed progression of large fibre neuropathy in both type 1 and type 2. Small fibre neuropathy seems to progress more rapidly in those with type 2.
Detection of early neuropathy in type 2 diabetes mellitus


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2National University of Malaysia, Community Health Department, Kuala Lumpur, Malaysia

**Question**

To determine the frequency and predictors of asymptomatic lower limb neuropathy amongst type 2 diabetic patients in University Kebangsaan Malaysia Medical Centre (UKMMC).

**Methods**

This was a cross sectional study which recruited diabetic patients in UKM Medical Centre who did not have any neuropathy symptoms. All patients who obtained a score of ‘0’ in diabetic neuropathy symptoms score (unsteadiness in walking, neuropathic pain, paraesthesia, numbness) (Table 1).

All patients were subjected to a neurological examination to ascertain their and nerve conduction studies.

**Result**

Ninety diabetic patients who were asymptomatic for neuropathy were recruited. Of these, 81 patients (90%) had abnormal NCS and 9 patients (10%) had normal NCS. From 81 asymptomatic neuropathy patients, 14 (15.6%) had pure motor neuropathy, 12 (12.2%) had pure sensory neuropathy and 56 (62%) had mixed sensorimotor neuropathy (Figure 1). Duration of diabetes, age of diabetic patients and presence of retinopathy were found to be significantly associated with the presence of asymptomatic neuropathy. Using multivariate analysis only the duration of diabetes more than 4 years was found to be an independent risk factor for neuropathy (Table 2).

**Conclusion**

The frequency of asymptomatic neuropathy in type 2 DM in this study was high. This study highlights the importance of the NCS in determining the presence of asymptomatic neuropathy in type 2 diabetes mellitus patients. The early detection of DPN in type 2 DM patients who had diabetes for more than 4 years may reduce the detrimental consequences associated with it.

**References**


**Figure 1**

*Figure 1: The frequency of nerve conduction parameters abnormalities in motor and sensory nerves.*
### Table 1

DNS score and guidelines:
1. Are you unable to concentrate when reading or watching television? Need for visual control, increase in the dark, work like a drunk and lack of contact with floor.
2. Do you have a burning, itching, or tingly sensation at your leg or foot? Occurring at rest or at night, unrelated to exercise, exclude epinephrine or menstruation.
3. Do you have paresthesia sensation at your leg and foot? Occurring at rest or at night, unrelated to exercise, exclude epinephrine or menstruation.
4. Do you have paresthesia sensation at your leg or foot? Occurring at rest or at night, unrelated to exercise, exclude epinephrine or menstruation.

<table>
<thead>
<tr>
<th>Maximum score: 4 points</th>
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<tbody>
<tr>
<td>0 points: absence of peripheral neuropathy</td>
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<tr>
<td>1-4 points: presence of peripheral neuropathy</td>
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</table>

### Table 2

Binary logistic regression analysis of variables analyzed for predictors of neuropathic changes:

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<th>Variable</th>
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<th>95% Confidence Interval</th>
<th>P value</th>
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<tr>
<td>Age of patients (&gt; 50 years)</td>
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<td>0.12-1.29</td>
<td>0.235</td>
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<tr>
<td>Duration of disease (&gt; 5 years)</td>
<td>4.25</td>
<td>1.68-11.37</td>
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<tr>
<td>Presence of retinopathy</td>
<td>1.95</td>
<td>0.59-6.24</td>
<td>0.362</td>
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</table>

Nagelkerke R square value: 0.328
Micromutations in PMP22 gene in patients with severe inherited neuropathies: report of a family.

*M. Alcantara¹, D. Portugal², L. F. Oliveira³, M. Venturini²

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²Sarah Rehabilitation Hospitals, Neurology, Fortaleza, Brazil
³Sarah Rehabilitation Hospitals, Pediatrics, Fortaleza, Brazil

Question

Charcot-Marie-Tooth (CMT) 1A is commonly caused by the duplication of peripheral myelin protein 22 gene (PMP22dupl). Micromutations of PMP22 are rare causes of CMT and may lead to variable clinical phenotypes, ranging from mild disease to severe demyelinating neuropathy.

Methods

We report an unusual presentation of CMT disease and its possible association with single nucleotide polymorphisms (SNPs) in coding exons of PMP22.

Results

Two siblings, brother and sister, age 4 and 7 years respectively, born of non-consanguineous parents, presented with claw hands, diffuse weakness and atrophy, pes cavus and steppage gait. Their father had mild distal weakness and ulnar and peroneal motor nerve conduction velocities (MNCVs) were unobtainable. Nerve conduction studies in the whole pedigree showed an asymmetrical motor-sensory neuropathy, worse in upper limbs and more severe in the offspring. One striking difference among the siblings was the preservation of median sensory nerves in the sister and the severe compromise of all upper limb nerves in the brother. Possible conduction blocks of motor nerves were present only in siblings. Two SNPs were detected in PMP22 sequencing in siblings (IVS3-17G>A and IVS4+33C>T) and one in the father (IVS3-17G>A). Mutations in EGR2, MPZ and PMPdupl/deletion were absent.

Conclusions

Atypical forms of CMT disease might be related to de novo micromutations in PMP22. Particularly severe autosomal dominant demyelinating neuropathies can appear and even bring about an anticipation phenomenon. Further studies are necessary to ascribe the value of SNPs in this context and sequencing of the gene is necessary when common mutations are absent.

figure 1
Abstracts of Poster Presentations – Poster Session 36 – Neuropathies 2

Figure 2: Nerve conduction studies recorded from the father.

Figure 2
P615
Polyneuropathy in HyperCKemia

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Question
Creatine kinase (CK) is a commonly used biomarker of neuromuscular disease. It is usually considered a marker of myopathy, but hyperCKemia is also described in polyneuropathy especially in amyotrophic lateral sclerosis and postpolio syndrome. We aimed to assess whether the prevalence of polyneuropathy is increased in persons with elevated CK compared to persons with normal CK.

Methods
Individuals with persistent hyperCKemia (n=121) and age and gender matched controls (n=129) were identified in a population study (n= 12,828). They were examined with neuropathy impairment score (NIS), nerve conduction studies (NCS) and electromyography (EMG). The neurophysiological diagnosis of polyneuropathy was based on NCS-criteria according to Dyck and neuropathic EMG pattern.

Results
We identified 63 persons with polyneuropathy according to our neurophysiological definition. Prevalence of polyneuropathy was higher in the hyperCKemia group (n=39, 32,8%) compared to the control group (n=24, 18,6%) (p= 0,013). NCS of the tibial nerve showed decreased compound motor action potential (p&lt;0.0001), decreased motor conduction velocity (p=0,002) and increased F-wave latency (p=0,003). EMG showed significantly increased average motor unit potential amplitude in three of four muscles.

Conclusion
Polyneuropathy was more common in persons with persistent hyperCKemia in our population sample. This finding indicates that even mild to moderate polyneuropathy may lead to some instability of the muscle cell membrane and leakage of Creatine Kinase.
NEUROPHYSIOLOGY AND ULTRASOUND IN DIAGNOSIS OF ISOLATED PERIPHERAL NERVE TUMORS. LITERATURE REVISION AND PERSONAL EXPERIENCE.

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²Università Cattolica del Sacro Cuore, Institute of Neurology, Rome, Italy
³Don Gnocchi ONLUS Foundation, Milan, Italy

Question

Primary nerve tumors can affect any peripheral nerve and can be benign, malignant, symptomatic, or asymptomatic. In this pathology, neurophysiologic examination presents an important role to define the possible lack of function of the nerve. However, sometimes, this evaluation cannot give all the information to make diagnosis. On the other hand, ultrasonography allows us to visualize the peripheral nerves and underline the morphologic changes in nerve structure. Our work shows the usefulness of the association of neurophysiology and ultrasound.

Methods

We present a literature revision of the use of ultrasound in peripheral nerve tumor study and a collection of 10 cases where the combined use of clinic, neurophysiology and ultrasound guided the diagnostic process of nerve tumors.

Results

All the patients presented a clinic pattern of nerve involvement and everyone was evaluated with neurophysiology which confirmed a mononeuropathy, but without the possibility of a sure diagnosis. The following ultrasound evaluation allowed to visualize a focal lesion, compatible with a nerve tumor.

Conclusions

These cases show that neurophysiology and ultrasound together contribute in diagnosis of peripheral nerve tumors. Ultrasonography is not able to certainly define the type of tumor, but it gives suggestions about discrimination between schwannoma and neurofibroma.
P617

Large and small nerve fiber investigation in chronic alcohol-dependent subjects using newer objective methods.

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²University of Heidelberg, Germany.

INTRODUCTION

Polyneuropathy (PN) is the most frequent complication of chronic alcoholism, mainly due to the direct toxic effect of ethanol on the peripheral nerves. Especially concerning small nerve fibers, newer objective neurophysiological methods are available to determine the various manifestation types of peripheral damage. The aim of the present on-going study was to evaluate the occurrence of large and small fiber neuropathy among alcohol dependent patients compared to healthy subjects.

MATERIALS AND METHODS

We examined 21 patients, 16 men and 5 women aged 32-63 years. They were all alcohol-dependent volunteers subjects without signs of malnutrition treated for detoxification in the specialized unit of the Athens University Psychiatric Clinic. The healthy group included 19 age matched controls. Polyneuropathy was confirmed using the neuropathy symptoms score, the neurologic disability score, nerve conduction velocity studies, quantitative sensory tests (QST), quantitative sudomotor axon reflex tests (QSART), and the axon reflex area test evaluated with a laser Doppler imaging (LDI) camera. Patients were considered with small fiber neuropathy when they revealed abnormal at least one of the specific tests (QST, QSART, LDI) with or without clinical symptoms of small fiber injury.

RESULTS

PN was diagnosed in 17 patients (80,95%). Subclinical large fiber neuropathy was observed in 6/21 (28,6%). In 5 of them the PN was not involving small fibers. PN of both large and small fibers was found in 8 patients (38,1%); exclusively small fiber neuropathy was observed in 4 (19%) . There was a reduction of electrically induced flare area in 8 (38,1%) and of electrically induced sudomotor response in 9 (42,86%) subjects (values under the lower 5% percentile of the control groups). Additionally, 3 (14,3%) patients had abnormal heat threshold values in the foot compared to the control group. No pain or autonomic symptoms were mentioned in 38,1% of patients with neurophysiological indications of small fiber neuropathy.

CONCLUSIONS

Complementary testing of large and several small somatic and autonomic fibers is necessary in order to reveal neuropathy in chronic alcohol dependent subjects, as different types of nerve fibers are often damaged independently and selectively.
**P618**

**MULTICENTER PROTOCOL ON THE ROLE OF ULTRASOUND IN IMMUNE-MEDIATED NEUROPATHIES**


1Catholic University of the Sacred Heart, Department of Geriatrics, Neurosciences & Orthopedics, Institute of Neurology, Rome, Italy
2Don Carlo Gnocchi Onlus Foundation, Milan, Italy
3Duke University Medical Center, Department of Neurology, Durham, N.C., USA, United States
4University of Padova, Department of Neurosciences, Padova, Italy, Italy
5“Sapienza” University, Department of Orthopaedic Science, Rome, Italy

Immune-mediated neuropathies include clinically heterogeneous disorders such as Guillain-Barré syndrome (GBS) and its variants, chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), neuropathy with monoclonal gammopathy and others.

High-resolution ultrasound (US) is a helpful technique for the evaluation of peripheral nerves. In previous studies on immune-mediated neuropathies, nerve US showed diffuse enlargement of cross sectional area (CSA) of peripheral nerves trunks and cervical roots and morphological alterations at conduction block site. Data are however heterogeneous, correlations with clinical history or disease severity are lacking and there are no longitudinal studies in literature.

The objective of the protocol is to prospectively evaluate, through a multicenter longitudinal study, nerve US findings in patients with newly diagnosed immune-mediated neuropathies and evaluate the relationship with clinical and neurophysiological findings and changes over time (natural history) or in response to therapy.

The protocol includes clinical assessment, neurophysiological examination, US examination of median, ulnar, radial, fibular, tibial, sural nerves (and brachial plexus in extended protocol) with evaluation of maximal/minimal CSA for each nerve, inter- and intra-nerve variability, US classification depending on echogenicity and fascicles enlargement. US and neurophysiological follow-up timing examinations follow different schedules in acute and chronic immune-mediated disease.

We present preliminary results and feasibility of the protocol.
P619
Is Electrophysiology Overused to Diagnose Carpal Tunnel Syndrome in Turkish speaking Cypriot population

*F. Selcuk¹, S. Mut¹,²
¹Dr Burhan Nalbantoglu State Hospital, Neurology, nicosia, Cyprus
²Near East University Hospital, Neurology, Nicosia, Cyprus

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy seen in our neurodiagnostic laboratory referrals. We describe the electrophysiologic profile of CTS patients with electrophysiological diagnosis seen in our centre during a period of three and a half years.

METHODS

A retrospective hospital based study was carried out from January 2009 to July 2012 and included 1667 consecutive patients suspected of CTS who were referred from neurologists, neurosurgeons, orthopaedic surgeons for nerve conduction study confirmatory testing.

RESULTS

The majority of patients were female (81.3%) with mean age of 47.8 years. The male patients mean age was 48.1. Among female patients 21% had right carpal tunnel syndrome, 10% had left, 28% had bilateral while 40% had no evidence of carpal tunnel syndrome electrophysiologically. Among male patients 18% had right carpal tunnel syndrome, 12% had left, 25% had bilateral while 45% had no evidence of carpal tunnel syndrome electrophysiologically.

CONCLUSION

In this study we found 40% of all the referred patients having no evidence of carpal tunnel syndrome electrophysiologically. This high percentage may indicate either overuse of referral (electrophysiological study) or may indicate a need to follow up to see if there is a higher possibility of these patients having CTS in the future.
P620
Acute idiopathic sensory neuronopathy presenting as a different form of length dependent polyneuropathy

*S. Z. Tun*, K. K. Lwin*

1Calderdale Royal Hospital, Clinical Neurophysiology, Halifax, United Kingdom

A previously fit and well, 20 year old mother had acute onset unsteadiness, numbness, tingling in her fingers and feet for a week. A baby was delivered normally after an uneventful pregnancy six weeks earlier.

She was unable to walk unaided. Despite sensory symptoms, sensory system exam was normal. She had generalized areflexia with good motor strength. Other neuro exam was unremarkable. A diagnosis of GBS was reached. 1st EMG was obtained ten days after symptom onset. Motor NCS are normal. Lower limbs sensory NCS are normal. Median, ulnar and radial sensory action potentials are low in amplitude. A non-length dependent sensory polyneuropathy diagnosis was made.

CSF studies, MRI of spine were normal. Various immunological profiles and other lab tests are normal.

IV IgG was given empirically.

EMG was repeated nine days later. Median, ulnar, radial and peroneal nerves SNAPs were absent. Sural sensory responses are low in amplitude. She walked home unaided after three weeks stay in the hospital. Follow up EMGs were done nine weeks and 17 months later. Motor NCS were consistently normal in all four tests. SNAPs remained unobtainable from all upper limbs sensory nerves and peroneal nerves even after 17 months later. Sural sensory potentials remained low in amplitude. Clinically she feels back to normal however reflexes remained hyporeflexic.

**Conclusion**

Ganglionopathy is a rare condition. Idiopathic, acute onset and monophasic course is presented. NCS obtained during acute illness revealed a different length dependent nature of neuropathy. Clinical recovery is not matched by routine NCS findings.
### Third NCS/EMG Study (23-12-2011) - 9 weeks after symptoms onset

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### Fourth NCS/EMG (09-04-2012) - 17 months after symptoms onset

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<td>Finger (F)</td>
<td>Ankle</td>
<td>Normal</td>
</tr>
<tr>
<td>Motor</td>
<td>2.0</td>
<td>9.2</td>
<td>12.2</td>
<td>2.4/4.2</td>
<td>2.8</td>
</tr>
<tr>
<td>Sensory</td>
<td>3.8/3.7</td>
<td>7.5/7.2</td>
<td>12.2/12.2</td>
<td>6.4/13.9</td>
<td>45.9/47.6</td>
</tr>
</tbody>
</table>
A case of acquired neuromyotonia. Slow potassium channel dysfunction and the effect of voluntary contraction.

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Question

Prior nerve membrane excitability studies using QTRACK in acquired neuromyotonia were reported as normal. A 15y-old girl had a 6 month history of progressive generalized muscle cramps initiated by movements and preceded by flu-like illness. She had no family history.

Methods

Electromyography was used to show myotonia. Nerve conduction studies were performed at rest and after a short and a long exercise test. QTRACK (Trond protocol) examined excitability properties of motor and sensory nerve membrane.

Results

Electromyography (EMG) revealed 2-60 seconds 200Hz myotonic discharges. Recruitment pattern was normal. Motor unit potentials were normal without diplets, triplets or multiplets. Motor and sensory nerve conduction studies were normal and showed no decrement of the compound motor action potentials on 3 Hz repetitive stimuli.

A short exercise test induced a 56% decrement. Subsequent 3Hz repetitive stimuli increased the decrement to 90%. A long exercise test was without decrement.

A median nerve motor excitability study revealed an abnormal membrane accommodation (phase s2) after polarization and a reduced late subexcitability after a supramaximal stimulus. Sensory nerve excitability study was normal. Excitability studies in both parents and a sister and a brother were normal.

She had no significant autoantibodies directed towards the voltage gated potassium channel. A test for intron point mutations in KCQN2 and KCQN3 was normal. We did not perform gene sequencing. A genetic test for congenital myotonia was normal.

Conclusion

In this rare case of neuromyotonia both standard nerve conduction studies and QTRACK were abnormal.

The excitability study supported the suspicion of an abnormal accommodation in this patient, and pointed to an abnormal function of the slow potassium channel responsible for the s2 phase.

We suggest the abnormality in slowly inactivating potassium current as causative in a subgroup of patients with neuromyotonia.
Lumbar Spinal Stenosis: an underestimated diagnosis?

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²St Antonius Hospital, Neurology, Nieuwegein, Netherlands
³St Antonius Hospital, Cardiology, Nieuwegein, Netherlands

Introduction

With overlapping symptoms and signs it can be difficult to differentiate lumbar spinal stenosis (LSS) from polyneuropathy (PNP). LSS is potentially treatable while PNP is often not. We assessed the prevalence of LSS in patients with symptoms of the legs and evaluated the value of history, neurological examination and electrophysiological investigation in recognising patients with LSS.

Methods

Patients with sensory symptoms and/or weakness of both legs were included from June 2011 - March 2012. Patients with a history of typical neurogenic claudication or with symptoms of the hands were excluded. Every patient was seen by a neurologist and underwent nerve conduction studies, needle electromyography and an MRI of the lumbar spine. Patients were divided between a group with absolute LSS and a group without absolute LSS.

Results

59 patients were included, of whom 20 (34%) had an absolute LSS. Older age was a predictor for LSS (mean 75 versus 67 years, p = 0.021). Patients with LSS significantly more often reported to experience cramps in the legs (6% versus 31%, p = 0.049). Nerve conduction studies and needle electromyography could not differentiate patients with LSS from patients without LSS.

Conclusions

LSS might be an underestimated diagnosis in patients with symptoms of the lower legs. Electrophysiological examination is not a potent tool to discriminate between PNP and LSS. It might warrant starting the work-up with an MRI of the lumbar spine to differentiate between PNP and LSS.
P623
Added value of the blink reflex in the evaluation of diabetic neuropathies

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Question
Is there a correlation between the blink reflex (BR) and the electroneurography (ENG) in diabetic patients?

Methods
The BR has been recorded in 35 diabetic patients, together with the ENG on motor and sensory peripheral nerves. The BR was obtained by stimulating separately the left and right supraorbital branch of the trigeminal nerve and recording each time the response in both orbicularis oculi muscles. The measures contained the latency of R1 and R2 responses, as well as the difference between sides. The ENG testing included the ulnar motor, median motor, radial sensitive, peroneal motor, tibial motor and sural nerves bilaterally. The following parameters were considered: distal latency, conduction velocity and amplitude of the CMAP and SNAP.

Results
In the majority of patients (97%) both R1 and R2 latencies were prolonged with respect to normal values from the literature. These values did not correlate with the diabetes type, but showed a linear relationship with the time from the onset of the disease. The latency differences between sides were not statistically significant. ENG measures displayed the most prominent modifications in the sensory nerves of the inferior limbs, more axonal than demyelinating, then in the sensory nerves of the upper limbs, and finally the least affected being the motor nerves. The sural nerve was often unexcitable and in such instances it proved even more valuable to find an altered BR. The best correlation between BR and ENG was obtained when the R1 and R2 latency on the one hand, and the amplitude of the SNAP on the other hand were considered.

Conclusions
Although a multitude of tests (mainly BR and ENG) allow a more reliable diagnosis, our study suggests that the BR can solely be a reliable determinant of a diabetic neuropathy in cases where the sural nerve cannot be excited.
P624
ULTRASOUND EVIDENCE OF CONCOMITANT TRAUMATIC NERVE LESIONS FAR FROM THE TRAUMA SITE

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Question

High-resolution ultrasound (US) of peripheral nerves is a valuable tool in the assessment of traumatic nerve lesions. Sometimes in traumatic nerve lesions multiple site damages can be observed. To identify cases of traumatic double site radial nerve involvement assessed through US.

Methods

We retrospectively evaluated 36 patients admitted to our neurophysiology lab from January 2010 to March 2013 for traumatic radial nerve lesions following humeral fractures. All those patients underwent clinical, electrodiagnostic and sonographic evaluation.

Results

In 14 patients a double site involvement of radial and posterior interosseous nerve was observed through US.

Conclusions

Multiple site nerve lesions following a trauma can be suspected based on clinical evaluation (presence of non homogeneous motor or sensory deficit) but are difficult to demonstrate through electrodiagnostic assessment. US can help to detect unexpected nerve impairment and can help identify multiple site traumatic nerve lesions showing that they are often more frequent than we can diagnose with neurophysiology alone.
Multimodal assessment of small fiber neuropathy: Laser Evoked Potentials or skin biopsy?

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3CHU Saint-Etienne, Neurology, Saint-Etienne, France

Question

Laser Evoked Potentials (LEPs) and Skin Biopsy (SB) are both considered as reliable methods for assessing a diagnosis of Small Fiber Neuropathy (SFN). The issue is whether these two methods are redundant or not.

Methods

We selected 67 patients (42F, 25M; 54±14 years) with probable pure painful SFN including the feet. All of them had thermo-algesic hypesthesia (either observed clinically or confirmed by quantitative sensory testing). LEPs was considered as abnormal if N2P2 was abnormal on at least 2 areas out of the 8 explored (third cervical dermatoma, hands, thighs, feet). SB was considered as abnormal if the density of intra-epidermal nerve fibers (IENFD) was abnormal either on proximal (thighs) or distal (leg) areas. We compared the sensitivity of these techniques and explored clinical factors that may predict these results.

Results

Only 58% of patients had abnormal IENFD while 79% of patients had abnormal LEPs. The concordancy between SB and LEPs was 55% on proximal areas and 51% on distal areas. There was 2.5 fold more patients with abnormal LEPs and normal SB than patients with normal LEPs and abnormal SB (23 vs 9 patients). These results were not explained by the length-dependent characteristics of SFN nor by the duration of pain evolution. Burning pain was the only clinical factor predicting abnormal SB (OR=4.1; p=0.024).

Conclusions

The discrepancies between LEPs and SB may provide in part from differential lesions of A delta and C fibers. In practice we may recommend to record LEPs in a first approach in case of expected painful pure SFN.
P626
Preserved Thumb Reflex in areflexic Guillain Barré syndrome - a novel phenomenon

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\textsuperscript{2}KLES Dr Prabhakar Kore Hospital and MRC, Neurology, Belgaum, India

Question

Generalised areflexia is one of the cardinal clinical features for the diagnosis of Guillain Barré syndrome. Few patients with Guillain Barré syndrome may have sluggish proximal muscle stretch reflexes. Isolated preservation of thumb reflex, a distal stretch reflex consisting of contraction of flexor pollicis longus has not been documented in areflexic Guillain Barré syndrome.

Methods

We prospectively evaluated thumb reflex in patients with Guillain Barré syndrome and age matched controls from April to September 2013.

Results

There were 31 patients with Guillain Barré syndrome (17 males, 14 females) with age ranging 13 to 78 years during the study period. Majority (84\%) presented in the first two weeks. Nerve conduction studies showed demyelinating neuropathy in 69\% and axonal motor neuropathy in 31\%. At the initial evaluation, thumb reflex could be easily elicited in all the 31 patients (24 normal, 7 hypoactive) whereas all other muscle stretch reflexes were absent in 29 patients. The remaining two had hypoactive biceps and quadriceps reflexes. Thumb reflex could be elicited in 27 among the 31 control subjects (normal 13, hypoactive 14) and absent in four (control vs. patients P = 0.001). Serial examination in the patients during hospital stay revealed gradual decline in the briskness of the thumb reflex (P < 0.001). Recording of the thumb reflex with surface electrodes from flexor pollicis longus revealed consistent electromyographic response correlating with the reflex. Early loss of thumb reflex was seen in patients who had rapid progression of the weakness.

Conclusions

Thumb reflex, a distal stretch reflex is preserved in the early phase of Guillain Barré syndrome. The presence of thumb reflex is intriguing and needs further clinical and electrophysiological correlation.
P627

Is precautionary neurophysiological monitoring useful for beta-thalassemia patients?

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²University General Hospital of Thessaloniki AHEPA, First Propedeutic Department of Internal Medicine, Thessaloniki, Greece

The thalassemias are the most common single gene disorder in the world. Over the last years, a limited number of studies, mainly in children, have demonstrated a mild peripheral neuropathy in b-thalassemia patients. Chronic hypoxia, iron overload, desferrioxamine (DFO) neurotoxicity and bone marrow expansion are implicated, but sufficient explanatory evidence and biomarkers development is envisaged. We perform motor conduction studies of the median, ulnar, peroneal and tibial nerves, as well as sensory conduction studies of the median, ulnar, peroneal and sural nerves in adults. For the first time to our knowledge, we use extended EMG studies (brachioradialis, abductor digiti quinti (hand), extensors carpi radialis, anterior tibialis, quadriceps rectus femoris) to reveal and better analyze peripheral neuropathy in these patients. Our findings are correlated with the history, the laboratory findings and the medication followed. As life expectancy for b-thalassemia patients extends, we support the use of neurophysiologic monitoring in order to achieve the appropriate management and as a result a better life quality for this patient group.
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P628
Electrophysiological data of DSMA1 patients in the Netherlands

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¹Canisius Wilhelmina Hospital, Neurology, Nijmegen, Netherlands
²Emma Children's Hospital, Academic Medical Center, Pediatric Neurology, Amsterdam, Netherlands
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⁷Wilhelmina Children's Hospital, University Medical Center Utrecht, Medical Genetics, Utrecht, Netherlands
⁸Wilhelmina Children's Hospital, University Medical Center Utrecht, Neurology, Utrecht, Netherlands
⁹University Medical Center Groningen, Neurology, Groningen, Netherlands
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¹¹Academic Medical Center, Neurology, Amsterdam, Netherlands

Question

What are characteristic electrophysiological findings in DSMA1 patients?

Background

Distal spinal muscular atrophy type 1 (DSMA1) is a rare disorder with distal muscle weakness, hypotonia and early respiratory difficulties as most striking symptoms. The pathophysiology is unknown. Some think the anterior horn cell is primarily affected, followed by degeneration of axons, others think it is vice versa. The former is supported by spinal cord autopsy data and findings in the animal model, the latter is supported by sural nerve biopsies and the early and severe changes in nerve conduction studies.

Methods

We collected electrophysiological data of 10 Dutch DSMA1 patients.

Results: Electrophysiological findings showed mostly reduced or absent compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) amplitudes. Nerve conduction velocities are markedly reduced and could be in the demyelinating range. Distal motor latency (DML) was generally not in the demyelinating range, considering CMAP amplitudes below 1mV being less trustworthy. None of the patients showed evidence for conduction block. Electromyography could be normal or show spontaneous muscle fiber activity and reinnervation. Electrodiagnostic findings best fit an axonal neuropathy (table 1).

Conclusions

In these 10 Dutch DSMA1 patients, electrodiagnostic findings suggest a severe axonal neuropathy. Our findings make the anterior horn cell as the primary site of the disorder less likely.

References


Table 1: Electrophysiological findings in DSMA1 patients

Pt = patient, M = male, F = female, m = months, y = years, mNCV and sNCV = motor and sensory nerve conduction velocity (in meters per second), - = not available, A = absent, n =normal, FCU = flexor carpi
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ulnaris, IOI = first dorsal interosseous, BB = biceps brachii, TA = tibialis anterior, VM = vastus medialis, APB = abductor pollicis brevis, GC = gastrocnemius, RF = rectus femoris, D= deltoid, AH = abductor hallucis, Y = yes, N = no. DML, CMAP and SNAP = in milliseconds, millivolt and microvolt respectively.

**figure 1**

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Gender</th>
<th>DML/CMAP/NCV</th>
<th>SNAP/NCV</th>
<th>DML/CMAP/NCV</th>
<th>SNAP/NCV</th>
<th>Spontaneous muscle fiber activity (Muscle stretch reflex, positive sharp wave, fasciculations)</th>
<th>Reinnervation</th>
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<tbody>
<tr>
<td>1M</td>
<td>2.7m</td>
<td>-</td>
<td>2.8 - 0.0 - 0.3</td>
<td>9.1 - 1.7</td>
<td>-</td>
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<td>D = yes, Y = no, N = no. A</td>
<td>A = no.</td>
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<tr>
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<td>2.7m</td>
<td>-</td>
<td>4.8 - 0.3 - 0.6</td>
<td>2.1 - 0.2 - 0.2</td>
<td>8.1 - 0.2</td>
<td>-</td>
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<tr>
<td>3M</td>
<td>0.5m</td>
<td>-</td>
<td>3.2 - 0.4 - 0.6</td>
<td>2.1 - 0.2 - 0.2</td>
<td>6.5 - 0.2</td>
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<td>2.7m</td>
<td>-</td>
<td>3.0 - 0.3 - 0.2</td>
<td>-</td>
<td>8.5 - 0.2</td>
<td>-</td>
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<td>A = no.</td>
</tr>
<tr>
<td>9F</td>
<td>2m</td>
<td>A</td>
<td>A</td>
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<td>A = no.</td>
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<td>D = yes, Y = no, N = no. A</td>
<td>A = no.</td>
</tr>
<tr>
<td>9F</td>
<td>8m</td>
<td>A</td>
<td>A</td>
<td>A = no.</td>
<td>A = no.</td>
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<td>A = no.</td>
</tr>
<tr>
<td>9F</td>
<td>3m</td>
<td>A</td>
<td>A</td>
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<td>A = no.</td>
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<tr>
<td>9F</td>
<td>7m</td>
<td>A</td>
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<td>A = no.</td>
<td>A = no.</td>
<td>A = no.</td>
<td>D = yes, Y = no, N = no. A</td>
<td>A = no.</td>
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</tbody>
</table>

**figure 1**
P629
A neurophysiological study of A-delta fibres in demyelinating and axonal polyneuropathies through cutaneous silent period recordings

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2Marmara University, Istanbul, Turkey

Introduction

Cutaneous silent period (CSP) is a brief pause in voluntary muscle contraction following noxious cutaneous nerve stimulation which allows to study small myelinated fibres. We investigated CSP in patients with demyelinating or axonal polyneuropathy (PNP) in order to evaluate the involvement of A-delta fibres. Furthermore we estimated the correlation of CSP parameters with presence of neuropathic pain in these group of patients.

Materials and Methods

Eighty demyelinating PNP patients, 178 axonal PNP patients and 265 healthy controls underwent clinical [neurological examination, Medical Research Council Score, DN4 Questionnaire] and electrophysiological [motor root conduction time (MRCT), compound muscle action potentials (CMAP), sensory nerve action potentials (SNAP) and CSP of the ulnar nerve] investigations. Another electrophysiological parameter, called "afferent CSP time" (a-CSP time), showing the difference between the CSP latency and the MRCT, was also calculated, in order to evaluate the conduction of the afferent fibre network.

Results

In the demyelinating PNP group, the a-CSP time was significantly longer, with respect to the axonal PNP group and the healthy subjects, as well in the axonal PNP group when compared with the healthy subjects. Axonal PNP group had shorter CSP durations respect to demyelinating (P= 0.0059) and healthy subject (P= 0.0001); CSP duration in the demyelinating PNP group was not different from the healthy subjects. Axonal PNP group had neuropathic pain more frequently than the demyelinating PNP group (P=0.02), but CSP parameters were not different in painful patients with respect to the painless ones in both groups (P > 0.05, for all comparisons).

Discussion and conclusion

Our study confirms for the first time in a large number of patients that CSP represents a viable method of easy execution for detecting small diameter fibres involvement in the afferent sensory pathway in both axonal and demyelinating PNP. The abnormalities of a-CSP time found mainly in demyelinating PNP demonstrate the involvement of A-delta fibres in the pathological demyelinating process; the short duration of CSP mainly in axonal PNP supports the strong influence of the number of axon on this CSP parameter.

On the other hand, our study show that a reduced duration of the CSP does not correlate with the presence of neuropathic pain, suggesting that neuropathic could be related to pathophysiological mechanisms different from the mere A delta fibre loss.
**Abstracts of Poster Presentations – Poster Session 36 – Neuropathies 2**

**P630**
**Slowing of peripheral nerve conduction in patients with adult onset sporadic neuronal intranuclear inclusion disease (NIID) with leukoencephalopathy**

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²National Hospital organization Minami Kyoto Hospital, Rehabilitation, Joyo, Japan
³Nagoya University Graduate School of Medicine, Neurology, Nagoya, Japan

**Question**

Neuronal intranuclear inclusion disease (NIID) is a progressive neurodegenerative disease characterised by eosinophilic hyaline intranuclear inclusions which are widely observed in neuronal and somatic cells. NIID shows variable clinical manifestations such as dementia, ataxia, extrapyramidal signs, autonomic dysfunction and neuropathy. Infantile, juvenile, and adult-onset cases have been reported. Decreased deep tendon reflex in lower limbs and slowing of peripheral nerve conduction has been described in some NIID patients. However there were few documentations of nerve conduction study in adult onset sporadic NIID with leukoencephalopathy.

**Method**

We studied 3 NIID patients. Age at onset and duration of the disease were 74yrs (2yrs) in case 1, 62yrs (8yrs) in case 2 and 68yrs (4yrs) in case 3. All the patients had slowly progressive dementia and ataxia without muscle atrophy. Deep tendon reflex was decreased in case 1 and case 2. All showed typical MRI findings of high-intensity areas in the cerebral white matter in FLAIR images and high-intensity signals in the corticomedullary junction in DWI. In addition, Case 2 revealed high intensity lesions in brainstem and spinal cord at C1-C2 level. The clinical diagnosis was confirmed by skin, rectal and sural nerve biopsy.

**Results**

Case1 and Case 2 showed diffuse slowing of motor and sensory conduction with markedly prolonged F wave latency (Fig.1,2). CMAP amplitudes and waveforms were relatively preserved. No conduction block and temporal dispersion was found. Sural nerve SNAP amplitudes were decreased and median nerve SEP showed peripheral and central conduction delay in both cases. Case 3 showed prolonged F wave latency with normal SNAP amplitudes. These findings are similar to other inherited leukodystrophy such as metachromatic leukodystrophy and suggest abnormal myelination in peripheral nerves. Thinly myelinated fibers observed in sural nerve biopsy in case 1 and case 2 supports the notion.

**Conclusion**

Conduction slowing of peripheral nerve is an important finding for the diagnosis of adult onset sporadic NIID with leukoencephalopathy.

![Figure 1](image-url)
### Case 2

<table>
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<tr>
<th></th>
<th>DL (ms)</th>
<th>MCV (m/s)</th>
<th>CMAP* (mV)</th>
<th>SCV (m/s)</th>
<th>SNAP* (µV)</th>
<th>F wave (%)</th>
<th>F minimum latency (ms)</th>
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<tbody>
<tr>
<td>Lt. Median</td>
<td>5.2 ↑</td>
<td>39 ↓</td>
<td>5.1 ↓</td>
<td>49 ↓</td>
<td>6.5 ↓</td>
<td>69 ↓</td>
<td>34.5 ↑</td>
</tr>
<tr>
<td>Lt. Ulnar</td>
<td>2.7</td>
<td>46 ↓</td>
<td>5.3 ↓</td>
<td>52 ↓</td>
<td>6.6 ↓</td>
<td>94</td>
<td>33.8 ↑</td>
</tr>
<tr>
<td>Lt. Tibial</td>
<td>6.0</td>
<td>31 ↓</td>
<td>3.9 ↓</td>
<td></td>
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<td>0 ↓</td>
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<tr>
<td>Lt. Sural</td>
<td></td>
<td></td>
<td></td>
<td>34 ↓</td>
<td>4.2 ↓</td>
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*baseline to peak  

Height 163cm

#### Median SEP

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<tr>
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<th>Ep (ms)</th>
<th>N13 (ms)</th>
<th>N20 (ms)</th>
<th>CCT (ms)</th>
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<tr>
<td>Right</td>
<td>11.4 ↑</td>
<td>16.3 ↑</td>
<td>25.5 ↑</td>
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#### Tibial SEP

<table>
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<td>not evoked</td>
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</table>

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898
P631
Clinical features of recurrent Fisher syndrome and Bickerstaff brainstem encephalitis

*J. Ishii¹, M. Kawamoto¹, H. Yoshimura¹, N. Kohara¹
¹Kobe City Medical Center General Hospital, Neurology, Kobe, Japan

Question

Fisher syndrome (FS) is a variant of Guillain-Barré syndrome (GBS) characterized by ophthalmoplegia, ataxia, and areflexia. FS is usually monophasic, but on rare occasions, it may recur after a long asymptomatic interval. We examined the clinical and laboratory features of patients with recurrent FS. We also examined recurrent Bickerstaff brainstem encephalitis (BBE), recently regarded as a variant of FS with CNS involvement.

Methods

We examined retrospectively all the patients with GBS, FS and BBE who admitted to our hospital from January 2001 to March 2013. FS and GBS are defined based on a GBS criteria (1). BBE was defined FS with CNS involvement. FS with limb weakness was classified into FS. Totally 95 patients were found. We evaluated the frequency of recurrence of GBS, FS and BBE and analyzed the clinical and laboratory features of patients with recurrent FS and BBE.

Results

Ninety-five patients were classified into 54 (31 males) with GBS, 34 (23 males) with FS and 7 (5 males) with BBE (Fig. 1). The incidence of FS in our hospital was 36% of all GBS variants. There are more men than women in all groups. Two (4%) out of 54 GBS patients, 4 (12%) out of 34 FS and 2 (29%) out of 7 BBE patients had recurrences. The mean age at the onset was 39.5 yrs. in non-recurrent FS and that at initial onset in recurrent FS was 23.0 yrs. (p<0.001). Mean age of the recurrence in FS was 32.5 yrs. Symptoms were generally less severe at recurrent time than at the initial episode in recurrent FS patients. Anti-GQ1b antibody is positive in 22/30 (73%) of non-recurrent FS, 4/4 (100%) of recurrent FS (Fig. 2), 2/5 (40%) of non-recurrent BBE, and 2/2 (100%) in recurrent BBE. No significant difference was found in nerve conduction between non-recurrent and recurrent FS and BBE.

Conclusions

The frequency of recurrence of FS/BBE is higher than that of GBS. The age of onset in recurrent FS is younger than that in non-recurrent FS.

Reference


Legends of figures

Fig. 1 The frequency of recurrence of GBS, FS, and BBE

Fig. 2 Comparison of recurrent and non-recurrent FS
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**figure 1**

![Bar chart showing the number of cases for GBS, FS, and BBE, with recurrence and non-recurrence percentages.]

**figure 2**

<table>
<thead>
<tr>
<th></th>
<th>non-recurrent (n = 30)</th>
<th>recurrent (n = 4)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at first episode (years)</td>
<td>39.5±18.0</td>
<td>23.0±2.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at recurrence (years)</td>
<td></td>
<td>32.5±3.4</td>
<td>0.07</td>
</tr>
<tr>
<td>Male</td>
<td>21 (70%)</td>
<td>2 (50%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Preceding infection</td>
<td>24 (80%)</td>
<td>2 (50%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Anti-GQ1b antibody</td>
<td>22 (73%)</td>
<td>4 (100%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Days to peak</td>
<td>8.8±6.5</td>
<td>6.8±2.1</td>
<td>0.55</td>
</tr>
</tbody>
</table>
Electrophysiological findings in POEMS syndrome during four years follow-up: a case report

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POEMS syndrome is classified as a rare type of plasma cells dyscrasias, with polyneuropathy as its main feature and sometimes the first symptom. We describe a case report of a female with POEMS syndrome, treated with chemotherapy and autologous hematopoietic stem cell transplantation. Results of four electrophysiological examinations are presented, with considerable axonal changes, quite stable conduction blocks and signs resembling carpal tunnel syndrome. Variability of electrophysiological features in POEMS syndrome should be considered during approaching acquired demyelinating polyneuropathies.
A rare case of Foot Drop in Children - Diagnostic and electrophysiological aspects

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Introduction

Foot drop is a gait abnormality in which the dropping of the forefoot happens due to weakness, damage to the peroneal nerve or paralysis of the muscles in the anterior portion of the lower leg. External popliteal nerve palsy is one of the most common causes of foot drop in children.

Presentation

The authors present a case of a child admitted in our clinic with gait disturbance and common peroneal nerve palsy with onset at the age of 4 - 5 years. He presented a slowly progressive evolution over time. Extended investigations revealed an unusual cause of SPE lesion. The electrophysiological studies we performed had a very important role in the management of this particular case.

Conclusions

When the physician is faced with a child presenting dropping of the foot, one needs to approach with care and adopt a thorough plan of investigations in order to appropriately treat the patient. Considering the vast etiology of this condition a careful evaluation of the child often can overcome the diagnostic challenge that is a peoneal nerve paralysis.

Key words

external popliteal nerve, foot drop, child
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P634
The Electrophysiological Differences Between Acquired Inflammatory Demyelinating Polyneuropathies
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Question
Acquired inflammatory demyelinating polyneuropathies (AclDP) are the most common autoimmune neuropathies. AclDPs are categorized into 3 groups as acute (GBS), sub-acute (SIDP) and chronic (CIDP). The electrophysiological differences between the AclDPs have not been defined in the literature clearly. The purpose of this study is to reveal the electrophysiological differences between 3 groups AclDPs.

Methods
GBS was diagnosed when the progression period is less than 4 weeks, SIDP was diagnosed when the period was between 4 and 8 weeks, and CIPD was diagnosed when the period was longer than 8 weeks and the history of previous episodes.

Results
Within the study, 129 GBS, 123 CIDP and 31 SIDP patients were included. Whereas mean sensory nerve amplitudes of GBS patients were statistically significantly higher than the CIDP and SIDP patients, motor nerve amplitudes were lower. Both mean sensory and motor NCV of GBS patients were higher than the CIDP and SIDP patients. Mean F wave latency of SIDP patients were significantly longer than the CIDP and GBS patients. Mean motor distal latencies were slightly longer in SIDP patients, but the difference was not statistically significant.

Conclusion
Nerve conduction studies of GBS patients were better than other AclDPs except from the motor amplitudes. Changes in nerve potential amplitudes indicate nerve regeneration, nerve degeneration, or the presence of conduction block. The lower motor amplitudes of GBS patients can be arisen from the conduction block.
Clinical and electrodiagnostic findings in vitamin B6 induced polyneuropathy

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**Question**

High dose vitamin B6 is neurotoxic. Previous case reports were sparse and little is known about the clinical and electrodiagnostic findings.

**Methods**

To report three patients with vitamin B6 induced polyneuropathy and a review the involved literature.

**Results**

Three patients whose ages were 80, 83 and 83 years old presented with numbness and ataxia for 3 to 8 months. Examination showed signs of polyneuropathy and sensory ataxia. Underlying diseases included radiculopathy in two patients and DM in two patients. They took vitamin B1-6-12 combination tablet, which contained vitamin B1 100 mg, vitamin B6 200 mg and vitamin B12 200 µg, one tablet three times a day, for three to ten years. Investigations for other causes of neuropathy were unremarkable. Blood level of vitamin B6 were markedly elevated at 104.6, 81.4 and 66.9 times of upper normal limits. Electrodiagnosis showed symmetric axonal sensory polyneuropathy in two patients. However, coexisting C7 or L5 radiculopathy was present in two patients. One year after vitamin discontinuation, two patients showed no significant improvement in neuropathy and gait.

**Conclusions**

Consumption of high dose vitamin B6 causes axonal polyneuropathy and sensory ataxia which may not be reversible.
P279
Effects of increasing the number of return electrodes in tCS

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Question
Transcranial current stimulation (tCS) has been shown to influence cortical excitability and is currently being studied as a putative therapy in several neuropsychiatric disorders. Bipolar electrode configurations are usually used, with one electrode placed over the region of interest and a return electrode (RE) positioned away from it. In these configurations the induced electric field (E-field) magnitude is very similar under both electrodes, which leads to unwanted activations in regions close to the RE. In this study we examine whether multiple REs may reduce these activations effectively.

Methods
Using the finite element method, the induced E-field was calculated in a realistically shaped heterogeneous head model, built from the template Colin27. All models contained cylindrical electrodes (radius of 1 cm), where the anode was placed over C3 (injected current: 1 mA). The number of REs (n) varied from one to five (return current 1/n mA). For all models, the average E-field norm was calculated in a cylindrical ROI located in the cortex and centered under each electrode.

Results
The average E-field under the anode / cathode in the bipolar configuration was of 0.180 V/m / 0.156 V/m. Increasing the number of REs did not influence the field under the cathode (reduction to 96 % of the maximum value) but did so under the REs (reduction to 37 % of the maximum value, with five REs).

Conclusions
These multiple RE configurations might be effective in protocols where highly focal stimulation is needed under one electrode with little secondary activations.
P635
Quality of Life and visual impairment in patients with optic neuropathy before and after non-invasive electrical stimulation

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University Magdeburg-Stendal (FH), AHW, study paths Rehabilitation Psychology, Stendal, Germany

Question

Does non-invasive repetitive transorbital Alternating Current Stimulation (rtACS) of patients with optic neuropathy induce changes of detection accuracy within visual fields? Are these changes related to improved vision-related Quality of Life (vrQoL)?

Methods

Within a double-blinded, randomised trial 44 patients received 10 days rtACS (20-40 min daily) while 37 received 10 days sham-stimulation. Detection accuracy within visual fields (High Resolution Perimetry, HRP) and vrQoL (National Eye Institute-Visual Function Questionnaire, NEI-VFQ 39 + neuroophthalmologic supplement) were recorded before intervention, after 10 days stimulation, and at a 2-months follow-up.

Results

An improvement of 4.52% in HRP could be observed after rtACS compared to 0.04% after sham at follow-up. Factor analysis disproved the original structure of the NEI-VFQ 39 + supplement in favour of two factors visual field defect and related impairments (factor 1) and general health and mental distress (factor 2). At follow-up both groups reported subjective benefits (p

Conclusion

These results confirm the potential of rtACS to ameliorate deficits in visual functioning after optic nerve damage. However, the missing relation between changes of visual field detection accuracy and vrQoL strengthens the need for further research.
P636
Comparison between adaptive and fixed stimulus paired-pulse TMS in normal subjects

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Question

Paired-pulse TMS (ppTMS) is used to examine cortical excitability. Typically, ppTMS consists of a facilitating or inhibiting conditioning stimulus followed by a test pulse delivered at a constant strength. Alternatively, the test pulse stimulus intensity can be adjusted to produce a MEP response of a certain amplitude. Such adaptive techniques (requiring statistical calculation at runtime) have been introduced to overcome some shortcomings with conventional ppTMS. At our institution, we have tried one adaptive method (“best-PEST”) for ppTMS, however, before changing our protocol we decided to compare results from the two different techniques.

Methods

Twenty healthy subjects were examined with ppTMS in two sessions (fixed stimulus ppTMS followed by adaptive ppTMS). Short-interval intracortical inhibition (SICI), intracortical facilitation (ICF) and long-interval intracortical inhibition (LICI) were examined. The conditioning stimuli where the same for the two methods. In the first session, the test pulse was delivered at 120% resting motor threshold. In the second session, the stimulus intensity was set to produce a 0.5 mV MEP response (according to a maximum likelihood model). MEP responses were recorded from the dominant first interosseus muscle.

Results

There were significant intraindividual correlations between the two methods regarding SICI (p=0.01), ICF (p<0.01) and LICI (p=0.02) measures. Adaptive SICI and ICF test pulse intensities were highly correlated to the motor threshold and seem to require normalization. ‘Conventional’ SICI data tended to cluster at near maximum inhibition (i.e., a well-known ceiling effect) which was not observed in adaptive ppTMS. ICF was, on the other hand, more difficult to establish with the used adaptive protocol.

Conclusions

Adaptive ppTMS excitability measures clearly correlated with those obtained with constant stimulus ppTMS. Some advantages with the adaptive technique were observed but also potential problems.
P637
Primary motor cortex theta burst stimulation does not enhance motor skill transfer from one trained hand to the other untrained hand

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⁴Clinic Nuremberg, Neurology, Nuremberg, Germany

Question
The human motor cortex is organized in a segregated integrative network with connected long-distance association fibers, e.g. between both hemispheres. This organization adapts to a changing environment according to Hebb (1949), for example during motor skill training. Training skill improvement of one hand also enhances training skill performance of the opposite non trained hand, termed as motor transfer. The aim of this study was, first to investigate whether a non-invasive transcranial magnetic stimulation (TMS) enhances retrieval of the trained motor skill from one trained hand to the other untrained hand, and second, whether such an influence is age-dependent, because it is suggested that during ageing white matter changes appear which may delay motor transfer.

Methods
39 healthy right handed subjects were included. Subjects was separated into three young groups (n=27; 27±6 years mean±sd) and one old group (n = 12; 63±6 years mean±sd). In one young group subjects were stimulated with intermittent theta burst stimulation (iTBS; termed as young-iTBS), one further group was stimulated with the continuous TBS (young-cTBS) and the third group was sham stimulated (young-sham). The old group was stimulated with iTBS (old-iTBS). ITBS and cTBS were applied over the contralateral M1 to the trained right hand (M1-left) after the training session. All subjects trained the Jebson-Taylor-Hand-Function-Test (JTHFT) ten times repetitively with their dominant right hand. The training effect of JHFT was tested for both hands before and after the stimulation.

Results
Time to perform the JTHFT was slower in older subjects throughout the whole training (initially 28,7 seconds vs. 26,8 seconds; at the end of training 21,8 seconds vs. 19,9 seconds, one-factorial ANOVA, p=0,019 respectively p=0,031). In all groups the time of the JTHFT improved significantly for the trained right hand (motor skill learning) as well as for the untrained left hand (motor transfer), whereas there were no differences in the relative amount of motor skill learning or transfer between young and old subjects. iTBS (young-iTBS and old-iTBS) over the M1-left did not significantly enhance the time of JTHFT of the left hand. The young-cTBS group also did not show a decrease of time for the JTHFT.

Conclusions
TBS stimulation over M1-left neither in young nor in old subjects did enhance manual motor transfer. We conclude and suggest that the premotor cortex rather than M1 is involved in information processing of manual transfer.
P638
Slow Oscillatory Stimulation simulating Gait Rhythm induces LTP-like effects on Corticospinal Excitability in Foot

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²Kyoto university, Integrative Brain Science, Kyoto, Japan

Human bipedal gait requires supraspinal motor control in addition to subcortical pattern generator system. In previous human studies, the corticospinal tracts from the primary motor cortex (M1) contribute to control foot flexors rather than extensors during gait. In animal studies, when monkeys were forced to walk by two hindlimbs, M1 neurons fired rhythmically according to gait cycle. Recently, slow oscillatory stimulation (SOS) over M1 hand area (0.8Hz) by transcranial electrical current stimulation induced LTP-like effects. Now, we investigated whether SOS given over M1 foot area simulating gait cycle can induce plastic changes of corticospinal tracts engaged in bipedal gait. Nine healthy subjects participated in the study. In the experiments, they were given SOS during gait (SOS+gait) and on another day, given sham stimulation during gait (Sham+gait). As a result, they showed significant enhancement of corticospinal excitability in TA muscles of the stimulated site immediately and 30 min after SOS+gait, but not after Sham+gait. We considered that SOS simulating gait cycle induced LTP-like effects in corticospinal excitability of foot and that it might be a promising method for enhancement of the supraspinal control during gait, especially in patients with gait disturbance from central nerve disorder.
P639
Effect of combined repetitive transcranial and peripheral magnetic stimulation on functional state of the brain in stroke patients

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Question
Repetitive transcranial magnetic stimulation (rTMS) induces functional cortical reorganization in stroke patients. It was also recently shown that repetitive peripheral magnetic stimulation (rPMS) promotes a functional reorganization of the motor cortex in healthy subjects. Based on this information we investigated the effect of combined rTMS and rPMS on functional state of the brain in stroke patients.

Methods
77 patients (mean age - 63.02±1.21 years) with cerebral hemispheric ischemic stroke were randomized to receive 1 Hz real or sham rTMS and rPMS for 10 consecutive days against the background of conventional rehabilitation and drug therapy. Single-pulse TMS and electroencephalography (EEG) were performed before and after treatment.

Results
Real stimulation group (RSG) showed a significant increase of motor evoked potential (MEP) amplitude and reduce resting motor threshold (rMT) of the affected hemisphere. No significant changes were observed of MEP amplitude and rMT of both affected and intact hemispheres of the sham group (SG), as well as the intact hemisphere of the RSG.

The power spectral EEG analysis revealed the hemispheric differences in EEG changes of both RSG and SG. In the RSG patients with left-side stroke observed a significant increase in alpha-1 band power in the affected and the intact hemispheres, increase in alpha-2 band power and increase in alpha rhythm frequency in the affected hemisphere. In the SG patients with left-side stroke observed a significant increase in alpha rhythm frequency in the intact hemisphere. In the RSG patients with right-side stroke observed a significant decrease in theta band power in the affected and the intact hemispheres, increase in alpha-2 band power in the intact hemisphere and increase in alpha rhythm frequency in the affected and the intact hemispheres. In the SG patients with right-side stroke observed a significant increase in theta band power and alpha-1 band power in the intact hemisphere and alpha-2 band power of both the affected and the intact hemispheres.

Conclusions
Combined rTMS and rPMS increased cortical excitability of the affected hemisphere and harmonized electrical activity of the brain of both the affected and the intact hemispheres in stroke patients.
Objective

To study the effect of transcranial static magnetic field stimulation (tSMS) over the parietal cortex on the size of somatosensory evoked potentials (SEPs) in humans.

Methods

SEPs were elicited by electrical stimulation of right median nerve at the wrist before, during and after tSMS (or sham) in 8 healthy subjects. tSMS was applied for 20 min to the left parietal cortex using a neodimium cylindric magnet with a diameter of 6 cm and height of 3 cm. Sham stimulation was obtained by applying for 20 min to the left parietal cortex a steel cylinder with a diameter of 6 cm and height of 3 cm.

Results

Amplitudes of N20/P25 and P25/N30 following right median nerve stimulation were significantly modified for at least 10 min after the end of tSMS, whereas P14/N20 were unaffected. There was no effect on SEPs evoked by right median nerve stimulation after sham stimulation.

Conclusions

tSMS over the sensorimotor cortex can induce a long-lasting changes in cortical components of SEPs.

Significance

tSMS can modulate cortical somatosensory processing in humans.
P641
Tele-Medicine approach in Non-Invasive Brain Simulation: case report in a pain patient

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Question

Chronic pain often shows insufficient response to pharmacological treatments. Non-invasive brain stimulation (NIBS) of the motor cortex has been proposed as an alternative therapeutic approach. Methods: We present a case of a patient treated in our Hospital using tDCS with good pain relief after 5 tDCS daily sessions, and with maintenance of the positive analgesic effects for more than one year with a single tDCS session every 7 days. The patient lives very far away from our Hospital and we decided to use modern information technology to start a Tele-NIBS treatment approach

Case presentation

Our patient, a 56 years-old male, was diagnosed of macrophagic myofasciitis. Macrophagic myofasciitis is a rare condition with few hundreds of definite cases identified in France, and isolated cases recorded in other countries. The main clinical complaints of our patient were pain and chronic fatigue. Pain was intense (mean VAS of 8, VAS scale scored pain from 0 to 10, where 10 meant worst possible pain) and the patient was treated with many different protocols of analgesic drugs. All these treatments failed. For this reason, the patient was screened as a possible candidate for NIBS. We received the patient 2 years ago and we decided to treat the patient with a tDCS protocol. The NIBS consisted of 20 minutes of anodal stimulation (with an intensity of 1.5 mA) over both motor cortices. This stimulation protocol was repeated on five consecutive days and maintained for months with one weekly session. Once the patient reached a good pain control, he stopped the treatment and VAS started to go up again in few months (VAS=5). The reason why the patient stopped the treatment was that he lived very far from the Hospital (about300 Km) and it was difficult for him to reach our Hospital.

Few months ago, we repeated the 5 days tDCS sessions with the same protocol and the patient’s pain diminished again (VAS=2±1). After more than one year of successful treatment, we decided - together with the patient - to use modern information technology to start a Tele-NIBS treatment approach. Conclusions: Here we report a case of a successful tele-NIBS approach using “at home” tDCS to treat pain. This strategy may increase the number of patients that may benefit from tDCS as an adjuvant treatment for pain (or other NIBS treated disorders).
P642
Modulating the interplay between exploration and exploitation in instrumental learning by prefrontal transcranial direct current stimulation

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Question

Accumulating experimental evidence indicate that instrumental learning situations in humans recruit both the striatal and the working memory system. However, the role of working memory system in instrumental learning is still not well understood.

Methods

In order to address this issue, we applied transcranial direct current stimulation (tDCS) optimized for targeting dorsolateral prefrontal cortex (see Figure 1), a key region in working memory for 15 minutes using 1.0 mA intensity. By following a double-blinded, repeated-measures study design, 16 male participants took part in a sham and anodal tDCS session separated by 1 week. Accuracy, reaction time and the number of behavioral shiftings (trial-to-trial changes after positive and negative outcomes) were taken as dependent variables.

Results

Although general accuracy and reaction time was not influenced by tDCS, we observed significantly greater amount of behavioral shifting in the active condition compared to the sham condition.

Conclusion

In line with previous findings, our results suggest that the working memory system may influence instrumental learning by actively maintaining reinforcement history and adjusting behavior on trial-to-trial bases.

figure 1
Safety and characterization of a novel multi-channel TMS stimulator

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Question

Currently available TMS stimulators have a single channel operating a single coil. This study presents benefits of a novel multi-channel stimulator, comprising five channels with independently controllable stimulation parameters.

Methods

Simultaneous and sequential operation of various channels was tested in healthy volunteers. Paired pulses schemes with various inter-stimulus intervals (ISIs) were studied for the hand APB and the leg AH muscles. Energy consumption and coil heating rates with simultaneous operation of 4 channels was compared to a figure-8 coil.

Results

Repetitive operation of separate channels with different stimulation parameters is demonstrated. The operations of various channels can be combined simultaneously or sequentially to induce multiple pulses with ISIs of µs resolution. A universal pattern of inhibition and facilitation as a function of ISI was found, with some dependence on coils configurations and on pulse widths. A strong dependence of the induced inhibition on the relative orientation of the conditioning and test pulses was discovered. The ability of this method to induce inhibition in shallow brain region but not in deeper region is demonstrated. Significant reductions in energy consumption and coil heating were demonstrated for several channels operated simultaneously compared to a standard figure-8 coil.

Conclusions

The multi-channel stimulator enables the synchronized induction of different excitability modulations to different brain regions using different stimulation patterns in various channels. Multiple pulses operation with coils with various depth profiles can increase the focality of TMS effect in deep brain regions.

Figure 5: Excitability modulation induced by paired pulses for the hand APB as a function of ISI for 4 capacitor combinations.

Figure 6: Excitability modulation induced by paired pulses at ISIs of 200, 400 and 600 µs.
P644
Anticipatory motor control is mediated via the left posterior parietal cortex (PPC)

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Question

Within the motor control network the posterior parietal cortex (PPC) has been related to anticipatory motor control while the primary motor cortex (M1) may be rather dedicated to movement execution. Assuming that cortical nodes within this network provide different contributions to motor control, the present study elucidates the specific relevance of left PPC for movement timing.

Methods

Anodal vs. cathodal transcranial direct current stimulation (tDCS) was applied for 10 min over left PPC in right-handed subjects in separate sessions. Left M1 tDCS served as control condition. Anticipatory motor control was assessed by means of a synchronization task requiring subjects to synchronize their own finger taps with a regular auditory metronome. In addition, subjects performed a continuation task investigating interval reproduction and a simple auditory reaction task. Tasks were performed with the right and the left hand, respectively, prior to and immediately after tDCS.

Results

Anodal left PPC tDCS decreased synchronization accuracy of either hand during the synchronization task. During continuation, cathodal left PPC tDCS increased the reproduced interval of the left hand but decreased the interval of the right hand. Reaction times were not significantly modulated by PPC stimulation. Left M1 tDCS was not efficient to significantly modulate performance in any of the tasks.

Conclusions

The present data underline the superordinate role of left PPC for anticipatory motor control of either hand - revealing a piece of evidence for left hemispheric PPC dominance. The observed effects cannot be explained by alterations of motor cortical excitability.
Case report: Seizure induction by single-pulse transcranial magnetic stimulation after anodal transcranial direct current stimulation in a stroke patient

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Transcranial direct current stimulation (tDCS) has been used as a safe therapeutic tool in neurological disorders, especially in stroke, because anodal stimulation given over the affected M1 area produces LTP-like effects on corticospinal excitability. Single-pulse transcranial magnetic stimulation (TMS) has been used as an evaluation tool of corticospinal excitability even in stroke, with a minimal risk of de novo seizure induction. Here, we report a 35 year-old male with postoperative subcortical hemorrhage in the left hemisphere, who developed a generalized convulsion starting from the affected upper limb after a single-pulse TMS subsequent to the anodal tDCS given over the ipsilesional M1 hand area for 10 minutes. He had no history of seizure or electroencephalogram (EEG) abnormality, and received several TMS tests without any side effects before tDCS intervention. EEG testing just after and 3 month after the event revealed no epileptiform discharges. He has been seizure-free at least for 3 months. The present case report raises the possibility that a single-pulse TMS after tDCS may be associated with a seizure risk in patients with brain lesion due to their accumulative excitatory effects.
**P646**

**Transcranial direct current stimulation (tDCS) in the treatment of adolescents with attention deficit-hyperactivity disorder (ADHD)**

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**Question**

The stimulation of the brain with weak direct current through the scalp (tDCS) is a safe, well tolerable and effective procedure which allows a focal modification of cortical excitability in brain areas of interest and causes changes of corresponding neurophysiological functions associated with the stimulated brain areas. In our study we investigated the influences of the anodal tDCS of the prefrontal cortex on the clinical symptoms of adolescent ADHD as well as on the neuropsychological parameters: working memory, executive functions and attention.

**Methods**

Sixteen adolescents with ADHD (12-16 years old) were treated according to the double-blind sham controlled cross-over design with anodal tDCS over the left dorsolateral prefrontal cortex (DLPFC, 1mA, 20 min) and with the sham protocol (impedance control, no direct current, 20 min) 5 days each with a 2 weeks pause between these conditions. The first tDCS and sham stimulation were performed in the MR scanner combined with the working memory task during the fMRI (3 Tesla Siemens Trio). The influence of tDCS on the neuronal networks of attention, impulse inhibition and working memory was investigated. The clinical effects were evaluated by patients and their parents in standardized questionnaires (FBB-ADHS). The dynamik of neuropsychological parameters was studied using a computerized continuous working memory test (QbTest, QbTech, Sweden) each day during the treatment and one week after.

**Results**

All 16 Patients tolerated the tDCS well. 5 Patients reported local sensation such as itching under the stimulation electrode, which occurred during the tDCS as well as during the sham condition. A significant improvement of the reaction time variability was observed in tDCS and not in the sham condition. Corresponding activation of attention/working memory network was registered in the tDCS condition compared with sham stimulation. This activation was observed not only in the brain area under the stimulating electrode (DLPFC) but also in brain areas remote from the stimulated region (inferior frontal gyrus, anterior cingulate).

**Conclusion**

Anodal tDCS revealed significant clinical effects in ADHD. The neuropsychological changes in RT variability correlated with an activation of attention/working memory networks. This project expands the perspective of a possible use of tDCS on the treatment of ADHD and other psychiatric disorders such as tics, anorexia and depression in children and adolescents.
P647
A dissociation between propriospinal facilitation and inhibition after bilateral transcranial direct current stimulation

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Propriospinal neurons receive bilateral input from both premotor cortex (PM) and primary motor cortex (M1) via the reticulospinal tract. In humans, the excitability of propriospinal neurons can be inferred by pairing an ascending volley from peripheral nerve stimulation and a descending volley from transcranial magnetic stimulation (TMS) to summate at the C3-C4 level. Previously conventional cathodal transcranial direct current stimulation (tDCS) was found to suppress C3-C4 propriospinal neuron excitability in the arm ipsilateral to stimulation (Bradnam et al. 2011). The effects of bilateral tDCS are unknown. The present study compared bilateral M1-M1 and PM-M1 tDCS effects on propriospinal excitability in the left arm. This was a randomised, double-blinded, sham-controlled study of 12 healthy adults (28.3 yrs, 5 males). Each participant received bilateral tDCS with the cathode over left PM or left M1, and the anode over right M1 in separate sessions (PM-M1, M1-M1 or Sham). Real tDCS stimulation was 1 mA for 15 mins. Sham stimulation was ramped down from 1 mA within 30 secs. TMS of right M1 elicited motor evoked potentials (MEPs) in left Biceps Brachii (BB) at a range of TMS intensities relative to active motor threshold (AMT). Left BB MEPs were conditioned by median nerve stimulation at an optimal interstimulus interval between 6 - 9 ms determined for each individual, and expressed as a ratio of conditioned / non-conditioned. Conditioned MEPs were facilitated (FAC, p<0.001) at TMS intensities near AMT, and inhibited (INH, p<0.001) at slightly higher intensities. After tDCS, FAC was reduced for M1-M1 tDCS compared to SHAM (p=0.039) but not after PM-M1 tDCS (p=0.67). INH was unchanged across all sessions. This pattern of results could mean that M1-M1 tDCS reduced basal facilitation of motor neurons via propriospinal neurons, while maintaining or sparing their inhibition, presumably via inhibitory interneurons. Compared to single hemisphere stimulation, M1-M1 DCS may provide bilateral input to inhibitory interneurons allowing for more selective suppression of only facilitatory propriospinal inputs. Since propriospinal inputs can be up-regulated in some patients after stroke (Stinear & Byblow, 2004), bilateral M1 tDCS may offer utility for promoting functional recovery of upper limb function.
P648
Transcutaneous spinal DC stimulation (tsDCS) modulates interhemispheric processing of motor and visual stimuli in a polarity-specific manner

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Question
Transcutaneous spinal Direct Current Stimulation (tsDCS) is a noninvasive technique based on the application of weak electrical currents over thoracic spinal cord. Although tsDCS can influence the conduction of spinal pathways and circuits, whether this technique can modulate human brain function is unclear. Here, we studied effects of tsDCS on interhemispheric processing of motor and visual stimuli by evaluating changes in duration of ipsilateral silent period (iSP) and in hemifield Visual Evoked Potentials (hVEPs) parameters.

Methods
In eight volunteers we evaluated changes in iSP and hVEPs amplitude, latency and interhemispheric delay, before (T₀) and at different intervals (immediately after = T₁, 60’ = T₂) after anodal and cathodal tsDCS (T10-T12 level, 2.0 mA, 20’). Motor Evoked Potentials (MEPs) were recorded from abductor digiti minimi (ADM) and abductor hallucis (AH). VEPs were recorded by reversal (1Hz) of a horizontal square wave grating (2c/deg) with the display positioned in the right hemifield.

Results
Anodal tsDCS reduced iSP (one-way ANOVA, ADM: T₀ vs. T₁: p = 0.0002; T₀ vs. T₂: p = 0.0001) and shortened the interhemispheric delay for N1 (T₀ vs. T₁: p = 0.0006; T₀ vs. T₂: p = 0.017) and P1 potentials (T₀ vs. T₁: p = 0.0025; T₀ vs. T₂: p = 0.0006), while cathodal stimulation has opposite effects both on ADM iSP (ADM: T₀ vs. T₁: p = 0.0001; T₀ vs. T₂: p = 0.0006) and hVEPs (N1: T₀ vs. T₁: p = 0.04; T₀ vs. T₂: p = 0.005; P1: T₀ vs. T₁: p = 0.048; T₀ vs. T₂: p = 0.019).

Conclusion
tsDCS seems to modulate interhemispheric processing of motor and visual stimuli in a polarity-specific manner: given the well-known inhibitory effect of anodal tsDCS, opposite from that induced by anodal transcranial direct current stimulation (tDCS), it may act at supraxial level also by dampening the callosal inhibitory input, then allowing a faster interhemispheric communication. tsDCS could be a new promising therapeutic tool in managing a number of human diseases characterized by an impaired interhemispheric balance, such as stroke, parkinsonisms and schizophrenia.
Transcranial direct current stimulation (tDCS) of left parietal cortex facilitates gesture processing in healthy subjects

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Question

Gesture processing deficits constitute a key symptom of apraxia, a disorder of motor cognition frequently observed after left-hemispheric stroke. The clinical relevance of apraxia stands in stark contrast to the paucity of therapeutic options available. Transcranial direct current stimulation (tDCS) is a promising tool for modulating disturbed network function after stroke. We here investigate the effect of parietal tDCS on gesture processing in healthy human subjects.

Methods

Neuropsychological and imaging studies suggest that the imitation and matching of hand gestures involves the left inferior parietal lobe (IPL). Using neuronavigation based on cytoarchitectonically defined anatomical probability maps, tDCS was applied over left IPL areas PF, PFm or PG in healthy participants (n=26). Before and after tDCS subjects performed a gesture matching task and a person discrimination task for control. Changes in error rates and reaction times were analyzed for the effects of anodal and cathodal tDCS (compared to sham tDCS).

Results

Matching of hand gestures was specifically facilitated by anodal tDCS applied over cytoarchitectonically defined IPL-area PFm, while tDCS over IPL-areas PF and PG did not elucidate significant effects.

Conclusions

Taking into account tDCS electrode size and the central position of area PFm within IPL, it can be assumed that the observed effect is rather due to a combined stimulation of the supramarginal and angular gyrus than an isolated PFm-stimulation. Our data confirm the pivotal role of left IPL in gesture processing. Furthermore, anatomically guided tDCS of left IPL may constitute a promising approach to neurorehabilitation of apraxic patients with gesture processing deficits.

figure legend

Depicted are the changes of RTs when RTs after tDCS are compared to RTs before tDCS for anodal, sham and cathodal tDCS applied over the cytoarchitectonically defined areas PF, PFm and PG of the left IPL. Exploration of the significant three-way interaction between TASK, STIMULATION and SITE by three two-way ANOVAs for each IPL-site separately and planned paired t-tests revealed a differential improvement in gesture matching (versus person discrimination) for anodal tDCS only, but not for sham or cathodal tDCS. Error bars indicate the standard error of the mean (SEM).
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figure 1
Dorsal transcutaneous spinal Direct Current Stimulation (tsDCS) induces remote effects on the Ia-motoneuron connections in the cervical spinal segments.

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Question
tsDCS is a novel non-invasive tool to modulate human spinal cord function (Cogiamanian et al. 2008, Lamy et al. 2012). To assess whether dorsal tsDCS modulates the cervical Ia-motoneuron connections, we tested the influence of tsDCS on the H reflex in the human upper limb.

Methods
tsDCS (2 mA, 20min) was delivered in 12 healthy volunteers (aged 22-50 yrs, 5 males) through a pair of surface electrodes placed over the spinous processes of T10-12 and above the right shoulder. The H reflex was elicited stimulating the median nerve at the elbow and recording the response with surface electrodes placed over the flexor carpi radialis muscle. Each subject underwent anodal and cathodal tsDCS in random order. H reflex was recorded i) before tsDCS (T0); ii) 5 (T1), 10 (T2), 15 (T3) minutes after tsDCS onset; iii) immediately after tsDCS offset (T4). The H reflex size is expressed as percentage of baseline amplitude (=100%). Values are mean ± SE.

Results
The two way ANOVA disclosed a significant “time” x “stimulation” interaction on the percentage change of H reflex amplitude. Post-hoc analysis revealed that anodal tsDCS significantly reduced the H reflex amplitude at T3 (78.3±8.2%; p= 0.040) and at T4 (76.3±7.6%; p=0.028), whereas cathodal tsDCS significantly increased the H reflex amplitude only at T1 (125.5±11.0%; p=0.018).

Conclusion
Dorsal tsDCS influences human cervical mono/oligosynaptic Ia-motoneuronal reflex in a polarity specific manner. Because the temporal dynamic of tsDCS-elicited H reflex changes differed between the two polarities, anodal and cathodal tsDCS might have different --not simply specular-- mechanisms of action.
P652
Where do we stimulate with tDSC?
Anatomical determinants of the electric field during transcranial direct current stimulation.
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Question
Transcranial direct current stimulation (tDSC) is characterized by a complex electric current flow which depends on many different factors. Computational models can help to determine stimulation areas based on realistic head models. In this study we quantified the influence of various anatomical factors on the electric field distribution in the brain during tDSC by applying cutting-edge modeling approaches.

Methods
We constructed two highly realistic finite element (FEM) head models from MR images. Different tissue types were segment using SimNibs (www.simnibs.de). Special attention was paid to accurately model the skull by segmenting different skull layers including compact and spongy bone. Conductivity anisotropy for WM was estimated from diffusion tensor imaging. Based on the standard montage for inducing motor cortex plasticity, we simulated the effect of small displacements of the stimulation electrode by translating and rotating it around the primary motor cortex over a region of 4 x 4 cm. We explored the effect of different anatomical features on the electric field using a multiple regression model.

Results
Local thinnings of the skull act as pathways for current flow which leads to localized hotspots of high electric fields in the brain (Fig. 1 A + B). This effect is independent from explicitly modeling spongy bone in spite of having an effect on how much current is shunted away from the brain (Fig. 1C). The explanatory variables skull thickness, sulcal depth, csf thickness and distance to electrode edge can account for 50% of the explained variance of the electric field (Fig. 2 A-E). Irrespective of electrode position the same regions in the brain are subject to stimulation (Fig. 2 F).

Conclusions
We quantified the influence of anatomical factors on the electric field distribution during tDSC. These factors explain about half of the variance of the electric field. We show that certain brain regions are especially prone to stimulation which is largely independent of electric position. Local skull thinnings lead to focused hotspots of high electric fields in the brain.

Our results have clear implications for the interpretation of stimulation effects of tDCS and can serve as a starting point for optimized electrode montages which can account for individual anatomical variations.
figure 1

A

B

C

figure 2

A

B

C

D

E

F
P653
Intermittent theta burst stimulation inhibits human motor cortex when applied with mostly monophasic (anterior-posterior) pulses

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**Question**

Does the current direction influence the effect of intermittent theta burst stimulation (iTBS) on human motor cortex excitability?

**Methods**

We stimulated the dominant hand representation of the motor cortex in 15 healthy subjects, using “unidirectional biphasic” pulses with an M-ratio (i.e., degree of monophasicity) of 0.2, generated by a prototype controllable TMS machine (cTMS-3, Rogue Resolutions Ltd., Cardiff, UK), connected to a standard figure-of-eight coil with physical attributes similar to a Magstim D70 coil. iTBS was applied conventionally, using 20 sequences of 2 seconds iTBS (10 bursts at 5 Hz burst repetition frequency, each burst consisting of 3 pulses of 80 % AMT intensity repeated at 50 Hz frequency). In two separate sessions pulses differing in current direction and shape were applied: a) posterio-anterior (PA) current direction in the brain, 75 microseconds (iTBS_PA75). b) AP current direction, 45 microseconds (iTBS_AP45). Before and for 30 minutes after iTBS, we monitored the modulation of motor evoked potential (MEP) amplitude from the dominant first dorsal interosseus using conventional, monophasic, suprathreshold pulses generated by a Magstim 200 stimulator, inducing PA currents in the brain, at 0.2 Hz frequency.

**Results**

The posterior effective current direction (iTBS_AP45) yielded a pronounced and slightly delayed inhibition of MEP amplitude in all but one subjects. iTBS_PA75 had a variable and inconsistent effect. The relatively consistent effect of iTBS_AP45 was unrelated to the MEP latency differences. The divergent iTBS_PA75 effects was in part related to the latency difference in that long latency differences were correlated with the induction of inhibition rather than facilitation.

**Conclusions**

Current direction influences the outcome of iTBS, with a preference for currents running from anterior to posterior in the motor cortex.
Effect of transcranial static magnetic field stimulation over the sensorimotor cortex on somatosensory evoked potentials in human

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Introduction

The motor cortex in the human brain can be modulated by the application of transcranial static magnetic field stimulation (tSMS) through the scalp. Oliviero et al. (2011) reported that 10 minutes of tSMS can reduce the amplitude of motor evoked potentials (MEP) for up to 6 min after the magnet has been removed. The mechanisms that underlie this reduction in excitability remain unclear; however, it is possible that this reduction in excitability is promoted by the distortion of ion channels. The aim of the present study was to investigate the possibility of a noninvasive modulation of the primary somatosensory cortex excitability by the application of tSMS in healthy humans.

Methods

tSMS and sham stimulation over the sensorimotor cortex was applied to 10 subjects for periods of 10 and 15 min. For tSMS, a cylindrical neodymium magnet (NdFeB; diameter,50 mm; height,30 mm) with a maximum energy density of 41 MGOe and a nominal strength of 735 N (75 kg) was used. Based on the accepted method for attaching scalp electrodes for experiments or EEG tests, the NdFeB magnet was centered over position C3 of the international 10-20 system, and thus stimulated both primary motor and somatosensory cortices (Fig. 1). Somatosensory evoked potentials (SEPs) following right median nerve stimulation were recorded before and immediately, 5 min, and 10 min after tSMS from the F3 (frontal component) and C3’ (parietal component;2.5 cm posterior to C3). In another session, SEPs were recorded from 6 of the 10 subjects every 3 min during 15 min of tSMS.

Results

Fig. 2 shows grand averaged wave forms of SEPs recorded before and immediately, 5 min, and 10 min after tSMS from the F3. Amplitudes of N18 (frontal component) and N20 (parietal component) significantly decreased immediately after 10 and 15 min of tSMS, and returned to baseline by 5 min after intervention. tSMS while recording SEPs every 3 min (peripheral nerve simulated) and sham stimulation showed no effect.

Conclusions

Our results suggest that tSMS over the sensorimotor cortex transiently reduces the excitability of the somatosensory cortex. tSMS is able to modulate cortical somatosensory processing in humans and might thus be a useful tool for inducing plasticity in cortical sensory processing. The lack of change in the amplitude of SEPs with tSMS implies that use of peripheral nerve stimulation to cause SEPs antagonizes diamagnetic ion movements (e.g. Na⁺, K⁺, Ca²⁺, Mg²⁺) and distortion of ion channels during exposure to static magnetic fields.
P655
Impact of dual-hemisphere transcranial direct current stimulation on complex whole body motor skill learning

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Question

Dual-hemisphere transcranial direct current stimulation (bi-tDCS) of both primary motor cortices (M1) has been shown to facilitate simple models of motor skill learning, possibly via complex network interactions involving alterations in transcallosal information processing. However, only few studies investigated the behavioral impact of bi-tDCS in complex motor skill learning paradigms. In the present study, we investigated the effect of bi-tDCS on a complex whole body dynamic balancing task (DBT). Bi-tDCS was applied using a single-blinded, parallel design over both M1 (anode centered over right M1, cathode centered over left M1, n=13). We hypothesized that bi-tDCS during skill acquisition augments motor skill learning relative to sham tDCS (n=10).

Methods

The study comprised of two experimental sessions. On day 1 (session 1), we applied 20 minutes of either bi-tDCS or sham tDCS over both M1 (arm area) while subjects performed the DBT: duration of the DBT including rest blocks was approx. 29 min. We used a discovery learning approach for the DBT, where no information about optimal performance strategies was provided to the participant. On day 2 (session 2), all participants performed the DBT again but without tDCS application.

Results

On day 1 (session 1), although all participants showed a significant improvement in the DBT, 20 minutes of bi-tDCS during DBT did not augment motor skill learning or task performance relative to sham. Furthermore, there was no statistical difference in learning slopes between groups. Analysis of DBT performance and learning slopes on day 2 (session 2) did not reveal any statistical difference between groups. Consolidation of the newly acquired skill was similar between bi-tDCS and sham.

Conclusions

Even though previous studies demonstrated that bi-tDCS seems to boost motor skill learning (even to a larger extent than single hemisphere tDCS), we here provide evidence that bi-tDCS (at least in more complex motor learning paradigms) does not seem to have a beneficial effect on motor skill acquisition in early learning phases. Future studies should provide proof-of-concept studies that bi-tDCS in other complex motor tasks is a valuable tool to facilitate learning capabilities and should investigate the impact of bi-tDCS on later learning stages.

figure 1
P656
S2 cortex - a promising novel target for the treatment of neuropathic pain with rTMS

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Question

To investigate the efficacy of repetitive transcranial magnetic stimulation (rTMS) in neuropathic orofacial pain comparing two active cortical targets (M1 and novel right S2) against placebo, and to assess the influence of dopamine D2 receptor gene (DRD2) related single nucleotide polymorphism (C957T) on pain and rTMS effects.

Methods

Sixteen patients with neuropathic orofacial pain participated in this randomized, placebo controlled cross-over study. High-frequency rTMS (10 Hz, 90% of resting motor threshold, 1000 pulses) was given to M1 and right S2 cortex with E-field navigated TMS device. C957T polymorphism was determined, and pain, mood and quality of life were assessed with numerical rating scales, pain diaries, and validated questionnaires.

Results

High frequency rTMS given to the right S2 decreased pain intensity scores more than stimulation of the M1 (p = 0.0071) or placebo (p = 0.0187). Effect size expressed in Cohen’s d values was 1.0 for S2, 0.4 for placebo and 0.1 for M1 stimulation. Neuropathic Pain Impact on Quality-of-life showed reduction in total score after S2 stimulation (p = 0.0031), but not after M1 or placebo. Scores of psychiatric questionnaires didn’t change with the treatments. DRD2 genotype TT was over-expressed in the patients (50%) compared to healthy Finnish population (27 %; p = 0.0191). TT homozygote patients reported more severe pain symptoms than patients with CT or CC genotype (p = 0.0351).

Conclusions

Stimulation of the novel right S2 target was more effective in relieving neuropathic pain than conventional M1 stimulation with excellent effect size of d 1.0. C957T polymorphism of the DRD2 gene seems to associate with liability to neuropathic orofacial pain and its symptom severity.
**Question**

Prolonged continuous transcranial Alternating Current Stimulation (tACS) at α-frequencies (8-12Hz) over posterior cortex leads to enhanced spontaneous occipito-parietal α-EEG activity after stimulation offset [1-3]. One proposed mechanism for this enhancement is that tACS entrains intrinsic cortical neuronal oscillations, implying that α-activity should phase-align to the phase of stimulation. Alternatively, the enhancement could reflect a (phase-independent) general change in excitability in response to prolonged stimulation [4,5]. This study investigates whether α-tACS can increase α-power when applied intermittently, and which factors determine the effectiveness of α-tACS in producing such an increase.

**Methods**

Twelve participants performed four sessions of a slow visual colour change detection task during which they received either active or sham stimulation using a bilateral posterior electrode configuration. Active tACS was applied at individual α-frequency (IAF) in three different protocols that manipulated the duration of tACS trains (30 vs 80 cycles of IAF) and phase continuity between successive stimulation events (phase continuous vs discontinuous), while keeping overall stimulation duration constant. EEG was measured before, during, and after tACS/sham.

**Results**

Preliminary results suggest that the strongest α-power increase occurred after α-tACS using 80 cycle trains with phase continuity between successive stimulation trains. In addition, individual differences in the stability of peak α-frequency seem to determine the effectiveness of α-tACS.

**Conclusion**

Overall, these results best fit the entrainment hypothesis of offline effects.

**References**

Investigation of the effects of transcranial Direct Current Stimulation (tDCS) on neurovascular coupling

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Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that alters cortical excitability and activity in a polarity-dependent way. Stimulation for a few minutes has been shown to induce plastic alterations of cortical excitability and to improve cognitive performance. Separately in neuroimaging studies, tDCS has also been shown to modulate changes in functional connectivity and cerebral blood flow. However, it is not known precisely how these effects between cerebral blood flow, functional connectivity and cortical excitability might be coupled. We aimed to investigate if there is a correlation, with regard to magnitude and time course, of tDCS-induced alterations in cortical excitability, functional connectivity and cerebral blood flow in the left primary motor cortex (M1) for up to 2 hours after the stimulation. To measure cortical excitability, TMS was performed over the motor cortex. Blood flow (CBF) changes, alterations of oscillatory activity, and functional connectivity were measured by functional magnetic resonance imaging (BOLD-fMRI & ASL) and electroencephalography (EEG). On 30 healthy subjects, anodal or cathodal tDCS was applied for 15 minutes in separate sessions, with the current intensity randomized across sessions of 0.5, 1.0, 1.5 or 2.0 mA. CBF and oscillatory activity changes were analyzed for functional connectivity patterns using a graph theoretical approach. Motor cortical excitability was monitored by transcranial magnetic stimulation (TMS)-elicited motor-evoked potentials (MEPs) from the right abductor digiti minimi muscle. The present results indicate a polarity-dependent linear correlation between TMS MEP recordings and the quantified CBF changes of the M1. Functional connectivity patterns significantly increased within premotor, motor, and sensorimotor areas of the stimulated hemisphere during motor activity in the 60-90 Hz frequency range. Additionally, tDCS induced significant intrahemispheric and interhemispheric connectivity changes in all the studied frequency bands. In summary, we show for the first time that the polarity and stimulation intensity of tDCS dictate a non-linear but causal relationship between cortical excitability and activity with cerebral blood flow.
P659
Differences of expression of transcription factor Zif268, proteasome subunits and regulators in the brain stem and frontal cortex of two rat strains

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Proteasome system is involved in brain neuronal plasticity. The goal of this study is to determine proteasome mechanism in brain stem and cortex plasticity of serotonin- and dopamine-deficient rats.

Brain stem and frontal cortex of mature rat males of August inbread strain (with serotonin and dopamine deficiency) and Wistar were studied. Levels of LMP2, LMP7, β1, β5, PA700, PA28α, PA200 and Zif268, and expression of neural markers NeuN and GFAP were determined by Western blotting. Chymotrypsin-like (ChTL) and caspase-like (CL) proteasome activities were estimated by fluorogenic substrates hydrolysis, Suc-LLVY-AMC and Z-Leu-Leu-Glu-MCA respectively. Immunohistochemistry was used for Zif268, LMP2 and LMP7 visualization.

Brain stem expression levels of constitutive proteasome subunits β1, β5, ChTL activity and Zif268 level were increased in August rats compared to Wistar strain. In frontal cortex constitutive and immune subunits, regulators PA28α and PA700, and Zif268 were at higher levels in August rats with no change of the ChTL and CA proteasome activities. Furthermore, in the brain stem of August rats were no differences in the expression of NeuN and GFAP compared to Wistar rats. The expressions of NeuN and GFAP in the cortex were higher in August rats compared to Wistar. The colocalization of Zif268 and immune subunits LMP2 and LMP7 was shown.

Observed increase of constitutive proteasome levels and ChTL activity as well as Zif268 level may serve as a proof of stability in the deficiency of serotonin and dopamine of August brain stem. Higher levels of constitutive and immune proteasome subunits, PA28 and PA700 regulators in August rats' cortex indicate the plasticity of this evolutionary young structure in the potential cognitive abnormalities’ compensation associated with failure of monoaminergic systems.

Supported by RFBR 12-04-00072-a.
Global and inter-motor areal changes in resting state EEG associated with motor consolidation

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Question

Although it is well established that procedural learning is associated with sleep, little is known about the relevance of pre sleep functional vigilance states for motor consolidation. The aim of this study was to examine whether pre sleep vigilance stages and network properties may influence consolidation of a motor sequence learning task (MSLT).

Methods

Twenty healthy participants (mean age 26 ± 5.1 a) were instructed to practice a five element left hand finger-tapping sequence (4-1-3-2-4, 1=Dig. II, 4=Dig. V) as fast and accurately as possible (MSLT training session). Performance was evaluated using the average time to perform a correct sequence (TCS). Motor consolidation was defined as TCS after 8 hours normalized to the performance at the end of the MSLT training session. 15 minutes of resting state EEG (32 channels) were recorded before (pre) and after (post) initial training. The EEG Vigilance Algorithm Leipzig (VIGALL) was used to stage vigilance before and after the training session. Associations of motor consolidation with non-linear general connectivity and specific connectivity strengths between motor areas (M1, SMA, PMC) were calculated using exact Low Resolution Electromagnetic Tomography (eLORETA).

Results

Preliminary analysis of 17 subjects showed that both pre and post training VIGALL stages correlated positively with consolidation (r=0.45 (pre); 0.39 (post) ; p<0.05 ). Furthermore, a pre-post decrease of VIGALL stages was associated with enhanced motor consolidation (r = 0.35 ;p < 0.05 ). Following MSLT training general connectivity globally increased in the theta and alpha-1 band and decreased in the delta and alpha-2 band. However, none of the changes was correlated with consolidation. In contrast, analysis of specific connectivity between M1, SMA and PMC revealed that the training-related increase of connectivity between right SMA and PMC within alpha-1 and beta band was highly correlated with consolidation (r=0.79 (alpha-1); r=0.73 (beta); p<0.05).

Conclusions: Our findings suggest that on a global level of brain function pre-sleep vigilance changes, rather than training associated changes in global connectivity, are related to motor consolidation. How pre/post training vigilance relates to connectivity changes in specific motor networks relevant for consolidation needs to be further investigated.
Experience-dependent structural plasticity in the adult rat brain.

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Question

Monocular deprivation (MD) has been established as an experimental model to study the plasticity of the adult brain. In interaction with the visual cortex, deprivation of one eye modulates as yet unknown pathways to enable enhanced sensitivity of the non-deprived eye. To advance the understanding on how this adaptation is implemented in the brain, we tracked changes in the grey matter macro-structure over time.

Methods

T2-weighted brain magnetic resonance images were acquired longitudinally at baseline and 3, 7 and 10 days following MD (rats, 2 months) and processed by deformation-based morphometry. Spatial frequency sensitivity of the optokinetic response (visual acuity [VA]) was monitored for the open eye. Changes in astrocytic morphology, neuronal activity and spine pool were analyzed by using immunohistochemistry (GFAP, Arc) and Golgi impregnation.

Results

VA of the non-deprived eye increased rapidly during the first 3 days of MD and stabilized at ~35 % above baseline around day 7. Fast regional expansion of gray matter ranging 2-6 % evolved in multiple brain areas which were followed either by renormalization (e.g. entorhinal cortex) or shrinkage (e.g. visual cortical areas). Slowly evolving and stable expansions were found in the cerebellum. Entorhinal expansion corresponded with speed and amount of VA-enhancement and was accompanied by increased neuronal activity and reduced astrocytic complexity. Normalization of entorhinal volume manifested with an enlarged spine pool and increased complexity of astrocytes.

Conclusions

Changing binocular experience by loss of one eye’s visual field increases the sensitivity of the other eye - associated with reorganization of the entorhinal cortex. Deeper knowledge of its interaction with additional areas, mainly showing non-linear relationships between volume alterations and behavioural outcome, is needed to evaluate the causality of our finding.
BDNF pretreatment prevents morphine-induced amnesia in rats

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**Question**

The aim of this study was to find answer to this question whether infusion of Brain Derived Neurotropic Factor (BDNF) in the CA1 regions of the dorsal hippocampi could ameliorate amnestic effect of morphine.

**Methods**

Thirty three male Wistar rats were divided into three experimental groups (morphine, BDNF, BDNF+morphine and one control group). Two weeks after stereotaxic surgery, animals received 0.5 μl bilateral infusion of saline, BDNF (2 μg/rat) intrahippocampally 30 minutes before morphine treatment (7.5 mg/kg, i.p). Step-through inhibitory avoidance task of memory has been used to examine retrieval of memory formation, 1.5 and 24 h after the training in rats.

**Results**

The results showed that post-training administration of morphine impaired memory retrieval (p<0.01). Intra-CA1 microinjection of BDNF prior to injection of morphine significantly prevented amnesia-induced by morphine administration (P<0.001).

**Conclusions**

These findings suggest that increase in the level of BDNF in the CA1 region of the hippocampus during 30 minutes time window before morphine administration is capable to enhance long term memory & memory consolidation.
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P663
Statistical learning and relative processing of tone sequences

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Purpose

We investigated how the statistical learning of auditory sequences is reflected in neuromagnetic responses.

Methods

Complex tones with fundamental (F0) frequencies in a five-tone equal temperament and seven different combinations of the first (F1) and second (F2) formant frequencies, as two distinct sets of five Japanese vowels, were generated by a formant synthesizer. The tones were ordered with the constraint that the probability of forthcoming tone was statistically defined (80% for one specific tone; 5% for the other four) by the latest two successive tones (second-order Markov chains) to form different types of tone sequences: F0-variable music-like tone sequences (F1, F2: constant) and F1, F2-variable language-like tone sequences. Each sequence consisted of 500 tones and successive 250 tones with a relative shift of fundamental and/or formant frequencies based on the same Markov transitional matrix. Neuromagnetic responses to music-like tone sequences in explicit and implicit learning conditions (experiment 1) and to music-like and language-like tone sequences in explicit learning conditions (experiment 2) were recorded from fourteen right-handed Japanese participants. Temporal profiles of the N1m responses to the tones with higher and lower transitional probabilities were compared.

Results

The N1m responses to the tones with a higher transitional probability were significantly decreased compared with those to tones with a lower transitional probability in the latter half of the 500-tone sequence. Furthermore, this difference was retained even after fundamental and/or formant frequencies were relatively shifted (Figure 1, Figure 2).

Discussion

The N1m responses may be useful as a marker for statistical learning, and such statistically acquired knowledge may also be utilized when spectral frequencies are relatively shifted.

figure 1
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figure 2

Figure 2. Grand-averaged source strength waveforms for the N1m responses (experiment 2) (N = 14)
P664
Plasticity in primary motor cortex innervating the ankle flexor in football juggling experts

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Question

It has been well known that short-term skill practice or artificial methods (e.g., PAS, rTMS, TBS) can induce the plasticity in primary motor cortex (M1) innervating hand and leg muscle. However, effect of long-term practice on the leg M1 excitability is not well addressed. Here, we used the transcranial magnetic stimulation (TMS) to reveal the long-term practice induced plasticity in the leg M1.

Methods

Eight football juggling experts and eight novices participated in this study. Motor evoked potentials (MEP) and the H-reflex were recorded from the right tibialis anterior (TA) during isometric dorsiflexion at 10% of maximum voluntary contraction. We measured the MEP input-output curve, short-interval intracortical inhibition (SICI), intracortical facilitation, long-interval intracortical inhibition (LICI), and the ratio of the maximum H-reflex (Hmax) to the maximum M-response (Mmax).

Results

The steeper MEP input-output curve was observed in the experts compared with the novices. Additionally, SICI and LICI were reduced in the experts. The ratio of Hmax to Mmax did not differ between the groups.

Conclusion

Our results show that football juggling experts displayed the plastic changes on TA M1, which was induced by the long-term practice of the ankle movements required to perform football juggling well.
P665
Intracortical water diffusion can retain plasticity-induced changes after repetitive transcranial magnetic stimulation through coupling between the stimulated and remote regions.

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In humans, repetitive transcranial magnetic stimulation (rTMS), an established protocol to induce plasticity in the stimulated cortex, also affects remote regions. Although the effects of rTMS are retained in remote regions beyond the stimulation period, the neural substrates underlying retention of the carryover effects in remote regions are unknown.

Diffusion-weighed magnetic resonance imaging (DWI) probes water diffusion and can be used to estimate microscopic morphological changes in neural tissue. We hypothesized that rTMS-induced plasticity would alter water diffusion. Using DWI techniques, we estimated morphological changes induced by application of rTMS over the left primary motor cortex (M1). We found that rTMS altered water diffusion in multiple regions including the left M1. It is notable that the change in water diffusion was retained longest in the left M1 and remote regions that had coupling of baseline fluctuations in water diffusion prior to rTMS.

We conclude that coupling of water diffusion between the stimulated and remote regions is the key substrate for retention of the rTMS-induced changes in water diffusion in remote regions. These revealed that basal fluctuations in cortical microstructures were synchronized between the stimulated and remote regions and that coupling of micromorphology with the stimulated M1 might underlie retention of the morphological changes related to long-term plasticity in remote regions. DWI techniques could be used to evaluate presence or absence of morphological coupling between brain regions that modulates rTMS-induced morphological plasticity in remote regions and thus could provide a new biomarker to evaluate the therapeutic effects of rTMS in patients for brain disorders.
Lowering neuronal activity with cathodal tDCS shows no effect on anodal tDCS- enhanced online learning but improves the offline leaning

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Question

Anodal tDCS applied to the motor cortex was found to improve motor learning by increasing the synaptic activity in specific learning-involved cortical areas. The effect depends on the timing of stimulation and on the modification threshold for inducing synaptic activity changes. Experimental decrease of the threshold for induction of synaptic plasticity before practice, may facilitate motor learning. The study examines whether lowering the neuronal activity with ctDCS enhances the effect of subsequent atDCS on motor performance, learning and cortical excitability in comparison to atDCS applied solely before or during performance.

Methods

Four study groups were trained on the grooved pegboard test (GTP): 1. 15 min ctDCS before- and atDCS during training, 2. atDCS during training, 3. 15 min atDCS before training, 4. sham tDCS. Motor performance was assessed by the GPT completion time across 4 training blocks, one block was retested 14 days later to determine the off-line learning effects. On-line learning was obtained by normalizing the completion time values to the first training block, off-line learning was obtained by normalizing the retest values to the last training block. Cortical excitability was assessed via single and paired-pulse transcranial magnetic stimulation (TMS) at pre-training, post-training and 60 min post-training.

Results

Motor performance across the 4 training blocks was improved in all stimulated groups compared to the sham group, while on-line learning was not significantly affected by the stimulation. Off-line learning, tested 14 days after training, was improved in the stimulated groups compared to the sham group. This effect was stronger for the group recieving cathodal and anodal stimulation. The observed effects were accompanied by changes in the motor cortical excitability. Application of ctDCS decreased MEP amplitude and intracortical facilitation (ICF) and increased intracortical inhibition (SICI). Application of atDCS increased MEP amplitude and ICF and decreased SICI. When atDCS was preceeded by ctDCS, the facilitatory effects were retained over 1h.

Conclusion

Decreasing neuronal activity by ctDCS did not facilitate the effect of atDCS on motor performance. However the lasting stimulation-induced cortical excitability changes resulted into improved motor memory. The results hold potential for clinical applications, specifically for the development of learning-stimulation protocols.
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P667
How does the lesioned language network process phonotactic regularities?

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Question

Phonotactic cues describe the possible combinatory rules of phonemes in a given language. For example, /BR/ at the onset of a German or English word is phonotactically legal (e.g., bread) whereas /BZ/ is illegal. The EEG of healthy adults showed a larger N400 component for phonotactically legal in contrast to illegal pseudowords (/BROP/ vs. /BZOP) indicating stronger lexical search processes for onset clusters belonging to the subjects’ native language. The present study aims at investigating the electrophysiological correlates associated with the processing of legal and illegal phonotactic regularities in patients who suffer from a left-hemispheric brain lesion.

Methods

32 patients with unilateral left-hemispheric vascular lesions and 26 matched controls were included in the study. They listened to 252 monosyllabic pseudowords belonging to three different conditions: (i) phonotactically legal pseudowords, (ii) illegal pseudowords, and (iii) pseudowords played in a reversed manner as an acoustic control condition. A 32-channel EEG was recorded. In order to keep the subjects’ attention to the stimuli they should press a button whenever two identical stimuli occurred.

Results

ERP results for control subjects showed a differential processing for phonotactically legal and illegal pseudowords in the N400 time range clearly differing from the processing of reversed pseudowords. Such a modulation was not found in patients with a left-hemispheric brain lesion.

Conclusions

Results of the present study indicate an increased difficulty in processing phonotactic rules in the lesioned brain reflecting disturbed neuronal mechanisms due to the brain lesion.
P668
Lack of a relationship between MRS-GABA-levels, LTD-like plasticity and motor learning in the human cortex

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Question

Long-term depression (LTD) is a cellular mechanism involved in motor learning, which is significantly controlled by GABAergic inhibition. Here, we tested whether magnetic resonance spectroscopic (MRS) measures of GABA concentrations relate to physiological measures of synaptic GABA activity, LTD-like plasticity and motor learning (ML) in humans.

Methods

26 healthy subjects (mean age= 25, SD= 3) took part in this study. GABA-A receptor mediated synaptic activity was indexed by short-interval intracortical inhibition (SICI). LTD-like plasticity was induced by continuous transcranial magnetic theta-burst stimulation (cTBS) over left primary motor cortex (M1) and determined by input-output curves of motor-evoked potentials (IO-MEPs) from right abductor pollicis brevis muscle. Motor practice consisted of an established ballistic thumb abduction task, which is known to result in ML primarily consolidated in M1 (Muellbacher et al. 2002 [Nature] 415: 640). GABA-levels in M1 were measured before (baseline) and after cTBS and ML by 1H-MRS.

Results

cTBS decreased IO-MEPs significantly and showed a trend towards decreases in SICI. Motor practice induced a robust learning effect as indexed by significant increases in peak acceleration of thumb abduction movements in all subjects. GABA-levels in M1 were not changed by cTBS or ML. No correlations were found between baseline GABA levels and SICI, cTBS-induced changes in IO-MEP or ML.

Conclusions

Findings confirm that MRS-GABA does not primarily reflect synaptic GABA content (Stagg et al. 2011 [J Physiol] 589: 5845) and suggest that those GABA pools detected by MRS cannot serve to predict individual levels of cTBS-induced LTD-like plasticity and motor learning.
P669
Acute effects of moderate dynamic exercise on brain plasticity

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Question: Regular participation in physical activity has been associated with improved cognitive functions across the lifespan and would help in preventing cognitive decline and dementia. It has been suggested that modifications in cognitive processes in response to repeated individual bouts of exercise may be associated with increase in BDNF concentration and therefore brain plasticity. Our aim was thus to evaluate the effect of a single bout of aerobic exercise on visual perceptual learning, as measure of brain plasticity. Methods: 32 healthy males (age: 23± 2 yrs) volunteered for this study. The subjects were randomly assigned to an exercise-group (exe-group; n=16) or a control group (ctrl-group; n=16). All subjects exercised on a cycle-ergometer for 30 min: exe-group pedaled at an intensity eliciting 70% of individual maximal heart rate (HR), i.e. at 159±45 Watts; ctrl-group pedaled at 20 W, that represented an almost unloaded task. The subjects were administered an orientation discrimination task (ODT), in which they had to decide whether the presented stimulus was tilted clockwise or counter-clockwise relative to the previously presented stimulus. ODT was performed before (block-pre) and six times after the exercise (block1-6). The orientation sensitivity was calculated as d’ value for each subject and for each block. HR was continuously recorded throughout the experiment. Results: at the end of cycle task HR in exe-group was 152±12 b/min, corresponding to a mean increase of 70 b/min above resting value. In the initial 2 min of recovery HR dropped by about 50 b/min and then further slowly decreased. In ctrl-group, a slight increase in HR (8-12 b/min) was observed during pedaling. Performance in ODT improved at block1 compared to block-pre in both groups (d’ +130% in both exe- and ctrl-group; p>0.05). In exe-group, the orientation sensitivity showed a continuous increase in the successive blocks. In contrast, in ctrl-group no modification in d’ value occurred from block1 to block6. Performance in all blocks was significantly different in the two groups. Conclusions: The results of this study indicate that a single bout of aerobic exercise does enhance visual perceptual learning. Thus, suggestion can be made that acute exercise, at least of moderate intensity, can have an influence on brain plasticity.
P670
Neural correlates of semantic vs. perceptual analysis of Morse-Code stimuli (MC)

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Certain kinds of stimuli can be subject to different levels of analysis (LOA, e.g. perceptual or semantic). The neural correlates of different LOAs have been investigated using functional imaging methods, which have identified the left inferior frontal cortex (IFC) and the hippocampus to be critically involved of deeper cognitive processing. However, most of the studies investigating LOA effects involve skills already present when performing the task. The goal of this study was to further investigate the neural correlates of processing stimuli on either a perceptual or a semantic level specifically monitoring new activation sites emerging with a new acquired skill, enabling semantic analysis.

16 healthy volunteers (23 ± 2 yrs) learned and practiced to decipher 12 letters presented in MC with a standardized learning protocol (acoustically). Before and after the learning period all participants listened to the same 130 randomized MC stimuli during fMRI measurement. In the first task participants were asked to indicate, if the first signal and the last signal in a train of three letters (presented in MC) was the same or not (perceptual level). In the second task, participants were asked to translate the MC signals and to decide whether they made up a word, a non-word or SOS (semantic level). For both tasks the same set of stimuli was presented, a sine wave tone served as a control stimulus (in both tasks).

The perceptual task was associated with a bilateral activation pattern including the SMA, the precentral gyrus and the inferior parietal lobe and the left insula. The same activation was seen pre and post learning. When performing the semantic analysis (of the same set of stimuli) the tasks elicited new activations in the left inferior frontal gyrus, left superior parietal cortex, left fusiform gyrus and right insula which were only observed post learning.

Our data are in line with the current literature identifying the left IFC including Broca’s Area as being critically involved in semantic stimulus analysis. Secondly our data demonstrate functional neuroplasticity associated with a new skill, enabling a higher LOP, which highlights the brain’s dynamic capacity to profoundly alter its activation strategy depending on the task requirements.

figure 1
Modulation of GABA in the human somatomotor cortex following perceptual learning

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Hebbian learning as a well-known principle of neural computation goes with changes on cellular level, yet data linking perceptual Hebbian learning, behavior and short-term changes in neurochemistry are sparse. Inhibition, particularly GABA-mediated inhibition, has been proven to play an important role in cellular plasticity, and now due to methodological progress, neurochemical shifts in humans can also be non-invasively investigated. Therefore we took advantage of repetitive electrical stimulation (RSS) as a somatosensory learning paradigm and addressed intervention-related changes in tactile spatial acuity with respect to neurotransmitter concentrations using magnetic resonance spectroscopy (MRS) of GABA.

Experiments were performed on 19 subjects (all right-handed, 11 male, mean age 24.1 ±3.7 yrs) with no previous history of psychological disorders or severe hand or head injuries. Two-point discrimination (TPD) thresholds were assessed on the tip of the index finger (D2) of both hands by using the method of constant stimuli. All subjects underwent one training session to familiarize themselves with the testing procedure. GABA MRS was performed bilaterally using MEGAPRESS sequence within a 3x3x3 cm³ voxel covering the somatomotor cortex (Philips Achieva, 3T). Both MRS and tactile discrimination thresholds were measured before as well as after the perceptual learning paradigm.

RSS was applied for 45 min to the dominant hand. The RSS sequence was applied to the entire hand and consisted of stimulus trains of 2 s (including 2x 0.5 s ramps, single-pulse duration: 0.2 ms (square), frequency: 20 Hz) and intertrain intervals of 5 s.

We found substantial learning effects to be accompanied by a complex GABAergic regulation: We did not find a correlation between levels of GABA and accompanying TPD thresholds, yet levels of GABA change according to baseline conditions and predict the future benefit of perceptual learning. Indeed, a strong positive correlation between baseline GABA concentration and TPD improvement was found exclusively for the dominant side (dominant: R=0.75, P>0.001; non-dominant: R=0.30, P=0.215). Therefore, it seems that learning effects are not determined by the absolute impact of GABAergic inhibition, but the direction of change around a homeostatic equilibrium. Our results provide a new insight into inhibitory mechanisms of perceptual learning.
Inter- and intra-individual variability in learning-induced corticospinal excitability.

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Changes in corticospinal excitability (CSE) induced by motor learning are variable both between and within participants. Apart from Muellbacher et al., (Exp Brain Res. 136, 4 2001) who demonstrated that changes in CSE following ballistic motor learning are variable, the topic has received little rigorous examination. The aim of this study was to describe the inter- and intra-individual variability in learning-induced changes in CSE.

We assessed CSE using the transcranial magnetic stimulation stimulus-response (SR) curve and CSE map. SR curves and CSE maps were acquired from first dorsal interosseus in the dominant and non-dominant hands of 21 healthy participants before and after training on a visuomotor tracking task previously shown to induce changes in CSE (Perez et al., Exp Brain Res. 159, 2 2004). Participants hands were tested in a random order and the sessions were separated by 7 days. A reduction in tracking error served as a marker of learning.

Tracking error significantly decreased in all participants and in both hands as a result of learning (p>0.05 for all parameters).

This study highlights an important consideration for future studies of motor learning; CSE does not increase for everyone following visuomotor tracking. There is considerable variability in the magnitude and direction of learning induced changes in CSE and these changes are independent of hand dominance.
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TMS-assessed corticospinal excitability associated with visuomotor learning in proximal and distal muscles.

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Distal muscles have larger cortical representation in the primary motor cortex compared with proximal muscles. This increased representation would suggest a greater potential for learning induced changes in CSE for distal muscles in a motor learning task. The aim of this present study was to investigate changes in CSE following visuomotor learning in proximal and distal muscles.

In 15 healthy participants we acquired three stimulus response (SR) curves and three CSE maps for first dorsal interosseus (FDI) and biceps brachii (BB). All participants were assessed before and after an isometric visuomotor tracking task (e.g. Perez et al., Exp Brain Res. 159, 2 2004) involving either index finger abduction or elbow flexion. Motor learning performance was quantified by the root-mean-square tracking error across five different waveforms.

Across all participants, tracking error decreased by 23±17% for FDI and 28±17% for BB indicating the task was learnt (p<0.05) with no significant difference between muscles (p>0.05). CSE changes were variable between muscles with 4 and 5 participants exhibiting increased CSE in FDI for the SR curves and map, respectively; and only 2 and 3, respectively, in BB.

There were a greater number of participants in whom CSE increased for the distal muscle whilst motor learning performance was not significantly different between muscles. The surprising result that so few participants exhibited increased CSE following motor learning suggests that individual differences should be better reported in studies of motor learning involving TMS. In addition, the inter-individual differences in the changes in CSE should be further examined.
Human single-unit recordings from the hippocampal formation reveal spatial context during free recall

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**Question**

Place responsive firing of neurons in the hippocampal formation has been extensively investigated in rodents. Recently, place responsive neurons have also been demonstrated in the hippocampal formation of humans. In humans the hippocampal formation is known to be crucial for episodic memory. According to a theory of episodic memory place-responsive neurons may play a role in episodic memory by coding temporal context. Therefore, we investigated the role of place responsive neurons in the hippocampal formation in humans during episodic memory.

**Methods**

During pre-surgical invasive EEG-recordings six patients volunteered to participate in a hybrid spatial navigation episodic memory task while neuronal activity was recorded with micro wires. In this task items were learned in a specific spatial location in a virtual environment computer game. In the recall part patients freely recalled items in front of a black computer screen.

**Results**

In total, 95 neurons (25.6% of all neurons) significantly increased their firing rate in a circumscribed area of the environment, the place field, during navigation of the virtual environment. The ensemble activity of these place responsive neurons during recall was more similar to the average firing in the area near the location of item presentation compared to more distant areas of the environment. The maximum of this reinstatement effect was during a time window -300 to 700 ms relative to verbalization of recalled items. Furthermore, place responsive neurons increased their firing rate significantly during recall of items presented near the place field compared to items presented far from a place field.

**Conclusions**

Place responsive neurons identified during navigation displayed firing pattern during recall, when no spatial cues were presented, that reinstated spatial information. This implies a role of place responsive neurons in episodic memory by coding spatial context during encoding that can be reinstated during recall.
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P675
Interneuron networks involved in human associative plasticity

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Objective

Paired associative stimulation (PAS) is a method to study motor cortex synaptic plasticity. If a repetitive electrical stimulus to the median nerve is paired with a transcranial magnetic stimulus (TMS) pulse over the contralateral motor cortex at an interstimulus interval (ISI) of 21.5-25 ms, a long-term potentiation (LTP)-like synaptic plasticity is induced in the corticospinal system (Stefan et al., 2000). We investigated the synaptic spatial specificity of PAS25 and PAS21.5, considered to have similar synaptic mechanisms until recently.

Materials and methods

Eight subjects (28.6±8.3 years), with the expected facilitation after both standard PAS protocols, participated in two randomized sessions in which PAS consisted of 360 electrical stimuli of the right median nerve at the wrist paired with a single TMS over the hotspot of right APB muscle at randomly delivered ISIs of 25 ms and of 21.5 ms (180 pairs for each ISI) (PASvar). Since cerebellar transcranial direct current stimulation (TDCS) can abolish the plasticity effects of PAS with an interval of 25 ms and not at 21.5 ms (Hamada et al. 2012), either sham or anodal TDCS (2 mA, 30 min) was applied to the cerebellum simultaneously with PASvar (anodal-PASvar and sham-PASvar). We measured MEPs before and after each intervention.

Results

Randomly delivered PAS25 and PAS21.5 (sham-PASvar) blocked the induction of PAS plasticity while the concurrent anodal TDCS (anodal-PASvar) restored the expected effect.

Conclusions

PAS21.5 and PAS25 induce LTP-like changes in different sets of cortical synapses and show mutual inhibition during plasticity induction. Heterosynaptic LTD-like modulation might well explain the loss of effect of combining PAS21.5 and PAS25.

References


Dorsal hippocampus modulates the degree of anxiety in rats after chronic sensory stress

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The stress behavior depends on the activity of the limbic-reticular structures, among which great importance belongs to the hippocampus. Hippocampus function belongs in the adaptation to stressful influences. Fear and anxiety are the most important cognitive functions of the organism, and their relationship and determine the degree of predictive resistance to emotional stress.

The intention of the work was to identify correlations between the activity of area CA1 of the dorsal hippocampus and the degree of anxiety in rats in the test "open field" in chronic sensory stress.

Chronic experiments were carried out on 12 male rats with respect for the fundamental bioethical rules. All animals were tested in the "open field" with the Convention on the protection of experimental animals (1986). Chronic stress was simulated by sensory disintegration upon presentation of complex stimuli with different frequencies of various amplitudes within 20 days. Recorded of the electrical activity of dorsal hippocampus CA1 with calculation of the energy levels of decomposition of the wavelet spectrum using multifunctional system BIOPAC Sistems© and the software MATLAB®. Correlation analysis was performed by Spearman (ρ

During exposure to stress expands the involvement of the dorsal hippocampus in anxiety-phobic implementation behavior: to stress the impact this form of behavior is not determined by the activity of the dorsal hippocampus, on the 10th day of stress activation of the hippocampus resulted in increased anxiety animals that may be associated with changes in synaptic plasticity under stress. By the 20th day of stress predominance of low-frequency activity of the hippocampus led to the emergence of anxiety and phobic behavior, and high activity - in a reduction of fear and anxiety.

So, the area CA1 of the dorsal hippocampus is involved in the modulation of anxiety-phobic behavior during prolonged sensory effects.
The Attention deficit hyperactivity disorder (ADHD) has a high prevalence (5%) in school-age children. If on the one hand the literature shows that information enables conscious decision making, recent research shows there is a lot of misinformation about ADHD, even among health and teaching professionals. The main objective of our study was to determine whether knowledge about ADHD found in parents of Brazilian children and adolescents diagnosed with this disorder had a significant relationship with treatment acceptance. The sample consisted of 101 parents or caregivers (94 women and 7 men) of children and adolescents treated for ADHD at the Hospital das Clínicas, Universidade Federal de Minas Gerais. The profile was composed of young, low-income (52.5%), students, aged 4 to 18 years old, in the majority boys (76.2%). The instrument used consisted of a structured questionnaire with 100 questions, with six different scales, assessing the general knowledge about ADHD and quality of life. The results showed there is no statistical significance between any of the variables tested. However, individuals classified as the inattentive subtype showed significant differences in appearance greater acceptance of the hyperactive or combined subtypes. While individuals with higher scores for quality of life showed intermediate treatment acceptance, the group with the lowest quality of life scores showed high treatment acceptance. We suggest that further studies should be conducted to better understand the relationship between ADHD awareness and its influence on individual behavior. These results could be useful for improved health education, including the development of prevention campaigns to promote effective health.
Cortical Plasticity in Tinnitus Patients after Repetitive Exposure to Tailor-Made Notched Music

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Question

Tinnitus, the perception of a sound without an external source, is assumed to be a result of reduced inhibition of neurons corresponding to the tinnitus frequency. One possibility to reverse the effects of this maladaptation is to induce inhibition on neurons corresponding to the tinnitus frequency by auditory stimulation. The aim of this study was to investigate the impact of repetitive stimulation with tailor-made notched music on neural activity in temporal and frontal cortical regions of tinnitus patients.

Methods

Ten subjects suffering from chronic tonal tinnitus listened to music passing through a notch-filter centered at the tinnitus frequency (tailor-made notched music) for three hours on each of three consecutive days. Neural activity evoked by either a tone at the tinnitus frequency (tinnitus tone) or by a control tone of 500 Hz was measured by magnetoencephalography (MEG) before and immediately after music exposure. Tinnitus loudness was measured via visual analog scales. A distributed source model was used to investigate the neural activity in auditory as well as in frontal cortical regions in the N1m time window.

Results

Neural activity evoked by the tinnitus tone in the temporal lobe decreased significantly after music exposure, whereas neural activity evoked by the control tone remained unaffected. Additionally, tinnitus loudness was rated significantly lower after music exposure. There was a significant correlation between the reduction of neural activity in the temporal lobe evoked by the tinnitus tone and the tinnitus loudness ratings. Furthermore, there was a significant increase of neural activity evoked by the control tone in the frontal lobe after music exposure, which could not be observed in the neural activity evoked by the tinnitus tone.

Conclusions

Tailor-made notched music evokes neural plasticity in temporal as well as frontal cortical areas of tinnitus patients. Additionally, there is a clear connection between the reduction of tinnitus loudness and the neural reorganization in the temporal cortex. These effects could be demonstrated after a short period of music exposure, indicating a fast neural reorganization and behavioral adaptation.
Wakefulness delta waves increase after cortical plasticity induction

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Question:

Delta waves (Dw) during sleep are considered effectors of synaptic plasticity. During wakefulness Dw appear when brain lesions occur, but their functional meaning is not unanimously recognized. We aimed at testing whether Dw change after inducing cortical plasticity by intermittent theta burst stimulation (iTBS).

Methods:

13 healthy subjects underwent iTBS on left primary motor cortex to induce long term potentiation (LTP) like phenomena. Five-minutes resting opened-eyes 32-channels EEG, right opponens pollicis motor evoked potentials (MEP) and alertness behavioural scales were collected before and up to 30 minutes after iTBS. Power spectral density (PSD) from delta to beta frequency bands of bilateral sensorimotor areas was calculated.

Results

iTBS induced a significant increase of both MEP amplitude and bilateral Dw (+87.5%) lasting up to 30 minutes after stimulation. No changes on behavioural scales were found.

Conclusions

Our data showed that motor LTP induction during wakefulness, by means of iTBS, is accompanied by a large and enduring increase of Dw over sensorimotor areas. Present results evidenced that Dw own a prominent role in neural plasticity processes in the awake state.
Induction of neuronal plasticity by transcranial biphasic quadro-pulse stimulation with one or two full-sine cycles

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Question

Neuronal plasticity in form of long-term potentiation (LTP) is considered to be the underlying neurophysiological mechanism of learning and memory. Biphasic transcranial quadro-pulse stimulation (QPS) consisting of one full-sine cycle demonstrated to be effective in induction of neuronal plasticity in human primary motor cortex. Two full-sine cycles demonstrated to be effective in evaluation of local excitability. Here, we aimed to study the effectiveness of QPS with two full-sine cycles (quadro-burst stimulation, QBS) in comparison to biphasic QPS with one full-sine cycle in induction of neuronal plasticity.

Methods

We investigated healthy volunteers (n=10 per protocol) with quadro-pulse stimulation consisting of one (QPS) and two (QBS) full-sine cycles (duration: 160 µs) separated by an inter-stimulus interval of 5 ms and an inter-burst interval of 200 ms with a total amount of 1440 pulses. Resting motor threshold (rMT), and motor evoked potential (MEP) amplitudes with stimulus intensities to target amplitudes of 1mV (SI_1mV) were measured before (Pre) intervention, directly after (Post1), after 15 minutes (Post2), after 30 minutes (Post3) and after 60 minutes (Post4).

Results

We found a significant increase of MEPs after QPS and QBS at interstimulus intervals of 5 ms and interburst intervals of 200 ms. While the MEP increase was immediately present after the QBS intervention lasting for one hour (Post 1-4), QPS resulted in a delayed MEP increase which became significant one hour after the end of QPS (Post 4). No significant changes in rMT were observed.

Conclusion

QPS and QBS of the human primary motor cortex can be used to induce a lasting increase in cortico-spinal excitability. Considerable differences in time course may be suggestive of different underlying neurophysiological mechanisms. Varying the pulse configuration of quadruple stimulation offers new opportunities in investigations of neuronal plasticity in humans.
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INTEREMISPHERIC ASYMMETRY OF CORTICAL PLASTICITY: THE “DORMANT POTENTIAL” OF THE NON-DOMINANT HEMISPHERE

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Question

Transcranial magnetic stimulation (TMS) studies have documented handedness related functional asymmetries in corticomotor excitability. We used TMS to compare changes in cortical excitability of dominant (DH) and non dominant hemisphere (NDH) in both right-handed and left-handed subjects in function of a bimanual non-fatiguing motor task.

Methods

Thirty enrolled subjects were classified as right or left handed according to their description of the hand used for writing and completed the Edinburgh Handedness Inventory. For each subject, cortical excitability was separately assessed in each hemisphere. MEP amplitude, motor threshold, and silent period were assessed. Then subjects performed a bimanual motor task. MEPs were recorded before exercise, immediately after each exercise periods of 30, 60, 90 seconds and after 15 minutes of rest. We evaluated if post-exercise facilitation and delayed facilitation were present. Hemispheric differences of MEP amplitudes registered after rest were related to handedness score.

Results

Mean threshold was lower for DH compared to NDH. MEP amplitude was increased in exercise condition, independently of the hemisphere stimulated. In rest condition, only NDH presented increased MEP amplitude, showing delayed-facilitation. Handedness scores and MEP asymmetry in rest condition were positively correlated.

Conclusions

Delayed facilitation asymmetry was laterialized to NDH and varied as a linear function of handedness. Hemispheric differences emerge more in individuals exhibiting strong preference for one hand (either right or left) and large manual asymmetries in performance when compared to individuals with no clear preference for one hand (i.e., mixed handedness) and lower degrees of manual asymmetries. DH and NDH, however, don’t show a mirror-like behavior among right-handed and left-handed subjects.

DH and NDH answer differently to motor requests and recover differently after exercise. Bimanual motor task induces different changes in cortical excitability in the two hemispheres, in favour of the non-dominant.

NDH has a “dormant potential” that can be activated if necessary.

The examination of the effects of a bimanual motor task on cortical excitability may be relevant to better understanding cortical plasticity processes and may provide new tools to study neurological disorders characterized by central fatigue and less capacity to recovery.
**figure 1**

- MEP amplitude was increased immediately after the exercise periods, independently of the hemisphere stimulated showing a post-exercise facilitation.
- After rest condition, only the NDH presented increased MEP amplitude, showing delayed-facilitation.

**figure 2**

- Delayed facilitation is present only in the NDH in both right-handed and left-handed hemispheres. Differences emerge more in individuals exhibiting strong preference for their hand, and NDH, however, don't show a mirror-like behavior among right-handed and left-handed conditions.
Abstracts of Poster Presentations – Poster Session 38 – Plasticity and the neurophysiology of learning

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Heterogeneity of Stimulus-Specific Response Modification - an fMRI Study on Neuroplasticity in the Visual System

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Question

Long-term potentiation (LTP) is a key element of synaptic plasticity. At the macroscopic level, similar effects can be induced in the human brain using repetitive stimulation with identical stimuli. High-frequency stimulation (HFS) can increase neuronal responses whereas low-frequency stimulation may produce the opposite effect. Optimal stimulation frequencies and characteristics for inducing stimulus-specific response modification differ substantially from those applied to brain tissue slices but have been explored in recent studies. In contrast, the individual manifestation of this effect regarding its spatial location and extent are unclear.

Methods

Using functional MRI (fMRI) in 18 subjects, we attempted to induce LTP-like effects by HFS with checkerboard flashes at 9 Hz for 120 seconds. The fMRI signal in the visual cortex in response to low-frequency probe checkerboard stimuli shown before and after the HFS period was compared.

Results

Flashes induced strong activation in primary and secondary visual cortices. Contrary to our expectations, we found clusters of decreased activations induced by pattern flashes after HFS at the border between primary and secondary visual cortices, significant in the right hemisphere. On the level of the individual subject, some showed significantly increased activations in the post-HFS session while the majority showed significant decreases. The locations of areas showing altered activations before and after HFS were only partly overlapping. No association between location, extent and direction of the HFS-effect was observed.

Discussion

The findings are unexpected in the light of existing HFS-studies, but mirror the high inter-subject variability, concerning even the directionality of the induced effects shown for other indices of LTP-like plasticity in the human brain. As this variability is not observed in LTP at the cellular level, a better understanding of LTP-like mechanisms on the macroscopic level is essential for establishing tools to quantify individual synaptic plasticity in-vivo.

Figure 1

Group-level session effects. Neuronal responses in the visual cortex to pattern flashes were significantly decreased in the post- compared to the pre-high frequency stimulation (HFS) session (p < 0.01, uncorrected for multiple comparisons for display purposes).

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figure 1
P1098
Auditory evoked temporal “delta brushes” in human premature neonates

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The initial period of sensory cortical circuit formation during the third trimester of gestation in humans is characterized by a particular electroencephalographic activity pattern, “Delta-brushes” that consist in high amplitude slow wave superimposed with rapid oscillations. While delta-brushes are often thought to be spontaneously generated entirely within neo-cortex, recent work showed that they are reliably evoked in central cortical areas by sensory input resulting from spontaneous hand or foot twitches in a somatotopic manner and in occipital areas by light flashes. Here, we explored the role of auditory input in driving delta-brushes in temporal cortex in 46 premature neonates from 31 to 38 weeks of gestational age, using simultaneous electroencephalographic recordings and auditory stimuli mimicking ambient sounds, including low intensity technogenic “clicks” and human voices. Event detection, power frequency analysis and stimulus locked averaging showed that in the youngest premature (31-34 weeks of gestational age), both voices and low-volume “clicks” reliably evoke delta-brushes specifically in temporal cortical areas. Auditory-evoked delta-brushes consisted of temporal negative slow-waves and rapid oscillations similar to spontaneous delta-brushes. Around 35-36 weeks of gestational age auditory-evoked responses showed a dramatic change characterized by the disappearance of auditory-evoked delta-brushes and the emergence of low-amplitude auditory-evoked cortical potentials. “Click” and voice evoked auditory responses differentiated in their frequency-power topography starting from 34 weeks onwards. Along with findings in other sensory modalities (visual and somatosensory), these findings suggest that sensory driven delta-brushes represent a ubiquitous feature of the human sensory cortex during fetal stages thus probably contributing to the formation of cortical sensory maps by amplifying sensory input. Sensory evoked delta-brushes provide a test of functional cortical maturation during fetal development.
Unconsciously Implanted Memory in the Presence of Cholecystokinin Retrieved in a Behaviorally Relevant Context

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In a previous study, we established a long-term visuoauditory associative memory in rats after pairing a visual stimulus with electrical stimulation of the auditory cortex. In the present study we investigated whether such associative memory can be artificially implanted under anesthesia and then retrieved in a behaviorally relevant context. Rats with bilateral electrodes implanted in the auditory cortex were trained to approach the left or right hole of a behavioral apparatus to retrieve a reward depending on whether the right or left auditory cortex was electrically stimulated. An initially irrelevant light stimulus was then repeatedly paired with electrical stimulation of the auditory cortex in one hemisphere after infusion of cholecystokinin (CCK) under anesthesia, potentially establishing an artificial link between the light stimulus and the stimulation of the CCK-infused hemisphere. After intervention, auditory cortex neurons of this hemisphere started to respond to the light stimulus in both anesthetized and awake states. In subsequent behavioral testing, in response to the light stimulus, rats approached the hole that was “engineered” to be associated with reward availability. Three control experiments showed that this behavioral change was not caused by non-specific effects of CCK infusion or pairings of stimuli alone. Moreover, subsequent stimulus pairings in the contralateral hemisphere resulted in a switch in the direction of behavior, demonstrating the flexibility of the auditory cortex. Our finding that an artificial associative memory formed in the neocortex under anesthesia could be translated into behavioral action provides a scientific foundation for “memory implantation”.

figure 1
LP38
A new paradigm to induce plasticity in human motor cortex: action observation combined with peripheral electrical nerve stimulation

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Question

Action observation (AO) is known to affect the activity of the primary motor cortex (M1). However, the AO effects may vanish if motor practice is not concurrent or immediately follows it. This suggests that a prompt comparison between the visual and the somatosensory representations of movement could be necessary to induce plasticity in M1. The main aim of this study was to test whether action observation combined with a peripheral nerve electrical stimulation was able to evoke cortical plastic changes in the left M1.

Methods

In Experiment 1 we proposed a stimulation protocol (AO-PNS) where the observation of a video showing repetitive thumb-index tapping movements was combined with electrical stimuli delivered on the right peripheral median nerve, i.e., the nerve innervating the abductor pollicis brevis (APB) muscle (the target muscle of the video and electrical stimulation). Left M1 excitability, measured by mean of transcranial magnetic stimulation (TMS-recruitment curve), was compared with that assessed after action observation (AO) and peripheral electrical median nerve stimulation (PNS) alone. In Experiment 2 we tested the long-term effects of AO-PNS by recording MEP amplitudes in the APB muscle before (PRE), immediately after (POST 0) and 15, 30, and 45 minutes after (POST 15, POST 30, and POST 45, respectively) the stimulation protocol. Finally, the topographic specificity of the AO-PNS was assessed in Experiment 3, where the effects of AO-PNS on the MEPs amplitudes of the right APB muscle were compared with those elicited in the adductor digiti minimi (ADM) muscle.

Results

The results of Experiment 1 showed that left M1 excitability increased only after AO-PNS whereas the effects of AO and PNS alone on M1 excitability vanished immediately after video observation. Notably, the increased M1 excitability was still present 45 minutes after the AO-PNS protocol administration (Experiment 2) and was specific for the stimulated muscle - APB (Experiment 3).

Conclusions

In this work we showed that plasticity in M1 can be induced by the activation of the mirror neuron system but only in an associative context (e.g., afferent signals from periphery) opening a general debate on rehabilitative treatments using action observation.
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LP39
Electrophysiological Patterns of Word Learning in 6-Month-Old Infants

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Question

The present study investigates how brain activity is modulated by native (i.e., legal) and non-native (i.e., illegal) phonotactic regularities in 6-month-old infants, with phonotactics describing the combinatorial rules of phonemes in a given language. Being able to differentiate between such regularities is an important prerequisite for undergoing an unimpaired language development.

Methods

We acoustically presented phonotactically legal and illegal pseudowords embedded in a semantic training. Each infant underwent a pretest, training, and posttest on 3 consecutive days. Pretest and posttest included trained and untrained pseudowords. During training the pseudowords were combined with pictures of real objects to create an associative learning setting. Brain activity responses were monitored by means of event-related brain potentials (ERPs) and functional near-infrared spectroscopy (fNIRS).

Results

ERP results revealed significant changes from day 1 to day 3 for trained pseudowords but not for untrained ones in fronto-central regions within a 200-450ms time window. In addition, a differential processing of trained legal (i.e., increasing positivity from day 1 to day 3) and trained illegal pseudowords (i.e., decreasing positivity) was observed. FNIRS results revealed that training-induced effects were lateralized to the left hemisphere. Short-term neuronal modulations due to habituation to the auditory stimuli were present on each day in inferior temporal regions of the left and right hemisphere for both trained and untrained pseudowords.

Conclusions

These findings emphasize the importance of phonotactics on word learning eliciting different patterns of brain plasticity effects in subjects at the beginning of their language development. However, these findings might support the understanding of similar processing mechanisms in clinical populations such as stroke patients suffering from language impairments and having to re-acquire language.
Transcranial Magnetic Stimulation-A Window into the Influences on the Primary Motor Cortex

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Transcranial magnetic stimulation (TMS) is widely used to probe the neural pathways in the cortex. We reviewed studies showing influences on the primary motor cortex (M1) at rest and during movement from other brain regions.

Influences on M1 come from bilateral posterior parietal cortices (PPC), ventral (PMv) and dorsal (PMd) premotor cortices, and cerebellum as well as contralateral M1. Both facilitation and inhibition can be seen depending on the exact position and latency. An example is that a facilitatory effect is produced with stimulation of the right caudal intraparietal lobule (cIPL) at 4 to 15 ms interstimulus interval (ISI)s, while anterior IPL stimulation (aIPL) has shown an inhibitory effect at 2 to 6 ms ISIs. Studies have also shown different networks to be modulated by motor tasks, such as grasping. A precision grip modulated the aIPL-M1 interaction, whereas a whole hand grasp modulated the cIPL-M1 interaction. At rest, the PMv has an inhibitory role on M1, at 6 to 8 ms ISIs, which becomes facilitation during grasping.

There are various facilitatory and inhibitory influences that are time, task and condition-dependent. The observed effects might arise from differently weighted simultaneous facilitation and inhibition, and be mediated polysynaptically via other regions. For example, the parietal areas connect to M1 mainly through premotor regions. Changes of these effects are seen in neurological disorders, enhancing our understanding of the areas involved in pathophysiology. Moreover, connectivity can be influenced by interventions such as repetitive TMS, which can be paralleled by behavioral change.

References
Civardi C et al. Transcranial magnetic stimulation can be used to test connections to primary motor areas from frontal and medial cortex in humans. NeuroImage 2001;14:1444-1453.
Neural adaptations have been involved in the early gains of force observed with strength training, but controversies remain as to the nature and sites of these adaptations. In this pilot study, we used transcranial magnetic stimulation (TMS) to explore changes in corticospinal excitability and interhemispheric inhibition (IHI) associated with unilateral strength training of small hand muscles in young healthy adults (n=6). Prior to training, participants underwent hand function testing bilaterally consisting of grip strength, tapping speed (5th digit) and fine dexterity (pegboard speed test). Corticospinal excitability was assessed for each hemisphere by recordings of motor evoked potentials (MEPs) from the abductor digiti minimi (ADM). Several measures of corticospinal excitability were derived from each hemisphere: resting motor threshold (RMT), MEP amplitude at rest and the contralateral silent period (cSP) and ipsilateral silent periods (iSP). The iSP was used as an index of IHI. The training consisted of daily exercises for 7 days targeting the 5th digit of the left hand (non dominant) using a Gripmaster™ hand exerciser. After training, participants exhibited significant improvements (p < 0.05) in strength (median, +2.7 kg) and dexterity (median, -28 s) only in the trained hand. RMT and MEP amplitude were not significantly changed after training; although a trend was noted (p=.06) for reduced RMTs in the trained hand. The cSP elicited in the trained hand was significantly reduced in duration (median, -27 ms) but not in the untrained hand. A similar trend (p=0.07) was noted for reduction of the iSP duration (median -4.2 ms) in the trained hand. Overall, these results are in agreement with other reports (Kidgell & Pearce, J Strength Cond Res 25, 3208-3217, 2011) and show that measures of central inhibition seem more sensitive to changes in response to localized strength training for the hand area than basic measures of corticomotor excitability. Further, the reported reduction in cSP and iSP seems to point to a fine modulation of intra and inter-hemispheric inhibition to shape the corticospinal drive to the contralateral trained muscles and at the same time to reduce inhibition towards the opposite hemisphere to allow for cross-training effects. (Supported by Faculty of Health Sciences, UOttawa and BRI, Ottawa).
Modulation of cortical excitability after motor learning by action observation

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Objective

Action observation can lead to mapping of neural representations of learning at the motor system level. The aim of this study was to examine the neurophysiological changes associated with motor learning induced by action observation. We hypothesized that motor learning by observation: (1) improves behavioural performance in the untrained hand and (2) enhances excitability of the primary motor cortex (M1).

Methods

In two separate sessions, subjects observed a video depicting another person; (1) learning a sequence-specific serial reaction-time task (SRTT) with the right hand and (2) performing a repetitive right-hand movement on a random-sequence SRTT. Before and immediately after each experimental condition, we measured behavioural performance (speed and accuracy of untrained right-hand) and motor cortical excitability with single- and paired-pulse transcranial magnetic stimulation (TMS). These include (1) resting motor threshold (RMT); (2) motor evoked potential (MEP) amplitude bilaterally (3) short intracortical inhibition (SICI); (4) intracortical facilitation (ICF); (5) interhemispheric inhibition (IHI) from the right to left M1.

Results

Preliminary analysis found learning by observation not only decreased reaction time in the SRTT task in the untrained right-hand, but also increased M1 excitability in the left hemisphere. These changes were selective for learning by observation, as they did not occur after observing performance of the random sequence.

Conclusions

This suggests the importance of visual input to drive learning through systems linking observation and action.
A comparison between short and long latency interhemispheric inhibition from the active to resting primary motor cortex during a unilateral muscle contraction

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Question

Our question is whether a functional difference between short and long latency interhemispheric inhibition (IHI) form the active to the resting primary motor cortex (M1) is detected during a unilateral muscle contraction.

Methods

In nine right-handed healthy participants, IHI was tested from the dominant to the non-dominant M1 and vice versa during a unilateral isometric contraction with the right or left first dorsal interosseous muscle at 10 and 30 % of maximum voluntary contractions. IHI was evoked by that a conditioning stimulus (CS) delivered over the M1 contralateral to the unilateral muscle contraction before a test stimulus over the opposite M1 at inter stimulus intervals of 10 (S-IHI) and 40 ms (L-IHI) using paired-pulse transcranial magnetic stimulation. We employed four CS intensities (80, 100, 120, and 140 % of resting motor threshold) to investigate IHI systematically. The TS intensity was adjusted to evoke a peak-to-peak motor evoked potential amplitude of 1.0 mV across the experimental conditions.

Results

Although there was no significant difference between S-IHI and L-IHI observed in a resting condition, S-IHI significantly differed form L-IHI observed during the unilateral isometric contraction irrespective of the strength of muscle contractions and laterality of IHI. S-IHI during the unilateral isometric contraction was significantly increased compared with that in the resting condition, but L-IHI was not.

Conclusions

Our findings provide novel evidence that S-IHI plays a different role from L-IHI from the active to the resting M1 under the unilateral muscle contraction.
Effects of goal-directed finger movement on intracortical inhibition circuits in the ipsilateral primary motor cortex

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Question

Previous studies on transcranial magnetic stimulation (TMS) demonstrated that excitability of the ipsilateral primary motor cortex (M1) increases during unilateral compared with pseudo goal-directed finger movement. However, it remains unclear whether unilateral goal-directed movement modulates short (SICI) and long (LICI) interval intracortical inhibition circuits in the ipsilateral M1. The aim of the present study was to investigate whether SICI and LICI in the ipsilateral M1 are affected by execution of unilateral goal-directed finger movement.

Methods

Ten healthy right-handed subjects performed four finger tapping tasks with the right index finger. The tasks included the following: (1) maintaining the finger at rest, as a control; (2) self-paced simple tapping on the desk; (3) typing real words using a virtual laser keyboard; and (4) typing pseudo words. During each of the tasks, TMS was delivered to evoke a motor evoked potential (MEP) from the left first dorsal interosseous (FDI) muscle. The test stimulus (TS) intensity was adjusted to elicit an MEP of approximately 1 mV peak-to-peak amplitude in the left FDI. For paired-pulse TMS paradigms, the conditioning stimulus (CS) intensity was set to 80% of the resting motor threshold for SICI. To assess LICI, the intensity of CS was set identical to that of the TS. Interstimulus intervals (ISI) between both CS and TS were fixed at 3 and 100 ms for SICI and LICI, respectively.

Results

EMG activity in the right FDI was similar during all finger tapping tasks. At an ISI of 100 ms, MEPs were significantly increased during the real words typing task compared with both control conditions and the pseudo words typing task. However, with single pulse TMS and paired-pulses with an ISI of 3 ms, MEPs remained unchanged during all tasks.

Conclusions

These results indicate that LICI was significantly decreased during the real words typing task, indicating disinhibition of ipsilateral M1 excitability. Previous TMS studies reported that LICI in the contralateral M1 decreases during precision grip compared with simple finger abduction. Therefore, our findings suggest that performing unilateral goal-directed movement increases the excitability of not only the contralateral M1, but also that of the ipsilateral M1 via the transcallosal pathway.
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**Figure 1**

Test alone

Rest

Tapping

Pseudo words

Real words

![Waveforms](image)

Fig. 1. Typical MEP waveforms for LI CI in the ipsilateral primary motor cortex were recorded from one representative subject.

**Figure 2**

![Bar chart](image)

Fig. 2. Mean LI CI (±SE) induced within the ipsilateral primary motor cortex in each condition in response to paired-pulse TMS (n=10).
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Water flow stimulation increases excitability of primary motor cortex at rest and during movement—A transcranial magnetic stimulation and EEG study—

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Question

Previous research have found that water immersion induced attenuation of short and long latency afferent inhibition, whereas no change in the excitability of primary motor cortex (MI) was observed because of low stimulus intensity (Sato et al., 2013). Consequently, we investigated whether the MI excitability increased by increasing the stimulus intensity by water flow.

Methods

Ten healthy subjects participated in three separate experiments. We evaluated the motor-evoked potential (MEP) recruitment curve produced by a single transcranial magnetic stimulation (TMS) pulse at increasing stimulus intensities (experiment 1) and short-interval intracortical inhibition (SICI) and intracortical facilitation (ICF) using the paired magnetic stimulation technique (experiment 2) before and after 15 min of intervention periods. Three interventions were set at immersion of their right hand with water flow (flow trial), without flow (immersion trial), and no immersion control (control trial). SICI and ICF were evaluated using a conditioning stimulus of 80% active motor threshold and a test stimulus adjusted to produce MEPs of approximately 1-1.2 mV, and were tested at intra-stimulus interval of 3 ms and 10 ms, respectively. In experiment 3, movement-related cortical potentials (MRCPs) were evaluated to examine the MI excitability during movement with flow trial alone.

Results

With flow trial alone, the slope of MEP recruitment curve significantly increased (experiment 1) and the water flow stimulation led to a decrease in SICI and an increase in ICF in the contralateral motor cortex (experiment 2) after intervention. In contrast, there was no significant difference with immersion and control trials. Furthermore, the amplitude of motor potential (MP) in MRCPs significantly increased after 15 min of water flow intervention (experiment 3).

Conclusions

We concluded that water flow stimulation increases the MI excitability at rest and during movement and differentially modulates excitability in motor cortical circuits.
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Triple Stimulation Technique in paired-pulse TMS paradigms

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Background and Question

Paired-pulse TMS paradigms allow to explore motor cortex physiology. The Triple Stimulation Technique (TST) improves conventional TMS in quantifying cortico-spinal conduction. The objective of our study was to compare both methods in paired-pulse paradigms of inhibition and of facilitation.

Method

We investigated paired pulse paradigms of 2 ms (short intra-cortical inhibition) and of 10 ms intervals (intra cortical facilitation) in a randomized order in 22 healthy subjects applying conventional TMS and the TST protocol.

Results

Paired-pulse paradigms by both TMS and the TST yielded comparable results of short intra-cortical inhibition and intra cortical facilitation.

Conclusion

These results suggest no greater sensitivity of the TST for quantifying inhibition and facilitation.
Changes of motor function in elder persons induced by transcranial magnetic stimulation with maximum voluntary muscle contraction for serial 4 days.

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Background

Our previous study suggested that transcranial magnetic stimulation (TMS) during the maximum voluntary muscle contraction (MVC) has a potential to facilitate motor neuron function in humans.

Objective

To evaluate the effects of TMS with MVC for serial 4 days on motor function in elder persons, motor evoked potentials (MEPs) and the maximum pinching muscle force were recorded sequentially.

Methods

Four MEPs in the first digital interossei (FDI) muscle elicited by TMS during MVC to pinch a button-like strain-gauge transducer with MVC for 2 seconds were recorded before and at each 15 minutes interval until 1 hour after the onset of TMS with MVC (test condition). As a control condition, sham TMS was delivered during MVC. But, before and 1 hour after the onset of TMS with MVC, real TMS was delivered to record MEPs.

Results

MEP amplitudes or areas in FDI muscle and pinching muscle force were significantly increased by TMS with MVC (P

Conclusion

TMS with MVC for serial days has a potential to improve motor function in elder persons. However, we need further studies to confirm the effects of TMS with MVC on motor function.

figure 1
Selective measurement of forearm muscles after transcranial magnetic stimulation


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Question

Thirty percent of all stroke patients suffer from a paralyzed arm in the acute phase and improvement of upper extremity function is seen in 40% of the survivors. The extent of this damage to the motor system can be measured by measuring motor evoked potentials (MEPs), evoked by transcranial magnetic stimulation (TMS). MEPs have a high predictive value with respect to motor recovery. Depending on the location of placement of the surface electrodes, information about the nerves innervating the associated muscles can be obtained. The goal of this study was to examine which are the optimal electrode positions for peripheral stimulation of flexor and extensor muscles and whether these electrodes are also optimal when applying TMS.

Methods

For the determination of these optimal locations, 37 surface electrodes were placed on the right forearm of 12 healthy subjects. The muscle activity resulting from two different ways to stimulate was measured. The first type was supramaximal electrical nerve stimulation of both the radial and the median nerve. The second type was TMS with a round coil of the motor cortex at multiple intensities. The best responding electrode combinations were selected on the basis of amplitude and waveform.

Results

Distinction between the flexors and extensors based on the sEMG results could be made. It was found that the optimal electrode pairs for electrical stimulation were largely in accordance with those of TMS.

Conclusion

This study helped to identify the optimal electrode positions for the use of TMS in outcome prediction of upper arm functionality in stroke patients.


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INTRODUCTION
A conditioning transcranial magnetic stimulation (TMS) over the cerebellum reduces the excitatory state of the contralateral primary motor cortex. This reduction has been termed “cerebellar inhibition” and is supposed to be triggered by Purkinje cells activation leading to the inhibition of the motor cortex via dentato-thalamo-cortical pathways. The assessment of this cerebellar cortex inhibition can be required when discussing thalamic stimulation for action tremor in multiple sclerosis patients.

OBJECTIVE
The purpose of this study was to obtain quantitative data from patients with various cerebellar syndromes, in order to evaluate the loss of cerebellar inhibition, trying to correlate the tests with clinical phenotypes and MRI lesions.

METHODS
We studied the excitability of the primary cortex motor using a conditioned TMS by a 6-ms preceding cerebellar TMS in a group of 13 patients with diseases affecting cerebellum (spino-cerebellar ataxia, 5 cases; multiple sclerosis, 5 cases; traumatic cerebellar lesion, 1 case, mitochondriopathy, 1 case; undetermined cerebellar atrophy, 1 case and in 13 age-matched voluntary controls. Motor evoked potentials (MEPs) were recorded from the right and left Abductor Digiti Minimi muscle using surface electrodes.

RESULTS
Cerebellar inhibition was observed in all controls: the reduction of MEPs amplitude and/or area vs unconditioned one was 85.5 (95% CI: 69.6-91.7) and 82.5 (95% CI: 73.7-94.1) respectively. There was no difference between the inhibition of the right and the left cerebellum lobes. MEPs amplitude and area recovered entirely after the test. Cerebellar inhibition was absent or markedly reduced in 69% cerebellar patients (right, left or both cerebellum stimulations) including facilitated signals in 2 patients (multiple sclerosis patient and one patient with cerebellar atrophy). Patients with affected cerebellar inhibition also had efferent cerebellar pathways alterations.

CONCLUSION
Abnormal cerebellar inhibition could be a valuable marker to quantify efferent cerebellar pathways dysfunction. This new functional tool seems to be a simply performed and sensitive method to detect motor cortex excitability alterations due to efferent cerebellum pathways.
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Novel method for estimating size of cortical representation area in navigated transcranial magnetic stimulation

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**Question**

Navigated transcranial magnetic stimulation (nTMS) can be used to map cortical representation areas, which may experience alterations e.g., due to plasticity effects. The objective was to introduce and validate a novel method for estimating the size of the cortical representation area on the cortex surface. The novel method can be used without a stimulation grid also to determine the location of centre of gravity (CoG).

**Methods**

Motor cortex of 6 volunteers was mapped for the representation area of the thenar and hypothenar muscles of the hands at above threshold intensity using a conventional method, i.e. using a stimulation grid [2] and without the grid allowing for unevenly spaced stimulus locations. The novel method utilizes Voronoi tessellation to compute coverage for each stimulus location within cloud of stimulated locations. The representation areas were also estimated using two reference methods; 1) computing the average coverage of a single stimulus within the mapped area [1], 2) using convex hull to outline all positive responses [2]. CoGs were determined with the conventional and the novel method. The CoG was adapted for the novel method by weighting each stimulus with their coverage area.

**Results**

All methods displayed similar values for the representation size (p>0.657, Fig. 1). The mapping method (with or without grid) did not affect (p>0.496, Fig. 1) the size of the representation when analysed with the novel method. The CoG agreed well between the mapping methods, distance between CoGs 5.8±1.9mm.

**Conclusions**

As the novel method utilizes both the negative and positive motor responses, it has great potential in quantitative analysis of the motor representation areas. The method was validated against reference methods, and has the advantage that it does not require a stimulus grid, it utilizes both positive and negative responses, and can estimate both the representation location and size.

**References**

[1] Uy J et al., BrainTopogr 2002;14:293

**Fig. 1**

Estimated cortical representation size for thenar muscle at different MEP threshold amplitudes (A) for three different methods and (B) with or without using the grid during mapping.
Task dependency of long latency facilitatory effect on soleus H-reflex by cerebellar transcranial magnetic stimulation

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Question

This study’s questions were whether cerebellar transcranial magnetic stimulation (C-TMS) modulates excitability of motoneuron pool and whether the effect by C-TMS is regulated during task that cerebellar activity associated with.

Methods

In the first experiment, 11 healthy humans were recruited. The subjects were prone and their bilateral ankle joints were fixed with braces. The center of the junction region of the coil was placed at the site 1 cm below and 3 cm to the right of the inion to stimulate the right cerebellum. Intensity of conditioning TMS was set at 90 % of the active motor threshold of a right soleus muscle. The tibial nerve stimulus (NS) evoking the H-reflex from right soleus muscle was delivered after or before TMS. Conditioning-test interstimulus interval (ISI) was every 10 ms in section from 0 to 130 ms or every 1 ms in section from -6 to 0 ms. No-TMS condition test and sham TMS (S-TMS) condition test only ISI 0 or 110 ms were inserted at random.

In the second experiment, 9 healthy humans were recruited. The subject was set same as first experiment. NS after C-TMS 110 ms later was delivered during right finger tapping with 1 Hz auditory external cues (tapping task) or during staying the finger at 0-degree position for flexion/extension (stay task), and no-TMS condition test during each task was inserted at random.

Results

Amplitude of H-reflex was significantly inhibited at ISI -1, 0, 10 ms and facilitated at ISI 110, 120, 130 ms (Fig. 1). There was no significant difference between the amplitude in S-TMS condition and no-TMS condition at ISI 0 and 110 ms, and the amplitude in C-TMS condition was significantly higher than that in S-TMS condition (Fig. 2-A). There was no significant difference of amplitude of H-reflex between tapping task and stay task (Fig. 2-B), although the quantity of facilitation induced by C-TMS was significantly decreased during tapping task (Fig. 2-C).

Conclusions

Cause of short latency inhibitory effect by C-TMS may be auditory effect. On the other hand, long latency facilitatory effect by C-TMS can not be auditory startle response. The long latency facilitatory effect by C-TMS is modulated by finger tapping task that needs temporal control of movement due to cerebellum. So, the modulation of long latency facilitation by C-TMS can reflect the alteration of cerebellar activity with motor control.
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**Figure 1**

[Graph showing data with asterisks indicating significance levels.]

**Figure 2**

(A) Graph showing H-reflex amplitude (% of no-TMS condition) with different conditions and significance levels.

(B) Bar graph comparing H-reflex amplitudes between Stay and Tapping conditions.

(C) Graph showing H-reflex amplitudes with statistical significance.
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rTMS in treatment of neuropathic facial pain - a prospective study of 20 patients

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**introduction**

Atypical facial pain as a kind of neuropathic disorders could occur after traumatic lesions and remains difficult to treat. One option for management of intractable pain is stimulation of the motor cortex by implantation of an epidural electrode. This effect of invasive stimulation could be replaced by transcranial magnetic stimulation.

**objectives**

The objective of the study was to observe the pain reducing effect of non-invasive transcranial magnetic stimulation (rTMS) in patients suffering from facial pain, and furthermore to detect whether there is a predictable value for invasive motor cortex stimulation (MCS).

**materials and methods**

The study was prospective but not randomized. We included patients suffering from chronical neuropathic facial pain. The primary motor cortex has been stimulated with high-frequent, repetitive transcranial magnetic stimulation (rTMS). Stimulation was daily repeated for a period of 9 days. The individual pain level was assessed by the visual analogue scale (VAS) and documented daily for three weeks. The first follow up was done after 6 weeks.

**results**

We included 20 patients (14 female / 6 male) between 32 and 75 years of age. The follow up was done at least after six weeks, further intervals were determined individually with a maximum follow up time of 2,5 years. 8 patients suffered from posttraumatic pain, 12 patients suffered from idiopathic atypical facial pain. A pain reduction in terms of a decrease in the VAS scale was obtained in 14 patients, ranging from 2 to 8 points with a mean value of 5.0. The pain reduction occurred with a delay between 3 and 28 days (mean 16 days), and showed a long term effect up to 6 weeks. Two patients successfully underwent invasive motor cortex stimulation.

**conclusion**

Non-invasive transcranial magnetic stimulation seems to be applicable for some kind of neuropathic pain, i.e. atypical facial pain. Pain reduction has a long term effect. Furthermore, it may be used as a positive predictor for invasive motor cortex stimulation.
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Differential effect of muscle fatigue on short-interval intracortical inhibition and short-interval intracortical facilitation in motor cortex

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Questions

Muscle fatigue can reduce the excitability of short-interval intracortical inhibition (SICI) in the hand area of motor cortex. However, particularly at an interstimulus interval of 3ms, SICI can be contaminated by concurrent short-interval intracortical facilitation (SICF). Here we examine whether the change in SICI after fatigue is related to changes in SICF.

Method

Eight male subjects participated in two separate experiments. In each of them SICI and SICF was evaluated before and after three 2 min periods during which they contracted the right FDI isometrically at 50 % of MVC. SICI was evaluated with a conditioning stimulus of 80% active motor threshold whereas SICF was evaluated with S2 equal to 100% resting motor threshold. In experiment 1 (8 subjects), SICI and SICF were both evaluated with an ISI =3ms; in addition ICF was tested at ISI=10ms. In experiment 2 (7 subjects) SICI and SICF were tested at ISI=2ms; in addition SICF was also tested at ISI=3ms. Test stimulus were adjusted to produce an MEP about 1-1.2 mV throughout the two experiments. The amplitudes of the test MEP as well as SICI, ICF and SICF were assessed before, after each of the individual contractions and then at 5, 10, 15, 20, 30 min after the last contraction.

Results

MEPTEST did not change significantly throughout the testing periods. SICI3ms and SICI2ms significantly decreased after the fatiguing contractions whilst SICF3ms and SICF2ms did not significantly change.

Conclusion

Fatigue suppressed SICI whilst having no effect of SICF, suggesting that the reduction of SICI was not caused by superimposed facilitation from SICF.
In time processing, the role of different cortical area is still under investigation. Event-related potentials (ERPs) represent valuable indices of timing mechanisms in the millisecond-to-second range. We used an interference approach by rTMS and ERPs to investigate the role of different cortical areas in processing basic temporal information. Ten healthy volunteers were requested to decide whether time intervals between two tones were shorter (800 ms), equal to, or longer (1200 ms) than a previously listened 1000 ms interval and press different buttons accordingly. This task was performed at baseline and immediately after a 15-min-long train of 1-Hz rTMS delivered to supplementary motor area, right posterior parietal cortex, right superior temporal gyrus, or an occipital control area. We analyzed task accuracy, reaction time, and ERPs during (contingent negative variation, CNV) and after the presentation of inter-tone intervals. At baseline, CNV was modulated by the comparison interval duration and the amplitude of the positive ERP peak emerging approximately 200 ms later was higher for ‘Long’ compared to ‘Short’ intervals. RTMS had no significant effect on behavioural or ERP measures. Data suggest that these cortical areas are less crucially involved than other brain regions (e.g. non-cortical) in processing basic temporal information.
Lack of behavioral effects of high-frequency rTMS in vegetative state: a randomised, double blind, sham-controlled, cross-over study

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Background

In a patient with post-traumatic vegetative state (VS), a non-significant trend toward neurobehavioral gains has been reported after the application of a patterned rTMS protocol over the right dorsolateral prefrontal cortex (Louise-Bender Pape et al. Brain Stimul 2009;2:22-35). Recently, in a patient with minimal conscious state, Piccione et al. (Neurorehabil Neural Repair 2011;25:98-102) reported an arousal with transient increase of meaningful behaviours and EEG changes after 20-Hz rTMS over the primary motor cortex (M1). This has raised interest in the scientific community but has also had disproportionate resonance in mass media and strong expectations among the patients’ families.

Objective

To evaluate the effect of a non-invasive brain stimulation protocol with high-frequency rTMS in VS by a randomised, double blind, sham-controlled trial with a cross-over design.

Methods

Eleven patients classified as being in a VS (9 post-anoxic, 2 post-traumatic) were included in the study. Twenty-Hz rTMS or sham stimulation were applied to the left M1 for 5 consecutive days. Daily sessions consisted of 10 minutes stimulation (1000 pulses) at an intensity of 60% maximum stimulator output. Primary outcome measures were changes in the JFK Coma Recovery Scale-Revised (CRS-R) scale total score and Clinical Global Impression (CGI) scale. Evaluations were performed at baseline, after the first day of treatment, immediately after the end of the 5-days treatment, and 1 week and 1 month later.

Results

Slight changes observed in the CRS-R and CGI scores did not significantly differ between real or sham stimulation conditions. In addition, no concordance was seen between CGI changes observed by clinician and patient’s relatives.

Conclusion

Findings did not provide evidence of therapeutic effect of rTMS in VS, at least with conventional coils and current safety parameters.
Trigeminal nerve stimulation does not affect cortical excitability in healthy subjects.

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Question

The lack of efficient treatment alternatives to antiepileptic drugs and epilepsy surgery in patients with severe epilepsy has promoted the development of various types of neurostimulation such as repetitive transcranial magnetic stimulation, vagal nerve stimulation and, more recently, trigeminal nerve stimulation (TNS). It has been suggested that peripheral nerve stimulation such as TNS exerts its potential effects by altering cortical excitability. In this study, we used a paired-pulse transcranial magnetic stimulation (ppTMS) protocol to measure cortical excitability in relation to trigeminal nerve stimulation.

Methods

To measure potential changes in cortical excitability, ppTMS-measurements were undertaken before, during and after 40 minutes of trigeminal nerve stimulation in 20 healthy subjects. The resting motor threshold (rMT), short-interval intracortical inhibition (SICI), long-interval intracortical inhibition (LICI) and intracortical facilitation (ICF) were measured from the dominant hand using navigated ppTMS and a custom-made automated protocol based on a threshold-tracking algorithm.

Results

No significant changes in cortical excitability measurements were seen between the different sessions (before, during, and after TNS).

Conclusion

Trigeminal nerve stimulation does not affect cortical excitability in healthy subjects.
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Task-dependent changes of late inhibitory and disinhibitory actions within the primary motor cortex in humans

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The objective of the present study was to investigate the time course of long-interval intracortical inhibition (LICI) and late cortical disinhibition (LCD) as a function of the motor task (index abduction, thumb-index precision grip and rest). Motor-evoked potentials were recorded from the first dorsal interosseus (FDI) muscle of the dominant limb in 14 healthy subjects. We used paired-pulse transcranial magnetic stimulation (TMS) paradigms in which a test pulse was preceded by a suprathreshold conditioning pulse (130% of the resting motor threshold) with varying interstimulus intervals (ISIs). Each task featured fifteen different ISIs (ranging from 30% (~45 ms) to 220% (~330 ms) of the corresponding silent period (SP)). We found that LICI was followed by LCD (namely a period of increased cortical excitability lasting for about 200% of the SP) in both active tasks. The time-dependent modulation of LICI and LCD differed in the two active tasks; LICI was shorter (i.e. disinhibition occurred earlier) and LCD was more intense during precision grip than during index abduction (Figure 1). Long-interval intracortical inhibition disappeared well before the end of the SP in the precision grip task, suggesting that the mechanisms underlying these two inhibitory phenomena are distinct. Late cortical disinhibition was not observed in the resting condition. Our results suggest that disinhibition might reflect adaptation of neural circuits excitability to the functional requirements of the motor task. This finding is potentially important for understanding some of the troubles that appear in neuropathies such as focal hand dystonia in which cortical excitability is increased in certain skilled tasks.

Figure 1: Time course of conditioned MEP amplitude during index abduction (black circles, solid line) and precision grip (gray squares, dashed line) as a function of ISI in percentage of the SP duration. Vertical dashed line represents the end of SP and horizontal dashed line the unconditioned control MEP. The asterisk indicates a significant difference between abduction and precision grip at p&lt;0.05.
Chronic rTMS increases the expression of down-stream long-term effects regulatory molecules in rat brain and lymphocytes

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Question
We have recently demonstrated an increased BDNF-TrkB signaling and TrkB-NMDA receptor coupling after consecutive 5 days high frequency (5Hz) rTMS in rat brain prefrontal cortex and lymphocytes, and similar results were obtained from lymphocytes of healthy human subjects. In the present study, we have investigated whether rTMS could produce modifications in the activation of down-stream long-term effects regulatory molecules such as CaMKIIα and CREB in rat prefrontal cortex and in lymphocytes.

Methods
We treated 6 normal sprague-dawley rats with 5 days chronic low (1Hz) and high (5Hz) frequency rTMS in separate groups. After that we measured the CaMKIIα and CREB expressions in prefrontal cortex and in lymphocytes.

Results
We found that both low- and high-frequency rTMS significantly increased CaMKIIα and CREB expressions in prefrontal cortex. High-frequency rTMS stimulated expression was found to be increased more than low-frequency. In lymphocytes, no change was observed in CaMKIIα activation but CREB activation was increased by both low- and high- frequency rTMS.

Conclusions
These results have shown the molecular level modulation of rTMS at down-stream level and approaching lymphocyte as a putative source to study brain contexture in the peripheral system with rTMS application.
Modulation of cortical plasticity by decompression surgery for cervical spondylotic myelopathy

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Background

Cervical spondylotic myelopathy (CSM) is a progressive disease, resulting in sensorimotor limb deficits, bladder and bowel dysfunction. However, the physiological mechanisms underlying motor plasticity changes before and after surgery are unclear.

Methods

We studied 24 CSM patients who underwent decompression surgery and 15 healthy controls. Clinical parameters (modified Japan Orthopedic Association (JOA) score), hand function tests, H reflex measurements and transcranial magnetic stimulation (TMS) cortical mapping before and 3 months after surgery were obtained. TMS parameters include sum amplitude of motor evoked potentials (sMEP) and number of focal points (N) MEPs were elicited from the right first dorsal interossei. Changes in sMEP (cMEP) and number of focal points (NDiff) were correlated with changes in hand function. CSM patients with mixed upper and lower limb dysfunction (Group A) and only lower limb dysfunction (Group B) were then analysed separately.

Results

Modified JOA scores were significantly improved after surgery (p = 0.03).

The sMEP (p < 0.01) and N (p < 0.001) were significantly larger in CSM patients compared with controls. For Group A (16 patients), sMEP (p < 0.01) and N (p < 0.001) showed similar findings. However, for Group B (8 patients), only N (p = 0.03) was significantly larger in patients than controls.

For Group A, we found significantly increased grip strength (p = 0.02), reduced sMEP (p = 0.001) and N (p = 0.003) after surgery. cMEP significantly correlated with improved feeding (p = 0.03) and stacking (p = 0.04) times, as was NDiff with improved writing times (p = 0.03).

For Group B, there was a trend to significant reduction (p = 0.05) in sMEP after surgery, but no significant correlation were found for cMEP or NDiff with all hand function test.

No significant differences in H reflex parameters obtained from the flexor carpi radialis were noted before and after surgery.

Discussion

Compensatory expansion of motor cortical representation occurs in CSM, corroborating functional imaging studies, showing a tendency to normalization after surgery. Cortical plasticity modulation mirrored improvements in relevant tasks requiring utilization of intrinsic hand muscles. Our study also suggested that changes driving motor recovery occur largely at cortical rather than spinal levels.
P704
Low frequency repetitive transcranial magnetic stimulation in early phase of rehabilitation of patients with post-stroke aphasia

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INTRODUCTION

About 50% of post-stroke patients remain aphasic a condition that greatly impede their reintegration to society. Results of Repetitive Transcranial Magnetic Stimulation (rTMS) as supplementary treatment for sub-acute post-stroke aphasia are controversial.

AIM

We assessed the efficacy of inhibitory rTMS with conventional speech therapy to help recovery language performance in sub-acute stroke aphasia.

MATERIAL AND METHODS

In a randomised case-control double-blind study 12 non-fluent aphasic were consecutively enrolled. All patients suffered a first-ever stroke in the sub-acute stage defined as time since lesion onset from 1 month post-stroke. Patients were randomized either to receive real (low frequency on right-hemisphere homologue of Broca’s area) or sham rTMS, to a 3-week (5 day in a week). Immediately after each rTMS all patients received speech therapy. The speech performance was evaluated with Italian version of Aachener Aphasia Test (AAT), before (T0) and after (T1) treatments.

RESULTS

Seven patients were treated with real rTMS and 5 patients with sham rTMS. Total and sub totals AAT scores showed a similar improvement in real and in sham rTMS groups between T0 and T1.

CONCLUSIONS

In early phase of rehabilitation (< 1 month) inhibitory rTMS over the right posterior inferior frontal gyrus, in combination with speech therapy, did not seem significantly to improve language recovery respect to conventional speech therapy only.
Test-Retest Reliability of Single and Paired Pulse Transcranial Magnetic Stimulation Parameters in Healthy Subjects

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Question

The aim of this study was to determine test-retest reliability of different TMS parameters and several confounding factors (investigator, retest-interval and gender) while controlling other potential confounders (time of day and period of menstrual cycle in women) in a large sample of healthy subjects.

Methods

Four investigators applied two sessions of TMS in 93 healthy volunteers (57 male, 61%) with a mean retest interval of 34.0 ± 25.6 (SD) days. Women were assessed in the follicular phase of their menstrual cycle. TMS was mainly applied in the morning. Parameters: Test stimulus (TS), resting motor threshold (RMT), short latency intracortical inhibition (SICI), intracortical facilitation (ICF) and CSP. Data were analysed offline.

Results

Good test-retest reliabilities were observed for TS (r=.880) and RMT (r=.826). CSP durations determined by visual (r=.466) analysis was of moderate reliability. Lower correlations were obtained for SICI (r=.383) and ICF (r=-.159). Reliabilities were different across investigators for CSP and were low when TMS was applied by different investigators across sessions. Gender did not affect reliability of TMS parameters.

Conclusions

TMS parameters measured twice in a large sample of healthy volunteers results in moderate to strong test-retest reliabilities in all excitatory and in all but one of the inhibitory TMS-parameters. The main confounding factor is the investigator.

Figure 1. Significant correlation (p

![Figure 1](image-url)
Motor evoked potential as a predictor of clinical response in MS patients treated with 4-aminopyridine.

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**Question**

4-AP has been recently introduced as a symptomatic treatment of walking impairment in MS patients. The clinical benefits have been reported in about 1/3 of patients.

The study was intended to determine:

- measure sensitivity and specificity of MEPs in identifying disabled responders to treatment
- evaluate how action mechanism of fampridine is associated to improvement in conduction velocity of electrical impulse.

**Methods**

Patients were enrolled in a prospective study. Patients underwent a neurological exam, in order to determine EDSS, and a walking test, measuring speed and endurance (T25FW); then, patients underwent motor-evoked potentials (MEPs) following transcranial magnetic stimulation (evaluating central motor conduction time and MEPs amplitude) before starting and after 30 days of 4-AP treatment.

**Results**

On average, there wasn’t an improvement of the MEPs parameters after 4-AP treatment, while in the patients that had a significant improvement of the walking-test after the treatment (responder patients) the MEPs parameters at baseline showed a CMCT and a MEPs amplitude alteration, while in the non-responder patients were was only a MEPs amplitude alteration and a normal CMCT at baseline.

**Conclusions**

4-Aminopyridine is useful for walking improvement in patients with demyelinating failure of pyramidal tract (CMCT alteration), while is not useful in patient which had only an axonal damage (MEPs amplitude alteration). Future clinical trials may be able to enrich a patient population for potential responders using MEPs measures.
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P708
Co-activation of small hand muscles depends on the synergy of neighborhood contracting muscles but not M1 somatotopy

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Objective

Unintentional coactivation is the muscle activation induced by contraction of surrounding muscles. Small hand muscles (SHMs) are activated during coactivation, however, the detailed mechanisms are largely unknown. We hypothesized that the coactivation of SHMs would be greater by contracting muscles which are closer to M1 somatotopy. Thus, we compared the coactivation of first dorsal interosseus (FDI) muscle during contracting abductor pollicis brevis (APB) muscle with that of abductor digiti minimi (ADM) muscle contraction. It was anticipated that more coactivation of FDI would be observed during APB contraction than ADM contraction.

Methods

Seven healthy adults participated in this study. FDI was kept relaxed as much as possible while the subject contracted either of APB or ADM at about 10-20% maximum voluntary contraction. MEPs of FDI were recorded 15 times in 3 conditions: rest, APB contraction and ADM contraction.

Results

The mean FDI amplitudes were increased during APB or ADM contraction condition compared with rest condition. Moreover, FDI amplitudes during ADM contraction were significantly larger than that of APB contraction condition.

Discussion

The coactivation of FDI was greater in ADM condition than that of APB condition, which was contrary to our working hypothesis. Thus, the somatotopic relationship in M1 is not a major determining factor for the coactivation level. We suppose that ADM contraction causes synergy of abduction of 2-5 digits, which results in more coactivation of FDI. However, APB contraction is more independent movement that induces less synergistic effect.
P709
Dropping Objects in Carpal Tunnel Syndrome: Clinical Characteristics and Sensory-Motor Integration

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**Question**

Some patients with carpal tunnel syndrome (CTS) complain about dropping objects. Is this attributable to abnormal sensory-motor integration (SMI)?

**Methods**

Twelve CTS patients who frequently drop objects (dCTS), 10 CTS patients without this complaint (ndCTS) and 16 normal controls were included. Clinical characteristics were quantified with Boston Carpal Tunnel Questionnaire (BCTQ) and Purdue Pegboard test.

SMI studies were comprised of submaximal electrical stimulation of right and left median and ulnar nerves followed by transcranial magnetic stimulation (TMS) over the motor cortex with 20, 35, 50, 65, 80, 100 and 200 ms inter-stimulus intervals (ISIs). Amplitude and area ratios were calculated by dividing the mean of eight motor responses elicited at each ISI to those evoked by TMS alone.

**Results**

CTS severity was similar electrophysiologically in dCTS and ndCTS groups, while BCQT symptom scores were higher in the former. Purdue test score was significantly lower in dCTS as compared to the other groups.

In the SMI studies, median nerve stimulation in dTCS led to significantly elevated amplitude/area ratios of the motor responses recorded from thenar muscles at ISI 35 ms (Fig 1, blue: dCTS, red: ndCTS, green: controls) and those recorded from hypothenar muscles at 50 ms. In ndCTS, amplitude/area ratios after ulnar nerve stimulation were higher for the responses recorded from thenar muscles at 20, 80 and 100 ms.

**Conclusion**

dTCS patients' SMI strategy may be deficient by only considering the abnormal impulse bombardment of the abnormal median nerve, while the correct strategy of the ndCTS cases augments the effects of the impulses carried by non-damaged nerves.

**figure 1**

![Graph showing the results of the SMI studies](image-url)
**P710**  
Disinhbition of primary motor cortex function contralateral to the hemipseudoathetotic hand

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**Background**

Pseudoathetosis is one of the involuntary movements similar to athetosis but caused by impaired proprioception. Its pathophysiology has not yet been delineated. It is hypothesized that the excitability of primary motor cortex (M1) is exaggerated in the hemisphere contralateral to the affected hand. To test this hypothesis, paired-pulse transcranial magnetic stimulation (TMS) was applied in patients with hemipseudoathetosis.

**Objective**

The aim of this study is to elucidate the pathophysiology of hemipseudoathetosis by assessing the motor cortical function using TMS.

**Methods**

Eight patients (Female: 1, mean age: 64.5, 46–77) who showed hemipseudoathetosis in an upper extremity due to cerebral vascular lesion or spinal lesion after the tumor resection were examined. In addition to neurological examination, somatosensory evoked potential (SEP) by median nerve stimulation of both affected and intact hand were recorded and MRI scans were used to evaluate the responsible lesion. Paired-pulse TMS was applied over the M1 contralateral to both affected and intact hand to evaluate the intracortical inhibition and facilitation (ICI, ICF). The relative amplitude of the paired response compared to that of the control response (amplitude ratio) was used for further statistical evaluation using Student’s t-test. The mean ratio at interstimulus interval (ISI) of 2 and 4ms was calculated as an index of ICI and the mean ratio at ISI of 10 and 15ms was used as an index of ICF.

**Results**

At the affected hand, the proprioception of the index finger was impaired and N20 of the SEP by median nerve stimulation could not be evoked. The mean ICI in the hemisphere contralateral to the affected hand was significantly greater than that in the other hemisphere (77.7% and 35.2%, respectively, P<0.001). By contrast, there was not statistically significant difference for ICF (111.0% and 113.0%).

**Conclusion**

This result suggests the disinhibition of M1 contralateral to the hemipseudoathetotic hand.
Abstracts of Poster Presentations – Poster Session 39 – Transcranial magnetic stimulation

P711
Influence of an Inhibitory Theta-Burst Protocol on the Cortical Silent Period Induced by Magnetic Stimulation

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Question
Is the cortical silent period (CSP) induced by magnetic stimulation influenced by inhibitory theta-burst stimulation (TBS)?

Methods
We studied a group of 9 healthy subjects (8 woman; mean age 42.0 ± 17.7 years) in two separate days. To define the size of the Motor Evoked Potential (MEP) of the right abductor digiti minimi (ADM) muscle, magnetic stimulation (TMS) was applied on the left cortical motor area of the hand, 20% above motor resting threshold (MRT). To determine the CSP, 10 consecutive magnetic pulses (20 seconds interval) 1.1 x MRT were delivered during the full contraction of the target muscle. CSP was quantified from the stimulus artifact to the return of the electrical activity (minimum 100mV of amplitude). The inhibitory TBS protocol consisted of 360 stimuli in bursts of 3 stimuli at 50 Hz, repeated at intervals of 200 ms, with an intensity of 80% of MRT. The MEP was measured before and immediately after the TBS, and for 20 minutes after, at 5 minutes intervals. The CSP was measured before and immediately after the TBS. Paired samples t-test was used to assess differences before and after the TBS protocol both in MEP and in CSP. Intraclass correlation coefficient was used to study the reliability of CSP measurements.

Results
The tested TBS inhibitory protocol was effective, as it caused a significant reduction of the MEP amplitude (1.26 before vs. 0.49 immediately after; p=0.011). The CSP was not influenced by this TBS inhibitory protocol (125.59 before vs. 123.12 after; p=0.635). Intraclass correlation coefficient confirmed the consistency of our results.

Conclusion
Although, the tested protocol was effective in reducing motor responses, it did not influence the CSP, suggesting that inhibitory theta-burst stimulation does not influence post-synaptic GABA B receptors.

figure 1
Abstracts of Poster Presentations – Poster Session 39 – Transcranial magnetic stimulation

P712
Assessment of Sensorimotor Integration Pathways during an Illusory Multi-sensory Perception

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Objective

Impairment of sensorimotor integration in movement disorders is increasingly being recognized. Therefore, it is necessary to investigate a circuit involved in the sensorimotor integration in both healthy and pathological states. The aim of this study is to assess the effects of sensory afferents on the primary motor cortex (M1) while higher levels of sensory processing are evoked by an illusory perception. We used the rubber hand illusion (RHI) paradigm which has been shown to activate the premotor cortex (PM) and posterior parietal cortex (PPc) and these areas are considered as sensory-integration centers.

Methods

8 healthy subjects were tested using short-latency and long-latency afferent inhibition (SAI/LAI) at baseline. Electrical digital nerve stimulation (DNS) was applied prior to transcranial magnetic stimulation (TMS) over M1 and motor evoked potentials (MEPs) were recorded from hand muscles at rest. The RHI paradigm was applied to evoke multiple somatosensory illusory perceptions activating the PM and PPc. SAI and LAI were tested before and immediately after the induction of the illusory perception. SAI and LAI were assessed by comparing the conditioned to the unconditioned MEP amplitude.

Results

At baseline, the average ratios of conditioned to unconditioned MEP were 0.71 +/- 0.19 for SAI and 0.71 +/- 0.14 for LAI, indicating sensory afferent inhibition. After RHI, the both ratios were slightly increased to 0.85 +/- 0.16 for SAI and 0.85 +/- 0.26 for LAI indicating a reduction of inhibition.

Conclusions

Both short and long latency sensorimotor integration pathways appear to be involved in the processing of multisensory perceptions. The long-latency pathway may interact with cortical areas that are activated by the RHI paradigm such as the PM and PPc.
Transcranial magnetic stimulation (TMS) and mirror therapy: a promising rehabilitative approach for subacute stroke patients with severe disability

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Introduction

Mirror therapy (MT) has been proved to promote cortical reorganization and functional recovery of post-stroke patients. Also high frequency repetitive transcranial magnetic stimulation (TMS) - a noninvasive, safe tool that modulates local neuron excitability and induce short-time functional reorganization of cortical networks- has been recently studied for its contribution in stroke rehabilitation. The combination of the two techniques has not been explored.

Methods

Three Patients affected by subacute first-ever stroke - documented by a brain CT- with severe disability (NIHSS 10-14) and hand paresis were recruited at 1 month from the event and received a complete neurological examination including MRC, NIHSS and Fugl-Meyer grading. They underwent 12 session (3 time/week) of 15 minutes of excitatory TMS through a circular coil applied on the primary motor cortex of the affected emisphere, followed by 15 minutes of MT for the upper limb (imitation of presented postures and motor imagery through repetitive active-passive limb movements, according to already existing protocols).

Double-pulse TMS through a figure-eight focal coil was used to study intracortical inhibition (ICI) in primary motor cortex of both side at rest and during the preparation of movement . Mapping the motor cortex with TMS was also obtained in order to study acute and rapid plastic rearrangements of cortical motor output.

Results

A motor evoked potentials - previously absent - was elicited after 1 month treatment for the affected upper limb. A normalization of the silent period - previously prolonged - and reduction of and intracortical inhibition in the affected emisphere was evident, together with a significant modification of ICI over the unaffected hemisphere. Such results were reproducible also one month after the end of treatment.

Conclusion

TMS treatment combined with MT may be added to the conventional therapy of severely impaired stroke patients even in an early phase after the insult, with positive results on both neurophysiological and clinical parameters. We may suppose that TMS, when combined with MT enhances synaptic plasticity and induce nerugenesis, facilitating the motor recovery, even in those cases with predicted limited recovery offered by regular physical therapy. A follow-up study and an enlargement of the sample is ongoing.
Abstracts of Poster Presentations – Poster Session 39 – Transcranial magnetic stimulation

LP41
Language mapping with nrTMS: an experimental study in 2 healthy speech therapists

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OBJECTIVE
The use of Navigated Transcranial Magnetic Stimulation (nTMS) in presurgical mapping is increasing. Good correlations have been found for TMS and Direct Electrical Stimulation (DES) when motor mapping is studied. Language mapping with TMS is far more complex. Repetitive TMS (rTMS) is required to disrupt language processing. The deficits typically reflect a delay in response times rather than a decline in accuracy, but rTMS may also cause ‘speech arrests’. The interpretation of speech arrests is often neglected, although it provides useful information regarding the specific function-location relationship.

METHODS
In this study we used for the first time two speech therapists as healthy subjects to study language mapping with TMS during a naming task. Firstly, we wanted to investigate if TMS elicits pure language problems or mainly motor speech problems. Secondly, anatomoclinical correlations were studied. At the first test moment (T1), the speech therapists had to name 210 low-, middle-, and highfrequent unknown coloured pictures. 3 weeks later (T2) and 3 months later (T3) naming was assessed using navigated repetitive TMS (nrTMS) of the left perisylvian regions. Afterwards, the speech therapists were asked to classify the errors into language/motor/apractogenic/other deficits.

RESULTS
There was a large interindividual difference since many more deficits were observed for speech therapist 2. Performance errors (dysarthric/apractogenic distortions, restarts, prolonged reaction times) were the most frequently made errors followed by semantic paraphasias. Performance errors were triggered by stimulations in superior temporal gyrus, inferior frontal gyrus, supramarginal gyrus, precentral gyrus and angular gyrus. Semantic paraphasias were elicited when AG, PrCG and SMG were stimulated. There was a trend for prolonged reaction times at T2 versus T1. However, there was a significant difference between T1 versus T3 and T2 versus T3 with shorter RT at T3 for speech therapist 2.

CONCLUSION
nrTMS might prolong reaction times and elicits motor speech deficits as well as language deficits. Since a clear learning effect was found at T3, the time between the three trials should be extended in future studies. The use of different language tasks in a larger study group would be interesting.
P713
Ultrasound and nerve conduction studies in patients with ulnar nerve compression neuropathy and healthy controls - a prospective study

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**Question**

Can ultrasound (US) be used as supplement in diagnosing ulnar nerve compression neuropathies, and how does US correlate to near nerve conduction studies (N-NCS)?

**Methods**

41 patients and 42 healthy controls were included. The ulnar nerve was examined with a linear array transducer (6-18 MHz) and with the elbow flexed. The examination was preformed bilaterally, in a randomised manner, blinded to patients' symptoms and prior to the routine N-NCS. The N-NCS included sensory and motor nerve conduction study in the following segments: across the elbow, in the forearm and across the wrist. The patients were invited to a follow up US after three months. Healthy controls underwent both US examination and surface NCS bilaterally.

**Results**

The mean cross sectional area (CSA) at the sulcus level was different (p2, sd 0.015) compared to patients (0.112 cm\(^2\), sd 0.040). US had a sensitivity of 73.2% and N-NCS had a sensitivity of 70.7% of patients. US localized the lesion at the sulcus in 68.3% and N-NCS in 53.7%. There was a combined sensitivity of US and N-NCS of 73.2% of localizing the lesion. There was a significant decrease in mean CSA at follow up compared to baseline. There was a linear correlation between CSA and conduction velocity to ADM in both healthy controls and in patients. The best cut-off for US to predict a positive N-NCS was 0.11 cm\(^2\).

**Conclusion**

US correlates to N-NCS, may predict a positive N-NCS and may be used as diagnostic supplement in ulnar nerve compression neuropathies.
Peripheral Nerve Echogenicity: Range of Values for normals

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Question

Ultrasound imaging of the nerves is increasingly used for diagnosing nerve pathologies and is most commonly used for entrapment neuropathies. Chronically compressed nerves become enlarged and hypoechoic. Measurement of nerve size is standardized, but to usefully employ nerve echogenicity there is a need for identifying normal values. We set out to measure normal values of nerve echogenicity.

Methodology

We prospectively collected data from 23 healthy volunteers [13 males; aged 21-80yrs (mean 41) with normal nerve conduction studies and no peripheral neuropathy. Each nerve was recorded at standardised sites in parallel to what is used for documentation of entrapment neuropathies. Grey scale echogenicity of Ultrasound images were quantitatively analyzed, using the public domain software of Image J.

Results

The mean echogenicity of the nerves in each location was quantified as area fraction (%). These are as follows: Median Nerve a. At the distal wrist crease 89.8(78.8-100.8), b. at the Carpal Tunnel 91.3 (81.7-100.9), c. at the mid-forearm 64.3 (54.3-74.3); Ulnar Nerve a. at the distal wrist crease 86.5 (77.3-95.7), b. below the elbow 72.3(60.3-84.3), c. at the elbow 86.5(76.5-96.5), d. above the elbow 83.3; Radial Nerve a. at the spiral groove 79.8 (71.8-87.8), b. at the lateral cubital fossa 76.8 (68.4-85.2); Tibial Nerve a. at the popliteal fossa 73.2(64-82.4), b. at the Tarsal Tunnel 82.2(71.8-92.6); Peroneal Nerve a. at the popliteal fossa 77.1 (69.5-84.7, b. at the Fibular Head 78 (68.4-87.6); Sural nerve at 5-10cm above the lateral malleolus: 69.8 (61.8-77.8).

Conclusion

Our study provides normative data for the quantitative measurement of the nerve echogenicity which can be useful in delineating normal from diseased nerves more accurately.

References

- Rsbweb.nih.gov/ij
Abstracts of Poster Presentations – Poster Session 40 – Ultrasound

P716
Quantitative ultrasonographic evaluation of facial muscles

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Question
Some neuromuscular disorders, as Myasthenia Gravis, myopathies or facial nerve palsy, are characterized by muscles facial atrophy. There are few reports about quantitative evaluation of facial muscles in literature. Most of them are performed with MRI. High-frequency ultrasonography (US) is a suitable technique for the small muscles evaluation. Recently US was also used for this purpose. Those studies evaluated horizontal section of muscles and did not compare superior and inferior parts of orbicularis oculi and oris muscles. We aimed to quantitatively evaluate the muscle thickness of frontalis, orbicularis oculi, orbicularis oris and masseter muscles in a group of healthy subject, and to compare the superior with inferior part of orbicularis oculi and oris.

Methods
We used for the US evaluation an Esaote MyLab70 XVG, equipped with a high-frequency broadband probe (frequency band 12-18 MHz). Maximum muscle thickness and echotexture were measured in 37 healthy subjects (mean age 48.4 years-old; 20 female). All examinations evaluated sagittal section. We used as anatomical landmarks the middle of eye-blow for frontalis muscle, the middle of eye for orbicularis oculi, the medium point between the philtrum and the mouth angle for orbicularis oris, and the angle of jaw for masseter muscle; all muscles were evaluated bilaterally.

Results
The mean of maximum thickness of each muscle was: frontalis 2.45±0.37 mm (mean±SD), superior orbicularis oculi 0.79±0.14 mm, inferior orbicularis oculi 1.44±0.24 mm, superior orbicularis oris 1.58±0.18 mm, inferior orbicularis oris 1.69±0.18 mm and masseter muscle 13.3±1.9 mm. Statistical analysis showed a significant difference between superior and inferior parts in both orbicularis oris and oculi muscles, while there were no significant differences between right and left side in all muscles.

Conclusions
US is a useful tool to assess facial muscles thickness. Our data provide normative values of facial muscles that could be applied in the future for clinical practice.
P717
Ultrasonography of the sural nerve in patients with polyneuropathy

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Question

Although signs and symptoms of polyneuropathies (PNP) predominantly affect the lower limbs, our knowledge regarding changes in nerve caliber in patients with PNP is mainly based on ultrasonography studies, which investigated peripheral nerves of the upper limbs. We, therefore, aimed to explore structural changes of the sural nerve in patients suffering from PNP of various etiologies in comparison with healthy subjects.

Methods

We measured the nerve’s cross-sectional area (NCSA) of the sural nerve at 3 pre-defined sites of each limb with high-resolution B-mode ultrasonography in 36 patients with PNP and 18 healthy controls and calculated the mean (mNCSA) of these 6 measurements.

Results

In an overall analysis, the mNCSA did not differ significantly between patients and controls. However, we found a significantly higher mNCSA of the sural nerve in patients with an inflammatory type of PNP than in those with chronic idiopathic axonal PNP (M₀.₅ 2.2mm², interquartile range (IQR) 1.2mm² versus M₀.₅ 1.7mm², IQR 0.5mm²; p = 0.03).

Conclusions

Our study demonstrates that inflammatory PNP are associated with an enlargement of the caliber of peripheral nerves, which occurs not only in large nerves of the upper limbs, but also in small nerves like the sural nerve.
Ultrasound of the brachial plexus and peripheral nerves in healthy subjects and patients with neuralgic amyotrophy

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Question

Neuralgic amyotrophy is a painful multifocal disorder of the brachial plexus and upper extremity peripheral nerves. Some NA patients show T2 hyperintensity and thickening of the brachial plexus on MRI, indicative of focal inflammation. Focal nerve abnormalities can also be assessed with ultrasound. The aim of this study was to invest if the brachial plexus and the peripheral nerves are thickened in (some) patients with NA.

Patients and methods

50 adult healthy subjects and 50 adult NA patients were recruited. People with other upper extremity neurological disorders were excluded. A 5-17 MHz broadband linear probe and IU22 Philips ultrasound (US) machine were used. The brachial plexus was imaged at three locations (roots, interscalene and supraclavicular) and the peripheral nerves of the arm were imaged at five locations. The cross sectional area (CSA) was measured in cm² and Power Doppler was used to show vascularization. Mean CSA and standard deviation (SD) were analyzed with SPSS, with >2 SD the cut-off point for abnormality. Increased vascularization was defined as the presence of vascularization in the surrounding neural tissue. Multiple regression analysis was used to examine the influence of age, length, weight and sex.

Results and conclusions

The mean CSA of the healthy cervical roots was 0.09 cm² for C5 and 0.13 cm² for C6 and C7. Two NA patients had significantly increased CSA of the C6 root. Other parameters and patients results will be presented at the conference. Our study provides US reference values for Dutch NA patients and may help diagnose a subgroup with ongoing PNS inflammation.
Presynaptic dopaminergic function for the superiority illusion

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Question

Majority of people believe they are better than others. This is a cognitive bias, called the superiority illusion. Our previous study revealed that the functional network responsible for superiority illusion was innervated by postsynaptic dopaminergic function in striatum (Yamada et al., 2013). In the current study, in order to deeply understand the role of dopamine on the superiority illusion, we investigated the relationship between presynaptic dopaminergic function and the superiority illusion.

Methods

Twelve subjects performed the superiority illusion task to quantify the degree of the superiority illusion. They underwent two positron emission tomography scans, using L-[β-¹¹C]DOPA and [¹⁸F]FE-PE2I. The L-[β-¹¹C]DOPA uptake rate reflects the dopaminergic synthesis capacity ($k_{ref}$), while non-displaceable binding potential ($BP_{ND}$) of [¹⁸F]FE-PE2I reflects the dopaminergic transporter (DAT) availability. We performed correlation analyses to compare the superiority illusion with $k_{ref}$ and $BP_{ND}$ in striatum.

Results

A significant negative correlation was observed between the BP values of [¹⁸F]FE-PE2I and the degree of the superiority illusion ($r = -0.76, P = 0.0025$). No significant correlation was found between the $k_{ref}$ values of L-[β-¹¹C]DOPA and the level of the superiority illusion.

Conclusion

The finding suggests that reduced DAT availability, which indicates the decreased dopamine turnover, is associated with the superiority illusion. The contribution of presynaptic dopaminergic function for the superiority illusion was elucidated.

Reference:

Pre-treatment frontal quantitative EEG asymmetry as a predictor of antidepressant effects of low frequency rTMS in patients with major depression

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Question

Low frequency repetitive transcranial magnetic stimulation (LF rTMS) over right dorsolateral prefrontal cortex (DLPFC) has been successfully employed in treatment of major depression. In order to determine functional brain asymmetry as potential predictor of antidepressant effects of rTMS we have evaluate QEEG parameters.

Methods

Eleven patients (48.2 ± 6.1 yrs) with treatment-resistant unipolar major depression (HDRS ≥20), and homogenous demographic/clinical features, who were on a stable antidepressant treatment were treated with rTMS (intensity: 110% of the threshold; 3000 stimuli per protocol; 10 daily sessions), and with partial sleep deprivation in addition (once per week). The patients were evaluated by a blind rater at baseline and immediately after the end of treatment (W2). QEEG data asymmetry index between right (pooled derivations being F8-aF8, F4-aF4, C4-aC4, T4-aT4), and left anterior scalp quadrants (F7-aF7, F3-aF3, C3-aC3, T3-aT3) was calculated. Positive values indicate an accentuation of the power on the left hemisphere and vice versa.

Results

Spearman correlation analyses were carried out with a moderate correlation [rho (95% confidence interval); P value] between HDRS at W2 and QEEG asymmetry before intervention [rho=0.63; P=.02].

Conclusions

Pretreatment QEEG asymmetry between right and left anterior scalp quadrants could be a predictor for favorable therapeutic response in given rTMS protocol. The association between functional QEEG asymmetry and magnitude of treatment response warrant further studies.
P722
Roadmaps of Anxiety: Different dysfunctional processes interacting in symptomatic subtypes.

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BACKGROUND

A continuum from normal threat response to anxiety disorders (AD) has been debated for long time. Psychiatric classifications conceptualize AD as nosological entities, with further division into distinct entities. Comorbidity and pharmacological response suggest a single dimension. Each perspective entails different therapeutic approaches, all only partially supported. PURPOSE: Search for neurophysiological evidence of brain dysfunction and differences among panic (PD), specific phobia (SP), obsessive-compulsive (OCD) and generalized anxiety (GAD) disorders.

METHODS

We studied 192 unmedicated AD patients grouped by DSMIV-R subtype and 30 controls. Hypothesis-related neurophysiological variables were combined into ten measures to create a non-parametric discriminant function with group as dependent variable.

RESULTS

Epileptiform activity was found in 25 patients, focal dysrhythmias in 66. Multivariate analysis discriminated accurately 83.4% of the training and 82.9% of the validation samples. Decreased delta and P300 amplitude differentiated AD groups from controls. Decreased P300 latency was found in OCD and GAD, right midfrontal hyperactivities were seen in OCD, at mesolimbic regions in PD.

CONCLUSIONS

Our findings support brain dysfunction diffusely affecting cortical stability and information processes in all subtypes with individual variations, hyperactive neuronal populations at right orbitofrontal regions in OCD and bilateral mesolimbic in PD. Epileptiform and dysrhythmic patterns at corresponding surface sites suggests shared mechanisms with epileptic neuronal populations (ie.. genetic channelopathies and/or acquired kindle-like synaptic changes). Neurophysiological measures can be used to explore interacting brain processes independently; our findings encourage further research on neurophysiological measures in planning and monitoring personalized therapeutic strategies.
**P723**

**THERAPEUTIC EFFICACY OF CONTINUOUS THETA-BURST MAGNETIC STIMULATION (cTBS) IN MAJOR DEPRESSION: A DOUBLE-BLIND SHAM-CONTROLLED STUDY.**

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In a previous open study we have demonstrated safety, tolerability and antidepressant properties of continuous theta-burst transcranial magnetic stimulation (cTBS) in patients with major depression (MD). The aim of the present study was to evaluate the therapeutic efficacy of cTBS using a double-blind sham-controlled design.

A total of 29 patients with MD were recruited for the study. Initially, patients were randomized to receive either active cTBS to the right dorsolateral prefrontal cortex (n=15) or sham cTBS (n=14) for 10 consecutive work days. After the 10th session, patients who received sham TMS were crossed over to the active cTBS treatment which consisted of 10 daily sessions. Patients who received active cTBS continued with the same treatment protocol for another 10 sessions. Each treatment session consisted of 3600 stimuli delivered in four consecutive trains of 900 stimuli each separated by a 15 minute interval at an intensity of 100% of the active motor threshold. Severity of depression was assessed weekly by the Hamilton Depression Rating Scale (HDRS). Overall, there was no significant difference in the degree of clinical improvement between active and sham TBS groups. However, in patients whose medication status was not changed before the trial (n=8) and those who were medication free (n=3), active cTBS resulted in a significantly greater reduction of HDRS as compared to sham cTBS.

The results of this study failed to demonstrate overall superiority of cTBS compared to sham treatment. However, cTBS might be beneficial in MD patients who are nonresponsive to ongoing pharmacological treatment.
Modulation of cognitive control with transcranial direct current stimulation (tDCS) in healthy subjects and major depression

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Question

Cognitive control (CC) is of decisive relevance for adaptive human behaviour. Deficient CC is a central characteristic of various psychiatric disorders particularly major depressive disorder (MDD). Insufficient activation of the dorsolateral prefrontal cortex (dIPFC) has been linked with this deficit (Cole et al. 2012). The activity of distinctive brain areas can be transiently modulated by transcranial direct current stimulation (tDCS). To further explore the role of the dIPFC in physiological and disturbed CC we modulated dIPFC activity in healthy subjects and MDD patients by tDCS and tested its effects on CC as quantified by emotional distractibility.

Methods/Results

We found (Wolkenstein & Plewnia 2013) that activity enhancing anodal tDCS to the left dIPFC (1mA, 20 min, cathode at right upper arm) ameliorated emotional distraction prevalent in patients with MDD and quantified with a delayed working memory task (DWM). Reciprocally, inhibiting cathodal tDCS to the left dIPFC (1mA, 20 min, anode at right upper arm) impairs CC on the influence of negative stimuli as measured with the DWM in healthy subjects. Furthermore, we demonstrate the effects of anodal and cathodal 1mA tDCS to the left dIPFC during an adaptive serial addition task that taps executive control in the context of frustration.

Conclusions

Our findings demonstrate the malleability of CC by non-invasive brain stimulation and verify the important role of left dIPFC activity for this key feature of human cognition and its disturbance in MDD. Most importantly, our data point towards new opportunities for the treatment of MDD based on a specific combination of brain stimulation techniques and cognitive-behavioral treatment strategies.

References


P725
Water deprivation induced alteration on serotonin system and produced anxiety disorder on desert rodent *Meriones shawi*: immunohistochemistry and behavioral studies.

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Introduction

Dehydration is a powerful stimulus causing perturbations in brain neurotransmissions accompanied by several behavioral disorders including anxiety.

Objectives

we studied the effects of dehydration on serotonin system and the anxiety behavior disorder in the desert rodent *Meriones shawi* after long periods of dehydration (1 to 3 months).

Methods

In this study, we used 5-HT immunoreactivity (IR) to evaluate the effects of dehydration on the serotoninergic system in both dorsal and median raphe nuclei (DRN, MRN). In addition, the dark/light box test is used to evaluate the effects of dehydration on anxiety behavior disorder.

Results

Our results showed a reduction in 5-HT-IR in both DRN and MRN following 1 and 3 months of dehydration. This diminution of 5-HT-IR was accompanied by noticeable changes in anxiety behavior of Meriones, suggesting an anxiogenic-like effects caused by dehydration.

Conclusions

Overall, data indicate that dehydration is able to reduce the serotoninergic neurotransmission, which is probably responsible for generating anxiety in this desert animal.

Figure legends:

Fig. 1. Light micrographs of frontal sections through both DRN and MRN of adult Meriones shawi, immunolabelled with antiserum against 5-HT (A-C); in controls (a1, a2), after 1 month (b1, b2), or 3 months (c1, c2) of water deprivation. DRN: dorsal raphe nucleus; MRN: median raphe nucleus; mlf, medial longitudinal fasciculus; DL, dorso-lateral; DM, dorso-median; VM, ventro-median.

Fig. 2. Anxiogenic-like effects of dehydration in the Meriones dark/light box test.

*p < 0.05 vs. controls and p < 0.05 vs. dehydrated animals. C: controls, DH 1: dehydrated 1 month, DH3: Dehydrated 3 months.

References: None
P726
Anxiety assessment and obesity in medical students

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The connection between obesity and common mental health disorders is an important public health issue. The purpose of this study is to assess the anxiety among undergraduate students and to evaluate its correlation with obesity. Anxiety is easily assessed by Zung Self Rating Anxiety Scale questionnaires as they are easy to understand by the participants.

Objective

This study was planned to assess anxiety using in young obese adults. Zung Self Rating Anxiety Scale (SAS) of 1 year MBBS students and to correlate Waist to Hip ratio (WHR) with anxiety levels.

Material and Methods

56 were males and 82 were females medical students were included in the study. Without knowing the interpretation of the scoring system, subjects were asked to fill the anxiety inventories in speculated time using Zung Self Rating Anxiety Scale (SAS) ⁶, a 20-item self-report assessment device which included measures of state and trait anxiety.

Result

There was no statistical significance in the anxiety score between male and female group even though the mean levels of Zung were higher in WHR >0.9 and > 0.8 in male and female subjects respectively.

Conclusion

This study demonstrated no statistically significant difference in anxiety scores of overweight and normal weight young adults. Also there is no statistically significant association between anxiety and WHR. This type of study will help in detection of high anxiety students at an early stage which will be helpful in implementation of preventive measures at an early age. This will prevent harmful effects of stress on body functions.
Increased risk of depression subsequent to a femoral neck fracture: A nationwide population-based study

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Objective

Femoral neck fracture is common in the elderly, and its impact has increased in aging societies. Comorbidities, poor levels of activity and pain may contribute to the development of depression, but these factors have not been well addressed. This study aims to investigate the frequency and risk of major depression after a femoral neck fracture using a nationwide population-based study.

Methods

The Taiwan Longitudinal Health Insurance Database was used in this study. A total of 4,547 patients who were hospitalized for femoral neck fracture within 2003 to 2007 were recruited as a study group; 13,641 matched non-fracture participants were enrolled as a comparison group. Patients who had histories of any form of depression or femoral neck fracture before the study period were not included. Each patient was prospectively followed for 3 years to monitor the occurrence of major depression. Cox proportional-hazards models were used to compute the risk of major depression between members of the study and comparison groups after adjusting for residence and socio-demographic characteristics. The most common physical comorbidities that were present after the fracture were also analyzed.

Results

Fifty-five (1.2%) femoral neck fracture patients and 95 (0.7%) non-fracture comparison patients were diagnosed with major depression during the study period. The stratified Cox proportional analysis showed a covariate-adjusted HR of major depression among patients with femoral neck fracture that was 1.82 times greater (95% CI, 1.30-2.53) than that of the comparison group. Most major depressive episodes (34.5%) presented within the first 200 days following the fracture. Peptic ulcers (40.0%) were the most common comorbidity after fracture that differed between the study and comparison patients (P<0.05).

Conclusion

Patients with a femoral neck fracture are at an increased risk of subsequent major depression. Most importantly, major depressive episodes mainly occurred within the first 200 days following the fracture.
The medical records of one million people (obtained from the LHID)\(^a\)

Patients who were diagnosed as a new-onset femoral neck fracture (2003 - 2007)

Patients who did NOT have history of femoral neck fracture or depression in (or before) 2003 \(^b\)

Exclusion criteria:
(1) With old femoral neck fracture
(2) With history of any depressive disorder
(3) Younger than 18 years
(4) Incompletely completed medical records

Study group (\(n=4,547\))

Control group (\(n=13,641\))\(^c\)

Each patient was tracked for 3 years, starting from their index hospitalization, to identify those who experienced new-onset major depression

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Comparison patients
Patients with Femoral neck fracture

\(P<0.001\)
P729
Increased risk of depression during a three-year period after a spinal fracture: a nationwide population-based and followed up study

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Background

Although adverse medical outcomes and poor functional capacity after spinal fracture may contribute to the development of depression, this relationship has not been investigated. This study aims to investigate the frequency of depression after spinal fracture.

Methods

This study utilized the Taiwan Longitudinal Health Insurance Database. A total of 10,195 patients hospitalized for spinal fractures from 2003 to 2007 were recruited for the study group, and 30,585 matched non-fracture patients were enrolled in a comparison group. Each patient was prospectively tracked for three years to determine the occurrence of depression. A Cox proportional hazards model was used to calculate the risk of depression after adjusting for residence and sociodemographic characteristics. Depression-free survival curves were generated. The use of surgical interventions and medications were analyzed for their influence on depression.

Results

There were 521 fracture patients (5.1%) and 1,028 non-fracture comparison patients (3.4%) who suffered a new-onset depression during the study period. The stratified Cox proportional hazards analysis showed that the crude hazards ratio for depression among the study patients was 1.54 (95% CI: 1.39-1.72) compared with the comparison group. The largest proportion of depressive episodes (13.6%) occurred within the first 100 days after the fracture. The patients who had ever received narcotics during the first 30 days after the fracture had a lower incidence of depression than those who received other medications.

Conclusion

The patients with spinal fracture were at an increased risk of subsequent depression. These depressive episodes frequently occurred within the first 100 days after the fracture.

figure 1
Abstracts of Poster Presentations – Poster Session 41 – Depression and anxiety

Figure 2

- Control group (n=30,585)
- Study patients (with spinal fracture) who were treated with
  - Narcotics (n=583)
  - Muscle relaxants (n=4,251)
  - NSAID (n=8,054)
  - Acetaminophen (n=2,602)

* Significantly higher (p < 0.05) prevalence of depression compared with control group
Urticaria Increases the Risk of Depression in Adult Patients: A National Database Study

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Urticaria is a common ailment in adult patients. The unusual-looking rash limits daily activities, and recurrent itching may contribute to the development of depression. However, this potential link has not been well studied. We investigated the risk of depression following the first onset of urticaria using a nationwide, population-based study. Patient information was obtained from the Taiwan Longitudinal Health Insurance Database (LHID) for 2005 to 2009. A total of 46,039 adult patients (> 18 years) hospitalized for a first-attack urticaria episode were matched to 138,117 non-urticaria controls. Patients with a history of urticaria or depression prior to the study period were not included. The patients were followed for one year to identify whether depression occurred. Cox proportional hazard models were generated to compute the risk of depression for the study and control groups while controlling for place of residence and sociodemographic characteristics. Additionally, depression-free survival curves were analyzed. A new-onset episode of depression occurred in 431 patients (0.9%) with urticaria and 944 (0.7%) non-urticarial control subjects. The stratified Cox proportional analysis showed that the crude hazard ratio of depression among patients with urticaria was 1.37 times (95% CI, 1.23-1.54) that of the control subjects without urticaria. Most cases of depression occurred within the first 100 days after the onset of urticaria. In conclusion, individuals who experience a primary onset of urticaria are at high risk of developing depression.
Abstracts of Poster Presentations – Poster Session 41 – Depression and anxiety

LP42
Study of locomotor and cognitive disorders in the ovariectomized female Wistar rats

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Objective

Menopause is accompanied by a cognitive and neurodegenerative dysfunction. These disorders are mainly due to the collapse of the level of estrogen causing a chronic inflammation in the brain associated with a several unbalance in neurotransmission. This study has for objective to study the impact of the deficit in estrogens on the levels of anxiety on ovariectomized female Wistar rat.

Methodology

Female rats (172 to 226 g), aged 6 months, were used during this study. The animals were randomly divided into two groups: a control group "C" and an ovariectomized group "OVX". Three months later, the levels of anxiety were evaluated by valid behavioral tests, Open Field test (OFT) and elevated plus maze (EPM).

Results

The parameter values are collected and statically analyzed show partiality that:

* In the OFT, the number of central squares visited as well as the time spent in the central squares by the OVX rats are significantly lower than the recorded values among the control.

* In the test EPM test, the time spent in the open arms by the OVX rats is substantially lower than that recorded by the control rats.

Conclusion: These preliminary results suggest that the ovariectomy is associated with an increase in the level of anxiety, which would be due to a decrease in the secretion of ovarian hormones, particularly estrogen.

Keywords

Ovariectomized rat, cognitive disorders, OFT, EPM.
**LP43**

The role of perceptual and semantic processing on visually distracted time reproduction

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**Question**

In humans, valence, temporal location and perceptual complexity of distracters have been demonstrated to modulate the perception and precise reproduction of physical time intervals in the seconds to minute range (interval timing). However, perceptually complex distracters might also be semantically more complex. This study aimed to further investigate whether perceptual and/or semantic complexity of distracters significantly contributed to the magnitude of distracter-induced temporal distortions.

**Methods**

Human participants were trained to a fixed target interval, before they reproduced the memorized duration in trials with and without presentation of distracting visual stimuli. Distracters varied according to their arousal, perceptual and semantic complexity, as well as their location within the to-be-timed interval. Possible effects of distracter-induced saccadic eye-movements were taken into account by complementing psychophysical measurements with high-speed eye-tracking recordings.

**Results**

In line with previous studies, we observed relatively large overproductions of the trained target duration, when distracters were presented near the end of the critical interval. In addition, a significant interaction between distracter characteristics of arousal and semantic complexity was observed. High arousing distracters induced longer time reproductions, when semantically complex (vs. less complex) distracters were presented, whereas low arousing distracters induced longer time reproductions in trials with presentation of semantically less complex distracters. However, no correlations between the number of saccades and the magnitude of temporal misperceptions had been observed.

**Conclusion**

Within an internal clock framework, our results can best be explained by a time- or resource-sharing mechanism that becomes modulated by the expectancy, arousal, and semantic complexity of visual distracters. The importance of our data will be discussed in the context of psychiatric disorders and involved symptoms of temporal misperceptions.
Continuous and chronic bilateral deep brain stimulation of the medial forebrain bundle in rats

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Background

DBS for treatment-resistant major depressive disorder is emerging as a viable option offering some patients a long-lasting control of the disease. Recently, bilateral DBS of the supero-lateral branch of the medial forebrain bundle (MFB) rapidly and dramatically reduced depressive symptoms in a clinical trial. However, chronic continuous bilateral high frequency stimulation (HFS) of the MFB has not been investigated in a preclinical context.

Methods

Sprague-Dawley female rats (n=20) were submitted to bilateral stereotactic microelectrode implantation into the MFB. Chronic continuous HFS was applied for 3-6 weeks. Welfare monitoring and behavior changes were assessed. Post-mortem histological analysis of c-fos protein expression was carried out.

Results

MFB-HFS led to a mild and temporary weight loss of 4-6% in the animals, but the weight was regained even with continuous stimulation. Exploratory motor activity increased during the initial 72 hours of stimulation, and food intake decreased by 25% up to 2 weeks post MFB-HFS. Stimulation did not influence performance on either a test of anxiety or behavioral despair. MFB-HFS led to increased and long lasting c-fos expression in the shell of Nucleus Accumbens, medial prefrontal cortex, medio-dorsal thalamic nucleus and lateral habenula.

Conclusions

Bilateral continuous chronic MFB-HFS is feasible and safe without impacting on the rodent’s health. MFB-HFS results in temporary increase in exploration, which could explain the initial weight loss and decreased food intake. Chronic stimulation does not produce any apparent behavioral abnormalities. This platform represents a powerful tool for further preclinical investigation of the MFB stimulation in the treatment of depression.
P731
EEG POWER SPECTRAL ANALYSIS OF PATIENTS WITH OPIOID DEPENDENCE IN EARLY ABSTINENCE - A CASE-CONTROL STUDY

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Introduction

Drug addictive behavior may emerge from the dynamic activity of entire neural networks rather than from any single brain structure. Drug addiction may be conceptualized as an adapted state—a new metastable regimen of brain functioning around altered homeostatic levels. Given the large opioid using population and the paucity of EEG studies in this patient group, this study was aimed to compare the EEG power spectrum of patients with opioid dependence and normal controls.

Methodology

28 channel EEG recording was conducted on 15 patients with ICD 10 DCR diagnosis of Opioid dependence syndrome and 15 normal controls matched for age, sex, education and handedness. 30 second epoch was taken for computing power spectrum using MATLAB 7.12. Difference between the power spectral values between the two groups was obtained by independent t test.

Results

On socio-demographic variables, the two groups were well matched. Patients had increased power spectral values in almost all regions of the brain. The increase in power spectral values was more pronounced in frontal and temporal region.

Conclusion

Opioid being a neuronal activator increases the power spectral value and this effect is present over a wide region of brain.

Keywords

Electro-encephalography, Opioid Dependence, Power Spectrum
P732
The effects of acute alcohol consumption on new tests of vestibular function

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Question
We investigated the effects of acute alcohol intoxication on several recently developed measures of vestibular function: the video head-impulse test (vHIT), dynamic visual acuity (DVA) and cervical and ocular vestibular evoked myogenic potentials (cVEMPs and oVEMPs).

Methods
We recorded vHIT and DVA (in 8 normal volunteers) and VEMPs (in 14 different volunteers) using a repeated measures design to track vestibular function over multiple rounds of alcohol consumption up to a maximum breath alcohol concentration (BrAC) of 1.5‰.

Results
All tests were normal at baseline. Vestibulo-ocular reflex (VOR) gain measured by the vHIT decreased by 25% by the highest BrAC level tested, while cumulative catch-up saccade amplitude increased from 0.13° to 1.43°. DVA scores increased by 86% indicating a deterioration of acuity, while static visual acuity (SVA) remained unchanged. oVEMP amplitude decreased by 27%, but there was no significant effect on oVEMP latency or cVEMP amplitude or latency.

Conclusions
We found dose-dependent effects of alcohol consumption on all measures of VOR function (VOR gain, catch-up saccade amplitude, DVA and oVEMP amplitude), but no effect on the vestibulo-collic reflex (cVEMP) or on SVA. The effects on the oVEMP may have been influenced by the systematic appearance of gaze-evoked nystagmus with increasing intoxication. However, these consistent results across several different tests suggest that alcohol has a selective, detrimental effect of alcohol on the VOR in normal volunteers.
P733
Alcohol abuse influences on autonomic nervous system and praxis in young adults

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Considerable evidence has demonstrated that women (W) are more vulnerable than men (M) to the toxic effects of alcohol, but results confirming gender differences in ethanol-induced executive function and autonomic nervous system (ANS) impairment are still contradictory.

We have studied 46 patients (pts) with II stage alcohol abuse (AA) divided into 2 groups: 24-39 yrs (13 W and 4 M) and 40-64 yrs (23 W and 6 M). 30 young and 85 older pts with mild dyscirculatory encephalopathy (DE) due to arterial hypertension or CAD were served as controls.

All pts underwent ANS examination by heart rate variability (HRV, 5-min. recording in supine and standing position), the M.Luscher color preference test (8 color range), computerized bimanual finger tapping test (30 sec.) and precise motor task - rhythm test (3 series with 20 presentations).

Young W with AA had significantly bigger heart rate (HR) and higher tapping rate obtaining by dominant hand than young M and only trend - by non-dominant hand. Grey color in the color test placed in the 4.75+/-0.53 vs 7.33+/-0.33 position in the M (p=0.007) may reflect the greater fatigue in W. Rhythm test did not revealed any gender differences. In 84.6% of W and 50% of M total power (TP) of HRV was diminished, extremely (less than 800 ms2) - in 69% of W and 50% of M. In the older group TP was diminished in 71.4% of W and 83.3% of M with AA. TP in M was significantly lower then in W, but 17.4% of W had insufficient sympathetic excitation during active standing predisposing to syncope. No gender differences were found in the other tests.

Young W with AA had greater HR, elevated sympathetic drive; young M - worse rhythm test, lower relative power of low frequency band in supine, both W and M - hyper reactivity in ortotest than those with DE. No difference was found in the older group.

Thus, majority of the young W and M with alcohol abuse have autonomic dysfunction and M - impaired praxis. Limitation of this work is the small study sample.
P734
Reward-sensitivity, decisional bias and metacognitive deficits in cocaine drug addiction

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The present research explored the effect of reward-sensitivity bias and metacognitive deficits in Substance Use Disorder (SUD) in decisional-making process. BAS (Behavioral Activation System) was considered as a predictive marker of dysfunctional behavior at IOWA. Secondly, we tried to relate this motivational system bias to some self-reported metacognitive measures (self-knowledge; strategic planning; flexibility; efficacy) in decisional processes. Thirty-four SUD subjects (cocaine dependent) and thirty-nine controls (CG) were submitted to IOWA task. SUD were associated with poorer performance on the IGT and dysfunctional metacognition ability (unrealistic representation). Reward-sensitivity (higher BAS, BAS-RR and BAS-D) increasing was observed in SUD more than CG, and it was found to be able to explain (regression analysis) the main behavioral deficits. More generally BAS-RR increasing may be considered as a predictive measure of a more risk-taking and dysfunctional behavior not only in pathological (SUD) subjects but also in subclinical sample (higher-BAS controls). The likely brain correlates (ventromedial prefrontal cortex, VMPFC, dysfunction) of this motivational and cognitive deficits were discussed.
Objective

Pharmacological involvement in childhood poisoning vary and treatment of poison exposure can be a challenge for primary physicians when events are causing by neurological system agents and patients are unconscious. The aim of this study is to report on patient characteristics, outcomes and clinical features of pediatric poisoning by neurological system agents in the emergency department (ED).

Methods

This retrospective study comprised 168 children with pharmaceutical poison exposure ≤ 18 years in the ED. Demographics, clinical characteristics of and detailed information of neurological system agents causing poisons were reported. Poisons causing by non-neurologic system agents served as a control group in this study. Clinical outcomes including duration of hospital stay and severity of American Association of Poison Control Centers classification: (major, moderate and minor/no effects) were analyzed between different categories of pharmaceuticals. Finally, we also analyzed the sex and the reasons for poison (intentional and accidental) across different age groups.

Results

Of all, we found that the prevalence of poison exposure was highest among adolescents and pre-school age children. Among the all categories of pharmaceutical poisons, neurologic system agents were the most common cause of poisoning (53.6%) and they significantly resulted in higher percentage of patients in suffering moderate or severe effect (p<0.05). Anxiolytic and hypnotic drugs (Lorazepam and Zolpidem) were responsible for the majority of this category mentioned above. Intentional poisoning and a female gender were significantly predominant factors among older children (both p<0.05). Finally, we noted that the older patients favored neurologic system agents for intentional use (p<0.05).

Conclusions

Neurologic system agents were responsible for the majority of all pediatric pharmaceutical poisons and also caused the more severe outcomes.

figure 1
Abstracts of Poster Presentations – Poster Session 42 – Drug abuse

Figure 2

![Bar chart showing mean age of patients (years) for intentional and accidental poison exposure.](image)

- **Mean age of patients (years)**
  - Intentional: 18 years
  - Accidental: 4 years

**Legend**
- Black bars with star: Neurologic system agents
- Light gray bars: Non-neurologic system agents

*Reasons for poison exposure*

- Intentional
- Accidental
LP45
Exercise attenuates methamphetamine-induced disruption of the blood-brain barrier

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Moderate to vigorous exercise is a powerful means to influence health status and lower the risk of the development of chronic diseases. We hypothesize that increased antioxidant potential by endurance exercise plays a critical role in the protection against the development of cerebral toxicity associated with drug abuse. To address this hypothesis, mice were subjected to voluntary wheel running for 5 weeks. The control mice did not have access to running wheels. At the end of exercise training, mice were injected with methamphetamine (Meth, 10 mg/kg) for 24 h. Exercise markedly changed Meth-induced alterations of cerebral blood flow and protected against Meth-induced disruption of the blood-brain barrier as assessed by in-situ brain perfusion. Consistent with these results, exercise protected against Meth-mediated disruption and localizations of tight junction protein expression (ZO-1, occludin, and claudin-5). Importantly, exercise markedly attenuated Meth-induced oxidative stress in brain microvessels. It appears that protection against upregulation of NADPH oxidase may be responsible, at least in part, for these protective effects. The obtained results indicate that exercise is an important modifiable behavioral factor that can protect against Meth-induced CNS toxicity. Supported by MH63022, MH072567, NS39254.
Abstracts of Poster Presentations – Poster Session 43 – Dystonia

P736
Geste antagoniste as a predictive factor of botulotoxine treatment effectiveness?

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Question

The sensory trick (geste antagoniste) - a slight touch in the area of face or head - is a bizarre clinical feature in cervical dystonia patients leading to attenuation of the disease symptoms. Even if well known, the pathophysiology and clinical significance of it still remain shrouded.

Methods

In a semiquantitative, questionnaire based research, we have so far examined 81 patients with idiopathic cervical dystonia.

Results

While 77 % of subjects were able to correct the abnormal posture with force - pushing the head to the normal position; only about 41 % of subjects showed the classic geste antagoniste where just a slight touch sufficed. Out of these patients, 76 % were able to use both hands to provoke the trick. However, when another person touched the very head area, only in 27 % of patients it lead to partial or full alleviation of symptoms, showing there is a distinct motor pattern that needs to be maintained to induce the geste antagoniste. Only 33 % of the patients were able to provoke the trick using a foreign object, so the geste antagoniste seems to be not only a simple sensory feature requiring just touching of the area, no matter the object providing the touch. Surprisingly, about 21 % of patients showed at least a partial disease symptoms improvement when imagining doing the trick and about 82 % of patients were not able to fully provoke the trick when busy with some cognitively demanding activity (e.g. counting), allowing us to hypothesize that there is also a psychological dimension of the geste antagoniste requiring the subject to focus on it.

Moreover, there was an unexpected difference in subjective evaluation of botulotoxine treatment effectiveness - in a scale of 0 to 10 (10 corresponding to complete alleviation of symptoms, 0 to no change), patients able to perform geste antagoniste stated clearly higher effect of the treatment (6.93 vs. 4.93; p < 0.01).

Conclusions

These data show that geste antagoniste is a complex feature requiring distinctive motor, sensory and cognitive input combination, possibly pointing to lower dystonia severity. It definitely deserves more attention, not only due to a possibility of effective therapeutic use of sensorimotor stimulation in cervical dystonia patients leading, but its eventual predictive value may prove a major asset in determining future course of the disease treatment.
The treatment of spasmodic dysphonia with botulinum toxin: the accuracy of the injection with EMG guidance assessed by spectrography and videolaryngoscopy.

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**Question**

Botulinum toxin (BTX) injection in vocal cords is considered the best treatment for spasmodic dysphonia (SD). Disability vocal scales like the Vocal Handicap Index (VHI) are often used to assess the response to BTX injection (Albanese 2013) confirming the efficacy of the technique with neurophysiological guidance. Vocal investigations like videolaryngoscopy (VL) and voice spectrography (VS) are usually used in the diagnostic process and are not often performed during the course of the disease. Here we present a small collection of cases of SD treated with BTX under EMG guidance assessing the efficacy of the treatment with vocal investigations.

**Methods**

6 patients affected by adductor SD (5 F, 1 M) with a mean duration of disease of 5.8 years (range 1-13 y) and with a VHI mean score of 22 (range 28-15) were assessed with VL, VS and VHI questionnaire before receiving BTX and 2 weeks after the treatment; the injection was performed in thyroarytenoid muscles with a mean dose of 3.25 U of onabotulinumtoxinA (range 3.75-2.5) for each side by a phoniatrician and the EMG recording was evaluated by a neurophysiologist for every patient.

**Results**

All patients reported subjective improvement confirmed by a significant reduction of the VHI score. Videolaryngoscopy showed a lesser contraction of false vocal folds and a reduction of spasmodic adductory movements, while spectrography revealed noise reduction and maximum time phonation.

**Conclusion**

The assessment of treatment with BTX for SD with vocal investigations confirms the accuracy of the EMG guided technique of injection and support the results of previous studies (Fulmer S.L., 2011) based only on the use of subjective disability rating scales in people with SD.
P738
Long-lasting effect of botulinum toxin: description of a beautician’s dystonia case

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Question

Dystonia is the third most common movement disorder, after Parkinson disease and tremor. Therapeutic options for dystonia are symptomatic and not curative; the treatment of choice for focal dystonias consists of repeated injections of botulinum toxin.

Methods

A 46-year-old beautician with focal dystonia in the left hand was recruited. This condition widely affected her ability to work. Pharmacological treatment with clonazepam and gabapentin failed to solve her symptoms and was discontinued due to side effects (sleepiness, gastrointestinal disorders).

We performed a clinical examination and surface EMG (sEMG) that confirmed the diagnosis of focal dystonia and highlighted the most involved muscles. Than we performed intramuscular injection of botulinum toxin (incobotulinumtoxinA, Xeomin®) into the extensor digitorum communis (35 U); flexor carpi radialis (35 U) and flexor digitorum superficialis (30 U) muscles using muscle stimulation to identify precisely the injection site.

Results

The injection of botulinum toxin resulted in a complete resolution of symptoms. The patient was able to work already 1 month after treatment. The beneficial effect of botulinum toxin was assessed 1, 3, 6 and 10 months after the injections, and was confirmed by the results of sEMG performed 10 months after treatment. No re-injection has been necessary at the last evaluation (12 months after treatment).

Conclusions

IncobotulinumtoxinA is an effective and well tolerated agent for the treatment of focal dystonia. If it is used appropriately this approach can rapidly and for long periods relieve discomfort and provide a positive impact on patients’ quality of life.

REFERENCES


FIGURE LEGEND

Figure 1. Surface EMG at rest (A) before treatment with botulinum toxin A, and (B) 10 months after treatment. EDC, extensor digitorum communis; FCR, flexor carpi radialis; FDS, flexor digitorum superficialis.
Comparisons between muscle rigidity meter measurements and H-reflex amplitude to M-wave amplitude ratio as quantitative methods of evaluating the efficacy of botulinum toxin type A therapy for spasticity.

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Question

The modified Ashworth scale (MAS) is commonly used for qualitative evaluation of the efficacy of botulinum toxin type A therapy (BTX) for spasticity management; however, there is no standard for quantitative evaluation. In addition to the qualitative MAS, two quantitative analyses were simultaneously tested to investigate their efficacies.

Methods

We evaluated a 60-year-old female with hypertonia in the left calf because of cerebral infarction. A total of 300 units of BTX was administered into the gastronemius, soleus, tibialis posterior and flexor hallucis longus muscles. Evaluations were made before and after the treatment, using the MAS and H-reflex amplitude to M-wave amplitude (H/M) ratio, which uses the H-reflex and a muscle rigidity meter (MRM).

Results

Although MRM data confirmed a declining tendency only for resting ankle flexion of the triceps surae medial head, the other data were variable, with poor reproducibility. In contrast, the H/M ratio trends: from the day after injections, a prominent decline was confirmed from 82.7% to 37.0%; over the two-week range, there were nearly no changes.

Conclusions

The pharmacological effect of BTX were expressed within 24 h after administration of the toxin. We suggest that the H/M ratio sensitively reflects the pharmacological effect of BTX. However, the efficacy of BTX could not be verified because of the variability of data on muscle tone obtained using an MRM. The H/M ratio may provide a better quantitative measure of the efficacy of BTX on spasticity.
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P740
Saccade-related beta-band desynchronization in the internal globus pallidus of primary dystonia

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Background
Studies in monkeys report more prominent pallidal cell firing during antisaccades than prosaccades (Yoshida 2009). We reported saccade-related beta-band desynchronizations (beta-SRDs) in the subthalamic nucleus (STN) of Parkinson's disease patients. We found more prominent beta-SRDs during antisaccades than prosaccades, like due to additional neural processing required. Since the STN projects to the internal globus pallidus (GPI), we expected an enhanced beta-SRDs to anitsaccades in the GPI.

Objective
To investigate whether oscillations in the GPI are modulated by saccades, and to compare the responses to prosaccades and antisaccades. We hypothesized that antisaccades would produce earlier and/or more prominent beta-SRDs than prosaccades.

Patients and Methods
We recorded the local field potentials from deep brain stimulation electrodes implanted in the GPI in 7 primary focal dystonia patients. The patients performed prosaccade and antisaccade tasks. We analyzed the wavelet power spectrum averaged on saccade onset.

Results
The beta-SRDs were observed in the GPI just before and during saccades in 6 of 7 patients. The onsets, durations, and amplitudes of beta-SRDs were not different between prosaccades and antisaccades.

Conclusions
Beta-SRDs were observed in the GPI of dystonia patients. They were not related to inhibition of unwanted saccades, because they were not different between prosaccades and antisaccades. While it is well known that the basal ganglia output from the substantia nigra pars reticulata strongly inhibits the superior colliculus, our results suggest that the basal ganglia output from the GPI may contribute to the control of saccades, but are not a major contributor in dystonia patients.
P741
EMG coherence analysis is not a reliable method to identify dystonic muscles in cervical dystonia

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Question

Botulinum toxin injections in the dystonic muscles is the preferred treatment for Cervical Dystonia (CD). For optimal treatment response, proper selection of the dystonic muscles is essential. Previous papers have suggested the use of EMG coherence analysis and EMG autospectral analysis as a discriminative tool to identify the leading dystonic muscles in CD patients. Our objective was to first compare the occurrence of intermuscular coherences and EMG autospectral peaks between cervical dystonia patients and healthy controls, and secondly, to investigate the diagnostic accuracy of coherence analysis to identify the dystonic muscles in patients.

Methods

We analysed the EMG in several cervical muscles and compared to occurrence of 4-7 Hz intermuscular coherences and 8-14 Hz autospectral peaks between 10 CD patients and 10 healthy controls. To test the diagnostic accuracy of coherence analysis, we compared the muscles with significant 4-7 Hz coherences with the muscles that were selected clinically (based on clinical picture, previous treatment results and standard EMG) for botulinum toxin treatment.

Results

There was no significant difference in the occurrence of 4-7 Hz intermuscular coherences between patients and controls. However, autospectral peaks between 8-14 Hz were significantly more often absent in the splenius muscles of CD patients compared to controls (p<0.01). Within patients, the diagnostic accuracy of coherence analysis to identify dystonic muscles was low.

Conclusions

Intermuscular EMG coherence analysis could not reliably discriminate patients from controls. Autospectral changes in the SPL muscles seems to be a more discriminative feature of CD. In patients, coherence analysis did not help identifying muscles that should be treated with botulinum toxin. The clinical use of the autospectral changes need further studies.
**P742**

Botulinum toxin treatment with emg control in drug induce tardive dystonia patients

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**INTRODUCTION**

Drug induce tardive dystonia (TD), as part of the tardive syndrome, is a delayed form of dystonia caused by dopamine receptor blocking agents (DRBAs). Represent an involuntary movement disorder, predominated by dystonia that has some different features from idiopathic dystonia, that include predilection for some muscles.

**MATERIAL AND METHODS**

We describe the different forms of tardive dystonia and the response to BoTA treatment in the six patients we received for treatment in a secondary hospital, reference for an area of 400,000 habitants; two patients has oromadibular dystonia, one had axial and cervical dystonia, one cranial and cervical dystonia and one cervical dystonia.

**RESULTS**

After years of treatment, some of them have had optimal response while in others it has been suboptimal. We discuss the possible causes of the differences in the response to treatment.

**CONCLUSIONS**

Chemooodenervation with BotA is the first treatment of choice in focal and segmental TD, but the grade of response in some cases may be less optimal than in idiopathic dystonia, even with control EMG of the inyections.
P743
Altered cerebellar inhibition in patients with focal hand dystonia - a TMS study.

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**Question**

Pathophysiological findings suggest that the cerebellar influence on the primary motor cortex is altered in patients with dystonia. The objective of this study is to investigate whether an altered cerebellar influence on the motor cortex plays a role in focal hand dystonia.

**Methods**

Paired pulse transcranial magnetic stimulation (TMS) was performed at rest and during tonic activation of the right first dorsal interosseus muscle (FDI). The conditioning stimulus (CS) was be applied to the ipsilateral cerebellum using 95% of the threshold for pyramidal tract activation and preceded the test stimulus by interstimulus intervals (ISI) from 5 to 7ms, respectively. The test stimulus (TS) was applied over the motor hot spot of FDI in the primary motor cortex.

**Results**

16 patients with focal hand dystonia (2f) and 16 controls (3f) completed the study. During rest, mixed model analysis showed a significant inhibitory effect of cerebellar conditioning on the TS in both groups. During tonic activation, the main effect of ISI remained significant (p=0.001), while no difference was seen between groups. However, when rest vs. tonic was tested separately, a significant reduction of inhibition during activation at ISI 5 and 6ms was only seen in healthy controls (p=0.016; p=0.018), and was absent in patients with focal hand dystonia.

**Conclusions**

As shown in controls, cerebellar inhibition of the primary motor cortex is reduced during voluntary movement. While in our study we observed inhibitory effects of cerebellar conditioning in patients and controls, at rest as well as tonic activation, by comparing the difference of cerebellar inhibition from rest to tonic activation, we could demonstrate a reduced ability of focal hand dystonia patients to change cerebellar inhibitory output during tonic activation. Our data therefore suggests an impaired modulation of cerebellar inhibition during voluntary activation as potential neurophysiological correlate in focal hand dystonia.

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Background

Dystonia is movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both. Speech-induced oropharyngeal dystonia is quite rare and difficult to be diagnosed.

Case report

The patient is 38-year-old right-handed care worker man, who had suffered from epilepsy for 12 years, presented uncomfortable feeling around the right upper wisdom tooth. After the tooth extraction, he developed right temporal headache, rhinolaliaclausa and dysphagia for four months. When he touched his right temple, temporal headache and rhinolaliaclausa were reduced. As tooth brushing, gum chewing and taking right lateral position mitigated the symptoms, these actions were considered as sensory tricks. Laryngoscopy revealed that oropharyngeal space was narrowed following vocalization “la-la-la” periodically, and recovered to the normal state by touching his right temple. Epipharyngeal and hypopharyngeal space, movement of vocal cords and soft palate were normal throughout the examination. We diagnosed his symptoms as speech-induced oropharyngeal dystonia without vocal cords involvement. Routine blood and cerebral spinal fluid tests showed no abnormalities. Cranial MRI, an electroencephalogram, nerve conduction studies and surface electromyograms were within normal limits. Trihexphenidyl hydrochloride was slowly titerated from 2 to 6mg per day, and eventually his habitual symptoms were diminished.

Discussion

The patient developed oropharyngeal dystonia caused by vocalization. Few previous reports suggest that abnormal contractions of oropharyngeal muscles cause pharyngeal dystonia using laryngoscopy. In this case, laryngoscopy revealed the styloglossus was responsible for these symptoms. However, other muscles in oropharynx except styloglossus possibly related his symptoms, such as temporal headache and rhinolaliaclausa. In conclusion, we reported a rare case of speech-induced oropharyngeal dystonia. This report adds new information that dystonia could be diagnosed using laryngoscopy. Physicians should be aware of this rare type of dystonia associated with abnormal contractions of oropharyngeal muscles.
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P745
Dissociation between the ordered and spontaneous voluntary movement in corticobasal syndrome

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Question

Two patients who complained of gait disturbance showed the disturbed simple, voluntary movement like grasping when ordered. Spontaneous movement in the daily life was more skillful than imagined from the ordered movement. This dissociation was like psychogenic disorder. We explored the background organic abnormality using electrophysiology and neuroimaging.

Methods

A 64-year-old female patient (case 1) who was a clerk and a 67-year-old male patient (case 2) who was a leather worker were examined. The disease course was two years and there was no family or past history in both patients.

Results

These two patients showed gradual deterioration. Neurological findings revealed motor aphasia, dementia, cortical sensory disturbance disclosed by JVP dome test and constitutional apraxia. In addition, dystonia and myoclonus were seen in both legs and arms. The left hand (case 1) or right hand (case 2) was more affected in upper limbs. No systemic abnormalities were detected from routine laboratory tests. There was no definite cortical atrophy in MRI imaging in both patients. TMS study revealed the poor In/Out curve on the left (case 1) or on the right (case 2). Levodopa up to 600mg per day was not effective in both patients. According to the Cambridge criteria and Mayo Clinic criteria, they were diagnosed as CBS. ⁹⁹mTc-ECD single photon emission computed tomography (SPECT) imaging showed similar decreased blood flow in both patients at the regions of intraparietal sulcus (IPS) and medial side of left frontal lobe (see Figure).

Conclusions

IPS is reported as the region of sensory-motor integration, especially visually guided movement or working memory. The dissociation between the ordered and spontaneous voluntary movement may one characteristic in CBS and may be due to the dysfunction of bilateral IPS and left medial side of frontal lobe.
P746
Botulinum Therapy for Embouchuer Dystonia

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Background

Embouchure dystonia patients happen to be unable to control their brass or wind instruments, mainly due not to manipulate their orolingual or oromandibular muscles skilfully. Just as other musician's dystonia, it is very difficult to adopt botulinum therapy as too much effect on the muscles around oral cavity reslut in thier weakness, which would disturb the stable musical performance on the contrary.

Methods

Four wind player are treated by botulinum toxin; all had no good response to medications. Due to their symptoms, botulinum toxins are injection to orofacial muscles.

Results

Botulinum therapy exhibited noticeable effects to disappear the symptoms of embouchure dystonia with no recurrence in all 4 patients. Mean dosage of botulinum toxin requested is about twice as much as th patients of hemifacialspasm. It was a little bit difficult to detect the muscles to be treated accurately because the patients could not make sharp distinctions among muscles' actions for embouchure formation exquisitely. Therefore, the increase of the botulinum toxin dosage even to the same muscle leaded to the favorable outcome, or injections to the muscles with inarticulate symptoms were necessary.

Conclusions

Botulinum therapy can be useful to embouchure dystonia patiens. It is neccesary to detect the muscles in charge appropriately and determine the appropriate amount of the toxins injected.
Visuo-tactile motion congruency enhances neural synchrony in the gamma-band

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Recent studies suggested a role of neural synchrony for the integrative processing of multisensory stimuli. More specifically, cortical gamma-band activity has been suggested as a marker of object feature binding within and across modalities. Previous studies revealed spatial proximity and temporal synchrony as two main principles that govern multisensory integration. To date, little is known about how motion congruency, which represents a combination of spatial and temporal coincidence, affects multisensory integration. In this high-density EEG study, we addressed how visuo-tactile motion congruency modulates gamma-band activity.

Participants were presented with temporo-spatially aligned visuo-tactile stimuli, which moved in the same (i.e. congruent) or in different (i.e. incongruent) directions. To ensure attention to stimulation we instructed participants to respond to occasional non-motion target stimuli. Time-frequency analyses were carried out on single-trial data projected into source space using linear beamforming.

For the congruent compared to the incongruent motion condition, we found an enhanced stimulus-induced gamma-band activity (50-80 Hz). This effect was source-localized to the visual cortex.

Our data suggests that motion congruency enhances the integrative processing of concurrently presented visuo-tactile stimuli. This result provides further evidence for the prominent role of gamma-band activity for the integration of object stimulus features across sensory modalities.
P748
Correlation of EEG recorded from scalp, transcortical and depth electrode derivation in deepening desflurane anesthesia

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Question

Depth electrodes are usually believed to record EEG from subcortical structures in the close vicinity of the electrode contacts. However with increasing electrode size the contribution of small nuclei is likely to decrease and contribution of larger structures like cortex increases. In deep anaesthesia the activity of deep nuclei decreases but the cerebral cortex continues to produce higher amplitude EEG. We studied the increasing contribution of cortical activity in EEG recorded from subthalamic nuclei in deepening anaesthesia.

Methods

For patients undergoing implantation of subthalamic stimulation electrodes for Parkinsonism symptoms were anesthetized with desflurane to deepening anaesthesia until EEG suppression. EEG between two contacts in the depth electrode, scalp electrode and depth electrode, as well between two scalp electrodes were recorded. The signals were band pass filtered with different frequency windows from sub delta to gamma frequencies. The signals were compared visually and by calculation of correlation.

Results

The correlation of the different EEG channels increased in deepening anaesthesia. Before onset of suppressions and during bursts the patterns in these channels were virtually identical indicating common generator. In lighter anaesthesia the patterns in different channels were essentially different.

Conclusion

The identical pattern of depth and scalp EEG in burst suppression suggests common generators. As the transcortical EEG is always highest in amplitude and the amplitude of EEG between any two depth electrode contacts is one tenth of the transcortical signal at maximum, the signals from depth electrodes are also generated by the cortex. During suppression the depth electrode EEG was totally suppressed consistent with the results from metabolic studies which show silence of subcortical nuclei in deep anaesthesia.

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P749
Phase synchronization evaluation in sleep spindles coincident at different EEG channels

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Question
Synchronizations can be seen in natural oscillating systems, such as brain rhythms. In this work we investigate synchronizations in sleep spindles at different EEG channels using a quantitative approach.

Methods
We used signals from 8 EEG channels (f3, f4, c3, c4, p3, p4, o1, o2) of 3 polysomnographic examinations. Sleep spindles were founded using Matching Pursuit (MP) [1] approach for each EEG channel. The coincidences of sleep spindles between the different EEG channels were founded using the MP parameters (amplitude, frequency, duration, time location). An 11-16Hz bandpass filter was applied in raw EEG signal. The Kuramoto order parameter $r$ [2] was derived using the filtered signal at the time location of each coincident spindle to evaluate the phase coincidences.

Results
Figure 1 shows the raw signal, filtered signal and Kuramoto order parameter $r$ for a characteristic sleep spindle. Sleep spindles with phase synchronization in all channels showed a high Kuramoto order parameter $r$ (near to 1). Desynchronization in just one channel causes significant drops in $r$ value.

Conclusions
Through the order parameter $r$ we can evaluate the phase synchronization of a sleep spindle. A characteristic plateau in Kuramoto $r$ value also can be observed during the spindle occurrence. These results can be used to evaluate sleep pathologies, such Obstructive Sleep Apnea, to evaluate the synchronization degree considering different brain areas, or study physiological processes like memory consolidation.

Figure 1: Raw signal of sleep spindle in different channels (top); Sleep spindle in different channels filtered with an 11-16Hz bandpass filter (middle); and Kuramoto order parameter $r$ (bottom).

References


Supported by: FAPESP (process number 2012/22413-2).
figure 1
P750
Ictal electroencephalographic discharges in the preterm newborn: defining a new nosological entity?

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Introduction

Preterm newborns are at higher risk of neonatal seizures than term newborns. Among them, infants who developed neonatal seizures are at increased risk for adverse outcome and death. In term or preterm newborn, EEG ictal activity is commonly defined as "abrupt and transient change in background activity lasting at least 10 seconds"; authors have arbitrarily defined this duration. However, some of them have pointed that brief rhythmic discharges are frequent among preterm newborns and are significantly associated with an increased risk of abnormal neurodevelopmental outcome, especially when these discharges are repeated on a same EEG.

Question

In this study our primary objective was to analyse the different rhythmic discharges registered on EEG of preterm newborns.

Methods

We included the preterm newborns (born before 37 weeks of gestational age) who were hospitalized in the neonatal unit of the University Hospital of Lille during the year 2005 and who presented with ictal discharges or suspected clinical seizures during the neonatal period. We proceeded to the analysis of standards EEG (8 channels): background activity, ictal discharges (duration, pattern, propagation), electroclinical correlation, etiology, response to anti-epileptic drugs were evaluated.

Results

among 84 preterm newborns included, we studied the EEG of 26 children having EEG because of abnormal movements or rhythmic discharges on the EEG rapport. Finally only 14 children had discharges, 9 of them had brief discharges (duration lasting between 3 and 9 seconds) and 5 had long ones (during at least 10 seconds). Newborns with cerebral malformation and cerebral hypoxia had long rhythmic discharges, and those with intraventricular hemorrhages or sepsis had non specific discharges (brief or long ones). The main frequency of the discharges is delta, sometimes starting with theta frequency when it is a long discharge.

Conclusion

This preliminary study find that brief rhythmic discharges are sometimes associated with long ones, but sometimes not, specially in preterm children with neurological risk (sepsis, hypoxia, ...). It emphasizes the importance of using a larger definition for ictal activity in the preterm newborn, however the prognostic value and the meaning of these brief rhythmic discharges remains to be defined.
P751
DIAGNOSIS OF EPILEPSY BY MEANS OF MELATONIN-INDUCED OR SLEEP-DEPRIVED SLEEP EEG IN DIFFERENT AGE GROUPS OF CHILDREN

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One of the cornerstones in the diagnosis of epilepsy in children is electroencephalography (EEG). Recording EEG is challenging since a recording of good quality requires that the child lies still. Therefore, the method of choice so far has been EEG performed during sleep. Many laboratories use sleep deprivation, but it is, however, not easy to achieve in young children. Melatonin, given prior to the investigation, is currently used to induce sleep. To the best of our knowledge there are no studies that have described the effect of melatonin intake on epileptiform discharges during sleep in different age groups or compared it to the effects of sleep deprivation.

Objective

To determine if melatonin is equally reliable as sleep deprivation in inducing sleep without interfering with epileptiform discharges in the EEG when evaluating epilepsy in children 1-16 years old.

Methods

We retrospectively analyzed 129 EEGs recorded after melatonin intake and 113 EEGs recorded after sleep deprivation. Comparisons were made concerning occurrence of epileptiform activity or other abnormalities, the number of children obtaining sleep and also technical quality of the EEG recordings. Comparison between different age groups was made as well.

Results

No difference was found regarding the prevalence of epileptiform discharges (33% in melatonin induced sleep, 36% after sleep deprivation), as well as number of EEGs that were not interpretable (10 and 11, respectively). Melatonin and sleep deprivation were equally efficient in inducing sleep in children (70 % in both groups). Significantly more children between 1-4 years of age obtained sleep after melatonin intake in comparison with sleep deprivation (82% vs. 58%, p= 0.01). Sleep deprived children between 9-12 years old had higher percentage of epileptiform discharges (62%) than other sleep deprived children (p= 0.02).

Conclusion

Melatonin is equally efficient as sleep deprivation to induce sleep and does not affect the prevalence of epileptiform discharges in the EEG recording. Melatonin induced sleep have advantages, especially in younger children as they fall asleep easier than after sleep deprivation. Sleep deprivation can still be preferable in older children as an activating method to reveal epileptiform activity, but not as a sleep inducing procedure.
Electrophysiological mismatch response to somatosensory changes in young and elderly humans

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Aging-related decline in cognitive functioning is associated with alteration in event-related potentials (ERPs). Namely, recent studies in the auditory and visual modalities have shown that the mismatch negativity (MMN, or the mismatch response, MMR), an ERP elicited by a deviant stimulus in a background of homogenous events, is sensitive to cognitive decline related to aging and several neurological conditions. It is, however, unclear whether the somatosensory counterpart of MMN is similarly affected by aging. We used the MMR to study the effects of aging to brain’s automatic change detection mechanism in the human somatosensory system. The participants were 41 young (22-30 y) and 44 elderly (63-80 y) women. In the experiment, a run of 1000 electrical pulses of 200 µs with individually adjusted intensity were delivered on the left forefinger and little finger in randomized order of standard ($P = 0.86$) and deviant ($P = 0.14$) stimuli with randomly varying stimulus-onset asynchrony of 400-500 ms. The results revealed significantly different responses to standards than those to deviants in the both age groups at 150-190, 220-290 and 290-360 ms after the stimulus onset. Within the young, the responses differed only at central electrode sites indicating narrowed scalp distribution of somatosensory MMR in aged compared to young adults. The results might reflect age-associated alterations in the sources of the brain activity related to the somatosensory change detection mechanism.
P754
IS MYOCLONUS STILL A PREDICTOR OF POOR NEUROLOGIC OUTCOME IN THE HYPOTHERMIA ERA? Report of 4 cases.

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QUESTION
Several studies had assessed the validity of neurophysiological and clinical testing as prognosis predictor before the use of therapeutic hypothermia (TH). TH and its associated use of sedative and paralytic agents may modify the value of the prognosis parameters and further investigations are needed. The presence of myoclonus is considered a sign of severe brain ischemia and has been associated with high rates of mortality and poor neurologic outcome.

METHODS
We retrospectively reviewed the data of all the patients undergoing TH after cardiac arrest from April 2012 to October 2013. We identified the patients with myoclonus and analyzed the features that may be related to the outcome.

RESULTS
Thirty one patients were included. Four of them had myoclonus (12.9%) between the third and fifth day after cardiac arrest (CA). Two patients had myoclonus with EEG correlate or cortical myoclonus (CM) and two had myoclonus without EEG correlate. All patients who had myoclonus without EEG correlate died within 10 days. Patients with CM (50%) survived during the first thirty days and one patient (25%) survived along the six and twelve months of follow-up. All patients had a poor neurologic outcome (CPC 4). The EEG pattern was discontinuous in all patients when myoclonus appeared, however it did not meet the criteria of burst-suppression pattern. One patient who presented generalized periodic epileptiform discharges (GPEDs) and CM had reactivity on EEG 7 days after benzodiazepine treatment. Only the patient with a reactive EEG survived, although he remains in a persistent vegetative state.

CONCLUSIONS
The presence of early myoclonus in patients treated with TH after CA can still be a predictor of poor prognosis. Additional studies are required to establish this relation.
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A Case Report of Epileptoid EEG with Theta Burst

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Preface

We report a case with epileptoid EEG which showed spike-like components but was difficult to conclude that these patterns were definitely epileptic.

Personal history

The patient is 65 years old and has been hospitalized as schizophrenia since he was 27 years old. He is a son of a geisha and his father is unknown. We was brought up by his foster father and grew up without parents’ love. Apparently this environment distorted his personality. After he graduated from a high school, he repeatedly changed his jobs and was arrested for committing thefts and an abduction. He was imprisoned and his delusional idea was build up there. His intelligence was normal.

Data analysis

We recorded his digital EEG data and analyzed them using our original computer program. The sampling rate is 1000Hz and sectioned them off into micro-state (2.56 sec). Respective micro-state was processed with FFT and converted into power spectra (Δ=0.39Hz). We separated the data into theta burst sections and non-burst sections, and examined whether epileptic waves would appear or not respectively. Also, we examined amplitude distribution and phase distribution at alpha band theta band.

Conclusion

This case showed epileptoid abnormal basic rhythms and we are going to examine more detailed EEG data including his whole night EEG.
Time-Frequency analysis during an auditory oddball task

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Objective

To provide a more thorough approach of the electrophysiological processes involved in the detection of the auditory target during an oddball paradigm. What can we learn from an exhaustively time-frequency analysis of auditory Event-Related Potentials (ERP)?

Methods

Event Related Spectral Perturbation (ERSP) and Inter Trial Coherence (ITC) in the time-frequency domain were calculated for an auditory oddball paradigm (Target: 1000 Hz, Non-target: 500 Hz, pure tones with ¼ occurring probability ratio) in 24 young healthy subjects. ERSP show variations of the EEG power spectrum with respect to its baseline. ITC quantifies phase consistency of the EEG spectrum at a given frequency and time-window across trials.

Results

Relations between ERP and time-frequency-based methods (i.e. ERSP and ITC) were studied in details at different frequency bands and time-lags. ERP could not extract all the information in an oddball paradigm. There were some aspects of information that could only be extracted by ERSP and ITC methods. ERP (with its good temporal resolution) could give information about slow and fast synchronous brain activities and their locations specifically just after the stimulation. ERSP at alpha and beta bands could identify brain regions engaging in decision making. ERSP was the only method which could show how a beta oscillation generator is formed around 800 ms in frontal region after the alpha desynchronization phase (300-700ms). Synchronization/desynchronization stages and flow of information at different frequencies could be tracked by ERSP. ITC could point to brain regions having small but synchronous activities such as motor regions that are related to finger responses at alpha2-beta1 bands to target stimuli. Such an activity could not be observed by ERP and ERSP analyses.

Conclusion

Time-based (ERP) and time-frequency-based (ERSP, ITC) methods could bring complementary information in analysis and unveiling of underlying mechanisms of cognitive tasks. ERP is basically efficient in the study of early brain responses to external stimuli. ERSP may distinct brain mechanisms according to their frequency contents. It is much more efficient than ERP in the study of late brain responses. ITC is able to detect tiny synchronous regions at a given frequency and time.

Keywords

Event-Related Potentials (ERP), Event-Related Spectral Perturbation (ERSP), Inter-Trial Coherence (ITC), beta oscillation generator
Hyperventilation during routine EEG recording: are “3 minutes” really necessary?

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Introduction

The minimal duration of hyperventilation (HV) to elicit electroclinical absences during routine EEG recording is usually 3 minutes. This protocol has been implemented for decades and is still recommended by the American Clinical Neurophysiological Society. However, the clinical impression when children experiences an absence seizure while performing HV in the clinical setting is that in most cases, absences occur in less than 90 seconds. Hence, the “minimum of 3 minutes” procedure may not be necessary.

Methods

We reviewed all ambulatory records of children who experienced clinical or electrographical absences during EEG HV. Besides demographic data, we reviewed: 1. the time elapsed from the beginning of HV until absence occurred; 2. Time until 2nd or more seizures, if these occurred; 3. Time of post-HV absences, if these occurred.

Results

53 EEGs from Israel and Turkey were reviewed (32 F, 21 M). Age range 4-15 years. 27/53 aged 4 - 10 years, 26 aged 10 - 15 yrs. Absences occurred within 2 - 130 secs. Mean time till first absence was 42 sec (Israel 52 sec, Turley 33 sec), median 35 sec. 21 patients had at least a second absence: mean time: 101 sec (Israel 117, Turkey 52 sec), median 56 sec. Only 10 of the 53 patients had post-HV absences. By age groups: the 4-10 years mean time to 1st seizure was 30 sec, compared with 54 sec for >10 years old.

Conclusion

This preliminary study supports the clinical impression that most children with absence seizures will experience an event during HV within less than 90 seconds, as the median time to a first absence was 35 secs. Only 3 of 53 cases sustained the first event in over 90 seconds (95 - 130 secs) of HV. It appears that the current recommendation of a minimum of 3 minutes of HV during routine EEGs may need to be reevaluated in larger-scale studies.
Disposible surface electrode impedance evaluation for quick application EEG in emergency medicine

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It is challenging to evaluate the neurological state of an unconscious person outside of a hospital. An electroencephalographic (EEG) recording can illuminate the cause of the unconsciousness and direct treatment already in the field and help to guide the patient into the correct treatment path when arriving at the hospital.

Question

Previously our group developed a wireless EEG system for out-of-hospital use [1]. The impedance of the electrode-skin interface causes most of the noise in the EEG [2]. What is the performance of common disposable Ag-AgCl surface electrodes in quick application EEG recordings?

Methods

The tested electrodes were: Myotronics Norotrode, Spes Medica EEG-EMG, Ambu Neuroline 720, Vermed Silverest, 3M RedDot, Tyco Kendall Arbo and Skintact FS-VB01.

The impedances were evaluated using Embla Titanum polysomnography system (Natus Neurology, CA, USA) on one test subject. The Embla features a channel specific impedance checker. The impedance is measured between the REF and each measuring electrode using 1-16 Hz square waves.

Electrodes were placed in the positions Fp1 and Fp2, M1 and M2. The ground electrode was in the midline below the frontal hairline and the reference electrode was placed immediately below that. The same type of electrodes was used for each location. The electrode locations were prepared with a quick alcohol swipe (EtOH 80%). For each electrode type, an impedance time series was recorded over 15 minutes at one minute intervals.

Results

The desired < 5 kΩ impedance was immediately reached by Myotronics, Ambu, Vermed and 3M in Fp locations and none in M locations. After 15 minutes < 5 kΩ was seen in Myotronics, Ambu and Vermed in Fp and none in M. Electrode stability was quantified by the standard deviation of the impedance time series. Myotronics and Vermed showed 0.1 kΩ in Fp and Myotronics also in M. Others were higher. A scoring system was applied which gave equal weights to low impedance in the beginning, after 15 minutes and to high stability. The performance ranking was as follows (best first): Myotronics, Vermed, 3M, Skintact, Ambu, Tyco, Spes Medica.

Conclusion

The Myotronics Ag-AgCl electrode had the best performance judged by the impedance measurements and is a candidate for quick application EEG out-of-hospital studies.
Figure 1. The evaluated electrodes for the developed EEG system for out-of-hospital use. All the used electrodes were disposable Ag-AgCl wet gel or hydrogel surface electrodes.
Figure 2. Panel A, the impedances of each of the seven electrode types over 15 minutes at 1-minute intervals in Fp1, Fpz, M1, and M2. Panel B, the electrode types were scored according to their impedance measures. Myotronics Norotrode performed the best when low impedance in the beginning and after 15 min along with high stability were emphasized.

REFERENCES
Identical Bursts are phase locked to Infra-slow oscillations

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**Question**

Recently, we reported on burst suppression with identical bursts [1], which is a distinct EEG pattern that is exclusively observed in patients with postanoxic coma. We provide additional characteristics of these EEG patterns.

**Methods**

Patients with postanoxic coma admitted to the ICU were monitored with cEEG using a full-band EEG amplifier. If Burst Suppression EEG with identical bursts was observed, we studied these EEG patterns for the presence of infra slow oscillations (0.005-1 Hz) and studied the temporal relation of the bursts and the infra slow activity.

**Results**

In 11 of 42 patients we observed burst suppression with identical bursts, and in 6 patients bursts were phase locked to infra-slow oscillations with frequencies of 0.015-0.02 Hz (figure 1). The patterns may evolve from an initial iso-electric EEG (figure 2). All patients with identical bursts had a poor outcome.

**Discussion**

We present additional characteristics of burst suppression EEG with identical bursts showing that in the majority of these EEG patterns infra slow oscillations are present, where the bursts are phase locked to these rhythms. We speculate that the infra slow oscillations may reflect pathological homeostasis, e.g. abnormal calcium or sodium/potassium gradients.

**References**

P760
Lag synchronization in the brain

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Question

Lag synchronization of two different chaotic oscillators is phenomenon when the signal from the system with a lower frequency has some delay with respect to the system which has the higher frequency. The interaction among the multiple brain oscillators may produce such a phenomena. The purpose of this study was to determine whether the direction of phase difference between two channels in electroencephalography (EEG) does depend on the source characteristic frequency.

Methods

Independence of the phase shift on the mean frequency between two channels was tested on a group of 31009 healthy truck drivers. Mean phase difference between two EEG channels was estimated by Hilbert transform and compared to the difference of characteristic frequency.

Results

Number of EEG segments with the phase delay from the electrode with a lower frequency to the electrode with a higher frequency was significantly higher than to the electrode with lower frequency. The most significant direction of phase delay was occipito-frontal.

Conclusions

The results support hypothesis about presence of lag synchronization in the human brain. This work provides alternative explanation of the phase shift between oscillations in different part of the brain.
Factors influencing the utility of Ambulatory EEG at a tertiary neurological centre.

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Question

Ambulatory EEG (AEEG) is a potentially useful investigation for patients requiring prolonged EEG monitoring and may be a cost effective solution to increasing demands for inpatient video telemetry. There are currently no published criteria to guide use of AEEG. A retrospective study of AEEGs performed at a tertiary neurological centre was carried out to identify factors influencing utility.

Methods

68 ambulatory EEGs performed at the University Hospital of Wales between 2006-2012 were included. With reference to the indication for the study; it was determined whether the AEEG had been contributory or non-contributory to the patient’s subsequent management. Baseline differences between contributory and non-contributory studies were identified by comparing data derived from AEEG request forms, standard EEG reports and clinical letters.

Results

50% of AEEGs provided information that contributed to the patient's subsequent management.

The majority of non-contributory AEEGs were a consequence of a normal or non-specific AEEG trace and the absence of any clinical event during the recording period (82%), with smaller proportions due to technical faults (9%) significant artefact (6%), and failure to return the seizure diary (3%). Contributory EEGs were helpful for confirming non-epileptic events (44%), corroborating the diagnosis of epilepsy (26%), categorizing epilepsy (24%), and quantifying seizures (9%).

Contributory and non-contributory studies were similar at baseline in terms of patient demographics, indications for the study, and proportion of patients with a previous normal standard EEG.

Marked differences were observed in average seizure frequency; 26 events per month compared with 14 events per month for contributory and non-contributory studies respectively, and average time passed since the last seizure/clinical event by the time of the AEEG; 26 days compared with 39 days for contributory studies and non-contributory studies respectively.

Conclusions

AEEG is potentially useful investigation in patients requiring EEG monitoring. Seizure/event frequency and amount of time passed since the last seizure/event by the time of the AEEG are key factors influencing utility. These findings may inform guidelines for AEEG referral and optimal timing of investigation.
MARA: An EEGLAB plug-in for the classification of artifactual independent components

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EEG signals are often contaminated by artifacts stemming either from muscular activity of the subject or from external technical sources. Consequently, the removal of artifactual activity is essential to prevent misinterpretations both in the clinical and the neuroscientific context. A common artifact rejection method is based on the idea that artifactual components and neuronal activity are generated independently. Using Independent Component Analysis, the original EEG signal is decomposed into independent source components (ICs) and reconstructed after dismissal of hand-labeled artifactual ICs. However, manual identification of artifactual ICs is time-consuming and tools for its automatization are needed.

For this task, we provide a ready-to-use EEGLAB plug-in called MARA ("Multiple Artifact Rejection Algorithm"). The core of MARA is a linear supervised machine learning algorithm that learns from expert ratings of 1290 EEG components by extracting six features from the spatial, the spectral and the temporal domain. Features were optimized to solve the binary classification problem "reject vs. accept". The algorithm is able to handle muscle artifacts as well as eye artifacts and loose electrodes and achieves low classification error on components from unseen EEG experiments [1, 2]. MARA includes a semi-automatic mode designed to support the practitioner's decisions. The plug-in is published under the General Public License (GPL) and can be downloaded from http://www.user.tu-berlin.de/irene.winkler/artifacts/. As existing ICA-based plug-ins primarily focus on the detection of eye artifacts, we hope MARA will deliver a substantial contribution to the EEG community.


Abstracts of Poster Presentations – Poster Session 44 – EEG 2

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Video-Polysomnography findings after functional hemispherotomy in a case of Rasmussen syndrome

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Question
Consideration of Video-Polysomnography (VPSG) findings after functional hemispherotomy in a case of Rasmussen syndrome

Method
The patient was a right-handed 14-year-old female. Around the age of 8 years, the patient suffered clonic convulsions of the right eyelid and right side of the body, later progressing to intractable epilepsy. Accompanied with enlargement of a left insular lesion in a brain MRI, epilepsia partialis continua (EPS) and intellectual deterioration advanced gradually. When the patient was 13 years old, a functional hemispherotomy was carried out. The patient was referred to our department for perioperative evaluation of brain function.

Result
In the preoperative VPSG, cyclic EEG changes (CECs) in which the following 3 phases repeatedly appear were observed: Phase A, a period when irregular spikes and slow wave discharges sporadically appear in the left hemisphere; Phase B, a period when irregular spikes and slow wave discharges rhythmically appear in the left hemisphere; and Phase C, a period when spikes and sharp wave discharges rhythmically appear in the left hemisphere dominance. Moreover, the rate of appearance of each phase differed during waking hours, NREM sleep, and REM sleep. CECs were more remarkable during sleep than waking hours. Phases B and C were dominant during NREM sleep, whereas Phases A and B were dominant during waking hours and REM sleep. Furthermore, there were no correlations between each phase and seizure symptoms. In the brain waves obtained via the postoperative VPSG, Phase A was dominant and Phase B was minor, and no Phase C was observed. Moreover, no correlation between sleep and waking was observed. Spike and spike-and-slow waves in the left hemisphere epileptogenic focus were observed sporadically. During the observation, clinical seizures ceased.

Conclusion
The changes in VPSG findings after functional hemispherotomy suggest that cortical and subcortical interactions are important for CECs formation in Rasmussen syndrome.
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Effects of mCIMT-BiT intervention in unilateral Cerebral Palsy: Hemispheric dominance of motor control of the affected hand influences outcome of treatment.

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Question

Research has demonstrated efficacy of both modified-Constraint-Induced Movement Therapy (mCIMT) and Bimanual Training (BiT) in children with unilateral Cerebral Palsy (uCP). However, the outcome of intervention differs widely between individuals. The present study examines whether differences in hemispheric dominance for motor control adds to these varying results.

Methods

Ten children (aged 8-12) with uCP were tested before and after a one week combined mCIMT-BiT intervention. The Lateralized Readiness Potential (LRP) preceding whole-hand button presses were used to determine hemispheric dominance for the control of the affected and non-affected hand. Based on LRPs, 2 subgroups were determined with respect to the control of the affected hand: a contra-lateral and an ipsi-lateral group (both n=5). In addition, Event Related Potentials (ERPs) evoked during a simple cue-target paradigm were compared before and after intervention.

Results

The two subgroups did not differ with respect to manual ability. However, a main intervention effect was observed in both groups with respect to the Canadian Occupational Performance Measure (COPM). In addition, the contra-lateral group showed overall higher scores on the COPM than the ipsi-lateral group. Finally, intervention effects with respect to the ERP P300 component to both cue and target stimuli were observed in the contra-lateral group.

Conclusions

In all, intervention effects were more marked in the contra-lateral group than the ipsi-lateral group. Thus, EEG provides an easy and non-invasive method to determine hemispheric dominance of the affected hand function. Future research should be aimed at how to use hemispheric dominance classification in determining optimal treatment protocols.
Abstracts of Poster Presentations – Poster Session 44 – EEG 2

P767
EEG as a prognostic tool for classic absence.

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Purpose

The main purpose of this paper is to offer some guidance to expect the prognosis of classical absence from the EEG.

Method

This was an observational study conducted from July 2006 to July 2012. Data of 42 newly diagnosed patients with typical absence seizures was collected retrospectively and analyzed.

Results

The mean time until seizure and EEG control for those with +ve 3 Hz. SWC during routine EEG recording was (9.9 +/- 14.4) months. While the mean total follow up period for all cases were (19.3 +/- 20.5). 100% of patients with +ve 3 Hz. SWC during the 3rd minute and after HV were controlled and 80% of the overall no. of controlled patients in this study was found during 3rd min HV (p value= 0.049). The majority of the controlled patients with 3 Hz. SWC after HV and during 2nd minute or 3rd minute HV was prescribed only monotherapy.

Conclusion

Overall prognosis of typical absence was good yet the presence of the 3 Hz. SWC with late onset either during the 3rd minute HV or even after had a better prognosis as regard; All of this group were controlled, monotherapy was used to control the majority of patients with late onset 3 Hz. SWC. These data was only significant for the association between the 3Hz. SWC and the percentage of control of absence seizures during the 3rd minute HV (80%) [p value= 0.049]. A multicenter study should be done in the nearby future to confirm these results.
P768
Quantified EEG reactivity predicts both good and poor outcome. A pilot study on cardiac arrest patients.

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Question

EEG reactivity (EEG-R) to noxious stimulation is an important prognostic parameter in comatose patients. Assessment of reactivity however, relies on a visual qualitative evaluation prone to subjective interpretations. The aim of this study was to test if QEEG analysis has a potential as an objective and sensitive method for the evaluation of EEG-R.

Methods

We conducted EEG in 14 lightly sedated out-of-hospital cardiac arrest (CA) patients during the first 12 to 24 hrs of therapeutic hypothermia. We marked three periods of 30 seconds both with and without noxious stimulation, and used the average to calculate a stimulation/rest ratio in the alpha, theta and delta bands. Then we compared the alpha/theta-, alpha/delta-, and theta/delta ratios. Outcome was assessed by the Cerebral Performance Category Score (CPC) 28 days after CA.

Results

Alpha/delta reactivity ratio (ADRR), defined as the ratio of the alpha/delta ratio during noxious stimulation to the alpha/delta ratio without stimulation, was the best predicting parameter. All 9 patients with an ADRR below 1 (range 0.32 - 0.95), i.e. a decrease in alpha-power and/or an increase in delta-power during stimulation, had a good outcome (CPC 1-2) and 4 of 5 patients with an ADRR of more than 1 (range 1.11-1.43) had a poor outcome (CPC 4-5). One patient with an ADRR of 1.12 had a good outcome (CPC 2).

Conclusions

This pilot study suggests that quantification of EEG-R by ADRR may predict both good and poor outcome in sedated CA patients, even within the first 24-hours of therapeutic hypothermia.
Creation of a clip type electrode for recording an electroencephalogram non-invasively from scalp hair

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INTRODUCTION

We created a clip type electrode (CE) for recording an electroencephalogram (EEG) non-invasively from scalp hair and analyzed its reliability and utility.

METHODS

1) Reliability. (1) We compared interelectrode voltage (IV) and resistance (IR) between traditional disc electrodes (DEs) and CEs using LCR HiTESTER (HIOKI E.E.Corp.). Electrodes of each type were placed at the distance of one centimeter across electrode paste (Elefix, EF, Nihon Kohden Corp.) for DEs or across skin preparation gel (Skinpure, SP, Nihon Kohden Corp.) for CEs. (2) Next, we measured IR on the scalp from 12 adults normal volunteers (eight males and four females) under following conditions: (a) DEs with EF at F2 and P2 in the ten-twenty electrode system, (b) DEs with EF after skin preparation with SP at F2 and P2, (c) CEs pinching scalp hair immersed with SP at F1 and P1 and (d) CEs pinching scalp hair immersed with SP after skin preparation with SP at F1 and P1. 2) Utility. EEGs were recorded by an electrode arrangement of Fp1, Fp2, C3, C4, O1, O2, T3 and T4 from three normal volunteers using Neurofax (Nihon Kohden Corp.). DEs were placed for right side recording and CEs were for left side. EEGs were recorded from other eight normal volunteers. Each recording time was 15 minutes.

RESULTS

1) Reliability. (1) IV/IR of DEs and CEs were 17mV/1.1kΩ and 24mV/1.1kΩ. (2) Mean values (standard deviations) of scalp IR were (a) 263.6 (300.8), (b) 5.3 (5.3), (c) 130.3 (83.4) and (d) 7.4 (5.6). There were no significant differences between (a) and (b), and (c) and (d). 2) Utility. Frequency analysis of EEGs recorded from right DEs and left CEs revealed no significant difference in frequency spectrum between DEs and CEs. EEGs from eight volunteers using CEs were all recorded stably. Mean time for setting CEs was 8 minutes (a half of DEs).

CONCLUSION

Recording an EEG from scalp hair with CEs had the same reliability and utility to recording from scalp with DEs.

figure 1
P770
Co-maturation of Theta and Low-beta rhythms during child development

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Question

Present report examines a possible pattern of co-maturation between different frequency ranges in the spontaneous electroencephalogram (EEG) during child and young adulthood development.

Methods

One hundred and sixty seven subjects, between 6 and 26 years old were recorded during three minutes of spontaneous EEG. The logarithm of the Power Spectral Density (PSD) was computed.

Results

There was a decrease in all frequency bands ranges between 1-46 Hz. Correlation matrix for these frequencies was computed. A general trend of correlation of PSD with neighbor frequencies was obtained. Furthermore, there was a high correlation during development between theta and the beta ranges, and between high beta and gamma frequency ranges. The topography of theta vs. beta correlation was particularly high between anterior and posterior networks. Principal Component Analysis (PCA) permitted to extract six components explaining the variance associated to the delta, theta, alpha, low beta, high beta and gamma. Interestingly, the component explaining theta rhythm was also explaining beta rhythm during development.

Conclusions

Results suggest that there is a pattern of co-maturation in the PSD of spontaneous EEG between theta and low beta, and between high beta and gamma. The reason for this co-maturation could be in the maturation of neural tissue underlying the sources of different frequencies. The possible functional role of the co-maturation of theta-beta in fronto-parietal areas is suggested.
Early EEG patterns and prognosis in neonatal asphyxia treated with hypothermia

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Question

Hypothermia decreases death and disability in neonatal hypoxia-ischemia encephalopathy. Neonatal electroencephalography (EEG) has shown clinical utility for predicting neurological prognostic outcomes in hypoxia-ischemia. We examined the evolution of EEG patterns after hypoxic injury to explore the moment with the highest clinical efficiency for predicting outcomes.

Methods

Retrospective review of consecutive EEG in newborns diagnosed with encephalopathy and treated with hypothermia. Background EEG activity was analyzed from 6 hours to 27 days of life and neurologic outcome was assessed (abnormal outcome if disability or death). EEG patterns were classified in normal/mildly abnormal if continuous EEG activity was recorded or abnormal if discontinuous or amplitude <10 µV of background EEG activity appeared. We estimated the sensitivity, specificity, positive (PPV) and negative (NPV) predictive values of performing an EEG at 12, 24, 48, 72, 96, 96-144 and >144 hours.

Results

Out of the 58 recruited patients, 30 (51.7%) had abnormal outcomes. 1-4 serial EEG examinations were analyzed (average per patient: 2.45; 142 in total). EEG performed at 3-4 days of life has the highest efficiency for predicting the outcome (sensibility 100%, specificity 80%, PPV 0.82 and NPV 0.8). Normal/mildly abnormal EEG results at 0-24 hours had 100% NPV; however the greatest PPV (90%) was not reached until 4th day.

Conclusions

Serial EEG are useful to predict neurologic outcomes in neonatal hypoxia-ischemia encephalopathy treated with hypothermia. Normal/mildly abnormal EEG patterns within the first 24 hours after birth were associated with normal neurodevelopment outcomes. To predict abnormal outcomes (disability or death), EEG background must remain abnormal until the 4th day of life.
P772
EEG PATTERNS AS PREDICTORS OF OUTCOME IN PATIENTS WITH VEGETATIVE STATE AND MINIMALLY CONSCIOUS STATE

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Methods

Totally 23 Comatose patients investigated. Vegetative state (VS) and minimally conscious state (MCS) diagnosed. Patients evaluated by Glasgow Coma Scale (GCS). Coma recovered patients accessed by Disability Rating Scale (DRS). Etiologically coma was divided in 5 groups: hemorrhagic, ischemic, subarachnoid/parenchimal, post hypoxic, traumatic. EEG activity patterns detected by 16 channel EEG. Statistical analysis performed by SPSS 11.0.

Result

Among 23 VS patients 9 patients evaluated as MCS according to the international criteria. In 1st group 1 VS patient (with GCS =4) revealed delta EEG pattern and at 1 year classified as PVS, from 5 VS patients (GCS=5) with theta EEG pattern 2 were defined as MCS, one recovered (DRS=14), and one died. 3 other patients defined at 1 year as PVS. In second group 3 VS patients (GCS= 5-7) with beta EEG pattern 2 patients developed PVS, 1 patient defined as MCS and recovered (DRS=18). In 3rd group 2 VS patients with alpha EEG pattern (GCS=6) died. In 4th group from 4 VS patients (GCS=5-7) with delta EEG pattern 2 patients defined as MCS, 1 patient died and 3 patients developed PVS. 5th group from 8 patients with VS (GCS=5-8) 4 patients diagnosed as MCS, 4 with delta EEG patterns and 4 with theta EEG patterns. 4 patients with VS remained with delta EEG pattern. At 1 year 1 patient with MCS recovered (DRS=11), 2 patient with MCS and 3 patient with VS died and the rest 2 patients developed PVS. Correspondence analysis of all researched factors including photo reaction, corneal reflex, tracheal reflex, oculo-cephalic reflex, localization of sound and pain, EEG pattern, coma outcome revealed that sound localization (Chi-sqr.=31.10493;p=0.000001) is significantly associated with EEG theta rhythm and with outcome. The high amplitude frontal and temporal lobe theta frequencies in MCS patients were strongly correlated with auditory long latency evoked potentials (p300) arising by binaural stimulation(r=+0.47;p

Conclusion

High amplitude theta frequencies in VS patients where significant for favorable outcome.
THE EEG ANALOGUES OF THE KAROLINSA SLEEPINESS SCALE BASED ON THE KAROLINSA DROWSINESS TEST

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Question

Simple methods of sleepiness assessment are greatly needed for both fundamental research and practical applications. We applied the Karolinska drowsiness test (KDT) to construct 6-point physiological alertness scales and to validate them against such well-known instrument of subjective assessment of sleepiness/alertness as the 9-point Karolinska sleepiness scale (KSS).

Methods

Seven-min EEG recordings were obtained with 2-h interval from frontal and occipital derivations during the last 32-50 hours of 44-61-hour wakefulness of 15 healthy study participants. Occipital alpha-theta power difference and frontal and occipital scores on the 2nd principal component of the EEG spectrum were calculated for each one-min interval of 5-min eyes closed section of the record. To obtain scores (points from 0 to 5) on alertness scales for each of these three EEG indexes, all positive one-min values of the index were assigned to 1, and all remaining (negative) values were assigned to 0.

Results

Scores on any of the three physiological alertness scales were strongly associated with KSS scores (Fig.1). We also demonstrated that the study design provides a possibility to compare validity of subjective and physiological scales.

Conclusion

Physiological analogues of KSS were offered by the study utilizing the EEG recordings on eyes closed interval of KDT (Fig.2).
Distinguishing dementia with Lewy bodies from Alzheimer’s disease using EEG

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Present diagnostic criteria for dementia with Lewy bodies (DLB) regard prominent slow wave activity with temporal lobe transient sharp waves on the EEG as a supportive feature. It has also been suggested that EEG abnormalities in DLB are more extensive than in Alzheimer’s disease (AD). Still the use of the EEG as a diagnostic tool to differentiate between DLB and AD remains rare in daily practice because of conflicting studies and the absence of a reliable scoring method. Roks et al. (1) used the Grand Total EEG (GTE) score to differentiate between DLB and AD with good sensitivity and specificity.

Methods

We reproduced the former study and visually rated EEGs using the GTE score in 29 patients with DLB and 54 with AD recruited form a memory clinic in a general hospital in the Netherlands. 6 items were scored: rhythmic background activity, diffuse slow-wave activity, reactivity, paroxysmal activity including frontal intermittent rhythmic delta activity (FIRDA), focal abnormalities and sharp-wave activity. Two of the authors rated the EEGs separately blinded to all clinical information.

Results

Patients with DLB had significantly higher total GTE scores than patients with AD: 9 vs. 4. ROC analyses revealed that patients with DLB could be distinguished from those with AD at a GTE cut-off score of 6.5 with a sensitivity of 79% and a specificity of 76%. The association between GTE and DLB was independent of age, gender, Mini Mental State Examination and use of medication. In the subscore analyses, scores on all 6 items were also significantly higher in the DLB group. FIRDA was found in 17.2% of patients with DLB compared to 2% with AD. The weighted kappa between the two raters was 0.89.

Conclusions

The GTE score has proven to be a reliable and easy to apply scoring method with low inter-rater variability. The EEG can help to differentiate between DLB and AD with good sensitivity and specificity and should play a more prominent role in distinguishing DLB from AD. Future revisions of the diagnostic criteria for DLB should consider FIRDA as a suggestive feature.

Reference

P775
Interrater agreement of EEG interpretation in comatose post cardiac arrest patients

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Question
What is the interrater agreement of EEG interpretation in adult comatose post cardiac arrest patients using the American Clinical Neurophysiology Society (ACNS) standardized critical care EEG terminology?

Methods
The EEG-data were obtained from patients included in the Target Temperature Management trial (TTM), an international, multicenter, clinical trial of temperature management in comatose cardiac arrest patients [N Engl J Med 2013]. In the TTM trial a routine EEG was performed in patients still comatose 12-36 hours after rewarming.

For this study, one EEG-specialist (IR) chose 20 EEGs, covering important aspects of the ACNS EEG terminology. Four EEG-specialists with different nationalities (Sweden: EW, Denmark: TWK, The Netherlands: AFvR and Switzerland: AOR) acquired the ACNS EEG terminology [J Clin Neurophys 2013;30:1-27] and studied a web-based training-module. The four EEG-specialists subsequently interpreted (blinded to patients' identity) the 20 EEGs, reporting the findings according to the ACNS EEG terminology. Percent agreement and Fleiss kappa values for every category in the terminology were calculated. Percent agreement was defined as the proportion of the 20 EEGs in which all interpreters reported identical findings.

Results
There was 65% agreement on whether a rhythmic or periodic pattern was present or not (Kappa 0,44). If a rhythmic or periodic pattern was present there was 93% agreement on which type of pattern (periodic discharges, rhythmic delta activity, rhythmic spike-and-wave/polyspike-and-wave/sharp-and-slow-wave) (Kappa 0,65).

Conclusions
Using the ACNS EEG terminology in adult comatose post cardiac arrest patients there was moderate agreement on the presence and type of periodic and rhythmic patterns.
P776
Oscillatory transcranial current stimulation (tDCS) and transcranial alternating current stimulation (tACS) stimulation affect spontaneous low-frequency EEG activity


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### Question

Five different experiments were carried out to assess how oscillatory tDCS and transcranial Alternating Current Stimulation (tACS) stimulation affect spontaneous EEG activity during wakefulness (experiments - Exp.- #1-4) or during subsequent sleep (Exp. 5): (1)

### Methods

Waking EEG was recorded from 28 derivations before and after stimulation in 42 subjects -Ss.- (Exp. 1=10 Ss.; Exp. 2=10 Ss.; Exp. 3=10 Ss.; Exp. 4=12 Ss.), and sleep EEG during a post-stimulation nap in 6 Ss. Mean EEG power was calculated for the following bands: delta (1-4 Hz), theta (5-7 Hz), alpha (8-12 Hz), beta1 (13-15 Hz) and beta2 (16-24 Hz). Relative changes of EEG power were compared by t-tests, separately for each band and for each derivation.

### Results

On the whole, the experiments show that tDCS and tACS affect post-stimulation resting EEG, by increasing slow-frequency EEG activity. Effects were however small, and larger as a consequence of tACS than tDCS protocols. Figure 1 shows the results of Exp. 3, in which frontal tACS at 0.8 Hz or at 5 Hz affects post-stimulation slow-frequency EEG. Figure 2 reports similar results of the Exp. 4, in which 5 Hz stimulation was administered over the temporal areas. EEG changes do not show a clear specificity for frequency and region of stimulation.

### Conclusions

Although still preliminary, our results point to an effectiveness of transcranial stimulation protocols at inducing a slowing of spontaneous EEG activity. The lack of a coherent pattern of changes dependent on frequency and region of stimulation suggests some caution in the interpretation of the neurophysiological mechanisms involved in these changes.

### Figure legends.

**Figure 1.** Experiment 3: Frontal tACS stimulation (0.8 Hz vs. 5 Hz vs. sham)

Topographic statistical differences (assessed by paired t-tests) between post-stimulation (post-S) vs. pre-stimulation (pre-S) slow-frequency resting EEG bands. Values are expressed in terms of t-values: positive t-values indicate a prevalence of post-S over pre-S, and vice versa. Average values are normalized by total power, color coded, plotted at the corresponding position on the planar projection of the scalp surface, and interpolated (biharmonic spline)

**Figure 2.** Experiment 4: Temporal tACS stimulation (5 Hz vs. sham)

Topographic statistical differences depicted as in Fig. 1
The neural function outcome of patients’ with burst-suppression changes in the amplitude integrated electroencephalograph

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**Background**

The paper aimed to observe the sequelae of the amplitude-integrated electroencephalographs (aEEG) with different types of burst-suppression changes and the relationship between the changes and patients' neural function outcome.

**Method**

We monitored the cerebral function bedside using the aEEG on the first and third day after the patients were admitted to the intensive care unit (ICU) of the hospital, who experienced cardiopulmonary resuscitation (CPR). We chose the ones with burst-suppression changes to study and others were included in the control group. We analyzed the differences between different types of burst-suppression wave, performed follow-up observations in the first month and recorded the Cerebral Performance Category score (CPC).

**Result**

There were 25 patients monitored in the ICU and 5 patients with burst-suppression changes, which could be categorized three types. The first one (1/5) had idiopathic suppression, whose essential rhythm was more than 7Hz in the interval stage and the amplitude was higher in the ictal stage and turned to normal level in the interval stage and well response for the antiepileptic drugs or sedative drugs. The second one (3/5) had idiopathic suppression too, but whose essential rhythm was from 4 to 6Hz in the interval stage and the amplitude was higher than normal value in the ictal stage but lower than normal level in the interval stage and not response for the antiepileptic or sedative drugs. The third one (1/5) was periodicity burst-suppression wave and the essential rhythm was less than 4Hz and the amplitude was significantly lower than normal level in the interval stage and without clinical and EEG epileptic seizure. There were significant difference in the amplitude and the CPC score between the three burst-suppression types and both of the p were less than 0.01. And the patients’ neural function prognosis were different, with or without burst-suppression changes in the aEEG, the p was less than 0.05.

**Conclusion**

The aEEG with burst-suppression wave did not always mean nicious prognosis for patients after CPR. The one with idiopathic suppression and well response to therapy signified good outcome.
NEUROPSYCHOLOGICAL CORRELATES OF VISUAL P300 RESPONSES IN ALZHEIMER’S DISEASE AND MILD COGNITIVE IMPAIRMENT

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Background

The growing interests for event-related potential (ERP) studies are derived from the success in helping to diagnose and measure the cognitive functions of neuropsychiatric diseases. Aim of the present study is to examine the correlation between neuropsychological test scores and visual P300 responses in Alzheimer’s disease (AD) patients, Mild Cognitive Impairment (MCI) patients and healthy elderly.

Method

Age, education and gender matched 20 AD patients (mean age: 73.20), 20 MCI patients (mean age: 72.50) and 20 healthy controls (HC) (mean age: 72.35) were recruited. All participants performed neuropsychological evaluation before participating classical two-stimulus visual oddball paradigm. Repeated measures of ANOVA, independent sample t-test for post-hoc and bivariate correlation tests were performed.

Results

ANOVA results showed that all three groups were significantly differed in terms of target and non-target amplitude and latency responses (p=0.000). Post-Hoc analysis using independent sample t-test showed that compared to HC both MCI and AD groups had significantly lower target amplitudes. Target amplitudes of MCI were significantly higher in frontal, central and parietal locations than AD group. P300 target latency of HC decreased in compared to both AD and MCI, but there was no significant difference between AD and MCI groups in terms of latency. MMSE and verbal memory tests scores were significantly high correlation with target amplitudes. Also there were significantly medium amplitudes and latency correlations between stroop and verbal fluency test scores.

Discussion

There are significant differences across groups with regards to P300 amplitude and latency responses. Decreased P300 responses of patients’ groups are related to decline in cognitive functioning primarily in memory, executive functions and attention. Analyzing the ERP responses in MCI and AD patients can be helpful to understand the underlying electrophysiological mechanism of cognitive function of these disorders.

Acknowledgements

This project is supported by TUBİTAK with project number 112S459.
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P300 TARGET AND NON-TARGET RESPONSES IN ALZHEIMER'S DISEASE, MILD COGNITIVE IMPAIRMENT AND HEALTHY ELDERLY IN COMPARISON TO NEUROPSYCHOLOGICAL TESTS

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Background

According to previous research studies it is known that Alzheimer’s disease (AD) and mild cognitive impairment (MCI) patients' responses to target stimulation are different from healthy elderly controls (HC) due to cognitive impairment. Therefore this study is aimed to investigate to brain dynamics of AD and MCI by using event-related potentials (ERP) and neuropsychological tests.

Methods

EEG was recorded from the F3, Fz, F4, C3, Cz, C4, P3, Pz, P4, O1, O2 and Oz channels. Age, gender and education matched 15 AD, 15 MCI, and 15 HC subjects were included to the study. Target and non-target P300 amplitude and latency were measured. Repeated measures of ANOVA, post-hoc t-test and bivariate correlation tests were used for statistical analyses.

Results

Target amplitudes of all groups were significantly different on Fz, F4, C4, P4, O1, O2, Oz channels. P300 latency was significantly different on frontal, central and parietal sites among three groups. In non-target amplitudes, frontal and central electrodes were significantly different between HC and MCI, whereas MCI and AD patient’s responses did not differ. Non-target latencies were significantly different on all electrode sites among three groups. Moreover, verbal memory scores and P300 target amplitudes showed high correlation and stroop and verbal fluency tests showed moderate correlations with the amplitudes of all locations.

Conclusions

Brain pathology of AD and MCI affects P300 responses to target and non-target stimulation in correlation with cognitive impairment in both groups. P300 target amplitudes and latency can be an objective marker of cognitive impairment in MCI and AD.

Acknowledgements

This project is supported by TUBITAK with project number 112S459.
P777
Reduction in motor nerve strength-duration time constant during the anti-voltage-gated Na+ channel therapy in epilepsy

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Question
Anti-epileptic drugs targeting voltage-gated Na channels (VGSC) are not selective for the brain and establishing the optimal therapeutic dose remains challenging. The aim of this study was to investigate the excitability of myelinated median nerve motor axons in patients treated with carbamazepine (CBZ) and other anti-VGSC drugs.

Methods
Stimulation was carried out at wrist and evoked compound muscle action potential (CMAP) was recorded from the abductor pollicis brevis muscle using a standard setup for distal median nerve conduction studies. The current required to evoke threshold responses (40-50% of maximal CMAP amplitude) was determined by manual trial-and-error, for cathodic pulses of 0.2, 0.5 and 1 ms duration. The strength-duration time constant (SDTC), a measure of chronaxie, was determined as the x intercept of linear regression between charge (duration x current) and duration for the 3 data points.

Results: In controls, the SDTC was 411 +/- 81 µs (n=25, mean +/- SD) and did not differ among the 4 medical centers contributing to the study. By comparison, in the age-matched anti-VGSC treated group the SDTC was 30% reduced (P

Conclusions: Our data suggest that, at the therapeutic doses of anti-VGSC drugs, the SDTC of peripheral motor axons is reduced. As this excitability impairment is not sufficient to cause conduction failure in axons with normal safety factor for conduction, the SDTC measurements could prove useful for monitoring the functional consequences of the anti-VGSC therapy in epilepsy.
Abstracts of Poster Presentations – Poster Session 45 – ENG

P778
Study on late responses’ parameters at patients with lumbar radiculopathy

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**Background**

The indications of electrodiagnostic evaluation at patients with lumbar radicular symptoms are when the neurological examination is not correlated with the MRI finding or if there is a suspicion of an entrapment neuropathy, polyneuropathy or a myopathy. The result of this investigation can change the patient’s management therefore a thorough investigation is necessary.

**Method**

65 patients (mean age 49.87 years) were examined, all with uni or bilateral lumbar radicular symptoms. Tibial, peroneal and sural nerves were tested bilateral, with F waves and H reflex studies. Also a bilateral examination of vastus lateralis, tibialis anterior, gastrocnemius medialis and paravertebral muscles was made.

**Results**

Considering the more frequently used F wave parameters, only 27.7% had F wave abnormalities (15.4% chornodispersion, 10.8% latency and 7.7% A wave) but calculating the F ratio, 79.31% of patients (46.55% unilateral and 32.75% bilateral) showed abnormal values. 71.86% of patients had abnormal H reflex (41.4% absent, 13.8% amplitude/latency changes and 16.66% abnormal H index). Pathologic spontaneous activity was present at only 33.8% and the MUP analysis showed alterations in the controlateral limb in 61.5% cases. Considering the patients with unilateral symptoms, 54.8% had bilateral EMG signs. The correlation with MRI findings was 100% for the patients with unilateral EMG findings and 77.8% for those with EMG evidence of bilateral alteration.

**Conclusions**

The examination must always be bilateral because of the evidence of controlateral EMG changes. Frequently used F wave parameters ‘abnormalities were present only at about one third of patients, more frequent at those with bilateral changes according to MUP analysis and at those with a good correlation with imaging. Using the calculated F ratio, the proportion of patients showing abnormal values increased almost 3 fold. In the same way, considering only latency, amplitude changes, or the absence of H reflex, only one half of the patients had abnormal values. Calculating also the H index we noticed an increase in the number of cases with abnormal H reflex parameters.
Abstracts of Poster Presentations – Poster Session 45 – ENG

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segmental nerve stimulation and needle electromyography in Guillain-Barré Syndrome

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Question
As they are mainly performed at distal nerve parts, routine nerve conduction studies (NCS) can fail to detect the abnormalities of proximal nerve segments in patients with Guillain-Barré syndrome (GBS). And it is still not clear whether acute inflammatory demyelinating polyneuropathy (AIDP) has axonal loss. The aim of this study is to describe the electrophysiological characteristics of GBS using segmental nerve stimulation and needle electromyography.

Methods
26 patients with AIDP and 6 patients who initially be considered as acute motor axonal neuropathy (AMAN) were retrospectively reviewed. Demyelination at different segments (for median nerve: below wrist, wrist-elbow, elbow-axilla, axilla-Erb’s point, Erb’s point-anterior horn; for ulnar nerve: below wrist, wrist-below the elbow, below the elbow-above the elbow, above the elbow-axilla, axilla-Erb’s point, Erb’s point-anterior horn) were calculated.

Results
For patients with AIDP, number of demyelination from distal to proximal median and ulnar nerve segment was shown as: 14, 12, 16, 18 and 18; 14, 13, 17, 18, 18 and 19, respectively. conduction block (CB) was more common at Erb’s point and above the elbow of ulnar nerve. 21 patients had low compound muscle action potential (CMAP) amplitude. 5 of 12 patients had fibrillation potentials and positive sharp waves. For patients who initially be considered as AMAN, 1 patient had proximal demyelination (above the axilla).

Conclusions
This study shows that proximal segmental nerve stimulation was very important. In patients with AIDP, demyelination was more common above the elbow, CB was mainly observed at Erb’s point and axonal loss can be found in AIDP. For patients who initially be considered as AMAN, proximal NCS should be performed in order to reclassify the subtype of GBS.
P780
Ulnar nerve injuries in Guyon canal: a report of 20 cases.

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OBJECTIVE

Ulnar nerve injury in the Guyon canal is seldom encountered in clinical practice. Its symptoms can be nonspecific and usually include sensory loss to the small and ring finger, as well as impairment of motor function of intrinsic hand muscles.

METHODS

The authors present a series of 20 cases of the ulnar nerve injury at the Guyon canal. The diagnosis was based on electrodiagnostic testing which revealed severe ulnar nerve injury in the Guyon canal.

RESULTS

In the study group with the diagnosis of ulnar nerve injury at the Guyon canal, women constituted 60%, while 40% of men. The average age onset of symptoms was 53 years. Among the main causes of complaints should be replaced traumatic injury, damage arising from congestion or compression, in one case ganglion was observed. The principles of diagnosis and treatment in adjacent of wrist the damages of ulnar nerve were presented.

CONCLUSION

Electrodiagnosis is an important tool in identifying ulnar nerve lesions at the wrist but it needs supplementation of US or MRI tests.
Electrophysiological difference between acute inflammatory demyelinating polyneuropathy and chronic inflammatory demyelinating polyneuropathy

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Questions
There is little known about electrophysiological difference between acute inflammatory demyelinating polyneuropathy (AIDP) and chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods
Electrophysiological data of 19 patients with AIDP and 15 patients with CIDP were retrospectively reviewed.

Results
Slow motor conductive velocity (MCV), prolonged distal latency, low amplitude, conduction block, abnormal F waves and H reflex were often seen in two groups, but MCV in patients with CIDP was slower than in patients with AIDP (p<0.05), disappeared compound muscle action potentials (CMAP) (about 20%) and sensory nerve action potentials (SNAP) (more than 50%) were more common in patient with CIDP, especially at the lower extremities. About 20% patients with AIDP while 100% patients with CIDP had abnormal sensory nerve studies (NCS). Also fibrillation potentials and positive sharp waves were more common in patients with CIDP.

Conclusions
Patients with CIDP had more severe demyelination and axonal loss, especially at the lower extremities. Patients with AIDP had motor nerve demyelination while sensory nerves were relatively not involved, also axonal loss was not so common as in patients with CIDP.
P782
Lumbrical-interosseus motor latency
- a useful test when the motor response of APB is absent

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QUESTION
Is measurement of the lumbrical-interosseus latency a useful test in clinical routine?

BACKGROUND
The recording of lumbrical-interosseus latency is a sensitive test for carpal tunnel syndrome (CTS). The test has been shown to be especially useful in severe cases of CTS, when motor responses are absent from m abductor pollis brevis (APB).

METHOD
As part of implementing the lumbrical-interosseus motor latency in clinical routine at our lab, we examined 20 healthy volunteers aged 21-75 years, and an additional 59 patients referred for carpal tunnel syndrome with conventional nerve conduction studies as well as the lumbrical-interosseus motor latency.

RESULT
The sensitivity for CTS was slightly lower than our standard combination of CTS tests. However, in patients lacking median nerve motor responses from the APB, registration of the lumbrical motor response gave essential information about the diagnosis. This was the case for patients with severe CTS in our cohort, and also two additional patients (not in our cohort, but attending the outpatient clinic) with median-ulnar nerve anomaly and lack of median nerve innervation of the thenar muscles.

CONCLUSION
the lumbrical-interosseus latency is a useful test for severe cases of CTS and other patients with absent median nerve motor response of APB.
P783
The effect of surface round electrode locations in median nerve antidromic sensory nerve conduction study -an investigation with high density surface electrode-

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Objective

Although ring electrodes generally used in antidromic sensory nerve conduction studies of the hand, disposable surface round electrodes for recording, which offer numerous advantages in terms of infection control and usability, are becoming increasingly popular. Potentials elicited by surface round electrodes are strongly influenced their location whereas ring electrodes pick up mean potentials whole circumferences of the finger. However, no studies on optimal electrode placement for surface electrodes have been reported. The aims of this study were to clarify the current distribution on the finger and to determine optimal surface recording electrode placement in antidromic median sensory nerve conduction studies.

Methods

The sensory nerve action potentials (SNAP) were recorded in both hands of the ten healthy subjects evoked by median nerve stimulation at the wrist. The potentials were recorded from ring electrode at the base of the second digit as commonly used and disposable round surface electrodes (diameter 7mm) placed at 4 different locations (radial, volar, and medial aspects of the second digit, and radial aspect of the third digit).

To clarify precise current distributions, bipolar SNAP were recorded from both lateral aspects of the second digit by using high density surface electrodes (diameter 1mm, interelectrode distance 5mm).

Results

The latency and the amplitude of the SNAP delivered by surface round electrodes placed on midline volar aspect of the second digit were similar to measurements obtained by using ring electrodes. The responses delivered on radial aspect of the second digit had lower amplitude and shorter latency than responses using ring electrodes with statistically significance (P<0.001, paired t-test). The SNAPs delivered by high density surface electrodes placed on radial aspect of the second digit showed small amplitudes without initial positivity, suggesting a unique volume conduction of the current propagating along the medial aspect of the digit.

Conclusion

We presented that an electrical fields were not uniformly-distributed within human finger tissues by using high density surface electrodes. In case of use surface round electrode for SNAP recording, electrodes must be placed on the second digit volar midline.
Characterization of the action potential derived from anodal stimulation in orthodromic sensory nerve conduction studies

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Objective

The origin of the anodal action potential (anAP) elicited by submaximal orthodromic sensory nerve stimulation of median nerve is still mostly unknown. Because of its possible applicability to clinical studies, we considered worth to examine how various physical factors modify the anAP in comparison to the conventional cathodal action potential (caAP) of the same amplitude.

Methods

The study was undertaken in 15 healthy subjects, aged 21 to 52. As baseline, we applied electrical stimuli to the digital nerves of the third finger to record anAP and caAP of similar amplitude over the median nerve at the wrist. We examined the effects of stimulus duration and intensity, skin temperature and conditioning by a stimulus of the same characteristics. All changes in anAP and caAP were expressed in percentage of baseline.

Results

The anAP was facilitated by longer stimulus duration, but it reduced until disappearance with increasing stimulus intensity. Paired stimulation, with conditioning and test stimuli of the same intensity showed earlier recovery of anAP than of caAP, with significantly higher amplitude of anAP than caAP between 2 and 3 ms (figure1). Cooling or menthol application caused faster reduction of the anAP than of the caAP.

Conclusion

Our results suggest that the physiological properties of the fibers generating the anAP are different from those generating the caAP. This may be due to different modes of generating the action potentials or to activation of a different population of sensory afferents.

figure 1
A new, expanded, scale for grading the severity of neurophysiological changes in carpal tunnel syndrome derived automatically from nerve conduction data.

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Grading scales based on data obtained from nerve conduction studies are currently in use to show severity of changes seen in carpal tunnel syndrome. Commonly used Canterbury scale divides the severity of changes seen into six grades(1). Grading scales serve a useful purpose while communicating the results to the referring clinician. On the whole they take into account the reduction in velocities, prolongation of distal latencies and presence or absence of potentials. Reduction in sensory and motor amplitudes are taken into account only when they are extreme. The proposed new scale allows inclusion of moderate reductions in amplitudes while determining severity. It has the added advantage that it can be calculated automatically from the nerve conduction data obtained. It is based on a points system ranging from 0 to 10, 0 being no change to 10 being extremely severe.

Routine nerve conduction data obtained from 50 hands was graded using the new scale. The results were compared with conventional grading. The results show a very close correlation.

This new scale can be adapted for future longitudinal studies of management of carpal tunnel syndrome after further validation. It should be easier to use as the grades are calculated automatically from nerve conduction data. It can be easily incorporated in to ENG software generating and displaying the grades automatically. Further studies are required to ascertain whether this would help to show subtle but significant nerve conduction changes in carpal tunnel syndrome either during its natural history or following treatment.

A link to an online template that would generate the points on the scale when nerve conduction data is entered will be made available at the end of the presentation.


A neurophysiological grading scale for carpal tunnel syndrome.

Bland JD.
P786
The Effect of Commercially Available Electrodes on CMAP Amplitudes and Latency

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Objective/Question
A number of surface electrodes of varying shapes, sizes and recording areas are being used for nerve conduction studies. The aim of this study is to assess if the type of electrode has any influence on motor amplitude (baseline to peak) and distal motor latency.

Methodology
We investigated in 10 normal young subjects (Male and female, age range: 20-40), measuring four commonly used motor nerves (median-Abductor Pollicis Brevis, ulnar-Abductor Digiti Minimi, peroneal-Extensor Digitorum Brevis and tibial-Abductor Hallucis).

Five different electrodes with varying characteristics such as usability (disposable/reusable), fixed and variable inter-electrode distance, different surface areas and structure were used. These were 1. Standard Ag/AgCl EEG electrodes, 2. Disposable surface electrode Kendall Tyco, 12 mm, circular 3. Ambu Neuroline disposable surface electrode 15mm x 20 mm rectangular rounded edge, 4. Surface stick-on, disposable ECG electrodes 22mm x 22 mm square and 5. Medelec bar electrodes with fixed inter-electrode distance of 20 mm.

Nerve conduction studies were performed using Kimura’s standard belly tendon protocol.

Results
We conclude that there is no significant difference when using electrodes of size/shape with varying inter-electrode distances, provided standard belly-tendon protocol is used. However, Compound Motor Action Potentials are significantly lower using Medelec bar electrodes with fixed inter-electrode distance and this difference was minimal with median-APB motor study. Distal Motor Latency was not found to be significantly different depending on the type of electrodes used.

Conclusion
The findings support the use of these commercially available surface electrodes with varying inter-electrode distances in routine nerve conduction studies. However, Medelec bar electrodes, with fixed inter-electrode distance, were found to be inferior in the majority of motor studies.

References
Epileptic signatures in cerebello-thalamic activity of the \textit{Cacna1a}\textsuperscript{tottering} mutant mouse

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**Question**

Hyper-synchronized thalamocortical network activity underlies spike-wave discharges (SWDs) in electrocorticogram recordings (EEG) during epileptic absence seizures. Cerebral regions involved in this type of epilepsy have been explored (e.g., Paz JT, et al., 2007, Polack PO, et al., 2007), but still, little is known about a cerebellar role in absence seizures (cf. Kandel and Buzsáki, 1993). We examined if the monosynaptic connection allows the cerebellum to mediate thalamocortical oscillatory activity and thereby control absence seizures.

**Methods**

We set up experiments in homozygous \textit{tottering} (tg) mice; a validated mouse model for absence epilepsy (Noebels et al., 1979). Awake, head-restrained tg mutants frequently show spontaneously occurring SWDs in EEG recordings. Simultaneously, we extracellularly recorded single-unit activity of neurons in the cerebellar nuclei and the downstream thalamic nuclei. In addition, we recorded the effects of optogenetic control of cerebellar output by virally encoded channelrhodopsin-2 on the thalamic activity as well as on the cortical EEG.

**Results**

During absence seizures, we found that in a subset of recordings the action potential firing pattern of neurons in both cerebellar nuclei and thalamic nuclei were significantly modulated at 6-9 Hz, i.e., the representative frequency for SWDs in \textit{tg} mutants. In addition, we were able to modulate the occurrence of SWDs by optogenetic control of the cerebellar output.

**Conclusions**

Together, our study provides new insights in how cerebellar output is implemented in thalamocortical network activity and underline that this subthalamic input is of general importance for absence seizure epilepsy.
P788
Electro-clinical characteristics of epileptic seizures in preterm infants

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Question

Although neonatal seizures have been evaluated in more detail over the last decade, seizures in preterm babies are still poorly described. In clinical practice aEEG rather EEG is often used to make the diagnosis. The aim of this study was to assess electro-clinical characteristics of seizures in preterm babies occurring before a corrected gestational age of 40 weeks.

Method

In this retrospective study we analysed electroencephalographically documented seizures in 19 infants born prematurely between 24 and 36 weeks of gestational age (median GA 30 weeks, sex ratio 0.9).

Results

Our results showed that seizures are diagnosed later in preterm infants born before 32 weeks gestational age than in preterm infants born after 32 weeks gestational age. Median duration of seizures was of 60 seconds, increasing with corrected age. Seizures are focal or multifocal and can involve any part of the cortex. In the very premature infants, they usually stay more localised and involve smaller regions of onset. With the increasing post-conceptional age spreading becomes more frequent and later on also more widespread, giving evidence of the progress of myelination. The electrographic pattern also evolved with age. The maximal frequency of oscillation within the seizure increased with the corrected age which reflects maturation of the ion channels and neuronal network. Only one of nineteen infants displayed electro-clinical seizures, thus neurophysiologic monitoring is essential for accurate diagnosis of seizures in preterm babies.

Conclusion

Our data indicate that seizures in preterm babies are shorter, involved smaller regions of onset and stayed more localised the younger the preterm babies were making diagnosis with aEEG difficult.
P789
Interictal EEG activity is associated with mood disorders in temporal lobe epilepsy.

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Objective
Psychiatric comorbidities are frequent in temporal lobe epilepsy (TLE), and symptoms of these comorbidities may be related with epilepsy activity. Here we evaluate interictal EEG activity in TLE patients with or without psychiatric comorbidities.

Methods
Cohort study of 78 patients with TLE, evaluating wake/sleep interictal scalp EEG. All subjects were submitted to psychiatric structured interview (SCID) for the diagnosis of lifetime psychiatric comorbidities. Four major diagnostic categories were studied: mood disorders, anxiety disorders, psychosis, and alcohol abuse. We then evaluated differences among interictal EEG activity in patients with or without these psychiatric comorbidities.

Results
Non-frequent EEG interictal spikes, defined as less than one event per minute, were significantly associated with mood disorders in TLE (OR=5.20; 95%CI = 1.05 - 9.12; p=0.02).

Conclusions
Mood disorders in patients with TLE might be associated with low interictal spike frequency on EEG. Low intensity of seizure disorder has been associated with a decrease in interictal EEG discharges, and with an increase in psychiatric symptoms in TLE, a phenomenon known as forced normalization. Here we observed a neurophysiological correlate in line with forced normalization.

Significance
Low spike index in TLE might be a neurophysiological substrate for the complex relationship between epilepsy and depression, as expressed by the phenomena of forced normalization and bidirectionality between the two entities.
P790
Sustained photic driving after the cessation of the flashes in epilepsy

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Question
What factors can be associated with sustained photic driving, defined as harmonic driving lasting after the cessation of the flash, in patients with epilepsy?

Subjects
Three-hundred and seventy-one patients with epilepsy (194 males), age 37 ± 15 years old (mean ± SD), who visited epilepsy clinic and were recorded electroencephalography (EEG) with photic stimulation, were included. Controls subjects were 6 males and 5 females, age 36 ± 13 years old.

Methods
EEG was recorded with scalp electrodes set in International 10-20 system. Photic stimulation was performed by placing the stroboscope in front of the subjects' eyes which were closed. The frequencies of repetitive photic stimulations were 3, 6, 8, 10, 12, 14, 16, 18, and 20 Hz, each delivered for 10 sec with the pause of 10 sec.

Results
Sustained photic driving was notices in 31% of patients with epilepsy and 91% of normal controls. Duration of sustained photic driving was significantly longer in patients with epilepsy (243 ± 59 ms in patients, 161 ± 35ms in controls, p<0.005). By epilepsy classification, the duration was significantly longer in partial epilepsies (frontal lobe epilepsy, temporal lobe epilepsy, and parietal lobe epilepsy) and idiopathic generalized epilepsy than in normal controls (p < 0.005).

Conclusions
Sustained photic driving is a physiological phenomenon seen in normal subjects. Rarer occurrence or longer duration in patients with epilepsy may associate with their abnormality in synchronization or desynchronization.
A case of temporal lobe epilepsy with sudden diarrhea

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Question

Can temporal lobe epilepsy manifest with repeated episodes of sudden diarrhea and loss of consciousness?

Methods

A 63-year-old right-handed female presented with chief complaints of sudden diarrhea and loss of consciousness for almost three decades. The first attack occurred in her 30s and similar attacks repeated several times in a year. Her attacks comprised of abrupt abdominal discomfort, diarrhea, sudden emergence of old memories that she had played with her brother in her childhood, and loss of consciousness during defecation. She had no convulsion or automatism and fully recovered in a few minutes. Every time she was transferred to emergency hospital by ambulance, she had examinations such as blood test, head computed tomography, electrocardiogram, abdominal ultrasound, and electroencephalography (EEG), but no specific diagnosis was made. She was admitted to our hospital for further evaluation of epilepsy.

Results

Vital signs, neurological examination, and blood tests showed no abnormal finding. During long-term video-EEG monitoring for forty hours she had no habitual event. Interictal EEG showed intermittent irregular delta waves and sharp transients regional left antero-midtemporal area. Sharp transients were not as outstanding from background activities as to be definite epileptiform discharges, but they were reproducible in morphology and distribution, and appeared not only in sleep but also in awake. Brain magnetic resonance imaging was unremarkable. Brain Single photon emission computed tomography showed decrease of blood flow in left frontal and temporal lobes. Wechsler Adult Intelligence Scale-III showed decline of verbal comprehension. We diagnosed that the patient was suffering from partial epilepsy originating from left temporal lobe. Carbamazepin markedly improved her attacks.

Conclusions

Temporal lobe epilepsy can manifest with diverse autonomic symptoms and signs. Abdominal sensations often herald the onset of epileptic seizures. Among them is an uncommon syndrome called abdominal epilepsy, in which gastrointestinal complaints are the primary or the sole manifestation of epileptic seizures. In patients who complain with diarrhea and other autonomic symptoms otherwise unexplained, a possible diagnosis of epilepsy should be considered.
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P792
Diffusion Tensor Imaging and Tractography identify structural changes in cryptogenic focal epilepsy

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Question

Here we investigate the contribution of Diffusion Tensor Imaging (DTI) and Diffusion Tensor Tractography (DTT) in identifying abnormalities in MRI negative patients with cryptogenic extramesiotemporal focal epilepsies.

Methods

14 patients with cryptogenic extramesiotemporal focal epilepsy were investigated. DTI data was acquired on a GE Signa HDx 3T Scanner, using an acquisition scheme with 64 diffusion weighted directions, a b-value of 1000m/s², 2.4 mm slice thickness and 2 mm in-plane resolution. Fractional anisotropy (FA) maps were investigated for focal changes and asymmetries. Streamline DTT of the whole brain was used as an exploratory method in the absence of a structural lesion and the number of reconstructed streamlines in homologous anatomical areas of the left and right hemisphere were compared. Asymmetries of more than 10% for FA maps and more than 20% for the streamline count were rated as a significant finding.

Results

Asymmetries in the number of reconstructed streamlines were found in nine of the 14 patients (64%). In eight of them, these changes were consistent with the clinically suspected seizure onset zone, based on video-EEG-monitoring and nuclear medicine data, however, in two patients DTT indicated more widespread, hemispheric changes, beyond the seizure onset zone. FA maps show asymmetries beyond 10% in only one patient. In two patients, the seizure onset zone was confirmed in the area of DTT abnormalities by intracranial electrodes, the other patients are still awaiting invasive evaluation, including the one with discrepant DTI findings. 

Conclusions

These preliminary data show the potential role of DTI and DTT as complementary lateralizing and localizing imaging modality in the presurgical evaluation of cryptogenic extramesiotemporal epilepsy patients. We hypothesize, the observed changes reflect migration disorders, where heterotopic neurons disrupt the microstructural order of white matter underlying the seizure onset zone. Follow ups with intracranial electrodes and correlation with histopathology are required for further interpretation of these findings. DTT appears to be more sensitive than FA maps, and this method may be less sensitive in patients with small circumscribed focal pathologies compared to patients with a more widespread pathology.
Consistency over Time of Electroencephalographic Connectivity Measures in Temporal Lobe Epilepsy

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Objective

Connectivity biomarkers of the EEG have been shown to reflect seizure propagation and to indicate the source of abnormal hyperconnectivity. Nevertheless, it is questionable if these patterns are stable over time in different measures of connectivity. Moreover, it would be of interest whether the consistency over time is different in patients with epilepsy.

Methods

To address this topic we examined 9 healthy participants and 13 patients with temporal lobe epilepsy (TLE) on the right (5) and on the left (8) hemisphere. We calculated 14 measures of connectivity from two EEG-recordings separated by two weeks. We correlated these measures for each group and compared the correlations.

Results

We found most consistent results for Geweke’s Granger Causality. For this measure, consistency was found in a different network in healthy participants than in patients. Patients with a focus on the right side showed only a few consistent connections, mostly on the ipsilateral hemisphere, while patients with focus on the left side showed large bilateral consistencies, which was extended frontocentrally over the left hemisphere and parietooccipitally over the right hemisphere.

Conclusion

It is important to note that a higher consistency on the focal side does not indicate that the connectivity is higher in this region. Instead, it suggests that while the brain concert of information flow is generally variable, it may be even more variable in patients with epilepsy, with an exception on the focal region. There, the consistency of connectivity indicates that the pathological changes are a stable pattern in the EEG, being detectable for example with connectivity markers such as Geweke’s Granger Causality.

Legends

GGC consistency for patients with right- (figure 1) and with left-lateralized TLE (figure 2). x-axis: 2-40Hz; y-axis: correlations -1 to +1; green: not significant; red: significant correlations (FDR-corrected p<.00004).
New modified Heart Rate Variability analyses as detector of epileptic seizures.

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Tachycardia is often seen during epileptic seizures, but it is also a characteristic result of physical exercise. In order to assess whether focal epileptic seizures can be detected by short term moving window Heart Rate Variability (HRV) analysis, we modified the geometric HRV method, Lorenzplot, to consist of only 50 R-R intervals pr. analyzed window. From each window we calculated the Cardiac Sympathetic Index (CSI) and compared the maximum CSI of the patient’s epileptic seizures with that of the patient’s own exercise and non-seizure sessions as control. The 11 patients analyzed all had complex partial seizures (CPS) (30 temporal, 1 frontal) during their 1-5 days Video/EEG long term monitoring. All CPS with electroencephalographic correlation were selected for the HRV analysis. The CSI was correspondently calculated after each heart beat depicting the prior 50 R-R intervals at the time. CSI showed a higher maximum peak during seizures than exercise/non-seizure (103-256%) for 7 of 11 patients within 2 seconds before till 86 seconds after seizure onset time even though exercise maximum HR exceeded that of the seizures. The 7 patients with higher CSI maximum during seizures vs. exercise/non-seizure had a tendency of higher maximum HR during seizures than the remaining 4 patients. The results indicate a sudden and inordinate sympathetic shift in the sympathovagal balance of the autonomic nervous system just around seizure-onset for certain patients. This new modified moving window Lorenzplot-method seems promising as an easy and inexpensive way of constructing a portable ECG-based epilepsy alarm for certain patients with epilepsy who needs aid during seizure.

figure 1

Cardiac Sympathetic Index

\[
CSI = \frac{sd2 \text{ (longitudinal)}}{sd1 \text{ (transverse)}}
\]

All graphs are examples of Lorenz-plot (50 R-R intervals) for the same patient with positive outcome.
Human intracranial High Frequency Oscillations (HFOs) detected by automatic time-frequency analysis.

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**Objectives**

High frequency oscillations (HFOs) have been proposed as a new biomarker for epileptogenic tissue. The exact characteristics of clinically relevant HFOs and their detection are still to be defined.

**Methods**

We propose a new method for HFO detection, which we have applied to six patient iEEGs. In a first stage, events of interest (EoIs) in the iEEG were defined by thresholds of energy and duration. To recognize HFOs among the EoIs, in a second stage the iEEG was Stockwell-transformed into the time-frequency domain, and the instantaneous power spectrum was parameterized. The parameters were optimized for HFO detection in patient 1 and tested in patients 2-5. Channels were ranked by HFO rate and those with rate above half maximum constituted the HFO area. The seizure onset zone (SOZ) - as defined in the presurgical workup - served as gold standard.

**Results**

The detector distinguished HFOs from artifacts and other EEG activity such as interictal epileptiform spikes. Computation took few minutes. We found HFOs with relevant power at frequencies also below the 80-500 Hz band, which is conventionally associated with HFOs. The HFO area overlapped with the SOZ with good specificity > 90% for five patients and one patient was re-operated. The sensitivity was markedly higher than with analysis by the Staba detector in four patients and equal in two patients.

**Conclusions**

In accord with the literature, the HFOs detected in our patients are biomarkers for epileptogenic tissue. The fast computation and reasonable accuracy hold promise for the diagnostic value of the detector.
P797
Callosal regulation of contrast gain control in photosensitive epilepsy
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Question
Visual areas of the two hemispheres interact via the corpus callosum (CC), but the precise role of CC in visual processing is unknown. Despite the predominance of the excitatory phenotype of CC neurons, callosal fibers produce a disynaptic inhibitory postsynaptic potential via a local GABAergic cell. CC appears to transfer preferentially information related to high contrasts and low temporal frequencies. Here, we explored the possible involvement of CC in the pathogenesis of photosensitivity.

Method
We enrolled eight patients with photosensitive seizures (5 males and 3 females: mean age ± 1SD: 14.6±8.7 years); None of the patients had been previously diagnosed as having epilepsy and they were all drug-free at the time of experimental procedure. Eight age- and sex-matched healthy volunteers served as controls. Visual evoked potentials (VEPs) triggered by grating stimuli of different contrasts (K90-50-20%) were recorded in response to abrupt reversal (3 Hz) of a horizontal square wave grating (spatial frequency 2 c/deg), before and after functional inactivation of the occipital cortex of one hemisphere via low-frequency repetitive transcranial magnetic stimulation (rTMS; 0.5 Hz, 20’). rTMS was applied over left occipital pole, at the border between areas 18 and 17, where callosal afferents densely converge. VEPs were recorded in V1 before (T₀), immediately after (T₁) and 45’ following the completion of rTMS (T₂).

Results
rTMS has an inhibitory effect on VEPs amplitudes at all contrasts in the treated side (p<0.05). Remarkably, reduction of VEP amplitudes in the inhibited hemisphere was accompanied by an increase in VEP amplitudes in the contralateral side only at mid-high contrasts and this potentiation was higher in patients than in controls (K50%: two-way ANOVA, p=0.004; K90%; p=0.0012, followed by Holm-Sidak post-hoc analysis). The disinhibitory effect remained stable through the whole session both at mid (T₁: p<0.01; T₂: p<0.001) and high contrasts (T₁: p<0.001; T₂: p<0.001) and was also observed with hemifield visual stimulation (K50%: p=0.004; K90%: p=0.0012).

Conclusion
Our preliminary data seem to suggest a key role of CC in the contrast gain control machinery. In this connection, photosensitivity could be due, at least in part, to a functional impairment of interhemispheric processing.
An investigation of fear potentiated transcranial magnetic stimulation, blink and audiogenic startle reflex after successful surgery of mesial temporal lobe epilepsy

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Fearful facial expressions are danger signals that rapidly trigger a cascade of neurobiological processes defensibly associated with action preparation. Direct evidence for the activating effects of fearful facial expressions on the motor system has been shown with transcranial magnetic stimulation (TMS) and auditory startle reflex (ASR) studies[1,2]. The present study investigated blink reflex (BR), fear-potentiated motor evoked potentials (MEP) and ASR results after successful surgery of mesial temporal lobe epilepsy.

We have included 15 healthy volunteers and 12 operated mesial temporal sclerosis (MTS) patients without seizures. Mean age for patients was 36.9±8.9 and 29.8±9.3 for controls. The current TMS and ASR study investigated whether fearful facial expressions selectively increase corticospinal motor tract (CST) excitability in patients with hippocampal sclerosis (HS) who successfully underwent selective amigdalohipocampectomy operation. BR responses of patients were also compared with those of healthy controls. Changes in CST excitability using the MEP and ASR data were recorded.

Results showed significant selective increases in MEP and changes in ASR data to fearful facial expressions in healthy volunteers but not in the patients(P=0.96). All though blink response results were in normal range in both groups, a statistically significant difference was investigated between the healthy volunteers and the patients. These findings provide evidence for selective increases in ST excitability to threat and the importance of amygdala in CST excitability.


**P799**  
**ELECTROCLINICAL CHARACTERIZATION OF SLC2A1 MUTATION IN THREE PEDIATRIC PATIENTS**

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**QUESTION**

Glucose transporter 1 deficiency syndrome (GLUT1DS) is a metabolic disorder manifesting as cognitive impairment, acquired microcephaly, epilepsy, and/or movement disorder caused by mutations in the *SLC2A1* gene.

Since its first description, many EEG findings have been described including normal findings, slow background activity, ictal and/or interictal generalized and/or focal epileptic discharges and fluctuations over time.

We aim to describe the different VIDEO-EEG findings in three patients with the SLC2A1 gene mutation, being twins two of them.

**METHODS**

VIDEO-EEG recording of three patients with the SLC2A1 de novo gene mutation.

Patients 1 and 2: Two fourteen year old boys, monozygotic brothers, who described episodes of progressive weakness and incoordination, related to exercise more or less prolonged; they also explained daily episodes of brief decreased attention and stare, interrupting briefly activity, diagnosed of absence epilepsy at the age of 8 years old.

Patient 3: Ten year old girl, who was studied for delayed psychomotor development since 2 year old. At the age of 7 year old staring spells, consistent in eye closure, blink along with cephalic fall, up to 20 per day, were observed with partial response to VPA.

**RESULTS**

VIDEO-EEG recordings for patient 1 and 2 showed the following anomalies: focal intermittent slow waves in anterior regions and 2.5 - 4Hz generalized spike-wave (frontal prevalence) that worsen while the hyperventilation was performed and associated with clinical absence. Additionally, a benign variant normality was found.

These pathological findings disappeared for a short amount of time after the administration of oral glucose.

Patient 3 VIDEO-EEG recordings showed focal delta bursts with occasional superimposed sharp waves in posterior regions, ictal and interictal 3 Hz spike-wave generalized discharges which worsen during sleep and a background activity that fluctuates over time.

**CONCLUSIONS**

EEG findings in GLUT1DS are still variable although serial recordings over ages show changes that suggest this syndrome.

Screening diagnose is recommended in patients with clinical absence epilepsy with characteristic clinical features and suggestive EEG findings over time.
P800
Slow spindles’ cortical generators overlap with the epileptogenic zone in temporal epileptic patients: an electrical source imaging study

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Question
to determine whether temporal epileptic patients and normal volunteers display similar sleep spindles’ cortical generators as determined by electrical source imaging (ESI), and whether such generators overlap in epilepsy patients with the epileptogenic zone identified by ESI.

Methods
thirteen healthy subjects and eight temporal lobe pharmaco-resistant epileptic patients underwent a 256-channel EEG recording during a daytime nap. Spindles were visually scored and marked; categorization in slow (10-12 Hz) and fast (12-14 Hz) ones was done by independently bandpass filtering in the appropriate frequency band. EEG was segmented on the marker position, and segments separately averaged for each category. Cortical sources were estimated using LORETA on the MNI brain. Maximal intra- and inter-individual intensities were compared through the Wilcoxon matched pairs test (p < 0.05). The same procedure was performed for averaged epileptic spikes, obtaining their cortical source. Source generators localizations were statistically compared between epileptics and controls via a X² test, and source intensities through a Mann-Whitney t test for independent samples (p<0.05). Overlap of spindles generators and spike generator was performed via a binomial distribution test (p<0.05).

Results
multiple, concomitant and equipotent generators were detected in both populations for slow and fast spindles. While in normal subjects slow spindles had a persistent source over the frontal cortex, in temporal epileptics they displayed a preferential localization over the temporal cortices (p=0.035), as well as higher source amplitude in comparison to healthy volunteers (p=0.042). Interestingly, at least one of slow spindles’ generators overlapped with the epileptogenic zone (p=0.016) as obtained by ESI.

Conclusion
slow spindles, but not fast ones, in temporal epilepsy are mainly generated over the affected temporal lobe cortex, and display overall higher intensities than spindles generators in healthy individuals. These results point to the strict relation between physiological sleep and epilepsy, and could underlie cognitive implications.
MODULATION OF SLOW WAVE ACTIVITY IN FOCAL EPILEPSY

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Objective

Slow wave activity (SWA) is one of the best-characterized markers of sleep pressure. Studies in healthy humans sustain SWA role in synaptic plasticity, memory, learning and brain maturation. However, literature is poor about SWA modulation in patients with focal epilepsy. Focal epileptic patients depict learning deficits and both structural and functional brain changes (atrophy of the epileptic network areas, cortical hyper-synchronization, maladaptive-compensatory plasticity). Consequently, on the basis of the close link that both focal epilepsy and SWA share with local brain plastic phenomena, we investigated if such patients exhibit an altered SWA with respect to the site of epileptic focus.

MATERIALS AND METHODS

15 patients affected by cryptogenic focal epilepsy originating within temporal areas and 14 healthy volunteers have been recruited. All subjects underwent an entire night domestic 14 channels EEG recording. Power Spectral Density (PSD) analysis was applied on SWA for stage 2-3 of sleep.

RESULTS

Compared to healthy controls, epileptic patients exhibit higher amount of SWA in the “affected” hemisphere, ipsilateral to the epileptic focus, specifically located in the temporal regions. The analysis of the ROI covering the epileptic zone showed a strong SWA difference between the two groups only for the affected hemisphere. Finally, in epileptic patients the increase of SWA over the hemisphere ipsilateral to the epileptic focus is evident during the first two sleep cycles. As expected, healthy controls did not exhibit any inter-hemispheric SWA difference.

DISCUSSION AND CONCLUSION

Compared to healthy subjects, epileptic patients exhibit a clear SWA increase partially restricted to temporal areas, where the epileptic focus was located. This plasticity could represent a compensative mechanism aiming at counterbalance the continuous and aberrant behavior of the epileptic focus.

Figure

Bottom: Whole night and cycle by cycle SWA differences between Epileptic Patients (red dot and lines) and Healthy Controls (green dot and lines). Top: Spatial distribution of SWA difference between the two groups (first line) and level of statistical significance (second line). Topoplot left side corresponds to affected hemisphere, right side to unaffected hemisphere.
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figure 1
Transcranial parenchymal sonography in adolescents and young adults with juvenile myoclonic epilepsy

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Question
Abnormal neural networks in the thalamus, limbic areas, brainstem and cerebellum seem to be associated with JME. Cognitive and behavioral difficulties in JME are suggested to involve alterations in basal ganglia (BG) and midbrain structures.

Method
Forty-two JME patients (13 male, 29 female, aged from 15.5 to 42 years (mean 27.6) and 30 gender and age-matched control subjects were studied. Trans-cranial sonography (TCS) study by trans-temporal approach was performed using a color-coded phased array ultrasound system, equipped with a 2.5 MHz transducer, with preauricular position. Influence of clinical parameters in the JME group was analyzed.

Results
Substantia nigra was markedly hyperechogenic in 6 pts with size ranged 0.26-0.39 cm², while its hyper-echogenicity was moderate and mainly unilateral in additional 9 (>0.19 cm²). In all but 4 pts, hyperechogenicity of red nucleus was found. It was marked in 9 patients (echogenic size ranged 0.21-0.38 cm²), unilateral in 6 and bilateral in remaining three patients. Echogenic size of red nucleus from 0.08 to 0.20 cm² was noted in 26 (bilateral in 19). Low echogenicity of brainstem raphe (gradus 0) was found in 12 and correlated with depressive mood in 7 pts. No correlation of hyper-echogenicity of substantia nigra and JME clinical parameters was found. Differently, marked echogenic size of red nucleus in 6/9 was found in patients with incomplete seizure control, short remission and psychiatric disorders. Our findings seem to be independent of the antiepileptic medication and intelligence scores.

Conclusions
TCS in JME patients suggest additional non-lesional abnormalities of BG and midbrain structures. Echogenicity of red nucleus was associated with seizure control and psychiatric profile.
A Case Report of Schizophrenic-like Pathology with Epileptic EEG

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Personal history

His father died in a traffic accident in his infancy. His mother and sister had mental retardation. He grew up without the proper home training.

Physiological diagnosis

Hallucination, insomnia and uneasiness. The left side of his skull was deformed. EEG shows theta wave of left side showed band spike, small-spike, sss, and theta train, especially at occipital and parietal regions. On MRI, the left side cisterna is wide and his left third ventricle expanded. A white matter infarction was found.

Psychological diagnosis

He was developmental disorder according to his Rorschach test. He had no skill to adapt himself to the society, never trusted anybody, didn't know to defend himself from others' violence. He had inadequate way to communicate with others, he had no friend. The epilepsy apparently caused supraversion of eyeballs, absentmindedness, ceremonial behavior, obsessive manner, sudden shouting, some peculiar pose, perseveration, excitement, and impulsive behavior.

Conclusion

He seems to be F06.8 "Other specified mental disorders due to known physiological condition" (epileptic psychosis).
P804

Electrical Source Imaging in cortical malformation related epilepsy: a prospective SEEG-HR EEG concordance study

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**QUESTION**

Delineating the epileptogenic zone (EZ) in refractory epilepsy related to malformations of cortical development (MCD) primarily relies on intracranial EEG recordings. It is crucial to promote the development of non-invasive methods such as electrical source imaging (ESI). We aimed to (i) analyze the localization concordance of ESI derived from interictal discharges and EZ defined by stereoelectroencephalography (SEEG), (ii) compare the sensitivity and specificity of ESI, MRI and electro-clinical correlations (ECC), and (iii) assess ESI added value in the EZ localization.

**METHODS**

We prospectively analyzed 27 consecutive patients undergoing presurgical investigation for MCD-related refractory epilepsy in 2009-2012. ESI derived from 64-channel scalp EEG was interpreted blinded to- and subsequently compared with SEEG. Sensitivity and specificity of ESI, MRI and ECC were computed using SEEG as reference method. We further assessed the ESI added value to ECC and MRI.

**RESULTS**

Twelve (44%) patients had temporal and 15 (56%) extratemporal epilepsy. MRI was negative in 11 (41%) and revealed a cortical malformation in 16 (59%). ESI was fully concordant with the EZ in ten (37%) and partly concordant in 15 (56%). ESI presented a sensitivity and specificity of 93% and 48%. ECC and MRI presented a sensitivity of 96% and 56% and specificity of 19% and 37% respectively. Of 11 patients with negative MRI, ESI was fully concordant with the EZ in seven (64%), partly concordant in four (36%) and presented a 100% sensitivity and 64% specificity. ESI correctly confirmed, restricted or added localizations to ECC and MRI in 12 of 27 patients (44%) and in eight of 11 patients (73%) with negative MRI.

**Conclusion**

ESI constitutes a valid method to localize the EZ in MCD-related epilepsy. The added value of ESI to ECC was particularly high in patients with negative MRI, who represent the most challenging cases for epilepsy surgery.

Figure1: Illustration of a negative MRI case with full sublobar concordance of ESI and EZ, and confirmed ESI added value.
Abstracts of Poster Presentations – Poster Session 46 – Epilepsy 3

Figure 1

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**P805**  
**Pulsed arterial spin labeling perfusion MRI in patients with localization-related epilepsy**

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**Question**

In localization-related epilepsy (LRE), ictal cortical hyperperfusion is a marker for identifying epileptogenic zones. Pulsed arterial spin labeling-perfusion magnetic resonance imaging (PASL-MRI) is a noninvasive method that measures regional cerebral blood flow (CBF). We examined whether peri-ictal or inter-ictal PASL-MRI could identify epileptogenic zones in patients with LRE.

**Methods**

We examined 10 patients with LRE and lesions caused by epilepsy. The lesions were as follows: subcortical hemorrhage (4), cerebral infarction (2), cortical dysplasia (1), herpes encephalitis (1), glioblastoma (1), and cerebral contusion (1). In 9 patients, PASL-MRI was performed immediately after the ictal state and during inter-ictal states. One patient experienced a seizure during MRI and the ictal PASL-MRI was obtained incidentally. All patients underwent diffusion-weighted imaging (DWI) analysis after PASL-MRI.

**Results**

During the peri-ictal state, all patients showed areas of hyperperfusion on PASL-MRI that were adjacent to their lesions. Six patients showed normal findings or hypoperfusion on inter-ictal PASL-MRI in areas where CBF increased during peri-ictal states. Three patients showed epileptic abnormalities on EEG in regions that were almost concordant with areas showing hyperperfusion on PASL-MRI. Although 5 patients showed hyperintense areas on DWI, the remaining 5 patients failed to show hyperintense areas where PASL-MRI showed hyperperfusions.

**Conclusion**

Although this study included a small sample size, PASL-MRI revealed significant changes in inter-ictal or peri-ictal states in patients with LRE and lesions. Thus, PASL-MRI is useful for identifying an epileptic focus.
P806
Effects of Spike Averaging on EEG, MEG and Combined EEG/MEG Source Analysis of Epileptic Activity

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Question
In most source localization studies either each interictal spike was localized separately or all spikes were first averaged (grand-average) and then localized. The former might give an estimate on the size of the irritative zone while the latter benefits from improved signal-to-noise-ratio (SNR). We chose a compromise between those by using sub-averages and compared its performance with single and grand-averaged spikes. Moreover we investigated if combined EEG/MEG (EMEG) has advantages compared to single modality EEG or MEG localizations.

Methods
A patient suffering from pharmaco-resistant focal epilepsy has been measured with simultaneous EEG (80 Electrodes) and MEG (275 gradiometers), and afterwards with stereo-EEG (sEEG) (167 contacts). We constructed a six compartment finite element head model which comprises anisotropic white matter derived from diffusion-tensor-MRI and calibrated the skull conductivity via somatosensory-evoked-responses. A bootstrap algorithm was used to calculate multiple sub-averages with varying number of spikes (1-50). We localized from the spike onset to the peak at 11 time instants.

Results
EMEG localizations were closer to the center of the irritative and seizure-onset zones, as estimated from sEEG, than EEG and MEG alone. Localizations obtained with different sub-averages differed considerably from each other and single spike localizations were localized more superior and deeper than sub-average results. The localizations at the spike onset and peak differed from each other and the scatter size was highly correlated to SNR.

Conclusions
Combined EEG/MEG source analysis can increase accuracy and confidence in the localization result. We have seen that using spike onset instead of peak could help avoiding mislocalizations due to propagation. The SNRs of single spikes at the onset are not always sufficient for reliable localizations and therefore, averaging should be performed. Sub-averaging might provide important and accurate information that neither single nor grand-averaged spike localizations can supply. The size of the dipole scatter depends highly on SNR; thus, one should be very careful interpreting this.

Acknowledgements
This research was funded by German Research Foundation (DFG) projects WO1425/2-1 and STE380/14-1, and Ruhr University Bochum FoRUM K062-11.
P807
Basal ganglia in temporal lobe epilepsy - SEEG and fMRI studies

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Epileptic activity may affect the basal ganglia (BG) as well as large-scale brain networks.

1. In the fMRI study the impact of epilepsy on the functional brain connectivity (FC) of the BG in two large-scale networks, the default mode network (DMN) and somatomotor network (SMN), was studied control subjects (HC) and patients with TLE. In HC, the BG were functionally negatively correlated with typical DMN regions. This negative correlation as well as the FC between the BG and SMN was significantly lower in patients [3].

2. SEEG studies: The human striatum and pallidum did not generate specific epileptic EEG activity, neither interictal nor ictal. The visually observed slowing and amplitude increase in the BG was found with the spread of the epileptic activity from the hippocampus to other areas [1]. Significant frequency components of 2-10 Hz were constantly observed in the BG [2]. The frequency of this component slowed by around 2 Hz during seizures. There was a significant ictal increase of power spectral density in all frequency ranges. The changes in the BG were consistent while the seizure activity spread over the cortex, and they partially persisted after the clinical seizure ended. They were inconsistently present in the first period after the seizure onset.

Significance: Unlike in HC, in TLE the BG are not correlated with a DMN component, and the FC of the BG is decreased with SMN. The epileptic process reduces the FC between the BG and large-scale brain networks. This may reflect an altered function of the BG in epilepsy. Based on our SEEG studies, the time course of the oscillatory activities together with the absence of the epileptiform EEG activities in the BG lead us to suggest an inhibitory role of the BG in temporal lobe seizures. The BG should be seriously considered as a potential target for neuromodulatory and pharmacological treatment of TLE.


Cortical substrates of interictal spikes in frontal lobe epilepsy: a simultaneous subdural- and scalp-EEG study

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Question

To assess the visibility and detectability in scalp EEG of cortical sources in frontal lobe epilepsy as to their localization, and the extent and amplitude of cortical activation.

Methods

We analyzed the simultaneous subdural and scalp interictal EEG recordings of 14 patients with refractory frontal lobe epilepsy associated with focal cortical dysplasia. Subdural coverage included a grid electrode over the lateral convexity and additional medial and orbito-frontal strip electrodes in ten and four cases respectively. Scalp EEG was mounted according to the 10-20 system. Subdural spike types were identified and averaged for electrical source localization and detection of their scalp EEG correlates. Both raw and averaged scalp EEG segments were reviewed for spikes, blinded to subdural segments. The area of dorso-lateral cortical activation corresponding to a scalp-detectable spike was determined from the number of subdural grid contacts involved in the electrical field. We further analyzed the correlation of spike-to-background amplitude ratios in subdural and scalp EEG.

Results

We identified 36 spike types in subdural EEG recordings, corresponding to 29 distinct sources. Four of 29 sources were visible by visual evaluation of scalp EEG and an additional six sources were detectable after averaging: four in the medial frontal, two in the dorso-lateral gyri, two in the depth of dorso-lateral sulci and two in the basal frontal region. Cortical sources generating scalp-detectable spikes presented a median of 6cm² activated surface of cortical convexity and a subdural spike-to-background-amplitude ratio over eight. These sources thus presented a higher number of activated subdural grid contacts and a higher subdural spike-to-background amplitude ratio than sources generating non-scalp-detectable spikes.

Conclusions

Our study showed that not only dorso-lateral but also basal and medial sources can be detectable in frontal lobe epilepsy. This is the first in vivo demonstration derived from simultaneous subdural and scalp EEG recordings of the complementary significance of extensive source activation and higher subdural spike-to-background amplitude ratio in the detection of cortical generators in frontal lobe epilepsy. Our findings contribute to the decoding of interrelations between cortical sources and their scalp EEG correlates and thus to the interpretation of scalp EEG in the presurgical evaluation of refractory frontal lobe epilepsy.
P809
Altered connectivity patterns during partial seizures with different types of impaired consciousness as ictal correlate.

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QUESTION
Are the connectivity patterns altered differently in different types of ictal consciousness impairment?

BACKGROUND
Consciousness is a central concept in epilepsy: transient loss characterizes generalized seizures and different types of consciousness impairment may occur during partial ones. Jackson postulated a “consciousness dissociation” caused by electrical disturbances at higher levels in hierarchical neural networks. The EEG breakthrough generated evidence of ictal experiential phenomena in focal epilepsies, raising several physiopathogenic hypotheses. Yet, even with intracranial recordings and electrical stimulation studies, the mechanisms of impaired consciousness remain elusive. Experiential phenomena defy focal interpretations. Current models consider brain function as the result of multiple processes in hierarchical modular assemblies with dynamical non-linear interactions. Flexibility and complexity are no longer obstacles within this framework.

METHODS
LORETA current source density correlations (CSDC) were calculated (Pearson) among Regions Of Interest (ROI) during EEG documented seizures with psychic content in 10 psychiatric patients, no history of epileptic or neurological disease. The Ictal Consciousness Inventory was applied scoring level (ICI-L) and content (ICI-C) of consciousness, psychotic features were extracted from the Positive and Negative Symptom Scale (PANSS-P), analyzed with ANOVA.

FINDINGS
Seizures defined by EEG ictal activity were accompanied by psychic changes in all subjects, no motor component. Psychic changes and CSDC patterns differed among patients. Decreased CSDC among structures of the Default Mode Network (DMN) were related to decreased ICI-L. Different patterns of increased CSDC among limbic and midfrontal ROIs were related to ICI-C and PANSS-P scores.

CONCLUSIONS
Our findings suggest that: 1) various types of consciousness impairment can be ictal correlates in partial seizures, 2) ICI-L, ICI-C y PANSS-P may vary independently, 3) variations correlate with different patterns of altered connectivity among ROIs, 3) DMN structures modulate ICI-L, 4) ICI-C and PANSS-P are independently related to altered CSDC within networks known to be related to monitoring and integrative processes.
We reported a paediatric series of invasive intracranial electroencephalographic (EEG) explorations with depth electrodes in patients of less than 5 years old (group 1, n=21) presenting refractory focal epilepsy. Children were explored with invasive EEG before surgery in the past 2 years in our institution. We compared their data to the one obtained with children more than 5 years old (group 2, n=44), explored during the same period of time.

In group 1, the mean age was of 39 months (range 20 to 60 months), and included 5 children presenting infantile spasms. In 24% of the group 1, scalp electrodes recorded bilateral EEG foci, and in 38%, multifocal interictal foci. Seizure onset was unique in 76% of the group 1, and multifocal inside a unique region in 19%. Therefore, the invasive exploration was wider in the group 1, as electrodes were implanted in at least 3 lobes and up to 4/5 lobes (76%). Only 2 patients were turned down for surgery after EEG, despite the great number of the patients (28%) with multifocal seizures onset. Subclinical seizures were very frequent since they are recorded in 67% of the children. In addition, the ictal onset was more heterogeneous in group 1 than in adults and the classic low voltage fast rhythms discharge could be missing. We were able to evoke seizures by electrical stimulation in 33% of the group 1. Cortical motor mapping was performed even in children less than 5 years old and motor response was evoked in 100% of the cases. After surgery, the follow-up lasted 26 months on average. The outcome in group 1 was Engel 1 for 76% of the children, whereas only 59% of the group 2 were seizure free.

In conclusion, children younger than 5 years old could be explored with intracranial EEG as well as could the oldest ones, even if electric and clinical correlations were more difficult regarding to the age. Group 1 outcome after epilepsy surgery seemed better than with group 2, even if they showed multifocal regional abnormalities, both on scalp and intracranial EEG. Apart for 2 patients, the others had no clearcut limits on the MRI and the EEG led to more wide tailored resection than a simple lesionectomy. Suitability of stereo-EEG and more frequent MRI abnormalities in youngest patients allowed a better guidance of the surgical process.
Pre-ictal changes of HRV rhythms in children with temporal lobe epilepsy

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Question

This study was undertaken to demonstrate that a combination of time-variant, frequency selective, linear and non-linear approaches can ameliorate the analysis of heart rate variability (HRV) in patients with epilepsy in order to reveal premonitory information regarding an imminent seizure and to provide more information concerning the mechanisms leading to changes of the autonomic nervous system. The combined approach should allow new insights into specific short-term patterns of HRV during pre-ictal, ictal, and post-ictal states.

Methods

10 min epochs (5 min before: pre-ictal state, 5 min after seizure onset: seizure and post-ictal state) of pediatric patients (≤18 years at age) with clinically ascertained temporal lobe epilepsy (TLE) due to mesial temporal sclerosis (MTS) - all of them at least 12 month seizure free after temporal lobe surgery - were investigated. EEG data were collected during presurgical video-EEG-monitoring. The continuous Morlet-wavelet transform was used to explore the time-frequency characteristics of the HRV using spectrogram, phase-locking, band-power and quadratic phase coupling analyses. These results are completed by time-variant characteristics derived from a signal-adaptive approach. Advanced empirical mode decomposition was utilized to separate out certain HRV components, in particular blood-pressure-related Mayer waves (≈ 0.1 Hz) and respiratory sinus arrhythmia (≈ 0.3 Hz). Their time-variant non-linear predictability was analyzed using local estimations of the largest Lyapunov exponent (point prediction error).

Results

18 children (median age 9 years 4 months; median seizure length 88 s) were included. Approximately 80 - 100 s before the seizure onset timing and coordination of both HRV components changed. A higher degree of synchronization was found and with it a higher predictability of the HRV. All investigated linear and non-linear analyses contributed specifically to these results.

Conclusion

Changes of organization (grouping) and signal properties of Mayer waves during the pre-ictal period can be seen as premonitory information regarding an imminent seizure in children with mesial TLE. Our approach serves as a starting point for further studies including not only HRV but also other autonomic parameters.
Usefulness of movement and heart rate as physiological signals to detect nocturnal epileptic seizures.

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Background

Many research groups focus on automatic seizure detection and prediction in scalp- and intracranial EEG for diagnostic purposes and novel closed-loop treatment options. Many patients with regular, intractable seizures, especially children with epilepsy syndromes and patients with cognitive impairments, have nocturnal seizures. Reliable seizure detection will provide a major step in patient safety, care, quality of life and disease management. In these patients invasive or uncomfortable EEG-sensors do not seem feasible, especially not in the near future. The use of other physiologic signals is investigated for automatic seizure detection. Heart rate and movement can be measured with simple and non-burdensome sensors making them very applicable for long-term monitoring of vulnerable patient groups.

Methods

ECG, accelerometer (movement sensor, ACM) and video data was collected with simultaneous clinical video-EEG as a gold standard. All generalized tonic, tonic-clonic, hypermotor and clusters of tonic seizures were included for detection. Seizures were scored for clinical relevance by an expert panel. Four features were extracted: heart rate, waveformlength (from ACM) and normalized energy of frequency for 2-10 Hz (from AVM and video after optical flow analysis). Features were calculated for 2-second epochs and -2, -4, -6, -8, and -10 second values were added as extra features. A non-linear SVM with 5-fold cross-validation for optimisation of parameters was used to identify an optimal combination of thresholds.

Results

Data was collected in 92 patients. 20 patients had major seizures and were included for interim analysis (191 hrs and 47 min of recordings). Initial analysis yielded a sensitivity of 61% and a false alarm rate of 1.3 per 24 hours for all included seizure categories. Only considering clinically relevant seizures yielded a sensitivity of 73%.

Conclusion

A combination of non-EEG physiological signals movement and heart rate seems feasible for automatic seizure detection in a home setting. Higher sensitivity and lower false alarm rates are needed for algorithms to be implementable in a workable seizure detection device. Currently, survival-analysis is investigated as a tool to improve detection rate and usefulness of HRV-features to increase yield of our algorithms.
Neurophysiological aspects of tuberous sclerosis complex

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Individuals with Tuberous Sclerosis Complex are associated with neuropsychological features as epilepsy, mental retardation, autism and other commonly cases are due to spontaneous mutation., psychological disorders.

Question: This study aims to assess neuropsychological features of Tuberous Sclerosis Complex and to correlate the psychological findings with neurological manifestations.

Methods: This descriptive study was conducted on patients of only definitive Tuberous Sclerosis Complex of both sexes.

Inclusion criteria: All the patients of both sexes included in the study follow the diagnostic criteria for TSC that have been revised (Roach and Sparagana, 2004).

Results: A group of twenty individuals in the pediatric age group with definitive TSC were included in the study, 12 males (60%) and 8 females (40%). Patients complaining of seizures were 18/20 presenting 90% of cases. Infantile spasms was the most common type of seizures representing 13/20 (65%). Infantile spasms were detected in all cases with moderate to severe (significant) mental retardation representing 100%. As for mild mental retardation, infantile spasms were present in 50% of cases. The mean number of tubers was significantly greater among individuals with mental retardation than among those without (P value= 0.005). All autistic patients had epilepsy with an EEG showing hypsarrhythmia.

Conclusion: There is a significant relationship between the number of tubers and epilepsy. The presence of more number of tubers is a risk factor for the development of infantile spasms or onset of seizures below one year. Patients of TSC with seizures are having higher incidence of mental retardation especially if they started below six months of life. There is no significant relation between the presence of autism and epilepsy especially infantile spasms, neither nor significant relationship between the number of tubers and autism. The presence of tubers in the temporal lobe might be associated with autism. The results show the presence of the temporal lobe tubers is most probably a necessary but not sufficient risk factor for the development of autism.
LP70
Post traumatic epilepsy due to traumatic brain injury by traffic accidents in neurophysiological explorations laboratory of Marrakesh university hospital

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Introduction
Post traumatic epilepsy (PTE) is defined by two or more unprovoked seizures after a brain traumatic injury (BTI). PTE after TBI can be secondary to traffic accidents. Its prevalence of 4 % increases after penetrating brain injury. Cortical lesions play a role of the genesis of the PTE. Morocco face a real “Road War” and Marrakesh city and its region is especially known by traffic accidents of motorcyclists.

Aim of the study
Was to analyze some characteristics of PTE cases secondary to TBI caused by traffic accidents in the area of Marrakesh city.

Patients and methods
retrospective Study on the cases of PTE registered over one year in the laboratory of neurophysiological explorations of Marrakesh university hospital. All cases had an electroencephalography (EEG) with selection of the cases associating epileptic seizure caused by TBI.

Results
Among 385 patients with epilepsy who had an EEG, 11 cases were associated with a TBI caused by a traffic accident (Among a total of 20 cases with TBI). TBI was severe in 9 cases. The average age of patients was of 27.5 years (ranged from 17 to 72 years) with a male predominance (10 cases). PTE diagnostic delay was of 4 years after the accident. Epilepsy seizures were mainly partial (9 cases). The neurological examination was normal in 5 cases. Elsewhere we found confusion (2 cases), a limb motor paralysis (2 cases), pyramidal signs (1case) and multifocal lesions (1 case). The EEG confirmed partial paroxystic abnormalities in 8 cases and was normal in 3 cases. All patients have a cerebral CT scan showing hemorrhagic contusions (3 cases), depressed skull (2 cases), frontal hematoma (2 cases). Five patients were treated by valproate at the time of the realization of the EEG.

Discussion
Traffic accidents constitute a significant cause of deaths and disabilities in Morocco with 3000 victims dying and almost 62 222 injuries every year. PTE caused by traffic accidents constitute 55% of all PTE secondary to TBI in our series over one year which is similar to rate of some other African countries less developed than Morocco (62 % in Tanzania for example). The incidence is known to increase with the severity of the TBI and the presence of hemorrhagic contusions and depressed skulls. AED prophylaxis seems not to be effective in preventing the late unprovoked seizures and PTE. Most used AED are phenytoin, valproate and carbamazepine.

Conclusion
PTE due to traffic accidents was seen in 55 % of all TBI cases seen in our neurophysiologic laboratory. The majority of victims of this “road war” are young active males with severe consequences in Marrakesh region. In spite of the deployed efforts to decrease road deaths, more prevention is needed with an early diagnostic and treatment of the PTE victims.
Somatosensory stimulation during routine EEG enables evaluation of secondary somatosensory cortex activation in extremely preterm babies at term

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With MEG we have shown earlier that secondary somatosensory (SII) response evaluation is useful in predicting neurodevelopmental outcome in extremely preterm infants. We examined whether, based on the knowledge gained with MEG, SII responses can be evaluated from multichannel somatosensory evoked potentials averaged from routine neonatal EEG that included electrical median nerve (MN) stimulation (so-called EEG-SEP).

Seven infants born extremely preterm (<28 weeks) underwent at term age routine EEG with 10-20 system electrodes, during which their median nerves were stimulated electrically. The interstimulus interval was 1 s in 7 and 2 s in one infant. All of these infants had had SII responses in MEG at term. SII responses from EEG-SEP were evaluated in quiet sleep stage (QS), which was available for four infants for right and six infants for left MN stimulation. In addition, one healthy newborn was studied.

Primary somatosensory cortex (SI) SEPs were present in all infants. The contralateral SII response in EEG-SEP was detected in all four infants to stimulation of the right MN and 4/6 infants to stimulation of the left MN. Ipsilaterally, the SII response was present in EEG-SEP to stimulation of the left MN in 2 of the 3 preterm infants in whom it was present in MEG. The healthy newborn had contralateral SII responses to stimulation of both hands.

EEG-SEP - i.e. a routine EEG with median nerve stimulation and averaging of SEPs - can be used to detect not only SI but also SII responses.
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P815
Automatic detection of change in emotional expression: comparison of different vMMNs

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Question

A large variety of changes of features in stimulation elicit in the brain a deviance-reflecting event-related potential (ERP) component known as the mismatch negativity (MMN). We asked whether visually presented schematic faces (neutral, happy, and angry; adapted from OEhman et al., 2001) elicit the automatic deviance detection in the brain (visual MMN) and whether obtained visual MMNs depend on stimuli and different comparisons (extending our recent findings from Kreegipuu et al., 2013).

Methods

Eleven observers (19-32 years, six women) took part in two experiments, in a traditional oddball design with frequent standard and rare target and deviant stimuli (12.5% each) and in an version of an optimal multi-feature paradigm with several deviant stimuli (altogether 37.5%) in the stimulus block. Stimuli were rapidly presented schematic faces and an object with face-features that served as the target stimulus to be detected by a button-press. Four different vMMNs were found and compared to each other: (1) An emotional schematic face (deviant) compared to a neutral standard in the same session; (2) Reversed design, i.e., a neutral deviant compared to an emotional standard in the same session; (3) An emotional schematic deviant stimulus compared to the same stimulus as a standard in another session; (4) An emotional schematic deviant stimulus compared to the same stimulus as a standard in the same session;

Results

(1) Differently calculated vMMNs differ from each other; (2) Allocation of attention to the angry stimulus was hard to avoid; (3) Automatic visual change detection was the most powerful during 140-260 ms after stimulus onset and at the posterior (P, O) sites); (4) Emotional faces were more efficient in eliciting vMMN in the brain than the neutral schematic face.

Conclusions

vMMN is affected by the way it is calculated. When interested in studying change detection in facial expressions we encourage the use of the optimum (multi-feature) design in order to save time and other experimental resources. Multi-feature design has obvious advantages in clinical settings.

References


1114
P816
Integration of an eye tracker with multichannel recordings of pattern VEPs in young infants

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Objective

Prior studies have shown that using patterned stimulation, especially orientation reversal, global form and motion, makes it possible to study cortical visual processing in a systematic fashion. This has raised an interest to use the paradigms in neurodevelopmentally compromised children known to develop visuospatial disabilities arising at cortical level. Our goal was to improve the reliability of such VEP recordings closer to the level required for clinical use by integrating an eye tracker to the EEG setup, which enabled us to develop the analysis methods, as well as the whole experiment workflow more suitable for studies on young, poorly cooperative infants.

Method

Healthy 3-month-old babies were presented continuous VEP stimuli orientation reversal and global form and motion paradigms.[1,2] The presentation was performed with the eye tracker and started upon fixation. The gaze coordinates were measured and synchronized with the 20 channel EEG recording. The collected gaze data was utilized in real time to control the interactive experiment and later in the EEG analysis. The presence of VEP responses was assessed using the circular-variance test and Fourier-based signal-to-noise-ratio calculation.

Results

The hereby developed workflow leads to considerable improvement of the experiment making it possible to i) control the study in real time without direct interaction with the baby, ii) present the stimuli so that the baby is fixated in an appropriate way, and iii) analyze the data in a selected fashion to improve the signal analysis. The quality of the analyzed data (the amount of gaze fixation on the stimulus) was improved by 50% by optimization of the EEG epoch selection compared to the way where the whole data was analyzed. In some cases this enabled us to detect the presence of a VEP response that we would have missed without the gaze data.

Conclusion

Our experience is encouraging in that eye tracking based VEP studies hold promise for improving the quality of early infant assessment in the clinical neurophysiology laboratories.


Development of visual P2, P3b and P3b components in a novelty detection paradigm in children

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Development of visual P2, P3b and P3b components in a novelty detection paradigm.

Question

The present study pretends to analyze the development of the late positive visual components P2, P3a and P3b in childhood.

Methods

One hundred and sixty seven subjects aged between 6 and 26 years old were recorded with 30 electrodes during a visual novelty paradigm, similar to the visual odd-ball.

Results

Behavioral results showed a decrease of RTs and errors with age. The sensitivity parameter d' increased with age and the response bias parameter C evolved from conservative to neutral bias with age. The modulation of the fronto-polar P2 by the target condition was statistically significant in all the age groups except for children (6-9 years). The P3a component was statistically significant in the young adult (18-21 years) and adult (22-26 years) groups. The P3b component was statistically significant in all the age groups, from 6 to 26 years old.

Conclusions

The results reveal differences in cognitive evaluation of the stimuli presented depending on the age of the subjects, as indexed by ERP components. The target condition modulation of the frontally distributed P2 and P3a emerges later in time with respect to the posteriorly distributed P3b, probably related to the postero-anterior gradient of cortex maturation.
P818
Neurological involvement in Systemic Lupus Erythematosus and primary Sjogren's Syndrome: an electrodiagnostic study with neurologically asymptomatic patients

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Question

Primary sjoegren syndrome (pSS) and systemic lupus erythematosus (SLE) can be complicated with neurological involvement. The prevalence for complications are reported to be 8.5-67% in pSS(Gono et al,2011) and 14-90% in SLE(Joseph & Scolding, 2010). In this study we tried to detect neurological involvement in SLE and pSS patients without neurological manifestations by the help of electrodiagnostic tests.

Methods

27 patients with pSS (27 female) and 13 (11 female) patients with SLE were enrolled. Neurological examination, conventional motor and sensory nerve conduction study, motor evoked potential (MEP) study were performed.

Results

Mean values for age were 54.2 (±8.18) for pSS patients and 41.8 (±12.08) for SLE patients. There was no neurological abnormality in physical examination. Nerve conduction velocities were pathologic in 17 (63%) pSS and 10 (77%) SLE patients. However only one patient with pSS was diagnosed with axonal sensory-motor polyneuropathy. Central motor conduction times (CMCT) were prolonged in upper limbs of 3 patients with pSS and lower limbs of 6 patients with SLE, 9 patients with pSS.

Conclusion

In the literature it is claimed that subclinical neurophysiological dysfunction can be detected by electrodiagnostic tests. However all pathological results cannot be named as neurological involvement. In our study we found prolonged CMCT and pathological results in nerve conduction studies. As we do not have any imaging evaluation we could not accept all of these pathological test results as neurological involvement of pSS or SLE.


Auditory brainstem evoked response in autistic children in central Saudi Arabia

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Question

Autism spectrum disorders (ASD) are a behaviorally diagnosed prior to 36 months of age. Several reports have proposed brainstem or midbrain dysfunction as the underlying pathology in ASD. The present study aimed to determine whether autistic children have difficulty in processing auditory sensory signals.

Method

The study was conducted on twenty-two children, age up to 10 years old, with confirmed professional diagnoses, according to diagnostic criteria DSM-IV and (Childhood autism rating scale) CARS. Auditory brain stem potential (ABR) was carried out under sedation (chlorohydrate 50 mg/kg body weight), using manoaural click stimuli with vertex, earlobe electrode placement. An evoked response audiometry was carried with click stimulus at 20, 40, 60, 80 dbs. Fine waves were recorded, absolute latency and interpeak latencies, prolongation of interpeak latencies I-III or III=V, all were measured.

Results

The hearing threshold for normal children and autistic was 20 dB. In all autistic subjects, waves I-V were within normal range, and the interpeak latencies were within normal, as compared to normal subjects. No interpeak latency abnormalities were recorded, and the latencies of peak I, III, and V were within the average range in both cases.

Conclusion

Despite the fact that no abnormalities were found in the autistic children examined, this does not rule out the presence of brainstem dysfunction in ASD. One of the major limitations for the current study is the small number of autistic children enrolled. Another study with larger numbers is strongly recommended to gain better knowledge and understanding of autistic children’s hearing and behavior patterns.


Table 1 - Auditory evoked potentials study in autistics as compared to controls (values are mean ± standard deviation).
P820
WITHDRAWAL REACTION IN RESPONSE TO A SINGLE NOCICEPTIVE STIMULUS IN MYELOPATHY

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QUESTION
In most cases the study of patients with myelopathic conditions is restricted to the evoked potentials (EP), i.e., electrical stimulation to evaluate afferent pathways and transcranial magnetic stimulation to evaluate efferent pathways. We considered that nociceptive stimulation would give us a better understanding of pathophysiological mechanisms of spinal withdrawal reflexes in patients with these conditions.

METHODS
We studied 16 patients with myelopathy (10 adrenomyeloneuropathy, 4 syringomyelia, one with a gunshot lesion at the dorsal spine, one patient affected by post-traumatic Brown-Sequard syndrome) and 5 normal subjects.

We recorded the withdrawal reflex responses evoked in the tibialis anterior muscle by either single laser stimuli to the lateral leg or electrical stimuli (single and trains) to sural nerve.

RESULTS
In patients, a withdrawal response with a minimum mean latency of 144 ms was evoked in all subjects by nociceptive stimuli at 1.5 times threshold intensity. No responses were elicited by single electrical stimuli at 6 times threshold intensity, while those obtained with trains of stimuli at an intensity 6 times perception threshold were less stable than laser evoked responses. Healthy subjects had no responses to laser stimuli, while those to trains of electrical stimuli had a minimum latency of 95 ms.

CONCLUSIONS
Single laser stimulation can evoke a withdrawal response in myelopathic patients, not elicited in normal subjects, at latencies compatible with a spinal cord reflex mediated by thinly myelinated fibers.

Inputs from purely nociceptive volleys may have easier access to subcortical integrative sensorimotor centres than those generated by mixed volleys from electrical stimuli.
Recognition of vocal emotional cues in children measured by ERPs

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**Objective**

Attention modulation to emotional stimuli is considered a critical aspect of understanding intentions and feelings of others. Little research has investigated children’s developmental performance to discriminate affective cues in the voice. We employed a task in which the emotional vocal stimulus (crying) was used and investigated the electrophysiological ERPs response (P3) in two groups of children of pre-school and school age.

**Methods**

10 children (5-6 years old) and 10 children (7-8 years old) with normal hearing were tested with a passive audio odd ball paradigm using a standard tone, deviant tone and a non-target vocal emotional stimulus - crying. EEG activity was recorded at 24 scalp locations following the extended International 10-20 System. The EEG signal was analyzed using the software package BrainVision Analyzer. The classical peaks of auditory ERPs were identified in the grand average responses. The statistical significance of these components was assessed using the unilateral t test and the ANOVA test. Each age group was analyzed separately. The comparison of the results between two different age groups was performed.

**Results**

Both age groups of children showed no differences in morphology, latency and amplitude of N1 response to standard stimuli. Therefore both groups of children reflect the same processing of auditory stimuli at the sensory level. Pre-school age children showed significantly smaller P3 amplitude to vocal emotional stimulus. Therefore pre-school children showed worse identification of emotional stimulus and worse stimulus triggered engagement of attention and categorization.

**Conclusion**

The age-related passive engagement of attention to affective vocal information improved considerably with age.

This study was supported by grant No. P407/12/1525 provided by the Czech Science Agency.
Brain Stem Auditory Evoked Potentials and Electrocochleographic Findings in Patients with Idiopathic Sudden Sensorineural Hearing Loss

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Objective

To determine the status of cochlea, auditory pathway and hearing threshold by recording brain stem auditory evoked potential (BSAEP) and electrocochleography in patients with idiopathic sudden sensorineural hearing loss (ISSNHL).

Methodology

This observational study was conducted Department of Clinical Physiology at King Abdul Aziz University Hospital, Riyadh, Saudi Arabia. Patients diagnosed with idiopathic sudden sensorineural hearing loss (ISSNHL) based on clinical features and pure tone audiometry were studied. Brain stem auditory evoked potential (BSAEP) and electrocochleography (ECOG) was performed in them according to standard protocols for assessment of auditory pathway and hearing threshold.

Results

Out of 23 patients (14 males and 9 females) left ear was affected in 9 (39.1%) patients, right ear in 13 (56.5%) and both in 1 (4.3%). Absolute latency of wave I and wave V were significantly prolonged in affected ear compared to unaffected ears (p=0.0031), while interpeak latency I-V latency was significantly higher in affected ears versus unaffected ears (p=0.0544). Six patients (26.1%) had type II Diabetes mellitus, five cases (21.7%) had hypertension and 5 cases (21.7%) had dyslipidemia. ECOG revealed absence of summation potential (SP) and action potential (AP) response even at 95 dB in 17 out of 23 cases (73.9%).

Conclusion

Patients with ISSNHL had significant abnormalities in BSAEP and ECOG recordings showing predominantly cochlear involvement. Thus, these tests provide useful diagnostic information in patients with ISSNHL in addition to pure tone audiometry.
Non-invasive recording of late spinal cord somatosensory-evoked potentials in humans

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Question

Short-latency spinal cord somatosensory-evoked potentials (SC-SEPs) can be recorded in humans, using surface electrodes positioned on the skin overlying the spine. These responses are thought to reflect arrival of the afferent volley within the spinal cord and/or early activation of dorsal horn neurons. In contrast, late SC-SEPs reflecting, for example, descending modulatory projections to the spinal cord have not been described.

Methods

We propose a novel non-invasive approach for the identification of SC-SEPs in humans. The electrospinogram was recorded using 13 skin surface electrodes overlying the full extent of the spinal cord referenced to the right iliac crest. SC-SEPs were elicited by stimulation of the left and right common peroneal nerve at the level of the popliteal fossae (1000 stimuli delivered at 1 Hz). A blind source separation algorithm based on an independent component analysis (ICA) was used to remove the contamination by electrocardiographic activity, considered as the main obstacle for the identification of SC-SEPs.

Results

In addition to early-latency SC-SEPs (e.g. N15), removal of electrocardiographic activity allowed identifying a series of late SC-SEPs at latencies extending from approximately 100 ms to 600 ms after stimulus onset. Some of these waves (e.g. N100) displayed an increase in latency in the caudo-cranial direction whereas other waves (e.g. N300, N600) displayed an increase in latency in the cranio-caudal direction, suggesting they reflect neural activity ascending and descending the spinal cord, respectively.

Conclusion

Blind source separation of multi-channel SC-SEP recordings can provide a more complete view of stimulus-evoked activity within the human spinal cord. The functional significance of the identified late SC-SEPs remains to be determined. Characterizing these responses, some of which could reflect descending projections, may lead to a better understanding of spinal cord function and dysfunction in humans.
P824
Utility of anal evoked potentials in patients with faecal incontinence

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Question

Faecal incontinence (FI) is associated with impaired recto-anal sensitivity. Animal studies suggest dysfunction may be the result of neuronal injury, particularly following obstetric trauma. Cerebral sensory evoked potentials (SEPs) have been proposed as a marker of the A-delta sensory afferent system from the anal canal despite being of low amplitude and variable morphology. This study aimed to determine the effect of sex, age and obstetric history on the quality of anal SEPs.

Methods

Twenty-nine healthy volunteers (HVs) (mean age 33 years; range 21-65; 21 females, 12 parous) and 13 patients with FI (mean age 49 years; range 28-79; 12 females, 11 parous) were recruited. Anal evoked potentials (AEPs) were recorded in response to stimulation with a bipolar electrode 1cm from the anal verge. Cortical recordings were made over the midline (Cz’-Fz). Anal SEP quality was evaluated by 2 blinded assessors.

Results

Eighty six percent (25/29) (86%) of HVs had a recordable anal SEP compared to only 1/13 (8%) of those with FI, p < 0.001. Hierarchical regression demonstrated that FI (p < 0.001), advancing age (p = 0.001) and female sex (p = 0.011) were associated with poor anal SEP quality. Sixty three percent in healthy females, (5/8) of healthy nulliparous females had excellent recordings compared to parity also appeared to be associated with reduced AEP quality (5/8 (63%) nulliparous vs. 3/12 (25%) of healthy parous women had excellent recordings) however this did not reach the level of statistical significance (p = 0.09). perhaps due to type II error

Conclusion

The inability to elicit anal SEPs in patients with faecal incontinence raises the possibility of underlying dysfunction in central sensory pathways.
OBJECTIVES
Cervical myelopathy occurs in mucopolysaccharidosis (MPS) patients with different degrees of functional impairment. MRI has been the method of choice to detect spinal cord compression. However, somatosensory (SEPs) and motor evoked potentials (MEPs) may offer a look at physiologic anatomy and provide a sensitive tool for assessment of spinal cord and brain stem posterior columns, lemniscal tracts and central motor pathways.

METHODS
We present twenty eight MPS patients (five MPS I, eight MPS II, one MPS III, five MPS IV and nine MPS VI) with spinal cord compression in whom we recorded ulnar and posterior tibial nerve SEPs [ulnar SEPs: brachial plexus potentials (N9), cervical spinal cord potentials (N13), cortical waveforms (N20); posterior tibial SEPs: lumbar potentials (N21) and thalamocortical potentials (P37)] and calculated central conduction time (CCT); we also performed MEPs using magnetic stimulation of roots and brain and calculated central motor conduction time (CMCT)

RESULTS
SEPs: initially waveforms were obtained under anesthesia, but in these conditions, we have experimented many difficulties in the ventilation of these patients; then we have changed the protocol (awaken patients) and SEPs became more accessible and we could perform many tests; SEPs were performed 32 times in 25 patients and the results were abnormal after upper and lower limbs stimulation in almost all cases (with only two exceptions) MEPs: waveforms were obtained in awaken patients; MEPs were performed 25 times in 17 patients and the results were abnormal in all cases (no exceptions).

CONCLUSIONS
Evoked potentials and MRI are complementary tests. The former provides a view of functional anatomy, whereas the latter registers structure. In the literature, is established that MPS patients often develop spinal cord compression during the course of the disease; in our opinion, the term 'disfunction' is more adequate in this context because, despite the different anatomic and physiologic background in each type of the disease, in all of them neurophysiological evaluation has shown severe impairment of conduction in sensory and motor central pathways. In MPS IV, for instance - primarily a progressive skeletal dysplasia in which spinal lesion is a major cause of morbidity and mortality - our data suggest that neurophysiological examination can refine the diagnostic of cervical myelopathy. Evoked potentials allow mapping the anatomic specificity, the functional sensitivity and have the ability to monitor changes over time.
P826
Time index of neural networks variability as physiological measurement of mental workload.

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Background

When subjects have to detect an infrequent stimulus amongst a series of standard stimuli (oddball paradigm), an event-related potential (ERP) component, the P3, is elicited. This component is of particular interest, as it is functionally related to complex cognitive functions such as the decision-making and/or the cognitive closure processes. Due to inter-individual variability and functional heterogeneity of mean averaging, its value as a marker of vulnerability is weak. Using averaging ERP block-sweeps, we describe the variation of repetition-dependent ERP amplitudes stimuli in controls, which are referred as time index of neural networks variability (TINNV). This new way to analyze P2 and P3 ERPs obtained in an oddball design may be a powerful tool to discriminate between psychiatric disorders.

Methods

Twenty-four healthy, cognitively intact adults were recruited. The participants were confronted with an auditory oddball paradigm with an easy task (press on a button) and a more constraining one (counting of rare stimuli).

ERPs were averaged over a window of 1000 ms with a 200 ms pre-stimulus onset period and band-pass filtered between 0.33 Hz (24 dB/octave) and 30 Hz. Amplitudes were measured from the pre-stimulus baseline to the maximum peak.

Analyses of the later P2 and P3a-P3b ERPs were restricted to Fz-Cz-Pz. To compute the TINNV, ERPs were calculated for rare tones. Variations of the ERP amplitudes were considered according successive blocks (8) of five targets.

Results

Comparable amplitudes of P3a and P3b were observed among each of the 8 blocks independently of task difficulty. In contrast, a rapid P3a and P3b amplitude decrease was observed in the highly demanding task, but clearly not in the easier. Similar TINNV patterns were observed on P2 component.

Discussion

The present data revealed distinct repetition-dependent ERP amplitude profile stimuli according to task difficulty. Interestingly, participants displayed a rapid disengagement in the allocation of attentional resources to target during realisation of the more difficult task, demonstrating that attentional-dependent brain networks are maximally recruited at the beginning of the task when effort is required. This procedure might be particularly adapted to study dysfunctions of attention allocation in psychiatric disorders.
Beyond P300: an auditory ERP paradigm with sequential stimulation

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Question

Brain-computer interfaces (BCIs) aim to establish communication channels which are independent of muscle movements, relying on the real-time analysis of brain signals instead. Typically, BCI paradigms which evaluate evoked potentials in the EEG follow the principles of the oddball paradigm with random sequences of target and non-target stimuli. We investigate whether this randomness can be removed, allowing a very user-friendly paradigm where the user knows the order of stimulation.

Methods

We performed an EEG study with 10 subjects. The subjects listened to a rapid sequence (SOA=83.3ms) of 30 auditory stimuli with the task to attend to only one stimulus/letter. The spoken alphabet with each letter lasting 250 ms was used as stimuli, which were presented either in a pseudorandom order (condition 1) or in a sequential order (condition 2).

Results

Despite the rapid stimulation sequence, we found that the oddball paradigm (condition 1) elicited typical class-discriminative ERP components, such as N200 and P300. The evoked potentials in the sequential condition also showed class discriminant features, such that the EEG signature from attended stimuli was different from non-attended stimuli. However Figure 1 depicts that the ERPs from the sequential condition were clearly distinct from those components observed in the oddball condition, since they were lacking N200 and P300 components.

Conclusions

Striving for the simplest-possible setup, we describe that one can also remove any randomness from an ERP-based BCI paradigm, by presenting 30 characters which are presented in a fix sequential order. We find that this paradigm - called CharStreamer - also elicits class discriminant EEG features which were however different to an oddball paradigm as they were lacking N200 and P300 components.

figure 1
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P828
The polyneuropathy associated with monoclonal gammopathy - the neurophysiological assessment of several sensory modalities

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Question

The acquired polyneuropathies can be the first symptom of the monoclonal gammopathy. The diagnostic tests (electroneurography, electromyography, evoked potentials) are very helpful with monitoring the neurological condition and give the suggestions about the further diagnostic procedures.

Methods and results

We present a 64-year-old male with a history of severe axonal-demyelinating polyneuropathy, which was the first symptom of Waldenstroem Macroglobulinaemia. On neurological examination (February, 2007) he presented a distal, flaccid paraparesis. The Achilles reflexes were absent. The “stocking” loss of sensation and the loss of the joint position sense of toes were observed. There were no symptoms of cranial nerves and upper limbs lesions. Due to the intrathecal chemotherapy we observed no marked progression of his clinical symptoms. The consecutive examination (May, 2011) revealed the similar neurophysiological data. The laser evoked potentials (August, 2013) showed no impairment of thermonociceptive pathways during stimulation both upper extremities and the right lower extremity. There were no response during stimulation of the left lower leg.

Conclusions

The assessment of the functions of small fibres' sensory pathways Ad and C can be helpful in prognosis for patients with acquired polyneuropathies.

Key words

polyneuropathy, Waldenstroem Macroglobulinaemia, electroneurography, electromyography, laser evoked potentials
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P830
Short-term Habituation in disorders of consciousness: a diagnostic/prognostic tool?

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Question
Short-term habituation (STH) is known as a fundamental component of attention since it represents a cortical “bottom-up” filter for salient stimuli. Our aim was to verify if STH is still preserved in patients with different levels of Disorder of Consciousness (DOC), namely vegetative (VS) versus minimally conscious state (MCS).

Methods
We selected 40 DOC patients assessed with a standardized neurobehavioral examination (Coma Recovery Scale-Revised). We performed a multimodal neurophysiological evaluation that included EEG, somatosensory evoked potentials, oddball protocol and STH paradigm. The STH protocol provides for the delivery of trains of three stimuli (S1-S2-S3): S1 and S2 always belongs to the same sensory modality (auditory or somatosensory) whereas S3 can belong either to the same modality or to the alternative modality. S1/S2/S3-related N1-P2 amplitudes were compared in order to detect any STH.

Results
STH was detected in each emerging and MCS patient, whereas it was found absent only in the VS group (10 out of 19): until now, none of these 10 patients has regained consciousness. Among the 9 VS patients showing STH, 4 have subsequently become MCS.

Conclusions
STH could represent a new potential diagnostic/prognostic neurophysiological tool in DOC. The STH protocol may be able to pick-up preserved elementary information processing in DOC patients since we found a STH in every patient with a preserved level of consciousness (emerging and MCS groups). It remains to be determined whether the presence/absence of STH in an early DOC stage can have a prognostic value and whether the absence of STH in chronic VS can assume the significance of a diagnostic confirmation.
P831
Laser evoked cutaneous silent periods in patients with chemotherapy induced polyneuropathy

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Question
Laser evoked potentials (LEPs) are one of the most reliable tools that assess peripheral and central nociceptive pathways following the stimulation of A-delta (Aδ) and C fibres. Whereas, cutaneous silent period (CSP) is an easy test that reflects mainly the function of peripheral Aδ afferents. CSP is a brief pause in voluntary contraction following the stimulation of peripheral Aδ and slow A-beta afferents. CSPs can be evoked with laser (Ls-CSP) or electrical stimulation (El-CSP).

In this study we wanted to see if Ls-CSPs could identify the patients with distal polyneuropathy.

Methods
Twelve women (51 ± 5.65 years old) with distal polyneuropathy due to chemotherapy were compared with 12 (46.58 ± 8.71 years old) age- and sex-matched healthy subjects. Neodymium:yttrium-aluminum-perovskite laser was used to evoke Ls-CSPs, and LEPs. El-CSPs, Ls-CSPs, and LEPs were obtained after palmar stimulation of the right median sensory nerve. We recorded CSPs from the right abductor pollicis brevis muscle and LEPs from the left temporo-parietal cortex. The CSPs were evaluated based on latencies and durations. LEPs were evaluated with N1, N2, P2 latencies, N1 amplitudes (baseline to peak), and N2P2 amplitudes (peak to peak).

Results
The N2P2 amplitudes were lower (36.69 ± 12.71 µV vs. 47.34 ± 14.45 µV, P = 0.048), El-CSP durations were longer (29.83 ± 16.04 ms vs. 27.9 ± 9.79 ms, P = 0.002), and Ls-CSP durations were shorter (9.66 ± 10.83 ms vs. 20.5 ± 8.01 ms, P = 0.004) in the patient group. The Ls-CSP durations were more sensitive (50%) than LEP-N2P2 amplitudes (25%) and El-CSP durations (8.3%).

Conclusions
The Ls-CSPs were better than the other tests to identify the patients with distal polyneuropathy, probably due to the fact that Ls-CSP evaluates mainly the peripheral Aδ-fibres starting from the free nerve endings. Ls-CSP can be considered as a quick and easy test to evaluate the peripheral nociceptive pathways non-invasively.
P832
Modulation of painful electrically evoked responses are best analyzed in the time-frequency domain

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Question
When studying modulation of afferent neural signaling it is of importance to use sensitive analysis methods. Are time-frequency domain analysis more sensitive than traditional time-domain analysis when studying modulation of evoked responses?

Methods
In study I, responses to painful electrical stimuli before and after sleep restriction were recorded in 22 healthy subjects (mean age 23 ± 4 years; 14 female) with a within-subject crossover design. In study II, responses to painful electrical stimuli before and after high-frequency electrical stimulation (HFS) were recorded in twenty subjects (mean age 26 ± 6 years; two female). Responses were obtained both subjectively and as cortical event related responses (ERP). ERPs were analyzed within both time-domain and within time-frequency domain.

Painful electrical test stimuli (TS) were delivered to the forearm with a custom made platinum electrode (0.2 mm). Pain intensity was estimated after each test stimulus by means of a 0 - 100 numerical rating scale (NRS). Sleep restriction (study I) consisted of 2 nights of 50 % sleep (self supervised). HFS (study II) consisted of 5 trains of 1 s long 100 Hz 2 ms square pulses (2.5 mA, 10 s intervals).

Electroencephalography was recorded (actiCap active electrodes, BrainProducts), filtered 0.5 - 100 Hz and ocular corrected with ICA (linked ear reference) before epoching (-1 - 2 s). N and P peaks were identified on averaged epochs. A time-frequency representation of each single EEG epoch was obtained using a windowed Fourier transform. The effect of modulation (sleep restriction and HFS) was analyzed with a linear mixed model with random intercept and random slopes.

Results
Subjective ratings of TS did not change after sleep restriction (p = 0.42), but a facilitating effect of HFS was found (p = 0.038). ERPs increased after sleep restriction (p = 0.021) when analyzed in the time-frequency domain, but when analyzed in the time-domain a weak trend towards reduced amplitude was found (p =0.16). ERPs increased after HFS for both analysis methods, but was strongest for the time-frequency domain method (F = 9.6, p = 0.004 and F = 4.4, p = 0.04, respectively).

Conclusions
Time-frequency methods have a better discriminating ability compared to the time-domain methods when studying modulation of painful electrical responses.
Long-term physical activity is associated with precognitive somatosensory brain processing and white matter volume in male twins

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Question
Leisure-time physical activity is a key contributor to physical and mental health. Associations between long-term physical activity and cortical structure and function are poorly known in healthy persons. Our aim was to investigate whether there are structural and/or functional differences by physical activity level in brains of young male twins.

Methods
Participants were 32 males (16 monozygotic twin pairs, mean age 34 y, differing in their physical activity habits). Brain MRI (1.5 T) and somatosensory mismatch response (multichannel EEG) to electrical stimulation of fingers (sMMR) were registered. White and grey matter (WM, GM) and total intracerebral volumes as well as sMMR amplitudes and latencies were compared with past 3 year physical activity measure (MET3y) and body composition data.

Results
WM, but not GM, volume correlated significantly with body mass index (r=.53) and waist circumference (r=.41) in males with mean weight of 75 ±11 kg. Both early and late component latencies of the sMMR waveform in sensory area of stimulated hand correlated significantly with waist circumference and body fat% (r=.54, r=.43, respectively). The sMMR latency correlated negatively with VO₂max and MET3y (r=-.57, r=-.60, respectively) as well as the sMMR amplitude with MET3y (r=-.38).

Conclusions
WM volume was larger and sMMR latency was longer in those who had bigger waist circumference and higher fat%, whereas those with better oxygen uptake and more leisure-time physical activity had shorter sMMR latency. Present findings indicate that even in normal-weight men physical activity pattern is associated with brain structure and precognitive function.
Nocebo effect dissociates the laser-pain rating from the N2/P2 laser evoked potential amplitude

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Question

The aim of this study is to investigate whether laser evoked potential (LEP) amplitude and subjective perception of laser-pain could be affected by a nocebo effect.

Methods

Ten subjects underwent either a conditioning nocebo session (CNS) or a learning nocebo session (LNS). At time 0 (baseline), LEPs were acquired from both right and left hand stimulation. At time 1, Vaseline was applied on the right hand and subjects were informed that they were receiving an hyperalgesic cream. In CNS, LEPs were recorded from both right and left hand using the same stimulus intensity as in the baseline. In LNS, right hand LEPs were recorded initially by a stimulus intensity secretly increased, so as to make the healthy volunteers believe that the hyperalgesic treatment really worked. Then, Vaseline was applied again and right and left hand LEPs were recorded at the same stimulus intensity as in the baseline. After each LEP recording, subjects were asked to rate laser-pain, by using a 101-points numerical scale.

Results

In CNS, laser-pain rating to right hand stimulation was increased after nocebo treatment, as compared to baseline. On the contrary, in both CNS and LNS the N2/P2 amplitude change induced by nocebo treatment, as compared to the baseline, was not different for both right (experimental) and left (control) hand stimulation.

Conclusions

Our results showed that, differently from the study conducted in the placebo experimental, in the nocebo setting LEPs do not change in both experimental setting (CNS and LNS) when compared to control, while the laser-pain rating in CNS increase after nocebo session. Our results support the hypothesis that LEP amplitude cannot be considered as an objective measure of laser-pain perception.
Clinical utility of auditory event-related potentials: effects of psychopathology and psychopharmacotherapy in psychiatric inpatients

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Question

With respect to early auditory processing (N1, P2) there is accumulating evidence from basic research and clinical studies that the loudness dependence of auditory evoked potentials (LDAEP) may serve as a marker for central serotonergic activity and potentially other monoaminergic neurotransmitters, too. However, there were hardly any acute psychotropic effects in human samples. As the LDAEP remains inconclusive for its suitability in clinical use at present, psychiatric patients undergoing chronic psychopharmacotherapy were to be investigated.

Methods

A cross-sectional sample of 162 psychiatric inpatients (major depression N= 86, bipolar disorder N= 12, schizophrenia N= 50, and schizoaffective disorder N= 14) and 40 healthy subjects was retrospectively examined for LDAEP and effects of psychopathology and chronic psychopharmacology using multichannel-EEG.

Results

The LDAEP was weaker in patients with affective disorders than in healthy subjects but did not differentiate between the total patient sample and healthy controls. LDAEP correlated significantly with dimensions of the Brief Symptom Inventory in the total patient sample (depression, paranoid ideation, psychoticism, Global Symptom Index, and Positive Symptom Distress Index), in patients with affective disorders (depression) and with schizophrenia spectrum disorders (depression, psychoticism, Global Symptom Index, and Positive Symptom Distress Index). Similar correlations were found in depressed patients with a single noradrenergic and specific serotonergic antidepressant or serotonin-norepinephrine reuptake inhibitor. There was a negative correlation between dosage of typical antipsychotics and LDAEP. Hypnotics generally led to a lower LDAEP.

Conclusions

The LDAEP in patients is related to severity of psychopathologic syndromes irrespective of diagnosis. Chronic psychopharmacologic treatment may also differentially modulate the LDAEP, but longitudinal studies are needed.
Tomographic imaging of fast neural activity with a resolution of 2 ms and 200 µm in the cerebral cortex of the anesthetised rat during whisker SEPs using Electrical Impedance Tomography and epicortical electrodes.

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Electrical Impedance Tomography (EIT) is a novel imaging method with which tomographic images of the electrical properties of a subject are produced with a box of electronics about the size of a DVD player, and ECG type electrodes placed around the head, chest or abdomen. Small, insensible, electrical signals are applied to the electrodes and sophisticated mathematical methods translate these into images with a PC in real time. It is portable, inexpensive, safe, and rapid. Unlike EEG source modeling, the images are in principle unique. It can be used to image small impedance changes which occur in the brain as ion channels open during neuronal depolarization and so provide a true tomographic imaging method able to image during evoked potentials or other cerebral activity with a temporal resolution of ~ 1msec. Biophysical modeling indicates such activity changes resistance by 1% locally in the brain; the model has been validated in crab nerve recording, and such changes are imageable in saline filled tanks.

Recent studies have demonstrated its accuracy during mechanical whisker stimulation at 2 Hz in the anesthetized rat. EIT was undertaken with an epicortical array, 7x5 mm square, with 30 platinised stainless steel electrodes, each 0.6mm in diameter. Images were collected using applied current of 50µA at 1.7kHz, applied to 30 electrode pairs sequentially, which produced reconstructed images every 2 ms after averaging. Images were acquired over 12 min of averaging 15 responses at each current injection site (450 in total) with a resolution of <200µm to a depth of 1.2mm (Layer V/VI). Reproducible peak resistance decreases of 0.15±0.01% (mean±SE, n=122 in 4 rats) were observed. It was possible to distinguish entry of activity at layer IV with spread to deeper and higher layers over 2 ms. The changes were validated by simultaneous recording of local field potentials and intrinsic optical imaging.

For the first time, it is possible to distinguish both lateral and columnar propagation throughout S1 with a method able to image throughout the cerebral cortex in 3D with non-penetrating surface electrodes. At present, it has only been validated for invasive animal studies but we plan to extend its use to imaging in 3D throughout the brain with epicortical electrodes and to use this in human studies with subdural mats implanted for presurgical evaluation.
P837
Comparison of the tibial nerve somatosensory evoked potentials (SEPs) between neuromyelitis optica and multiple sclerosis patients.

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Question
Evoked potentials including SEPs has been long believed to be a useful measure to detect lesions in multiple sclerosis (MS) patients. The concept of neuromyelitis optica (NMO) with aquaporin-4 (AQP4) antibody has been recently established as an independent entity that should be differentiated from the classical MS. The evoked potential profiles of NMO in comparison with MS have been investigated by only one report so far, in which SEP showed no significant difference between the two disorders. In this study, we investigated tibial nerve SEPs for NMO and MS patients.

Methods
NMO or MS patients who fulfilled respective diagnostic criteria were extracted retrospectively from the patient database at our institution between 2009 and 2013. Only patients whose AQP4 antibody was measured were included. AQP4-positive patients were classified as NMO and AQP4-negative patients were classified as MS. Other inclusion criteria were the presence of sensory symptoms in the lower limb and the existence of definite MRI lesions in the spinal cord. In this way, we investigated the nature of the lesions using SEPs, and did not test the ability of SEPs to detect subclinical lesions. Tibial nerve SEPs were measured using standard methods at our institution. Evaluated parameters were the N21 latency, the N21-P38 interval, and the P38 amplitude. Z-score was given to each parameter using our established normal values considering height, age, and gender. Absolute value of the Z-score exceeding 2.5 was considered abnormal.

Results
Enrolled subjects consisted of 7 NMO and 10 MS patients. N21 latency was within normal limits for every subject. N21-P38 interval was prolonged in 0/7 patients in the NMO group and 5/10 patients in the MS group. Mean±SD of the Z-scores were 0.30±1.05 in NMO and 3.90±3.28 in MS, the latter was significantly higher than the former (p

Conclusions
Demyelinative nature of the spinal cord lesion resulting in the prolonged central conduction was evident in the MS group but not in the NMO group, coinciding with the documented pathology of each disorder. Axonal and destructive nature of the NMO lesion was not detected by the P38 amplitude reduction despite the presence of sensory symptoms and MRI lesions, which may be due to the amplifying effect of SEPs.
P838
Low- and high-frequency subcortical SEP amplitude reduction during pure passive movement

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Question
We aimed to investigate the effect of a pure passive movement on the amplitude of the somatosensory evoked potentials (SEPs) recorded by intracerebral leads implanted for deep brain stimulation (DBS).

Methods
Eleven patients, suffering from Parkinson disease resistant to pharmacological treatment, underwent electrode implantation in the ventral intermediate nucleus (VIM) of the thalamus (2 patients), in the subthalamic (STN) nucleus (3 patients) and pedunculopontine (PPTg) nucleus (6 patients). The study was performed in the operating room with the patient under total intravenous anesthesia. Median nerve SEPs were recorded at rest and during a passive opposition movement of the ipsilateral thumb. Passive movement was performed at 1, 0.5, 0.33, 0.25, and 0.2 Hz. Beyond the low-frequency SEPs, also the high-frequency responses were analysed.

Results
Although both DBS lead potentials and scalp components reduced their amplitudes during passive movement at 1 Hz, as compared to the rest, amplitude reduction was higher for cortical than intracerebral responses. Also the high-frequency SEP amplitudes were significantly lower during passive movement than at rest.

Conclusions
Our study suggests that a two-level (cortical and subcortical) mechanism is involved in SEP amplitude reduction during passive movement (centripetal gating).
P839
Low and high-frequency Somatosensory Evoked Potentials recorded from the human pedunculopontine nucleus

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Question

To investigate the generators of the somatosensory evoked potential (SEP) components recorded from the Pedunculopontine Tegmental nucleus (PPTg).

Methods

Twenty-two patients, suffering from Parkinson’s disease (PD), underwent electrode implantation in the PPTg area for deep brain stimulation (DBS). SEPs were recorded from the DBS electrode contacts to median nerve stimulation.

Results

SEPs recorded from the PPTg electrode contacts could be classified in 3 types, according to their waveforms. 1) The biphasic potential showed a positive peak (P16) whose latency (16.05 ± 0.61 ms) shifted of 0.18 ± 0.07 ms from the lower to the upper contact of the electrode. 2) The triphasic potential showed an initial positive peak (P15) whose latency (15.4 ± 0.2 ms) did not change across the DBS electrode contacts. 3) In the last SEP configuration (mixed biphasic and triphasic waveform), the positive peak was bifid including both the P15 and P16 potentials.

Conclusion

While the P16 potential is probably generated by the somatosensory volley travelling along the medial lemniscus, the P15 response represents a far-field potential probably generated at the cuneate nucleus level.
P840
Somatosensory evoked potentials: clinical application in pediatrics - challenges and limits

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Question

Somatosensory evoked potentials (SEP) allow evaluation of the functional integrity of the somatosensory system from the peripheral nerve to the cerebral cortex. Although in childhood the clinical application of SEPs are less well established than in the adult population this is a useful method in a variety of pediatric neurologic conditions.

Methods

Clinical application of SEP in pediatric neurology is described with the experience of a pediatric neurophysiologic unit and the literature is reviewed.

Results

SEPs are useful in pediatrics for the evaluation of peripheral pathology, spinal cord lesions, lesions of the cervicomedullary junction, brainstem lesions and cortical lesions. SEPs can be used in predicting outcome in perinatal asphyxia or in coma. Maturational changes and normative data have to be considered in clinical application. Methodology should be adapted to the need of children.

Conclusions

SEPs in pediatrics are a reasonable diagnostic tool if there is a clear clinical indication. Interpretation must be done in the clinical context. Age dependent normative values have to be considered. Methodology has to be adapted to the children's needs.
P841
Quantifying the effect of sternocleidomastoid muscle contraction strength on cVEMP amplitude and symmetry

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Question

Cervical vestibular evoked myogenic potentials (cVEMPs) are vestibular-dependent muscle reflexes recorded from the sternocleidomastoid (SCM) muscles in humans. They are thought to reflect the function of the otoliths, and when evoked by air-conducted sound stimulation are thought to originate predominantly in the saccule. The cVEMP can be modulated by both stimulus intensity and SCM muscle contraction strength, but the effect of muscle contraction is not well-documented. Therefore, in this study the effects of stimulus intensity and SCM contraction strength on the cVEMP were compared.

Methods

Seventeen normal subjects and 10 patients with possible vestibular migraine were tested. cVEMPs were recorded at different intensities while holding the SCM contraction constant and at different contraction levels while holding stimulus intensity constant.

Results

The cVEMP was first seen at an activation level of around 20 μV, but in one subject could be recorded with just 7 μV mean rectified EMG. The maximal SCM contraction ranged from 110 to 540 μV across subjects, producing cVEMPs ranging from 150 to 904 μV in size. The effect of muscle contraction (mean R² = 0.95) was linear for most of the range of values, although there were some nonlinearities when the contraction was either very weak or very strong. Some subjects were more sensitive to changes in stimulus intensity and others to changes in muscle contraction. Comparison of the regression equations showed that a 50 μV difference in SCM muscle contraction produced on average the same change in cVEMP amplitude as a 20 dB change of stimulus intensity (range 6-55 dB). When muscle contraction was ignored and raw amplitudes used to calculate asymmetry 2/10 patients had false-positive cVEMP test results. These became normal once a ratio of raw amplitude to contraction strength was used.

Conclusions

These data provide detailed information on the effect of muscle contraction on the cVEMP and highlight the importance of considering SCM contraction strength when recording cVEMPs.
P842
Effect of focal mechanical vibration on the nociceptive pathways

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Question
To evaluate whether the focal application of a vibratory stimulation on the skin may change the laser evoked potentials (LEPs) and the laser pain to pulses delivered on the same cutaneous area.

Methods
In 10 healthy volunteers, LEPs were recorded after stimulation of the radial and ulnar dorsal hand territories, bilaterally. After each LEP recording, the subjects were asked to rate the laser-pain according to a 100-point VAS. All subjects were evaluated in two different sessions in order to test both effective and sham vibratory stimulation. In each session, the experiment included two times: 1) LEPs were recorded without any conditioning vibratory stimulus, 2) LEPs were recorded during effective or sham vibratory stimulation within the right radial territory.

Results
No difference in N2/P2 amplitude changes was found between the effective and the sham vibratory stimulation. Also the subjective perception of pain was not influenced by the simultaneous vibratory (effective or sham) stimulation.

Conclusions
Our negative results suggest that focal vibratory stimuli, currently used for motor rehabilitation, are not effective as analgesic physical treatment.
P843
Influence of anesthetic agents on sensory nerve excitability testing in mice

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Introduction

Nerve excitability study in experimental animals can directly test a hypothesis at a molecular level by a specific pharmacological agent or a genetic model. Unlike human subjects, animal study is often performed under anesthesia, however, the anesthetic effects on peripheral nerve excitability has not been fully investigated.

Methods

We performed nerve excitability testing under two commonly used anesthetic agents in normal male mice: (1) 1.5% isoflurane inhalation (N=10) and (2) the triple agents - medetomidine (0.3 mg/kg), midazoram (4 mg/kg) and btorphanol (5 mg/kg) - intraperitoneal injection (N=10). Sensory nerve at the tail was orthodromically recorded, immediately after the animal was under control for maximal duration of 2 hours to assess the time course of the excitability changes. QtracS software (Digitimer, UK) was used.

Result

Threshold changes by long hyperpolarizing stimulation (i.e., threshold electrotonus and current-threshold relationship) increased approximately 30 minutes after induction of anesthesia that sustained thereafter. By contrast, recovery cycle, strength-duration time constant and depolarizing threshold electrotonus showed no remarkable change during the recording.

Conclusion

The results suggest anesthetic blockade of HCN channels which are activated by long hyperpolarizing current. When we assess the nerve excitability in experimental animals, the influence of anesthesia on nerve excitability should be taken into account.
P844
H-Reflex Recovery Cycle as an Electrophysiological Correlate of Spasticity

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OBJECTIVE

To investigate correlation between spasticity and spinal cord excitability, the recovery cycle of the H reflex (HRRC) was assessed using novel threshold tracking method.

METHOD

A subset of patients with spastic paraparesis (11) were recruited for the study. Before HRRC, muscle strength and spasticity (with modified Ashworth Scale) of lower limbs were evaluated. HRRC was performed with two equal suprathreshold stimulus paradigm with different (between 2-200 ms) interstimulus intervals (ISIs) by using the threshold tracking method.

RESULTS

Preliminary results indicate that there is good correlation between inhibition of HRRC at ISIs of 56-2 ms and modified Ashworth scale scores (r> 0.740).

CONCLUSIONS

Findings of the study suggest that HRRC using the novel threshold tracking method is a good electrophysiological correlate of spasticity.
P845
Interpretation of excitability studies in multifocal motor neuropathy and chronic inflammatory demyelinating polyneuropathy

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Question
Pathophysiology of multifocal motor neuropathy (MMN) and chronic inflammatory demyelinating polyneuropathy (CIDP) is not fully understood. Nerve excitability studies have been performed to improve understanding of disease mechanisms, but results were difficult to interpret. Although cold paresis is frequently reported in MMN and was attributed to depolarized nerve lesions, effects of cooling on excitability were not previously studied in MMN and CIDP. The aim of this study was to explore nerve excitability in MMN and CIDP to assess changes in passive and active axonal membrane properties.

Methods
We performed excitability studies of the median nerve at the wrist in 5 MMN and 7 CIDP patients with nerve conduction abnormalities in the forearm segment and 10 normal controls. Tests were performed following warming to 37°C and cooling to 25°C. Results in MMN and CIDP were compared with those in normal controls. Inverse modeling was used to interpret the results.

Results
Following warming, MMN patients showed fanning-out and increased accommodation of threshold electrotonus, shortened refractory period and increased superexcitability. In CIDP, stimulus-response slope was decreased, rheobase was increased, threshold electrotonus showed fanning-out and refractory period was shortened. Inverse modeling showed decreased fast K-conductance, increased myelin conductance and hyperpolarization-activated cation conductance in MMN and increased myelin conductance and hyperpolarization-activated cation conductance in CIDP. Following cooling, changes in excitability-indices were largely similar in all groups.

Conclusions
The present findings support permanent axonal hyperpolarization and demyelination in MMN, demyelination in CIDP, and normal effects of cooling on ion-channels in both diseases.
P846
The effect of hand dominance on peripheral nerve excitability.

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Question
The threshold tracking technique has been used for exploring the peripheral nerve excitability in normal subjects and patients with various neuromuscular diseases. Murray et al. reported that nerve excitability of the median and ulnar nerve was significantly different in normal subjects by using threshold tracking. However, it is unclear whether hand dominance can affect the peripheral nerve excitability. The aim of this study is to elucidate whether the properties in nerve excitability of the dominant hands are different from those of the non-dominant hands.

Methods
Both median nerves were examined in healthy subjects using Trond NF program with Qtrac® system. Nerve excitability parameters were compared between dominant hands and non-dominant hands. In each individual, the dominant hand was determined by Edinburgh Handedness Inventory.

Results
All subjects (n=10, 8 men and 2 women; aged 24-45 years) were right-handed. Strength-duration time constant (SDTC) demonstrated no difference between dominant hands [0.37 ± 0.084 ms] and non-dominant hands [0.37 ± 0.074 ms] (p = 0.872). Second, all parameters in threshold electrotonus tracking showed no difference in hand dominance (TEh [90-100ms]; -117.3±13.6% [dominant hands], -116.4±7.8% [non-dominant hands], p =0.846, TEd [90-100ms]; 44.6±4.6 % [dominant hands], 45.0±3.0% [non-dominant hands], p=0.794). In recovery cycle testing, no side difference was noted both in superexcitability and in subexcitability.

Conclusions
Nerve excitability measures in dominant hands were not different from those in non-dominant hands. This study provides the practical basis for the hypothesis that it may be unnecessary to consider the handedness when exploring nerve excitability in patients with neuromuscular diseases.
Abstracts of Poster Presentations – Poster Session 48 – Excitability of nerve and muscle

P847
Signs of motoneuronal hyperexcitability with reinnervation after peripheral nerve lesions

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Question

Several abnormalities complicate reinnervation after complete section of a peripheral nerve. Axonal growth may lead to abnormal branching and reinnervation errors. Enhancement of excitability at motoneuronal level may entail generation of abnormal reflex responses. We examined the neurophysiological characteristics of these two types of abnormalities in 20 patients with complete traumatic section of either ulnar or median nerves.

Methods

Patients were examined at predetermined periods between 3 and 24 months after the lesion. We recorded the motor and sensory nerve action potentials and performed needle electromyography in the affected muscles. For comparison, we also analyzed the motor and sensory nerve conduction of the same nerves in the contralateral (unimpaired) extremity. For the analysis of abnormal sensorimotor responses, we recorded with needle EMG the muscle action potentials elicited by cutaneous stimulation to territories supplied by the impaired nerve and by unimpaired neighbour nerves.

Results

We recorded two types of responses: The first response, of relatively short latency (12 to 45 ms), consistently appeared at the same latency with repeated stimuli. The second response, of longer latency (48 to 114 ms), appeared less constantly and had a noticeable latency variation with repeated stimuli. Only the second response was elicited with stimuli applied to unimpaired nerves. In both cases, response latency progressively shortened with successive exams.

Conclusions

At least two types of abnormal muscle action potentials can be elicited by sensory stimuli during reinnervation after a mixed nerve lesion: Axo-axonic or ephaptic responses at relatively short latency and transynaptic reflex responses at longer latency.
P848
Silent period in the mentalis muscle in healthy subjects and hemifacial spasm

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**Question**

Action potentials of a voluntary contracting muscle undergo a transient suppression during continued effort after electrical stimulation of the nerve innervating the muscle. We reported this silent period in the mentalis muscle (J Clin Neurophysiol 2001). 1) How is the excitability of the facial nerve during this silent period? 2) Can the electrical stimulation of the zygomatic branch not innervating the mentalis muscle induce this silent period in the mentalis muscle in patients with hemifacial spasm?

**Methods**

The marginal mandibular branch 1) or the zygomatic branch 2) of the facial nerve was stimulated at a frequency of 1Hz, a stimulus intensity of supramaximum during slight voluntary contraction of the mentalis muscle and the baseline contained evidence of random muscle activity was obtained electromyographically in the mentalis muscle. 1) To estimate the excitability of the facial nerve, the facial F waves were elicited by the paired stimulation (interstimulus interval(ISI): 40ms(during voluntary contraction of the silent period) or 80ms(during late phase of the silent period)). 2) To examine the silent period of the hemifacial spasm, the baseline activity was obtained in the mentalis muscle following the zygomatic branch stimulation.

**Results**

1) The F waves elicited by the second stimulation were enhanced (ISI: 40ms) and inhibited (ISI: 80ms). 2) The silent period was recorded in the mentalis muscles by the zygomatic branch stimulation in the patients with hemifacial spasm.

**Conclusions**

The silent period expresses the facial nerve excitability as well as the facial nerve F waves elicited by paired stimulation. The silent period was recorded by not innervating nerve stimulation in the hemifacial spasm as well as the abnormal muscle responses.
Abstracts of Poster Presentations – Poster Session 48 – Excitability of nerve and muscle

P849
The relationship between Muscle strength and Transcranial Stimulation Motor evoked potential

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Question

Transcranial electrical stimulation Motor evoked potential (TCS-MEP) has been used as an intraoperative monitoring of motor functions. But TCS-MEP has inherent variability. This variability has disturbed that we push forward an analysis of TCS-MEP. How can we resolve this variability problem? We tried to show the absolute relationship between muscle strength and TCS-MEP by the unique method.

Methods

We hypothesized that the fluctuation of MEP amplitudes took the distribution of the amount according to Gaussian distribution in the same condition. And the mean values of MEP amplitudes were measured within the constant period. The effects on motor tracts were digitized by using the ratio of the mean values that were measured before and after the invasive maneuvers. And we investigated the correlations between those ratios and the changes of muscle strength. TCS-MEP were monitored at 26 operations of 18 intramedurally spinal cord tumor cases. TCS-MEP was in the habit of recording every 10 minutes at the direct manipulation to spinal cord after the dura matter incision. 150 muscles’ data were analyzed. All muscles’ innervation was under the tumor level in spinal cord. We gathered the MEP data in two periods. One was in one hour before tumor resection, and the other was in one hour after tumor resection. And the change ratios of MEP amplitude by one operation were described with the ratio of two mean values in each period (MEP amplitude ratio). We classified the muscle strength in six phases using Medical Research Council’s Manual Muscle Testing (MMT). The change of muscle strength were showed by the difference of two MMT values (dMMT) that were measured just before operation and at the time when postoperative awaking enough. All MEP amplitude rate values were classified in each dMMT groups (figure 1).

Result

Between adjacent dMMT groups, the significant difference was not found in two-side statistical test. However, the mean and median values of the dMMT group which muscle strength more decreased were smaller. We found the positive relation between the change of MEP amplitude by one surgery and postoperative muscle strength (figure 2).

Conclusions

There is the positive relation between the MEP amplitude and the muscle strength. So, the fixed quantity evaluation method using the statistical technique makes TCS-MEP reliable. And TCS-MEP may enhance us to remove tumors in central nervous system and at the same time preserve motor functions. Moreover this relation between MEP and muscle strength is useful for understanding the motor control system.

figure 1

The relationship between the change of MEP amplitude and the change of muscle strength by one surgery

![Image](figure1.png)

MEP amplitude rate = last value / first value

beginning of dura mater incision time end of dura mater closure

First value (mean) Last value (mean)
The relationship between Muscle strength and Transcranial Stimulation
Motor evoked potential

- MEP amplitude rate (%)
- dMMT -3, dMMT -2, dMMT -1, dMMT 0

<table>
<thead>
<tr>
<th></th>
<th>dMMT -3</th>
<th>dMMT -2</th>
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<tr>
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<td>(33.6-9.1)</td>
<td>(57.0-26.8)</td>
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<td>Median</td>
<td>18.9</td>
<td>39.9</td>
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p = 0.0084
p = 0.2312
p = 0.3125

Wilcoxon signed-rank test (two-sided test)
P850
Electrophysiological pattern in GLUT1 Deficiency Syndrome (A275T mutation)

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Question

Glucose transporter type 1 deficiency syndrome (GLUT1DS) is characterized by impaired glucose transport across the blood-brain barrier due to SLC2A1-gene mutation. GLUT1DS infancy onset shows epileptic encephalopathy, ataxia and microcephaly although paroxysmal exercise-induced dyskinesia and epilepsy may also be observed. Exercise and recovery-induced modifications of GLUT4 and GLUT1 expression in human muscle have been reported. We describe clinical and electromyographyc correlates of a GLUT1DS patient with adult-onset of exercise-induced dystonia.

Patients and Methods

A 19 year old male with mild mental retardation presented with a two-year history of episodic stiffness in his calves and feet and painless flexion of the toes followed by leg weakness triggered by exertion and starvation and alleviated by rest and eating. His father had experienced exercise-induced leg dystonia at younger age. A heterozygous missense of mutation (c.823G>A; p.A275T) of SLC2A1 gene was found in the proband and his father. The proband underwent an electromyographyc study after voluntary contraction (5 minutes) to investigate muscle membrane excitability with the evaluation of compound muscle action potential (CMAP) amplitude.

Results

The test disclosed significant decrement of CMAP amplitude up to -42% (n.v. ≤ -20%) after 40 minutes from exercise with respect to the pre-exercise CMAP amplitude (baseline). The same test repeated after carbohydrate-rich food intake showed a significant improvement of CMAP from baseline (-26%).

Conclusions

The electrophysiological study after exercise showed a reduction of CMAP amplitude in this patient with GLUT1DS (A275T mutation). Our data suggest a possible involvement of muscle membrane excitability in GLUT1DS.
P851
Tracking the spatiotemporal profile of cortical and peripheral motor axon hyperexcitability in amyotrophic lateral sclerosis

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Question
Recent studies using magnetic and electrical excitability tracking tools have confirmed early hyperexcitability in ALS. This study sets out to use excitability testing to examine directly the spatiotemporal profile of cortical and peripheral hyperexcitability in ALS patients simultaneously, to associate these parameters to the clinical course of the disease and to compare them with healthy controls.

Methods
Nineteen patients with first-diagnosed definite ALS (group A), four patients with advanced disease (group B) and ten control healthy volunteers (group C) were included in the study. Multiple axonal excitability properties (threshold electrotonus, strength-duration time constant, recovery cycle, current-threshold relationship) and TMS investigations including measurement of resting motor threshold (RMT) and motor evoked potential (MEP) were measured.

Results
In group A there were greater changes in depolarizing threshold electrotonus (TD) compared with group B (t-test p<0.03 ). No differences in recovery cycle, strength-duration time constant, current-threshold relationship were noted between the three groups. Regarding the cortical excitability parameters, there was a significant decrease in the slope of MEP amplitude to TMS intensity in group B with the advanced disease in comparison to controls (Mann-Whitney U test p<0.05). ANCOVA showed strong correlation between TD and slope of cortical excitability (p<0.01) after correcting for the status of the disease (groups A,B,C).

Conclusions
These are preliminary results of an ongoing study trying to understand the changes in axonal and cortical excitability in first-diagnosed and advanced disease in order to provide insight into the pathophysiological basis of the disease and furthermore provide useful information for the best treatment approach in the future.

References
P852
Temporal profile of the effects of regional anesthesia on the cutaneous silent period of foot muscles.

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Question
It is commonly accepted that cutaneous silent period (CuSP) is mediated by small fibers but median size or large afferents may also contribute. We examined the effects of blocking pain afferents by regional anesthesia on the silent period latency and duration in foot muscles.

Methods
We studied 10 patients with indication for surgical treatment of hallux valgus before and after ultrasound-guided popliteal sciatic nerve block (US-SPB). CuSP was obtained from the extensor digitorum brevis muscle to high intensity electrical stimuli applied to the big toe with ring electrodes. We also obtained the sympathetic skin response (SSR) from both feet to the same electrical stimulus and the skin temperature variation using an infrared thermometer. We evaluated motor fibers through the analysis of F waves.

Results
The SSR showed an early block of the efferent sudomotor fibers (mean of 4.5 m), which was almost immediately followed by a decrease in CuSP duration and a delay in CuSP onset latency. At the same time there was also an increase in temperature in the ipsilateral leg and a decrease in the contralateral one. The CuSP end latency remained unaltered up to 10 m after anesthesia in most patients, when the F wave began to show a significant change in persistence.

Discussion
The timing of involvement of the CuSP after US-SPB suggests that fibers of small to intermediate size are responsible for CuSP duration and onset latency but the end part of the CuSP might be contributed by larger diameter fibers.
Abstracts of Poster Presentations – Poster Session 48 – Excitability of nerve and muscle

P853
Nerve excitability change by chronic administration of methylglyoxal: implication for diabetic neuropathy

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Question

The methylglyoxal (MGO) pathway is an offshoot of glycolysis, which converts glucose into MGO. Frequently increased in diabetic patients, MGO is highly toxic, resulting in activation of apoptosis and mitochondrial damage. Recently, MGO was found to be a causative agent for neuropathic pain. Because abnormal nerve excitability is frequently present in peripheral neuropathy and neuropathic pain, MGO can alter overall nerve excitability. The objective of the present study was to observe the chronic effects of MGO on peripheral nerve excitability in vivo.

Methods

Eight adult male mice were examined. Sensory nerve multiple excitability testing (QTRAC) was performed from a tail nerve under inhalational anesthesia. The parameters were compared between at baseline and 1 week after intraperitoneal injection of MGX (0.005 ml/10g body weight) nine times (3 times weekly for 3 weeks).

Results

The tested animals were all survived. The excitability parameters were similar in strength-duration time constant and threshold changes by long depolarizing current (threshold electrotonus: TE). The threshold changes by long hyperpolarizing current (TE) became smaller by MGO; (1) TEh(peak) by -70% conditioning current: -203.8 ± 7.5 at baseline to -162.3 ± 9.1 post-injection, P = 0.003; (2) TEh(90-100ms): -94.3 ± 4.9 at baseline to -71.7 ± 5.5 post-injection, P = 0.006. The recovery cycle showed smaller refractoriness at 2ms by MGO: 23.5 ± 3.0 at baseline to 7.9 ± 4.8 post-injection, P = 0.01. The overall nerve excitability assessed by strength-response curves was slightly reduced after injection.

Conclusions

Chronic administration of MGO changed axonal excitability in vivo. It is likely that MGO facilitated hyperpolarization-activated cation current (Ih). The upregulation of Ih may be responsible for abnormal excitability and sensory symptoms of diabetic neuropathy.
P854

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**Question**

To test motor fibers excitability in early affected patients with transthyretin (TTR)-type familial amyloid polyneuropathy (TTR-FAP) before and during tafamidis treatment.

**Methods**

We examined the left median nerve of 21 healthy-matched controls and 10 TTR-FAP patients using the automated threshold-tracking program, QTRAC. TTR-FAP patients were tested one day before the initiation of tafamidis treatment, 3 and 6 months later.

**Results**

The drug was well tolerated in all patients; there was no drop-out. Six patients referred improvement from the neuralgic pain. No statistical difference was found between healthy controls and TTR-FAP patients at study entry. On treatment, both stimulus intensity for 50\% of the maximal motor response and rheobase increased progressively and significantly from the entry to the last evaluation at 6 months (p<0.009). No other change was noticed.

**Conclusions**

Threshold-tracking of motor fibers of the median nerve is not a sensitive test to support early diagnosis of TTR-FAP patients. Tafamidis was well tolerated and decreased sensory symptoms of most patients. We observed a significant reduction of some measures of nerve excitability.
Funny currents in human axons: the contribution of $I_h$ to axonal excitability.

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Question

Hyperpolarization-activated cyclic-nucleotide-gated (HCN) channels are unusual in that they open with hyperpolarization and pass a depolarizing current ($I_h$) which actively opposes the long-term hyperpolarization of membrane potential, a process known as inward rectification. These properties allow $I_h$ to contribute to the determination of resting membrane potential and the frequency preference of activity in human peripheral nerve.

Normal sensory axons appear to have greater inward rectification than motor, and this has been attributed to a greater expression of HCN channels. Altered inward rectification has been observed in the large myelinated fibres of the peripheral nervous system in diseases such as porphyria, stroke and diabetes, and has been implicated in epilepsy and pain.

Methods

Threshold tracking studies using strong and long hyperpolarization and a novel application of resonance techniques were used to probe the biophysical properties of $I_h$ in human motor axons and cutaneous afferents. A mathematical model of the human motor axon was adapted to incorporate the new data and was further modified to fit the observed excitability of sensory axons.

Results

No structural or morphological changes were required to model the differences between motor and sensory axons. This study suggests that the sensory axons of human peripheral nerve operate at a depolarized membrane potential compared to motor axons.

These studies provide evidence that sensory axons limit further hyperpolarization more readily than motor by bringing the voltage dependence of the fastest HCN isoform (HCN1) closer to resting membrane potential.

Conclusions

Changes in and regulation of the voltage dependence of ion channels may be as important as differences in channel expression when considering altered axonal behaviour in both health and disease.
Objective

The aim of this study was to investigate whether axonal excitability indices of potassium currents are associated with the speed of regional spreading between body regions in amyotrophic lateral sclerosis (ALS).

Methods

In 99 patients with sporadic ALS, the period of spread from onset region to other body regions were measured. Multivariate analyses were performed using the Cox proportional hazard model. Threshold tracking was used to measure multiple axonal excitability indices in median motor axons.

Results

The overall median spread-free survival from onset was 8 months. No indices of potassium current in motor axon were associated with regional spreading time.

Conclusions

Axonal potassium currents in lower motoneurons are not associated with mechanisms for more rapid inter-regional spreading in patients with ALS. The past study showed that the changes showing depolarization in potassium currents could lead to shorter survival in ALS. The results of this study suggest that the changes of axonal potassium currents in ALS are possibly associated only with the local processes of lower motor neuronal degeneration in ALS.
Segmental nerve conduction studies for distinguishing carpal tunnel syndrome from diabetic neuropathy in diabetics presenting with hand paresthesia

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In a patient with long history of diabetes presenting with hand paresthesia, it is hard to accurately attribute the sensory complaint to either Carpal Tunnel Syndrome (CTS) or Diabetic Peripheral Neuropathy (DPN). Various electrodiagnostic techniques are utilized to reach the correct diagnosis. This study is concerned with segmental median nerve sensory conduction studies. Twenty patients were selected with clinical signs and symptoms of DPN (confirmed by electrodiagnosis), and compared with another 20 diabetic patients of matching age, sex and duration of diabetes but whose sensory symptoms and signs were more consistent with distal median nerve entrapment on top of a neuropathic process. A battery of nerve conduction studies that was performed of both groups comprised: routine motor conduction studies of median and ulnar nerves, routine sensory conduction studies of median and ulnar nerves, segmental sensory conduction study of the median nerve in the hand (wrist- midpalm and wrist-digit) and F-wave studies. Statistical analysis of the result showed a clear significant difference between the group with pure neuropathy and the one with entrapment on top of neuropathy in the median midpalm-wrist sensory latency midpalm-digit sensory conduction velocity and full length (wrist-digit) latency. Further analysis of the nerve conduction techniques (using receiver operated characteristics curves) showed that the midpalm-wrist sensory conduction velocity measurement was 90% sensitive and 100% specific in differentiating the 2 disease groups with a cut-off point of 40.9 m/s. Midpalm-wrist sensory latency study was found to be 90% sensitive and 80% specific with a cut-off point of 2.3 msec. The whole length sensory median latency had a sensitivity and specificity of 80% with a 4.11 msec cut-off point while the whole length sensory median conduction velocity was 90% sensitive and specific with a 41.7 m/s cut-off. This study shows that electrodiagnosis is a valuable tool in differentiating these 2 distinct neurological conditions when clinical examination is inconclusive.
P719
Verification of maternal “memory” by assessing testosterone level in pregnant women.

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**Question**

H - Y antigen, a male specific cell membrane component is encoded by the Y chromosome. Antibodies to H - Y antigen develops in the mother when conceives a male fetus. So, one can be presumed, that the titer of the antibodies increases in the maternal circulation when same mother conceives again with a male fetus. Thus, a pool of antibodies accumulates within the maternal circulation and it is hypothesized the name “older brother effect” or maternal “memory”. The purpose of the present study was to verify the validity of “older brother effect” by measuring plasma testosterone (PT) level during pregnancy.

**Methods**

50 (Mean age 25.70±1.25) pregnant women were divided into 10 groups on the basis of their number and sex of previous children. PT level was measured by ELISA method on the 8th week of pregnancy. Statistical analysis of data was done by using ANOVA.

**Results**

The mean values of PT in 10 groups of pregnant women are comparable. Significant (p< 0.001) higher mean value of PT was observed among the mothers who conceived male fetus with compare to female fetus. Segregating pregnant women on the basis of their number of previous elder sons but carrying male fetus, the mean of PT differs significantly. Surprisingly, pregnant women on the basis of their number of previous elder sons but carrying a female fetus, the mean of PT differs significantly.

**Conclusion**

Women who conceive with one or more male fetus, developed maternal “memory” which might be responsible for the enhancement of PT level in subsequent pregnancy.
Complex repetitive discharges (CRD:s) are occasionally seen in needle EMG of neuromuscular diseases as well as myofascial syndrome and even in some normal muscles. The aim of this study is to compare CRD:s in muscles affected by neuromuscular diseases and CRD:s of muscles with myofascial pain but without any other alterations in needle-EMG.

**METHODS**

74 patients were studied with needle EMG, 53 (14 men; mean age 69 y SD 10) suffering from neuromuscular diseases (NMD), mainly neuropathies, and 21 (4 men; mean age 59 y, SD 9) suffering from myofascial pain (MFP) in the given muscle. 51 CRD:s were recorded in various striated muscles in NMD and 28 CRD:s in MFP. All CRD:s were drawn on paper. The frequency, maximum amplitude of the main component, number of spikes in the main component and blocking of some of the spikes were studied. Some of CRD:s were studied with two of three needles in parallel of the muscle fibres (fascicular EMG) to study the propagation of CRD. The difference between variables of CRDs were analysed with t-test.

**RESULTS**

The CRD variables did not show any significant differences, when CRD:s in NMD and MFP were compared. Fascicular EMG showed that some CRD:s are strictly local, especially high-frequency CRD:s. On the other hand some CRD:n propagate along muscle fibres as motor unit potentials do.

**CONCLUSIONS**

Similar results on variables of CRDs in NMD and MFP point out that the basic mechanism of the occurrence of CRDs is the same in both diseases. Ephaptic muscle fibre circuit does not explain CRD:s in myofascial pain, where the membrane properties of muscle fibres are normal and ephaptic transmission is improbably. On the other hand also denervated muscle fibres develop membrane alterations with a long (>100 ms) refractory period, which does not allow rapid recurrence of the basic component. Blocking experiments with curarization and local anaesthetics have been performed to exclude spinal reflex mechanisms of CRD:s but there are no neurophysiological recordings to prove a successful total block. CRD:s may thus have a spinal reflex mechanism, originating from intrafusal drive of II-, III- and IV-afferents to efferent gamma- and beta motor systems. These have also different neuromuscular junctions compared to alpha motor neurons which may explain the small jitter.
P857
Thoracic outlet syndrome with more then 8 years subclavian artery involvement?

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Question

Are all forms of thoracic outlet syndrome (TOS) with subclavian artery involvement serious?

Methods

This study reports a cases of a 25 year old Caucasian female with a very long history (>8 years) of thenar muscles atrophy with no functional impairment and no pain. Electrophysiological and imaging studies were done.

Results

Initial electrophysiological studies shown normal SNAP both on ulnar and median nerves with just a reduction on CMAP amplitude on both nerves on the affected side. Electrophysiological follow up (six months) showed a combinations of reduced ulnar SNAP on the affected side with normal latency and low amplitude CMAP, normal median SNAP with reduced CMAP and prolonged f wave responses. Cervical CT scan reviled the existence of a bilateral cervical rib. Doppler studies showed a right subclavian artery involvement.

Conclusions

Thoracic outlet syndromes includes various clinical entities that can affect brachial plexus and/or subclavian artery. Among the causes of this syndrome cervical ribs or bands are included. Although pain is one of the most common signs in TOS some patients can present with no clear anamnestic history. In this case a monomelic amyotrophy cannot be rolled out as the initial cause of thenar atrophy due to age and history. But because of the imaging aspect and the dramatic changes on electrophysiology examination within six months, a clear TOS diagnosis has been made.
Modulation of motor cortex plasticity with transcranial direct current stimulation in spinal cord injury patients: intensity dependent quantitative EEG study

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**Question**

Existing strategies to enhance motor function following Spinal Cord Injury (SCI) are suboptimal leaving patients with considerable disability. Available evidence suggests that Transcranial Direct Current Stimulation (tDCS) is a promising non-invasive neuromodulation method that can improve motor behavior.

Using Neuroelectric’s Starstim novel multichannel wireless device, which allows for simultaneous electroencephalography (EEG) and tDCS, we aim to determine the effects of anodal tDCS on EEG to assess changes in brain system activity after stimulation, and understand further the mechanisms of this technique in modulating cortex plasticity and its potential in protocols for motor rehabilitation.

**Methods**

We conducted a randomized, single-blind, sham-controlled, cross-over study in four chronic SCI subjects with cervical lesions, investigating the effects of 20-minute anodal tDCS applied over the primary motor cortex (M1) on electroencephalography (EEG) power spectrum density, coherence and frequency band power (theta (4-8Hz), alpha (8-10Hz), beta1 (16-25Hz), beta2 (25-35Hz)). Subjects were randomized to one of the three study groups: 1mA, 2mA or sham stimulation. The EEG data consisted of 5-minute takes of 24 bit, 500 S/s 8-channel EEG collected with StarStim Ag/AgCl EEG electrodes (positions at C3, AF8, F3, F4, Cz, C4, P3 and P4; and Pi Ag/AgCl electrodes at C3 and AF8) acquired at two time points for each subject (pre and post stimulation). C3 was used for anodal stimulation and AF8 as a return electrode (Figure 1).

**Results**

Our results showed that, in comparison to sham stimulation, 20-minutes of active 1 and 2mA tDCS induced a decrease on the total power spectrum density (1-40 Hz), with significant changes in the 2mA vs. sham group in the theta and alpha bands, that were not present in the 1mA group (Figure 2). Changes in coherence were found across the 1mA vs. sham group in the beta2 and gamma bands. Also, significant changes were found in mean frequency across 1mA vs. sham in alpha1, alpha2 and beta2 bands, while the 2mA vs. sham group showed significant changes in full bands and beta-1.

**Conclusions**

These findings show that tDCS is capable of inducing intensity-dependent modulation of ongoing oscillatory brain rhythms and may provide further elements for understanding the underlying mechanisms of tDCS alteration of motor function. Overall, we show in this study that active tDCS effects on the modulation activity of the motor cortex are associated to a decrease of the total power spectrum of the full bands.

Figure 1. Electric field induced by montage (+ C3, - AF8 using Pi electrodes (3.14 cm2 Ag/AgCl electrodes).

Figure 2. Full band results for the normalized Pre-Post Power changes of 1mA vs sham (left) and 2mA vs sham (right) groups. The bottom map provides the p-value (Wilkox) of Sham vs. active stimulation.
P859
Differences in Resting-State Functional Magnetic Resonance Imaging Functional Network Connectivity between Patients with Restless Legs Syndrome and Controls

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Question

Restless legs syndrome (RLS) is generally considered to be a central nervous system (CNS) disorder, although no specific lesion has been found with a conventional MRI scan. The purpose of our present study was to explore the intrinsic changes in the functional network connectivity (FNC) in RLS patients, using resting-state fMRI data.

Methods

We obtained resting state fMRIs for 45 idiopathic RLS patients (28 drug naïve; 17 drug treatment) and 16 healthy gender matched controls. The GIFT group ICA toolbox was used to identify temporally independent resting state components. Among them, 19 independent component networks were deemed valid resting state networks and they yielded 171 total pairwise combinations. We compared the two groups with a correlation coefficient of 171 total pairwise combinations using SPSS v19.0 (controlled for both age and gender, uncorrected p-value).

Results

RLS patients showed higher correlation than controls among three network pairs: visual processing network-discrimination of the location network, visual processing network-theory of the mind and social cognition network, sensorimotor network-interoception processing network. Four network pairs including visual processing network-auditory network, visual processing network-sensorimotor network, action and somesthesis network-auditory network, interoception processing network-discrimination of location network showed lower correlations in RLS patients than controls.

Conclusions

We identified several abnormal resting state network connections of patients with RLS. Significant differences between the RLS patients and the controls connectivity in these different networks revealed possible deficiencies in cortical processing of the RLS patients.
A study of investigation request form designs across Clinical Neurophysiology departments in the United Kingdom: towards a better design.

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**Question**

The information on the Neurophysiological request form is of paramount importance in determining the appropriate investigation to answer a clinical question. We surveyed the Clinical Neurophysiology departments across the United Kingdom to investigate how they collect clinical information prior to seeing the patient.

**Method**

A letter was sent to 77 Clinical Neurophysiology Departments in the UK asking for their request forms. The forms were then analysed to look at the data requested on the form and the method of gaining information prior to meeting the patient.

**Results**

58/77 departments replied of whom 2 used electronic requests. The following were requested by the remaining 56 departments: name 98%, address 91%, telephone number 57%, hospital number 92%, ward 95%, date of birth 86%, age 13%, date of admission 5%, gender 40%, title 32%, referring physician 95% and referring specialty 23%. 17-70% of the page was devoted to demographic information. 66% used a tick box/ring to request a test; 20% used separate forms and 14% left space for free text. Prompts for clinical information were made by requests for: history 93%, previous test results 27%, clinical examination findings 74% and medication 88%.

**Conclusions**

It is clear from our survey that there is a wide variety in the range of demographic data required by the departments. In one case this used up over 2/3 of the form and left little space for clinical information to be added. A significant proportion of the request forms direct the referrer to fill in clinical information and we feel that this is a useful tactic, as it is our experience that the request form is often incomplete and the clinical information sub-optimal. Thus we feel that the information required should be the minimum required to correctly identify and contact the patient, to be able to perform appropriate and directed clinical investigation and to be able to return the clinical report to the referring physician. As a result of this study we have changed our referral form to request less demographic data and give more space for the referring question. It will be interesting to repeat this study in a several years time to see how electronic requests have developed compared to their paper equivalents.
P861
The long-range corticomuscular synchronization as the neural correlate of the internal stochastic resonance phenomenon

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Noise can have beneficial effects as shown by the stochastic resonance (SR) phenomenon. The internal SR phenomenon occurs in nonlinear systems in which an intermediate level of Gaussian noise can enhance the response of such systems to weak signals. Modern attempts to improve human performance utilize this phenomenon. The purpose of the present study was to investigate whether performance improvement by an optimum noise is related to increased long-range synchronization between motor cortex and muscles reflected in an increase in corticomuscular coherence and spectral power (SP), i.e. cortical motor synchrony. Eight subjects performed with the right index finger a visuomotor task requiring to compensate isometrically a static force generated by a manipulandum on which stochastic noise could be applied. The finger position was displayed on-line on a monitor as a small white dot which the subjects had to maintain in the center of a green bigger circle. EEG from the contralateral motor area, EMG from the active muscles and finger position were recorded. The performance was measured by the mean absolute deviation of the white dot from the zero position. Optimum noise compared to the zero noise condition induced a significant improvement in motor accuracy together with an enhancement of cortical motor SP and corticomuscular coherence. These data suggest as the neuronal basis of the improved sensorimotor performance via SR an increase in local cortical motor and long-range synchronization between cortical motor and spinal circuits.
Multicenter collection of reference values for jitter obtained with concentric needle electrode.

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QUESTION

In some countries only disposable needle EMG electrodes can now be used. Thus, an alternative must be sought for the Single Fiber EMG (SFEMG) electrode to measure the neuromuscular jitter. The so-called “facial” concentric needle electrode (CNE) has been recommended for this purpose. Although small, its recording surface is still much larger than that of the SFEMG electrode, giving a significant risk of recording action potentials from many, rather than single muscle fibers. “Apparent single fiber action potentials (ASFAPs)” recorded with the CNE can be used for jitter analysis. Since these signals still differ from the SFEMG signals, new reference values are required. We aim at collecting those in the age group of 20 to 80 years.

METHODS

Electromyographers experienced in recording jitter have been invited to participate. Each participant must earn an “entrance ticket” by submitting 5 full CNE studies from orbicularis oculi, frontalis or extensor digitorum (ED) muscles with voluntary or electrical activation, the quality of which must be considered acceptable by 2 study monitors.

RESULT

Centers from Japan, Brazil, USA, Slovenia and Sweden have so far received their entrance ticket. It is obvious that it is more difficult to obtain good quality signals with the CNE, particularly in the ED.

CONCLUSIONS

In deciding between accepting somewhat distorted signals, which would give wide reference limits, and stricter signal quality, we have chosen the latter. Jitter is a sophisticated biological event that should not be buried in undefined artifacts. With poor recordings, the sensitivity of this technique will be lost.
P863
EEG response to different odors in healthy individuals: a promising tool for objective assessment of olfactory disorders

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Objective
The aim of this study was to examine human CNS response to three different odors: lemon, vanilla and peppermint.

Methods
Sixteen healthy participants, 7 females and 9 males (mean age 29+-3), were included in this study. Electrophysiological activity was recorded with EEG-cap with 32 active electrodes in the baseline state and for three odors, lemon, peppermint and vanilla. Fast Fourier Transformation (FFT) analysis was performed on every set. Mean value of activity in theta interval (4-8Hz) was exported from every data set and statistical analysis was conducted.

Results
A significant reduction of theta band was found for each odor and the mean value of all three odors. Electrodes grouped into five regions (left anterior (LA), right anterior (RA), central (C), left posterior (LP) and right posterior (RP)) showed the mean theta activity for the lemon and peppermint differed statistically significant between regions (P < 0.0005 and P = 0.035, respectively), while for the vanilla there was no statistically significant change (P = 0.309). Lemon and peppermint elicited greater reduction of theta band in the C region comparing to other regions (C vs LA, P = 0.002; C vs RA, P = 0.002; C vs. LP, P = 0.001 and C vs RA, P < 0.0001; C vs LA, P = 0.001; C vs. RP, P

Conclusions
EEG response to odors is characterized with the significant reduction of theta band. Lemon and peppermint have the greatest effect in the central region.
Motor and sensory function in smartphone users

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Objective

Smartphone users use their finger pads more frequently than smartphone non-users, because touch screen is a common input mechanism in smartphone. The aim of this study is to investigate the effect of smartphone usage on motor and sensory function.

Methods

We assessed finger dexterity with the Grooved pegboard test and spatial discrimination with Johnson-Van Boven-Philips (JVP) domes and two-point discriminator in smartphone users and smartphone non-users. All smartphones in this study had touch screen input method. Smartphone non-users were defined as people who had never used smartphones, and their mobile phones used only keypad input method. The motor and sensory measurements were compared between smartphone users and smartphone non-users. In smartphone users, the correlation between the usage and the motor-sensory function was also analyzed.

Results

Fifteen smartphone users and six non-users participated. There was no difference of finger dexterity between the smartphone users and the non-users, but the threshold for spatial discrimination tended to be lower in the non-users. In the smartphone users, the daily amount of smartphone use was not associated with the motor function, but negatively correlated with the threshold for spatial discrimination in the right hand.

Conclusions

This study suggests that more frequent use of smartphone might enhance sensory function, but we did not find any evidence that touch screen input method is superior to keypad input method to improve motor and sensory function.
RELATIONSHIP BETWEEN MUSCLE FIBER CONDUCTION VELOCITY AND EXPLOSIVE PERFORMANCE

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Question

Human performance in explosive activities is influenced by a number of neuromuscular factors. However, the contribution of muscle fiber conduction velocity (MFCV) in power demanding activities remains uncertain. Aim of the study was to describe the relationship between the MFCV and explosive performance.

Methods

Fifteen moderately-trained young females performed an isometric leg press test for maximum isometric force (MIF) and rate of force development (RFD), as well as a countermovement jump (CMJ). At a different occasion, MFCV was measured with intramuscular microelectrodes at rest (stimulation signal was set at 0.05ms duration, 1Hz frequency, 2-15mA and filtered between 2kHz-20kHz). The mean MFCV (MFCV_total) and maximum MFCV (MFCV_max) of all muscle fibers, as well as the mean MFCV of type I (MFCV_typeI) and type II (MFCV_typeII) muscle fibers, were determined and used in further analysis.

Results

RFD at 100ms, 150ms, 200ms and 250ms was significantly correlated with MFCV_total (r range between 0.796-0.887, p<0.001) MFCV_typeII (r=0.765-0.859, p<0.001) and MFCV_max (r=0.859-0.924, p<0.001). Similar correlations were found between MIF and MFCV_total (r=0.764, p<0.001). Lower but significant correlations were found between the power production during the CMJ and MFCV_total (r=0.656, p<0.001), MFCV_typeII (r=0.599, p<0.05), and MFCV_max (r=0.625, p<0.05).

Conclusions

These data suggest that the velocity with which the neural signals travel along the muscle fibers is linked with performance during explosive actions, most likely because MFCV is mainly determined by the size of the muscle fibers and/or the protein isoforms of the Na+-K+ pump.
Effect of prefrontal cortical activity in preparatory period on success or failure of response inhibition in stop-signal task

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Question

The prefrontal cortex plays an important role in response inhibition. How prefrontal cortex activity in the preparatory period contributes to an accurate response inhibition is less well understood. To examine this, contingent negative variation (CNV) were compared with success and failure of response inhibition.

Methods

In the present study, CNV during a stop-signal task (SST) was examined in 11 right-handed healthy subjects (age: 18-24 years). The subjects were required to press a button when a go signal was presented but, to withhold the response occasionally followed by a stop signal. Electroencephalogram data were recorded from the scalp using 128 channels. Six channels (Fz, F3, F4, Cz, C3, and C4) in accordance with the international 10-20 system were adopted as regions of interest (ROI). The preparatory period of successful and failed inhibitions were compared and analyzed.

Results

The early CNV amplitudes of Fz, F3, and C3 in preparatory period were significantly higher in the failed inhibition than in the successful inhibition. The late CNV amplitudes of all the channels except C3 were significantly higher in the failed inhibition than in the successful inhibition.

Conclusions

CNV reflects the preparation of response and the simultaneous anticipatory attention for the upcoming go signal. Higher prefrontal activities in the preparatory period facilitate the execution processes after the presented go signal. In fact, failure in response inhibition, due to prior starting of the execution process, completed faster than the process of inhibition starting later.
P867
Recording and reporting by Biomedical Scientists in Carpal tunnel syndrome

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Question
To reduce the increasing workload of the physician we need to use the skills and experience of other members of the staff, in this case the Biomedical Scientist (BS). We tested task shifting on the referral diagnosis of CTS.

Methods
The new task was well defined in collaboration between physician and BS. Education, application, evaluation, standardisation of the report and recurrent quality controls were undertaken. The principle consisted of interpretation and reporting by BS blinded to previous results in 100 cases. The result was compared to the report given by the physician. There was a very high concordance in the interpretation and decision was made to licence those BS that had undergone the test period. Agreement was made that the BS did not report cases of atypical pattern.

Results
The number of CTS that remained to be analysed and reported by the physician was 386 out of 1643 in three years - a reduction of 77% in workload regarding this patient group. Quality controls (peer reviews) are performed twice a year and clinical careers for Biomedical Scientists are introduced.

Conclusion
The success of task shifting is dependant on needs and positive acceptance from parties involved. A period of testing and evaluation from both parties followed by regular quality control is required. Due to the positive outcome of this task shift we have implemented the same principles in other areas of clinical neurophysiology. We consider this a way to optimize the work in our laboratory.
P868

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Nonverbal signals such as facial expressions have repeatedly been shown to be critical in the shaping of social behavior (e.g. Hari & Kujala, 2009). Their perception predominantly occurs quickly and subconsciously, often without the possibility of active cognitive intervention: Minute violations of the basic proportions of the human face, for example, lead to the feeling that "something is wrong", without being able to specify what (Lewicki 1986).

Question
Which (neural) mechanisms allow for the effortless and quick perception and interpretation of these pivotal signals in natural situations?

Methods
This was investigated using functional magnetic resonance imaging as well as eye-tracking technology in a face perception task.

Results
Our data suggest that the natural strategy for judging emotional faces is an intuitive one, relying on neural structures of the mirroring system (e.g. temporoparietal junction), along with areas involved in intuition and reflexive consciousness (medial orbitofrontal cortex [OFC]) and interoceptive awareness (anterior insula).

Conclusion
Based on our findings and expanding upon previous research, we propose that in intuitive judgments of emotional faces, the visual information is sent via extrastriate areas to the OFC and seems to entail a top-down influence of the OFC to further downstream activation, explaining the swiftness of these judgments that are not consciously accessible. We are only beginning to understand the neurobiological underpinnings required for the use of facial expressions in dyadic social interactions and will branch out towards a holistic understanding by including the study of the adaptive value of facial expressions in social communication.
Visual self-recognition: I am my actions

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Question

The Neuroscience of dance is a thrilling field which main goal is to study cognitive processes combining the human movement and neuropsychology. In our study we use fMRI technique to map the representation of the visual-self-body recognition while the subject is watching videos of expert flamenco dancers in both first-person (the subject themselves dancing) and third-person perspectives (a dancer model dancing). We compare this activation with the representations obtain after watching ballet steps or simple sports warms exercises.

Methods

Ten expert dancers viewed series of 15ms clips of three different movement conditions (flamenco, ballet and sport steps) and in two different perspectives (first vs. third view) during the registration of fMRI protocol. The fMRI data was analyzed with SPM8 in a factorial design, movement type and perspective, resulting in different activations depending on the analyzed condition.

Results

The visual self-recognition effect (for all actions, sport or any kind of dance) implicates the insula and inferior posterior parietal cortex, as well as the middle cingulum and the supplementary motor area, and not only for certain effectors of discrete actions, but also for ecological ones like dancing. Watching whole body actions implies a recognition of the action self (insula and BA40), preparation for the action or involuntary imitation (BA4 and 6), empathy (BA24/32), visual consciousness (BA18-19) and somatotopic activation (BA1, 2, 5, 7). Notably, subtracting flamenco condition (first vs. third view) there was left activation of BA11 (orbitofrontal cortex), the left inferior frontal gyrus (BA44), the left insula, the right postcentral gyrus (BA40) and the amygdala.

Conclusions

We propose that representation of the visual self-recognition is different for each kind of action: it is cognitive and qualitative in flamenco, sensorimotor in ballet and “by default” in physical exercise. Moreover, there is a specific network that takes over distinguishing between self and the others.

Figure 1: Cerebral image comparing the conditions First > Third person in Flamenco. Z is the sagittal coordinate and the vertical bar indicates the t value.
P870
Prevalence of chronic degenerative diseases of the nervous system in adolescents and adults people in physical therapy services

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Introduction

The aging processes, scientific advances in health care actions, and inadequate lifestyles have triggered population sensitive changes in the epidemiological profile within which chronic degenerative neurological diseases have become increasingly frequent with its implications to the quality of life.

Methodology

Cross-sectional study was performed statistical records taking care of Physiotherapy services Practices Physiotherapy Program Manuela Beltran University, for the period February to April 2009 within which we calculated prevalence of chronic degenerative diseases treated in adolescents and adults starting from 15 years onwards, which are calculated as raw and level specified with the corresponding standard error.

Results

In the study period were treated a total of 2087 patients, of which 10.20 % (n = 213, standard error = 0.06) were assisted by file type chronic degenerative diseases, of these people with a 23.94 % of them had chronic degenerative diseases affecting the nervous system (n = 51, standard error = 0.04).

52.94 % (n = 27, standard error = 0.06) of those who had chronic degenerative diseases of the nervous system were of male gender.

Among the chronic degenerative diseases of the nervous system by 19.6 % (n = 10, standard error = 0.09) were cases of multiple sclerosis and fibromyalgia with the same prevalence, which was followed by muscular dystrophy entity record in 17.64 % of cases of chronic degenerative diseases of the nervous system (n = 9, standard error = 0.09), and 11.7 % of patients seen were cases Alzheimer disease (n = 6, standard error = 0.09).

Conclusions

Chronic degenerative diseases of the nervous system have important prevalences, being multiple sclerosis and fibromyalgia chronic degenerative entities nervous system that most often are treated in Physiotherapy followed by muscular dystrophy.
Prevalence of traumatic neurological diseases in adolescents and adults people in physical therapy services

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Introduction
Modern societies have experienced noticeable changes in their epidemiological profiles within which traumatic diseases has become a major public health problem for its prevalence, costs and impacts on the quality of life.

Methodology
The study developed corresponded to a non-experimental, observational, cross-sectional descriptive secondary sources.

The collection of information that will work occurred from monthly statistical records of patient care in Physiotherapy Services Practice Sites Level Assistive Therapy Program Manuela Beltran University February period April 2009.

The processes of data analysis were handled raw prevalence estimates and specific measures to which they estimate their level of standard error.

Results
During the observation period 2484 patients were treated of which 54.18% (n = 1346, standard error = 0.00) were female gender.

A 19.9% of patients who were treated had traumatic diseases (n = 495, standard error = 0.01), of which 65.8% were male gender (n = 326, standard error = 0.01).

14.5% of traumatic origin entities affecting the nervous system (n = 72, standard error = 0.02).

50% of people with neurological diseases were cases of spinal cord injury (n = 36, standard error = 0.05), whereas 43.0% of patients with brain injury had these entities. Of the patients who were treated for spinal cord injury cases 94.4% (n = 34, standard error = 0.00) were male gender, and 100% of those who had brain injury cases were of this gender.

Conclusions
The traumatic neurological diseases have important prevalences in adolescents and adults peoples with principal afectation in the male gender mainly by spinal cord injury cases requiring actions to help promote personal safety by reducing the use of weapons and the occurrence of vehicular accidents.
Qualitative vs quantitative evaluation of arousal and valence associated to the chants in the terraces of football stadiums

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There exists a way of invading physically the area of game in football stadium. We can modify his acoustic field.

The pretension is to study the stimuli generated by the principal sources of the sound: the supporters from the terraces. The exhibition to these sonorous stimuli well could unleash feelings euphoria, lessen the physical weariness, to free from inhibitions, improve the skill ambidextrous, modify the relation temporary space, alter the perception or diminish the time of response.

Another application may be to reduce the recovery time of injuries, allowing to reduce the perception of effort and pain if not relevant. Similarly, the music has been used to reduce the length of stay in hospital care units.

Along the investigation have been registered the sonorous environments of six matches. Also there have been processed some other sonorous stimuli of equal duration and claimed emotional load but without any relation with the sport. Finally fans have been exposed to these stimuli in order to value, by means of the response format named SELF ASSESSMENT MANIKIN. We answer about arousal, valence and other variables. Also, we used Electrodermal Group Activity (EDAg) for study lateral answer of brain and compare with previously qualitative results. This measurement technique is possible with machine named Sociograph®.

Of this form we will be able to discriminate against the variable of belonging or not to the sports activity as fundamental characteristic of the stimulus to study the consequences in the brain.

In this first approximation, we have tried to explore as the brain answers before the sonorous stimuli of the fans. But on future phases of the Investigation we will submit these stimuli to study also to professional players with different innocuous technologies between which should stand out Magnetoencephalography (MEG).

**KEYWORDS:** FOOTBALL, FANS, CHANTS, AROUSAL, HOME ADVENTAGE, CROWD NOISE, TERRACES, ELECTRODERMAL ACTIVITY, SOCIOGRAPH

figure 1
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figure 2
P874
The adam10 gene plays an important role in the development of the cerebellum

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Adam10 gene is widely expressed in the cerebellum, suggesting that it may play an important role in the development of cerebellum. Adam10 gene knockout at early stage of embryogenesis in the central nervous system leads to prenatal death of knockout mice and prevents our further research on the function of adam10 gene in the development of cerebellum. Through the use of CRE-LOXP system, we selectively knocked out the glia cells (including radial glial cells) adam10 gene in mice. Thus, the adam10 gene knockout mice could survive as long as three weeks, which permitted us to study the role of the adam10 gene in cerebellar development. The adam10 gene conditional knockout mice (CKO mice) showed abnormalities from embryonic 18.5 (E18.5), mainly on the morphology defects of the cerebellar foliation and cortex architecture. Glial cells in CKO mice appeared abnormal from E 18.5 as indicated by the disorder of the cell bodies at the adjacent folia. With the development of cerebellum, the abnormal morphological differentiation of the Bergmann glial cells was obviously. Most of the Bergmann glial cells lost radial protrusions and could not attach to the pial surface. At the same time, the glial cells BLBP protein was down-regulated and the glial cell apoptosis was increased. The granule cells mainly showed abnormal distribution. After postnatal 4 days, the granule cells began to cluster lining the fused folia; 21 days after birth, a considerable part of granule cells could not migrate into IGL and these cells accumulated at the meningeal surface or adjacent fused folia. In addition, the proliferation of granule cell precursors was decreased and the granule cells apoptosis was increased. Purkinje cells also displayed abnormal development whereas these changes were secondary and non-cell autonomous. After birth, it did not cause abnormal development of cerebellum by ablating the adam10 gene in glial cells or granule cells. In CKO mice, the Notch I protein levels were down-regulated. However, adam10 knockout did not affect β-catenin, N-cadherin or L1 protein expression. The results suggest that the adam10 gene is critical for the formation of cerebellar foliation and cortex architecture and plays an important role in the migration of granule cells. More experiments are needed to dissect the underlying mechanisms.

figure 1
figure 2
Pelvic Floor Electrophysiology in Spinal Cord Injury

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**Question**

What is the utility of electrophysiologic testing of pelvic floor in patients with chronic spinal cord injury?

**Methods**

12 patients aged 18 to 63 years with chronic complete spinal cord (C8-Th10) injury were examined prospectively in relation to a project regarding nerve anastomosis of L5 and S2 ventral roots to obtain bladder and eventually bowel control. In all patients, external anal sphincter (EAS) electromyography (EMG), pudendal nerve motor nerve conduction studies (NCS) with St Marks electrodes and bulbocavernous reflex (BCR) with single electrical stimulation of penis/clitoris and recording from bulbocavernous muscle were performed. Assessment of fibrillations (fibs)/positive sharp waves (PSWs) and quantitative individual motor unit potential (MUP) and interference pattern (IP) analyses were done in EAS. The latencies and amplitudes were evaluated for motor NCS of pudendal nerve and minimum latencies for BCR.

**Results**

Patients had fibs and/or PSWs in EAS and mean MUP duration was prolonged in 8 patients. The persistence of BCR was high (100%). The minimum BCR latencies were normal (mean: 34.4 ms; range: 28-40 ms) in 11 patients and prolonged (51 ms) in one patient. Pudendal nerve motor latencies were between 1.4 ms and 3.1 ms without any significant side difference and amplitudes ranged from 0.4 mV to 1.9 mV with a side difference of more than 50% in 4 patients.

**Conclusions**

Sacral neurophysiologic studies may have diagnostic implications in patients with spinal cord lesions. Unexpectedly high incidence of neurogenic changes in EAS muscle, prolonged BCR and side difference in the amplitude of pudendal nerve may indicate some kind of lower motor neuron/peripheral nerve involvement. Further studies have to be conducted to understand the underlying cause and mechanisms.
Cholinergic stimulation and skin melanogenesis

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Question

Paracrine/autocrine activity of some neuromediators was also evidenced in non-neuronal tissues, including human skin. We investigated the possible role of acetylcholine in melanogenesis of the skin, by quantification of tissular activity of butyrylcholinesterase (BChE) and acetylcholinesterase (AChE), enzymes responsible for the inactivation of acetylcholine.

Methods

AChE and BChE (mU/mg protein) levels were analysed in pigmented melanoma (17 samples), acromic melanoma (14 samples), melanosis (12 samples), vitiligo (15 samples), perilesional tissue (22 samples) and healthy skin tissue (9 samples).

Results

AChE and BChE levels were significantly lower in acromic melanoma versus pigmented melanoma (3.07±0.9 versus 5.01±1.9 mU/mg protein, p<0.05 for AChE and 1.7±0.4 versus 2.8±0.7 mU/mg protein, p<0.05 for BChE), in depigmented skin versus pigmented skin (2.1±1.1 versus 9.4±3.6 mU/mg protein, p<0.05 for AChE and 1.8±0.5 versus 4.1±0.6 mU/mg protein, p<0.05 for BChE).

In addition, we obtained a significant difference between the level of enzymatic activity in pigmented skin and in the adiacent epidermis.

In vitiligo patients we observed a reduction of AChE and BChE levels, both in lesional tissue and in unaffected skin, versus normal skin of control group.

Conclusions

The reduction of AChE and BChE levels in depigmented tissues versus pigmented corresponding tissues was associated with an increase of tissular acetylcholine. These observations confirm the inhibitory effect exerted by acetylcholine on the synthesis of melanin. The restoring of normal metabolism of acetylcholine in noncholinergic tissues represent an attractive field of research.
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P877
TRANSCRANIAL DIRECT CURRENT STIMULATION IMPROVES SEIZURE CONTROL IN PATIENTS WITH RASMUSSEN ENCEPHALITIS

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PURPOSE

Rasmussen encephalitis (RE) is associated with severe seizures not responsive to antiepileptics as well as immuno-suppressants. Transcranial direct current stimulation (tDCS) is a non-invasive and safe method tried in drug-resistant epilepsies. Our aim was to investigate the effect of t-DCS on the seizures in RE.

METHODS

Five patients (mean age: 16.5; 3 females), diagnosed as RE with their typical clinical and neuro-radiological findings, were included after their signed consent. Patients received anodal, cathodal and sham stimulation (2 mA for 30 minutes on 3 consecutive days). Two type of cathodal stimulations were used; 1-tDCS 2-amplitude modulated tDCS. While three of the patients received cathodal tDCS, two patients received cathodal stimulation with amplitude modulation at 12 Hz. All patients received anodal stimulation with amplitude modulation at 12 Hz. Three patients received sham stimulation (60 seconds stimulation gradually decreased in 15 seconds).

RESULTS

Four patients except one had more than 50 % decrease in their seizure frequencies by cathodal stimulation. Two patients who received modulated cathodal tDCS had better results. One of those patients, had 8 days of seizure freedom despite her previous frequency of 20-30 seizures/day and the other patient also had 10 days seizure freedom. Longest positive effect of t-DCS lasted one month. On the other hand, anodal stimulation and sham stimulation were not effective. No adverse effect has been reported. The last patient had no change in seizure frequency by both anodal and cathodal t-DCS.

CONCLUSION

Although our series was small, it can be suggested that t-DCS may be tried as an alternative method for improving seizure outcome among RE patients before sending them to surgery. Further studies are needed to find out the best parameters of the cathodal t-DCS in large series.
Incidence of functional alterations of somatosensory pathways in the hereditary spastic paraplegia SPG4


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Questions

The most common forms of autosomal dominant hereditary spastic paraplegia (HSP) is SPG4, caused by mutation in the gene that encodes for the spastin. The main clinical features in this neurodegenerative condition are progressive spasticity and weakness of the lower limbs due to corticospinal tract involvement, accompanied with sensory and motor neuropathy. Are there any functional alterations of posterior columns somatosensory pathways in SPG4?

Methods

Somatosensory evoked potentials (SEPs) following stimulation of median and posterior tibial nerves were performed in 28 (18 men) genetically confirmed SPG4 patients from 18 families, in mean age 44.8 ±13.8y, with average disease duration24.2±12.9 y and in 30 healthy volunteers matched for age and height. The latency and amplitude of recorded SEPs were measured at the peripheral, lumbar, thoracic, cervical levels and from the contralateral scalp. Peripheral conduction velocity was calculated for the median and posterior tibial nerves. The spinal conduction time and central conduction time (CCT), were defined as interpeak latency: P9-P14, P14-N20, N24-P31 and P31-P40.

Clinical severity was evaluated by Spastic Paraplegia Rating Scale (SPRS). MRI of brain and spinal cord were performed to exclude other causes of spastic paraplegia.

Results

The clinical severity assessed by SPRS was 20.4 ± 11.4 (from 2 to 46) points and correlated with disease duration. Cortical SEPs by stimulation of median nerves were abnormal only in 25% of patients: prolonged cervical conduction time P9-P14 with decreased amplitude in three cases. Central conduction time of the posterior spinocerebral tracts from the lumbar segments to the medial medullar lemniscus (N24-P31) was prolonged only in a10 (38%) of cases. In two patients with long disease duration we disclosed total conduction block above N24. The recorded cortical SEPs from lower limbs revealed severe temporal dispersion with decreased amplitude in 17 (61%) patients. In these cases MRI disclosed the thin corpus callosum and white matter hyperintensities. Slowing of conduction velocity accompanied by loss of sensory fibers (diminished amplitudes) were found at the peripheral segments of posterior tibial nerves in 9 subjects.

Conclusions

This study provides evidence for the involvement of somatosensory pathways in the SPG4. Somatosensory evoked potentials may become important progression markers in upcoming interventional trials.

The study was supported by grant POIG 01.01.02-14-051/09/01 from the Ministry of Regional Development Operating Programme Innovative Economy.
P954
Altered awareness of action in Parkinson's disease

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Parkinson's disease (PD) is a neurodegenerative disorder affecting voluntary action. However, whether the awareness of action in this disorder is affected is yet to be known.

We used the intentional binding paradigm (Haggard, 2002) to measure the extent to which experiences of actions are influenced by subsequent effects (tone). It has been reported that voluntary actions were perceived closer in time to the effects and effects closer to actions in healthy and young participants. The actions were perceived more distant to effects and effects more distant to actions when the actions were involuntary.

We conducted this task in 15 PD patients (mean age = 64.9) and 25 age and sex matched healthy controls (mean age = 64.9) with each of their hands. There were no differences in the separate timing judgments of actions and tones between groups. When actions were followed by effects, effects were perceived closer to actions in both groups. On the other hand, while actions were perceived closer to effects in the control group, actions were perceived more distant from effects in PD group. This tendency was consistent in limbs with both stronger and weaker motor symptoms in PD (fig.1).

This may reflect an underlying abnormality in the subjective experience of voluntary action in PD.

figure 1
Longitudinal fVEP measurements in extremely premature infants

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Einleitung


Methodik


Ergebnisse

58 Patienten waren eingeschlossen davon 16 exkludiert wegen neurologischen und 7 wegen Optalmologischen Auffaelligkeiten. (24+1 bis 28+6 SSW). In jeder Messung wurden die Latenzen N2, P2 und N3 ermittelt und deren Mittelwert mit Standardabweichung als Referenz fuer die jeweilige Schwangerschaftswoche berechnet. Hier sind die Ergebnisse der 35 Patienten.

Eine negative Korrelation mit dem zunehmenden Gestationsalter ist zu erkennen.

<table>
<thead>
<tr>
<th>SSW</th>
<th>23-24</th>
<th>25-26</th>
<th>27-28</th>
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<tr>
<td>n</td>
<td>2</td>
<td>8</td>
<td>25</td>
</tr>
<tr>
<td>N2</td>
<td>323 (10)</td>
<td>308 (53)</td>
<td>353 (29)</td>
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<tr>
<td>P2</td>
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<tr>
<td>N3</td>
<td>577 (2)</td>
<td>646 (71)</td>
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P1060
Suppressing cortical hyperexcitability of right parietal cortex by repetitive transcranial magnetic stimulation (rTMS) relieved the anxiety symptom of patients with generalized anxiety disorder

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Question

Generalized anxiety disorder (GAD) is a common anxiety disorder. However, the underlying mechanisms of the disorder are poorly understood. Prior studies have shown dysfunction of right parietal cortex in patients with anxiety disorders. The purpose of the present study was to investigate the changes in cortical excitability of right parietal cortex using the recovery function of median nerve somatosensory evoked potentials (SEPs), and to assess the efficacy of repetitive transcranial magnetic stimulation (rTMS) of the right parietal cortex on anxiety in patients with GAD.

Methods

This study was comprised of two parts. In the first part, we studied the recovery function of left median nerve SEPs in 15 medication-naive GAD patients and in 15 age- and sex-matched healthy subjects. SEPs in response to single stimulus and paired stimuli at interstimulus intervals (ISIs) of 20, 60, 100 and 150 ms were recorded. In the second part, 42 patients with GAD were randomly assigned to receive 1 Hz low-frequency rTMS (rTMS group, 22 patients) or sham rTMS (sham group, 20 patients) to the right parietal cortex (over 10-20 EEG electrode site P4) for ten days. The Hamilton Anxiety Scale (HAMA), Hamilton depression Scale (HAMD) and Pittsburgh Sleep Quality Index (PSQI) scores were obtained before and after the treatment period, two weeks and one month after the treatment.

Results

In the first part, the recovery function of the cortical component of P25 showed significantly less suppression at ISI of 20 ms in GAD patients as compared to healthy controls. In the second part, the HAMA, PSQI and HAMD scores after the treatment period, two weeks and one month after the treatment, significantly decreased in comparison with scores before the treatment period. However, no significant changes of theses scores were observed in the sham group.

Conclusions

The present study suggests that cortical excitability of right parietal cortex is increased in GAD patients, and suppressing the hyperexcitability of it by low-frequency rTMS was effective in relieving anxiety in patients with GAD.
LP49
Electroneurographic evaluation of the utility of Botulinum Toxin A (BoNT) in severe post-paralytic facial synkinesis

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Aim
Prompted by the efficacy of BoNT in hemifacial spasm we assessed its utility in patients with post-paralytic facial synkinesis.

Patients and Methods
Forty patients entered in the study after informed consent, 1 or more years after onset of severe facial palsy (≥ 90% of axonal degeneration). All 40 patients had a severe degree of synkinesis according Zander Olsen criteria. Thirty eight (95%) had had Bell’s palsy, two (5%) Ramsay Hunt syndrome. Facial synkinesis were photographed before and after treatment. ENG was performed before and 10 to 20 days after injection of 30-40 U. of BoNT A (Xeomin or Botox), recording on the Orb. Oculi with surface electrodes after facial electric stimulation.

Results
Twenty per cent of patients found the results found the results "excellent", 60% "good" and 20% "negligible". Facial paresis increased by 20%, after BoNT, Synkinesis diminished by 70%. The mean pre-BoNT amplitude of CMAPs of the Orb Oculi was 1380 microvolts(SD, 825) and fell to 498 microvolts (SD,298) after treatment , indicating that 60% of motor en-plates were blocked.

Conclusion
BoNT proved to be the treatment of choice for patients with post-paralytic facial synkinesis, particularly those left with only mild residual paresis.
A Novel Method For Capturing Cerebrovascular Reactivity Using Near-infrared Spectroscopy During Transcranial Direct Current Stimulation: A Stroke Case Series

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Transcranial direct current stimulation (tDCS) has been shown to induce polarity-specific changes of cortical blood perfusion [1]. In fact, a significant correlation between tDCS current strength and increase in regional cerebral blood flow (CBF) has been found [2]. It has been postulated that CBF-alterations are causally related to tDCS-induced alterations in cortical excitability via neuro-vascular coupling. However, the mechanism of action is unclear where another study [3] demonstrated consensual changes in heart rate variability during unilateral tDCS. Therefore, our objective was to investigate these different biophysical models (see Figure 1) using near-infrared spectroscopy (NIRS), where NIRS recorded changes in oxy-haemoglobin and deoxyhaemoglobin concentrations during anodal tDCS-induced activation of the cortical region located under the electrode and in-between the light sources and detectors [4]. Here, it was postulated that Dynamic Causal Modeling (DCM) [5] will allow to disambiguate between competing biophysical models. A case series on four stroke survivors showed detectable CVR response (0-60sec) to a 0.526mA/m\(^2\) square-pulse (0-30sec) of anodal tDCS, as shown in Figure 2, where model parameters could assess subject-specific neurovascular functionality. Based on this encouraging result, CVR during tDCS is currently investigated for assessing impaired cerebral microvessels functionality where cross-sectional studies suggest that impaired cerebral haemodynamics precede stroke and transient ischaemic attacks [6].

References:
Figure 2: An illustrative CVR response (0-60sec) to a square-pulse (0-30sec) of anodal tDCS.
Haemodynamic correlates of fronto-central EEG delta and sigma power during slow wave sleep

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Question
The functional neuroanatomy of slow wave sleep (SWS, N3) has been characterized by low regional cerebral blood flow (rCBF measured by PET) in brain stem, thalamus, basal forebrain, basal ganglia, as well as in cortical areas (frontal, parietal, and mesiotemporal) (1,2). Here, we set out to identify brain regions exhibiting haemodynamic (BOLD) activity during N3 sleep in correlation with characteristic EEG frequency bands.

Methods
15 healthy subjects were scanned at 3 T (Siemens Trio, Erlangen, Germany) with T2*-weighted echo planar imaging (EPI). EEG was acquired simultaneously via a cap (modified BrainCapMR; Easycap, Munich, Germany) with a polysomnographic setting. MRI and pulse artifact correction was performed in Vision Analyzer 2 (Brain Products, Gilching, Germany, see 3). After EEG sleep scoring (4), slow wave sleep (N3) epochs were selected for further analysis. Based on the power time course of different EEG frequency bands (δ: 0.5-4 Hz, θ: 4-8 Hz, α: 8-12 Hz; ς: 12-15 Hz; β: 16-30 Hz; ϒ: 30-60 Hz) at electrode Fz (referenced to FCz) regressors for a general linear model (GLM) were built by convolution with the canonical hemodynamic response function (HRF) and down-sampling to the fMRI repetition time. Rigid-body motion correction parameters, cardiac and respiratory noise regressors were also included in the GLM.

Results
During N3 sleep, BOLD fMRI signal was negatively correlated with δ-power in the precuneus, the brain stem, prefrontal and orbitofrontal cortex as well as primary visual and auditory cortices, and positively correlated with σ-power in the thalamus (Figure 1).

Conclusions
Increased δ-power during N3 sleep is associated with reduced activity in default mode network and primary sensory cortices possibly reflecting a continuous modulation of reduced self-awareness and visual and auditory “imagery” during deep sleep which could be parametrized by EEG δ-power; in contrast, positive correlation of σ-power with activity in thalamus could indicate thalamic activation for sleep spindles (σ frequency band).

References
Figure 1. Random effects group analysis (N=15) revealed brain regions where BOLD fMRI signal is negatively correlated with EEG delta power fluctuations overlaid on brain sections (A) and a 3D brain rendering (B): precuneus, prefrontal cortex, parietal cortex (green circle), visual cortex, auditory cortex (purple), brain stem (red), orbitofrontal cortex (blue), and positively correlated with sigma power fluctuations (C): thalamus (p<0.001, uncorrected, extent threshold k=100 voxels, color coded t-values bar).
Changes in oxyhaemoglobin signal during cycle ergometer activity at moderate intensity: A near-infrared spectroscopy study

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Question

Near-infrared spectroscopy (NIRS) is a widely used, non-invasive method for measuring human brain activation on the basis of the cerebral haemodynamic response during gross motor tasks. However, systemic changes influence the measured NIRS signals. We aimed to determine and compare the time-dependent changes in NIRS signals, skin blood flow (SBF), and mean arterial pressure (MAP) during moderate, constant, dynamic exercise.

Methods

Five healthy volunteers (22.8 ± 2.2 years; 2 women) participated in this study. The study was approved by the Ethics Committee of our university. The oxyhaemoglobin signals (O₂Hb) were recorded using a NIRS system (OMM-3000; Shimadzu Co.) while subjects exercised on a cycle ergometer at 50% of peak VO₂ for 20 min. SBF and MAP were measured during exercise, and were synchronized using the NIRS system. The relationship between O₂Hb and SBF and that between O₂Hb and MAP was assessed using Pearson’s correlation coefficients with significance set at P < 0.05 during exercise.

Results

O₂Hb increased to 0.076 mM·cm over the first 8 min, decreased slightly over the next 2 min, and remained constant thereafter. SBF continued to increase over time. MAP increased to 23.1 mmHg at 4 min, and slowly decreased until the exercise ended. The correlation coefficients for SBF and MAP were r = 0.846 (p < 0.01) and r = 0.421 (p < 0.01), respectively, in the first 10 min, and r = -0.257 (p < 0.05) and r = 0.376 (p < 0.01), respectively, in the subsequent 10 min.

Conclusions

During moderate, constant, dynamic exercise, peak times in O₂Hb, SBF, and MAP differed, and O₂Hb might be affected by SBF in the first 10 min.

Figure legend

Fig. 1. Time-dependent changes in O₂Hb (a), SBF (b), and MAP (c) in all subjects (mean± SEM).
Investigating the predictive value of brain metabolism in the identification of laterality in temporal lobe epilepsy: a pattern classification approach

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Question

How well could Support Vector Machine (SVM) classification be used to separate between patients with right and left temporal lobe epilepsy (TLE) based on 18F-FDG PET imaging data and what are the most relevant brain areas to do so.

Methods

We selected a group of 30 subjects with intractable TLE who were awaiting surgical treatment. According to the EEG, MRI and neuropsychological data, half of the subjects had right TLE and the other half had left TLE. The two groups were matched as nearly as possible for age, sex and years of formal education. 18F-FDG PET images were acquired during interictal periods in a GE Discovery 690 (GE Healthcare, Millwakie, EUA) scanner. After gross manual image reorientation, the PET images were spatially processed using the Statistical Parametric Mapping toolbox (SPM8, Wellcome Trust Centre for Neuroimaging, 2008). All images were spatially normalized onto a PET template created in MNI space and then spatially smoothed using a 12 mm FWHM Gaussian kernel. Intensity normalization of regional tracer uptake to the global mean activity was applied to each scan. Voxel-based multivariate analysis of FDG PET scans was performed using the SVM algorithm built into PIPR v1.01 toolbox (King’s College London, 2013) and lead to “pattern recognition” in the data. A weight map with the classification weight of each voxel was generated. To access the accuracy of the method, leave-one-out cross-validation was performed.

Results

The SVM classification was able to separate right TLE patients from left TLE patients with 75% accuracy (p=0.01). The generated weight map is presented in figure 1 and shows a clear difference between the weight distributions in right and left brain hemispheres.

![Figure 1: map representing the weight of each voxel in 18FDG-PET images used by the SVM to classify between right (negative values) and left (positive values) TLE subjects.](image)

Conclusion

The weight map distribution shows that not only the epileptic focus, but the whole ipsilateral brain hemisphere, plays an important role in the computation of the hyperplane that separates the two groups in the SVM classification. This suggests that the metabolic consequences of temporal epilepsy, and therefore, the underlying cerebral dysfunction, have a much larger extent than the actual epileptic focus.
Diffuse optical imaging of activation in the infant brain

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Near-infrared optical spectroscopy (NIRS) and imaging [1] has during the last two decades been emerging as a method for imaging neuronal activations in the human brain, and for continuously monitoring the cerebral blood flow. In the simplest (spectroscopic) case, the attenuation of the optical signal between a single optical source and a detector can be related to changes in the hemoglobin concentration and oxygen saturation of tissue. In diffuse optical imaging, multiple optical measurements are used to obtain spatially resolved functional images. Due to its good sensitivity to changes in cerebral hemodynamics, and the relatively light instrumentation suited for bed side measurements, optical imaging is an attractive method for tasks ranging from monitoring cerebral hemoglobin concentration in prematurely born infants or adult stroke patients to localizing functional areas in the brain, such as lateralization of speech.

Optical imaging is very sensitive to confounding effects of blood circulation in the scalp, and, in the case of localizing functional brain areas, to global changes in cerebral circulation. This reduces the reliability of measurements. Ways to improve the situation include using dense array of optical measurements and accurate computational modelling of the imaging situation.

We measured the hemodynamic responses to neutral, glad, angry and sad human voices in the infant brain using time-domain optical instrument with 15 optical sources and 15 detectors. This allowed a dense measurement array. The optical data were analyzed using a pre-built anatomical atlas model based on MR imaging. Different functional responses to the four stimulus conditions were observed. The merits of the dense optical measurement and advanced computational analysis, and the implications for clinical use are discussed.

P885
Resting BOLD fluctuations in the primary somatosensory cortex correlate with tactile acuity

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Question

In this study we sought to investigate the relationship between local BOLD fluctuations in the S1 cortex (representational field of the hand) and 2-point discrimination of the corresponding index finger (right and left). Since tactile acuity shows high diversity throughout the healthy population, we asked whether sensory perception without intervention also relates to cortical activity. Specifically, is resting cortical activity, as measured by BOLD signal fluctuations, related to 2-point discrimination thresholds?

Methods

Two-point discrimination thresholds of the left and right index fingertips were measured in 19 subjects using a custom-made device consisting of one singular and 7 pairs of brass needles (0.7 mm-2.5 mm separation). Stimuli were presented 10 times in a randomized order and the threshold was taken as the needle distance to which the subject correctly perceived 2 stimuli rather than 1 fifty percent of the time. Additionally, mean fractional amplitudes of the low frequency BOLD fluctuations (fALFF) were determined using resting state fMRI and the Matlab-based toolbox, REST, for the hand regions of the primary somatosensory cortices bilaterally. This fALFF value was correlated with the 2-point discrimination thresholds of the index finger of the contralateral hand. Age was added as a covariate of no interest.

Results

Higher fALFF scores of the left and right S1 hand region positively correlated with better 2-point discrimination thresholds of the contralateral hand (R hand: p=0.02, $R^2 = 0.31$; L Hand: p=0.03, $R^2 = 0.19$; Figure 1).

Conclusions

Higher BOLD amplitude at rest, as a potential measure of cortical excitability, are related to better 2-point discrimination thresholds of the contralateral hand. Our findings extend the relationship seen between spontaneous BOLD fluctuations and behavior to sensory perception.

figure 1
Cerebral hemodynamic changes due to facial expression using near-infrared spectroscopy

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Question

We can usually recognize emotion induced by facial expressions. Cortical neural responses to facial expressions have been revealed in previous neuroimaging studies. NIRS enables a noninvasive monitoring of brain activity without severe motion restriction. Therefore, NIRS has been applied for exploring cerebral functions in various populations. Our future research goal is to objectively evaluate the perception of facial emotion in people with profound multiple disabilities. Thus, we examined neural correlates of facial expression changes in normal adults by using NIRS.

Methods

12 female adults participated in this experiment. The three cycles of the block design composed of 40-second rest period and 30-second task period were done in each condition for NIRS measurement. Participants were asked to view passively the fruit and face images. This experiment was done in the following conditions: 1) Face recognition: a fruit image in the rest period and a neutral face in the task period. 2) Eye-closed facial expression: neutral face images in the rest period and facial expression change into eyes closed face from eyes open face (neutral face) in the task period. 3) Happy facial expression: neutral face images in the rest period and facial expression change to a happy face from a neutral face in the task period. 4) Angry facial expression: neutral face images in the rest period and facial expression change to an angry face from a neutral face in the task period. NIRS was recorded from 66 channels in frontal and bilateral temporal area. Mean values of Oxy-Hb at each channel was compared between 10-second before and 30-second during task period in all conditions.

Results

Regardless of condition, Oxy-Hb significantly increased in right temporal area. On the other hand, Oxy-Hb in superior frontal area significantly decreased under all facial expression conditions, especially angry and happy face. In left inferior frontal area, a decrease of Oxy-Hb was observed in only happy face.

Conclusions

Oxy-Hb decrease in frontal area might be related to facial movement since such a phenomenon was robustly observed in angry and happy face images with larger motion. On the other hand, difference of positive and negative facial expressions might be able to explain by deactivation in left inferior frontal area.
Resting-state fMRI used for intraoperative neuronavigation in children

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Background

Functional imaging of primary motor areas is commonly used in the presurgical workup of patients with intraaxial tumors in the vicinity of these areas. In young children that are unable to perform task-related functional MRI, resting state examinations (rsfMRI) constitute a novel alternative.

Methods

We report on two cases of young children six and seven years of age, where we used resting-state fMRI for neuronavigation and correlated it with direct cortical stimulation. Both had low grade tumors near the primary motor area.

Functional resting-state imaging was performed on a 3T (TIM Trio System Siemens Medical Solution, Erlangen, Germany for case 1° and Philips Medical Systems, Best, The Netherlands for case 2°). Twenty slices (1 mm gap, 4 mm thickness) with a FOV of 210 x 210 mm and TE/TR 42/2000ms were acquired. Image preprocessing was performed with SPM8 (http://www.fil.ion.ucl.ac.uk/spm/), including motion correction and normalization to the corresponding anatomical image. Correlation maps were generated by computing the cross-correlation coefficient on a single-voxel basis for the regions of interest. Correlation maps were converted to z-values using Fisher’s r-to-z transformation, as implemented in Matlab (Matlab 7.8.0, Mathworks Inc., Sherborn, USA) to enable parametric statistical comparison. Resting state data was transferred to the neuronavigational system (Medtronic, Louisville, Colorado). Direct intraoperative navigation of the 3-D brain surface was additionally performed in one case by the use of Synergy Cranial version 2.2 software (Medtronic, Louisville, Colorado).

Both monopolar (500Hz, 5-20mA) and bipolar cortical (50Hz, 8-20mA) stimulation techniques were used to verify the topography of the primary motor cortex.

Results

Intraoperative correlation with direct cortical stimulation showed a good concordance with the functional imaging data. Thereby, identification of the primary motor cortex was facilitated in both cases and increased the safety of the tumor resection.

Conclusion

Resting-state fMRI can be used for intraoperative neuronavigation in children unable to perform task-related fMRI examination.
Clustering of interictal events for improved fMRI specificity in high density EEG-fMRI studies

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Question

During pre-surgical planning in focal epilepsy, high-density EEG-fMRI of interictal activity can be used to locate epileptic foci. The inter-event variability poses a problem for comprehensive identification of events. Our objective is to develop a semi-automated method of identifying and clustering interictal events for improved electric source imaging (ESI) and fMRI regressor design.

Methods

A 128-channel EEG was recorded of a patient with left temporal lobe epilepsy in an electrically shielded room and during fMRI (1.5T). The MR-gradient and cardiac pulse-related artifacts were removed. A representative interictal epileptic discharge (IED) from the shielded room recording was selected as the template and template matching using a set of indicative channels was performed to identify IEDs. Intertrial correlations were calculated and used to cluster the IEDs based on mean within-cluster correlation, which provided specificity. Clusters were averaged and a cortically constrained current density reconstruction (CDR, sLORETA) was performed around the first peak and from that an equivalent dipole was derived. ESI-based cluster selections were used to define the regressor for the fMRI analysis.

Results

In the shielded room recording 456 events were detected over 35 min and in the scanner recording 233 in 25 min. Concordant event clusters could be identified as well as a separate group of spikes that occur within the sharp wave of a preceding spike. Weakly correlated events, e.g. artifact corrupted or overlaid with other activity, could be separated and rejected. The left temporal blood oxygenation level dependent (BOLD) activation was concordant with ESI. Selecting ESI-positive concordant event clusters for fMRI regression notably reduced spurious activation regions and isolated an otherwise unclear second contralateral pre-central activation spatially concordant with the equivalent source of the post-spike wave complex.

Conclusions

Semi-automatic event discovery and clustering can notably improve BOLD contrast. Non-invasive ESI/fMRI of epileptic events shows promise in improving pre-surgical evaluation of epilepsy.
P889
Electrical Impedance Tomography (EIT) of epileptic seizures in rat models - a potential new tool for diagnosis of seizures

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Question

EIT is an emerging method for producing tomographic images of the internal impedance of a subject using a box of electronics connected to surface EEG-type electrodes. It is safe, portable and inexpensive and may be used simultaneously to EEG/ECoG. It can be used to image millisecond changes in brain impedance during epileptic seizures caused by: (1) neuronal depolarisation during inter-ictal spikes; and (2) cell swelling. The purpose of this work was to examine the potential of EIT for localising seizure foci in a rat model of epilepsy.

Methods

Cortical electrical impedance and ECoG were recorded in 9 rats anaesthetised with α-chloralose or fentanyl/droperidol using a 30 electrode epicortical array with an applied current of 60 µA at 1.7kHz. Seizures were produced by intracortical injection of 4-AP, Penicillin or Picrotoxin (n=9 in total, 3 each).

Results

Following inter-ictal epileptic spikes, there were reproducible fast neural impedance changes of -0.26±0.09% (mean±SD, n=9 rats, 3562 interictal spikes in total) 7 ms preceding the peak of the inter-ictal spikes, and impedance increases of 0.57±0.32 %, starting 50 ms after each inter-ictal spike and lasting up to 2 s. For seizures, there were significant impedance increases of up to 2.21±1.16% (201 seizures in total). The impedance changes occurred focally around the injection site and were consistently imaged with a resolution of ~0.4mm (see fig.).

Conclusions

Here we present the first-ever EIT images of fast neural activity and cell swelling during inter-ictal spikes and seizure activity in rat models of focal epilepsy. Cell swelling causes impedance increases within 50 ms of seizure onset and this could be used for early seizure detection. The present method could be ported to the clinical setting with use of subdural electrodes implanted for presurgical evaluation, or potentially scalp electrodes, which could provide a major improvement in neuroimaging technology for localising seizure onset zones.

Fig.1: Example of a 4AP induced seizure. (Left) Exp. setup. (Right) upper: Conductivity change (dσ) imaged at 1.1 mm depth; scale: 5x7 mm. Lower: EEG (continuous) and impedance (dotted). Seizure onset was marked by a DC shift at 2s followed by ECoG spiking at 4s. Tissue impedance increased due to cell swelling around the injection site within 50 ms of the DC shift.

def (%)
LP50
Atypical Cerebral Language Dominance in a right-handed patient: An anatomoclinical study with DES, fMRI and DTI

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OBJECTIVE

Approximately 97% of the right-handed individuals has left hemisphere language dominance. Within the language dominant hemisphere Broca's area is of crucial importance for a variety of linguistic functions. As a result, tumour resection in and around Broca’s area is controversial. However, studies showed that with the help of Direct Electrical Stimulation (DES) tumour resection in this region can be safely performed. We report unexpected anatomoclinical findings in a right-handed patient who underwent tumour resection in the left prefrontal hemisphere.

METHODS

Language functions in this right-handed patient were extensively examined in the pre-, intra-, and postoperative phase by means of a standardised battery of neurolinguistic and neurocognitive tests. Results obtained in the pre- and postoperative phase are compared. In addition, intraoperative DES findings and postoperative functional Magnetic Resonance Imaging (fMRI) and Diffusion Tensor Imaging (DTI) results are reported.

RESULTS

Tumour resection near Broca’s area was safely performed since no positive language sites were found during intraoperative DES. As no linguistic deficits were encountered in the pre-, intra-, or postoperative phase atypical language dominance was suspected. Neuropsychological investigations disclosed permanent executive dysfunctions. Postoperative fMRI and DTI in this right-handed patient confirmed right cerebral language dominance as well as a crossed cerebro-cerebellar functional link with the left cerebellar hemisphere.

DISCUSSION

Atypical right hemisphere language dominance in this right-handed patient can be hypothetically explained by brain plasticity mechanisms or maturational variation. A number of arguments favour the latter: 1) absence of language problems (even transient), 2) no positive stimulation sites during DES, 3) a clearly more pronounced arcuate fasciculus in the right than in the left cerebral hemisphere (DTI), 4) a crossed functional connection between the right cerebrum and the left cerebellum (fMRI). To conclude, this case of atypical cerebral language dominance shows that although fMRI is currently not considered to be a highly sensitive method to identify eloquent language regions, functional neuroimaging proves to be useful to identify language lateralisation.
Progressive Myelopathy Mimicking Subacute Combined Degeneration after Intrathecal Chemotherapy

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Intrathecal chemotherapy including methotrexate is well documented for neurotoxicity of diverse clinical manifestation. Acute or chronic leukoencephalopathy is the most common type of methotrexate-induced neurotoxicity and subacute myelopathy is rare. Although its pathogenesis is not fully understood, it is postulated that direct damage of methotrexate to the central nervous system plays a major part and elevated levels of homocysteine and its excitatory amino acid neurotransmitter metabolites (homocysteic acid and cysteine sulfinic acid) may mediate, in part, MTX-associated neurotoxicity. On the while, subacute combined degeneration is a progressive degeneration of the dorsal and lateral columns of the spinal cord, mostly due to vitamin B_{12} deficiency. The authors report a case of a 15-year-old boy with Burkitt’s leukemia who developed progressive myelopathy after intrathecal triple therapy (methotrexate, cytarabine, and hydrocortisone) whose clinical and radiological features were compatible with subacute combined degeneration. The pathogenic mechanism could be explained by biochemical alteration by methotrexate and a possible treatment strategy was discussed.

**Figure 1.** Magnetic resonance images on T1 (A, C) and T2WI (B, D) show diffuse high signal intensities along the whole spinal cord. T2-weighted axial images at C2 (E), T4 (F), T10 (G) levels respectively show high signal intensities on the dorsal columns which resembled typical findings of subacute combined degeneration.

![Figure 1](image-url)
New approach to understanding common mechanisms of pain disorders and chronic fatigue syndrome

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Stress is known to be the cause of non-communicable disorders, such as chronic fatigue syndrome (CFS), heart attack and many others. Better understanding of the mechanisms that are common to several disorders, is an important challenge for early diagnosis of disease and for the development of therapeutics.

Materials and methods

95 patients (38 men and 57 women, age of 48±6 years) with combined myofascial pain in the cervical part of the vertebral column and CFS were examined. Clinical examination was conducted to identify the role of biomechanically significant biomarkers for the cranio-cervical spine that affecting the cerebral blood flow. NEC-method of visualization was used to define the level of cerebral metabolism and adaptation possibilities.

Results

All the patients had disorders in the cognitive, personal, emotional status, fatigue, behavioral, sleep and memory problems. Vertebral examination revealed the biomechanical rigidity in the shoulder girdle, neuro-vascular syndrome of upper aperture of the chest and postural displacement. Musculoskeletal pain was caused by displacement of gravity center and located in the overburden muscles in the cervical part of the vertebral column that try to return the body to the vertical axis. NEC analysis revealed different levels of cerebral acidosis, as biomarkers for brain hypoxia. New chains of non-specific base of CFS and non-communicable disorders are: emotional stress, as the psychomotor reaction of the body, leads to muscle spasm and redistribution of liquid between muscle and skin level. Trigger points are formed in muscles and depot of interstitial liquid is formed in the skin. Those points of additional fixation keep the dysfunction of muscles, compression of subcutaneous nerves, vessels, lymphatic nodes and blockade interstitial liquid circulation. Disturbances in the connective-tissue construction lead to formation of 3-levels tunnels. Integrative schemes of rehabilitation were worked out for patients with different pain, postural and neurovascular disturbances. Methods of physiotherapy, adoptive and breathing gymnastics were used for improvement the cerebral metabolism and remove the brain hypoxia.

Conclusions

Integrative personalized rehabilitation of the patients with CFS improved their emotional background, memory and cognitive functions. NEC examination marked the tendency of recovery the cerebral metabolism. Neurovascular tunnel syndromes and disorders in interstitial circulation are considered to be the common mechanisms to several diseases.
Amelioration of Migraine Memory Impairment By Dizocilpin

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Migraine headache have been previously discussed as wave of depolarization in neural cell. Gorji at 2001 have named Spreading depression (SD) as corresponding phenomenon for Migraine. SD has near relation with some neurological disorder. SD is a depolarization wave, pass through the brain. SD wave initiation and propagation are linked with large changes in cellular and molecular phases. Many of these changes play role in SD injuries pathophysiology. Initiation of SD waves are consider to depend any mate, which increase extracellular potassium level, include direct trauma, pressure on cortex or any other.in the other hand, glutamate release are suggested to have essential role, which by glutamate receptor activation exacerbate ionic imbalances. ECoG recording is standard test to identify SD wave initiation. ECoG recording have showed a transient hyperactivity, which followed by depression of cellular activity. Cellular death and electrical changes are postulated to play central role in SD outcome as well as memory impairment.in present study 24 Wistar rat were used to investigate repetitive SD role in memory consolidation of by T-Maze test. Result showed that memory consolidation was significantly disrupt by SD wave. However neural damage play important role in this impairment compare to electrical wave distribution.

Key words

Spreading depression, memory, memory consolidation, T-Maze, memory impairment

Fig1. mean time of food finding in comparision of Sham and SD induced group, which showed significant increase in time of SD group.

Fig 2. Showed treatment with Dizocilpine could help to protect memory from SD wave. Mean time of food finding significantly improve in treatment groups compare to SD group.
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**Figure 1**

![Graph showing time in seconds for Sham and SD groups across three weeks with statistical significance indicated by asterisks.]

**Figure 2**

![Graph showing time in seconds for Sham, SD, Ctrl Treatment, and Treatment groups across three weeks with statistical significance indicated by asterisks.]

1203
Para nasal Sinus Nitric Oxide and Migraine: A new hypothesis on the sinorhinogenic theory

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Migraine is a debilitating illness that has no exact biomolecule to explain its pathology. After reviewing neurophysiological and biochemical basic of the research findings of nitric oxide and such migraine, I present to the best of my knowledge the first paranasalsinus nitric oxide mediated neurobiophysiological hypothesis for migraine of sinorhinogenic origin. The diffused paranasal sinus nitric oxide in the nasal mucosa could be the primarily molecule that initiates migraine and is termed Sinus Hypoxic Nitric Oxide Theory. This hypothesis regards repetitive or intermittent activation of the trigeminal sensory nerve and blood vessels in the nasal mucosa. Production of paranasal sinus nitric oxide is mainly induced by hypoxia due to several independent factors and the diffusion of paranasal sinus nitric oxide depends on the vulnerable surface area in the nasal cavity. Apart from the known trigeminal nociceptive impulse in the migraine, two main peripheral trigeminal nerve activating mechanisms may induce migraine. First the nerve endings of the nasal mucosa which are directly stimulated by diffused paranasal sinus nitric oxide are indirectly stimulated by vasoactive substances released by antidromic activation of the nerve, parasympathetic efferent of the nerve and sterile neurogenic inflammation. Secondly, the perivascular nerve of nasal mucosal and the meningial blood vessels are directly stimulated by either diffused paranasal sinus nitric oxide or by shear stress mediation.

Indeed this article explains a new pathophysiological initiation between sinorhinogenic nitric oxide effects and migraine and provide an initial steps for the obscured or neglected etiologically important neuro vascular impulse generating pathway. The patients who are clinically suspected of having headaches should receive comprehensive sinorhinological examination and evaluation based on the sinus hypoxic nitric oxide theory. A standard surgical and medical management of migraine links with the sinus hypoxic nitric oxide theory may restore the hypoxic state or reduce or remove the paranasal sinus nitric oxide diffusing surface. It warrants clinical testing.

P892
Effect of Nifedipine on Memory of The Rats Models of Spreading Depression

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Question

Spreading depression known by transient loss of spontaneous and evoked neuronal activity and changes in ionic, metabolic and hemodynamic characteristics of the brain. Many studies have focused on the role of Ca²⁺ channels in spreading depression, however this role is not completely clear yet. On the other hand it has proven that impairment of memory is one of the main effects of spreading depression. In our study we aimed at determining the role of Ca²⁺ channel-blockers on repetitive spreading depression in terms of its effect on memory.

Methods

Wistar rat (60-80gr) randomly chosen in 4 groups and Nifedipine 1 mg/kg were administrated weekly after 3 mol/L KCl injection for induction of repetitive SD in rat for 4 week. The groups were evaluated by T-maze memory test and SD group were compared with control groups.

Result

T-maze test data demonstrated that in repetitive spreading depression group memory was impaired during the weeks. In group which Nifedipine have been administrated memory improvement has been not significantly observed.

Conclusion

Our study showed that administration of Nifedipine as a Ca²⁺ channel-blockers could not significantly reduce the level of memory impairments, which naturally followed by repetitive spreading depression.
P893
Association between promoter region of the uPAR (rs344781) gene polymorphism in genetic susceptibility to migraine without aura in Iranian population

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Introduction

Migraine is a chronic neurological disorder. Inflammation has a key role in migraine pathophysiology. Urokinase plasminogen activator receptor (uPAR) directly involves in inflammatory conditions by facilitating migration of inflammatory cells to different tissues. The aim of this study was investigation whether uPAR rs344781, common genetic polymorphism in the uPAR promoter region, might be associated with migraine without aura susceptibility in Iranian population.

Methods

We enrolled 103 newly diagnosed patients with migraine and 100 healthy controls. Peripheral blood sample was used for DNA extraction and uPAR rs344781 gene polymorphism was determined. Patients filled HIT-6 as a tool to evaluate headache severity.

Results

The genotype frequency of uPAR is significantly different between migraine patients and control subjects. Heterozygote genotype (AG) was statistically more frequent in the patients than the controls (P=0.001; OR=2.67, 95% CI=1.51-4.7). Also G allele was more frequent in the patients. Total HIT-6 score was not significantly different between heterozygote and homozygote patients (55.50±2.22 vs. 49.60±3.68 respectively, P=0.075).

Conclusion

In conclusion, our study showed a significant association between uPAR rs344781 gene promoter polymorphism and migraine without aura susceptibility but not with headache severity.
Thermal pain thresholds in migraineurs do not change with migraine phase

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Question

Peripheral and central sensitisation may be important for the development of migraine attacks. Previous studies have shown lower thermal pain thresholds between, before and during migraine attacks. Can these findings be confirmed in a longitudinal study?

Methods

Pain thresholds (PT) for cold (CPT) and heat (HPT) were recorded on the forehead and the volar hand. Forty-nine migraineurs (17 with aura) and 31 headache-free controls were analysed in this longitudinal study. The migraineurs were tested on 4 different days. The examiner was blinded for diagnosis on the migraineurs' first session, and for migraine phase the next three sessions. Headache diaries were used to determine the migraine phase for each recording, defined by a 24 hours limit before/after the examination day. Interictal PTs were compared with preattack (23 pairs), attack (16 pairs) and postattack (10 pairs) PTs using Wilcoxon Signed-Rank Test. PTs of interictal recordings from 45 migraineurs and 31 controls were compared using Mann-Whitney U Test. Pain threshold definitions: CPTd = 32 °C - CPT and HPTd = HPT - 32 °C.

Results

- Cold pain thresholds on the hand were lower in the postattack phase (18.8 ± 7.1) compared to the interictal phase (20.3 ± 7.4) (p = .037). No other phase comparisons differed significantly (p > .156).

- Cold pain thresholds on the hand were lower in interictal migraineurs (20.0 ± 6.0) compared to controls (22.6 ± 5.3) (p = .022).

Conclusions

This longitudinal study could not confirm the previously reported lowered PTs in the preattack phase. However, a slight postattack allodynia was observed. Also, migraine patients had lower CPT than controls in the hand. Cold allodynia may accordingly be the more robust thermal pain feature that reflects a slight generalized hypersensitivity in migraine patients. Larger groups, investigated closer to attack onset, may be necessary to reliably quantify the previously reported preattack heat allodynia in migraine. Because of the large interindividual variation in the measurements, future studies should ideally apply a longitudinal design.
P895
TRIGEMINAL SOMATOSENSORIAL EVOKED POTENTIALS IN MIGRAINE

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Introduction

Migraine pathogenesis is suggested to involve many structures in cerebral cortex, brainstem and trigeminovascular system. Electrophysiologic studies revealed loss of habituation, decreased cortical preactivation, segmental hypersensitivity and decrease in control of inhibitory descending pathways. Given these information we aimed to evaluate the excitability changes of the trigeminal pathway in the cortex, and brainstem in migraine using trigeminal nerve somatosensory evoked potentials (TSEP).

Patients and method

Fifty-one women with migraine without aura and 25 age-matched healthy women were included. TSEP were recorded in migraine patients during interictal period and in healthy volunteers. The latencies of P1, N2, P2 and N3 waves as well as N2/P1 and N2/P2 amplitudes were measured.

Results

TSEP stimulation thresholds were bilaterally higher in migraine group. Other parameters including latencies and amplitudes did not show significant difference between patients and healthy volunteers. There were no differences of TSEP parameters considering the localization of headache and attack frequency in migraine group. However, patients with long disease duration had longer latencies of right N3, left P2 and left N3.

Conclusion

Our study did not show difference between migraine patients and healthy volunteers which may be attributed to the interictal design of the study similar to the limited previous studies. However, migraine with long duration even affects the excitability of the cortical and brainstem trigeminal pathways during interictal periods.
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P897
Acute and prophylactic treatment with inhibitory transcranial electrical current stimulation of the visual cortex: which method is better?

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Background and Purpose

The present study aimed to investigate the efficacy of 140 Hz alternating current stimulation (tACS) and consecutive repetitive cathodal direct current stimulation (rc-tDCS) over the visual cortex (V1) as acute and prophylactic treatments in migraine.

Method

56 patients participated in this double-blind, randomized and placebo-controlled study and were assigned to active or to sham stimulation. In the prophylactically treated group 20 patients received rc-tDCS or sham stimulation with 2 mA intensity for 20 minutes for five days. In the acute treatment group 36 patients were treated during the migraine attacks using tACS for 10 minutes with 0.4 mA intensity or with sham stimulation. The stimulation was done by the patients at home, using a preprogrammed stimulator. The frequency, duration of attacks and the intensity of pain were recorded during the study periods.

Results

A significantly decrease in the number of migraine attacks was observed during rc-tDCS compared to sham stimulation in the prophylactically treated group. 140 Hz tACS did not decrease the occurrence of the attacks compared to placebo stimulation.

Conclusion

The results suggest that cathodal stimulation applied over the visual cortex has a prophylactic effect and might be a promising tool as an alternative or additional treatment option in migraine, although more challenging and time consuming compared to drug intake. Though previous studies reported that 140 Hz tACS with 0.4 mA intensity applied over the motor cortex has an inhibitory effect, in this study it did not affect the duration or the frequency of the migraine attacks, probably due to the too low intensity.
VEP habituation distribution in the families of migraine children

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**Question**

In spite of the bulk of studies showing reduced visual evoked potential (VEP) habituation in adult migraineurs, this abnormality has never demonstrated in children with migraine. VEP habituation can be assumed as a marker of the visual cortex excitability, whose abnormality in migraineurs is related to the genetic background of this disease. In pediatric age, it is debated whether the presence of migraine in the families of young migraineurs is due to a hypothesized genetic background or is a consequence of the “psychological environment”. The aim of our study was to investigate whether neurophysiologic or psychological elements are segregated in families of migraine children.

**Methods**

We studied 11 children (2 siblings) with migraine without aura and their parents. VEPs were recorded in six successive blocks to test the change in amplitude of N75-P100 from the first to the sixth block (habituation). The psychological profile was made according to the CBCL/6-18 for children, YSR 11/18 for 11-18 years old patients and ASR for parents.

**Results**

VEP habituation was significantly lower in both patients and migraineur parents than in non-migraineur parents (two-way ANOVA: F=14.7, p < 0.001). As for the psychological tests, no significant “between groups” difference was found when we compared the Internalizing (p = 0.5), externalizing (p = 0.3) and Total scales scores (p = 0.1).

**Conclusions**

This is the first study showing a reduced VEP habituation in migraine children. Our results suggest that the familial distribution of the disease is due to a genetic background, while the “psychological environment” does not have a significant influence.
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P899
Spatial attention mechanisms in migraine children with imploding or exploding pain: A topographical SEP study

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Different pathophysiological mechanisms are supposed to work in migraineurs with either imploding or exploding pain. Previous studies demonstrated that spatial attention modulates somatosensory evoked potential (SEP) amplitudes as from 40 ms of latency. Our aim was to investigate the effect of spatial attention on the SEP amplitude and topography in migraine children with imploding or exploding pain. We studied 10 migraineurs with imploding pain and 9 migraine children with exploding pain. SEPs to median nerve stimulation were recorded from 31 scalp electrodes in a neutral condition (NC) and in a spatial attention condition (SAC), in which the subjects had to count tactile stimuli delivered on the stimulated hand. The P40 amplitude increase during SAC, as compared to NC, was higher in patients with exploding than with imploding pain. While in imploding migraineurs the N140 amplitude increase during SAC was prevalent in the centro-parietal region, it mainly involved the frontal region in exploding patients. Our results suggest that in pediatric migraine psychophysiological mechanisms subtending spatial attention depend on pain direction.
Treatment of acute migraines with Vagal Nerve Stimulator (VNS)

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OBJECTIVE

To describe the influence of vagal nerve stimulation on headaches in an individual with cryptogenic generalized epilepsy and migraine without aura.

BACKGROUND

Migraine is a common comorbidity in individuals with epilepsy, with 2.4 times greater incidence rate. Although the origin of comorbid migraine is unknown a similar genetic susceptibility is described. Vagal nerve stimulation as a treatment for medically refractory epilepsy is also thought to mediate nociceptive receptors via inhibition of the spinal nociceptive reflexes and influencing the trigeminovascular system. Therefore, it is logical to consider the impact of VNS on migraine in individuals with epilepsy.

METHODS

We report a 28-year-old woman with migraines and generalized convulsive seizures since age 4 who had a VNS implanted at age 15. At multiple visits, seizure and headache frequency were documented with close attention to the influence of VNS on seizures and migraine. Note that there was no clear temporal relationship between her seizures and headaches.

RESULTS

The patient exhibited slow but steady improvement of headache frequency after VNS implantation from 4-5 headache days per week to less than 1 per month. Importantly, she has been swiping the VNS magnet during the migraine attacks to activate the VNS during off cycle. This procedure was able to abort her attacks, resulting in complete resolution of disabling migraines.

CONCLUSIONS

The current case illustrates that vagal nerve chronic stimulation may gradually improve pain tolerance and decrease headache frequency. Further, activating the VNS during off cycle has the potential to abort acute migraines. These findings may represent a novel non-pharmacological therapy for comorbid migraine in people with epilepsy.
Visual evoked potential habituation in migraineurs: A longitudinal study with a blinded design

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Question

Lack of habituation has been called the neurophysiological hallmark of migraine. It has been hypothesized that this alteration is important to explain migraine, but the results of earlier studies have been discrepant. We investigated if VEP habituation changes in relation to an attack, and if lack habituation in interictal migraineurs could be reproduced with a blinded design.

Methods

50 migraineurs and 31 headache-free controls were included. VEPs were recorded once in controls and four times on different days in migraineurs. Investigators were blinded to diagnosis or relation to nearest attack. VEPs were averaged in 6 blocks of 100 single responses to measure habituation. VEP peaks were determined without knowledge of diagnosis or block number. Linear change over blocks of N70-P100 amplitude was applied as main habituation measure.

23 migraineurs had interictal (examination ≥2 days before/after attack) and preictal recordings (< 2 days before the next attack), 10 had interictal and postictal recordings (<2 days after the last attack), and 15 had interictal and ictal recordings (attack during or in near relation to the examination). These recordings were compared with a paired Student’s t-test.

Habituation in controls and in the first interictal recording in migraineurs was compared with an independent samples Student’s t-test.

Results

Habituation was more pronounced in ictal (-0.47 ± 0.43 µV/block) than interictal (-0.31 ± 0.25 µV/block) recordings (p = 0.029). No habituation differences were found between interictal and preictal or postictal recordings. No VEP habituation differences were found between headache-free controls and interictal recordings.

Conclusion

VEP habituation increased significantly in relation to the migraine attack. In contrast, no changes were detected in the preictal period. Earlier studies reporting changes in VEP habituation over the migraine cycle have mostly applied a cross-sectional design, which may not have been ideal because of the large interindividual variation of VEPs. Also, in this blinded replication study we could not confirm that migraineurs lack habituation compared to controls. This confirms our recently published data and, as far as we know, no studies that applied blinding during VEP recordings have found lack of habituation in migraineurs.
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P902
Visual evoked potentials in subgroups of migraine with aura patients

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Objectives

Patients suffering from migraine with aura could experience pure visual symptoms, and/or complex aura with sensory disturbances and dysphasia. The pathophysiology of these subgroups of common forms of migraine with aura has been studied rarely.

Methods

Forty-seven migraine with aura patients were subgrouped in migraine with pure visual aura (MA, N=27) and migraine with complex aura (MA+, N=20), i.e. those who had visual aura associated with paraesthesia and/or dysphasia. We recorded visual evoked potentials (VEPs, 15 min of arc cheques, 3.1 reversal rate, 600 sweeps) amplitude and habituation (slope of the linear regression line for N1-P1 amplitude from the 1st to 6th block of 100 sweeps) in patients and in 30 healthy volunteers (HV) of comparable age and gender distribution.

Results

Habituation (i.e. response decrement), which could be observed in most HVs (slope -0.54), was deficient in both MA (slope +0.01, p=0.001) and MA+ (+0.14, p<0.001) patients. However, VEP amplitudes across the blocks generally tended to be lower in MA patients, while were significantly higher in MA+ patients, than in HVs.

Conclusions

We found different patterns of visual responses in subgroups of MA patients. We hypothesize that a different genetic load and energetic metabolism may characterize migraine with aura patients with more severe focal symptoms.
P903
Assessment of course of tension-type headache in adolescents based on nonlinear multidimensional analysis (deterministic chaos) EEG

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The life prevalence of tension-type headache in the general population by various studies ranged from 30 to 78%, and in the children - 28.7% - 72.8%.

Question

Examine the condition of nonspecific cerebral regulatory systems based on the study of bioelectrical brain activity using the method of nonlinear multidimensional analysis (deterministic chaos) EEG in adolescents with episodic and chronic tension-type headache.

Methods

We observed 43 adolescents with tension-type headache at the age of 13-18. Two groups: 1st (23 pers.) - patients with episodic tension-type headache, 2nd (20 pers.) - patients with chronic tension-type headache. Registration the electroencephalogram (EEG) was performed at rest with eyes closed and intellectual load (countdown in mind in 1000, 993, 986, etc.). We conducted nonlinear multidimensional analysis (deterministic chaos) EEG and calculated Kolmogorov-Sinai entropy.

Results

Decrease in the value Kolmogorov-Sinai entropy is observed with increasing frequency of episodes of tension-type headache, i.e. the transition to the chronic form of the disease. This means reducing the number of active parallel functional processes in the brain, the possibilities for self-organization, the ability to form ranked adaptive dissipative structures, reducing neuroplasticity of the brain and, consequently, the capacity to adapt.

Conclusions

Study of nonlinear parameter - the Kolmogorov-Sinai entropy of EEG signal is an objective quantitative measure of the dynamic characteristics of cortical and limbic - reticular structures of the brain that are involved in the formation of adaptive processes in patients with episodic and chronic tension-type headache.
Normalization of EEG Power Spectrum in Patients with Migraine During Peri-ictal Periods

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Question

Previous resting EEG spectral analyses in patients with migraine showed inconsistent results. The inconsistency might be related to the spontaneous fluctuation of electrophysiological activity in a headache state-dependent manner in patients with migraine. In this study, we aimed to investigate the resting EEG power spectrum and its relation to migraine state.

Methods

Resting EEG data (30 seconds for 3 times) was recorded with 256 Hz sampling rate, and 19 electrodes positioned according to the international 10-20 system, while the subjects kept awake and alert. After artifacts rejection, independent component analysis was applied to remove noises. Minimum norm estimate analysis was then used to transform the original electrode-based EEG signal into region-of-interest (ROI)-based EEG activity. Then, normalization of spectral power was done by normalizing the power at each frequency band with total power to reduce the inter-individual variability. We then compared the relative power of each band across all ROIs in patients with migraine and control subjects. Statistical significance was defined as a $p$-value of < 0.05. All tests were two-tailed.

Results

One hundred and twenty-seven episodic migraine patients were recruited (M/F: 29/98, age: 35.1 ± 10.3, headache frequency: 4.3 ± 2.6 days/m). Compared to age- and gender-matched controls (n=20, M/F: 8/12, age: 36.4 ± 6.8), patients during inter-ictal period (n=75) showed decreased alpha and theta power over most of all brain regions and increased delta power over bilateral frontal regions. These spectral abnormalities were less obvious or normalized during pre-ictal (n=21), ictal (n=19) or post-ictal (n=12) periods. Of note, compared with controls, patients with migraine had a consistent increment of beta- and gamma-band powers regardless of their clinical headache state.

Conclusions

Resting EEG spectral analysis in patients with migraine showed a state-dependent fluctuation at delta-, theta- and alpha-band range, which tended to be normalized during peri-ictal periods. Besides, we found that gamma-band power, and beta-band power to a lesser extent, were consistently increased in patients with migraine, which deserves further studies to evaluate its potential as a non-invasive biomarker.
P905
Spreading Depression Detection by Different Methods of Imaging

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Neurosurgical diagnosis has been widely based on using neuroradiology methods such as Computed tomography (CT), Magnetic resonance imaging (MRI) and Positron emission tomography (PET). Cortical Spreading Depression (CSD) is a well-known pathophysiological phenomena, which is associated with propagation of electrophysiological hyperactivity followed by a wave of inhibition. CSD which mostly located in the visual cortex of the brain can spread as wave of depolarization, vasoconstriction and ischemia. In this study we aimed to have a review on the way of influence of CSD on most frequent imaging method.
Central mechanisms of migraine improvement with ketogenic diet

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Question

Ketogenic diet (KD) is a dietetic regimen that mimics fasting in producing ketone bodies, which seems to have a potential role in treating migraine. From animal and human models emerges that KD might affects CNS at multiple levels: it is able to normalize cortical dysexcitability and to reduce cortical spreading depression velocity of propagation, which mechanisms are potentially of interest in migraine pathophysiology. Here, with the aim of identifying cortical electrofunctional correlates of responsiveness to short-lasting preventive intervention with KD in migraine, we investigated visual evoked potentials (VEPs) before and after KD.

Methods

To find out whether ketogenic diet alters VEP habituation, we recorded VEPs (3.1Hz reversal rate, 15 min of arc checkerboard visual pattern) before and during ketogenesis, as confirmed by urinary sticks, in 12 migraine patients. We measured VEP N75-P100 amplitudes in 6 sequential blocks of 100 sweeps and habituation as the percentage change in N1-P1 amplitude between the 6th and the 1st block.

Results

After a mean of 1-month period of KD, a significant reduction of migraine frequency (from a mean of 6.4 to 1.9 attacks/month, p=0.02) and duration (from 50.6 to 17.0 hours/month, p<0.01) was observed. KD tended to increase VEP amplitude in block 1 and induced normalization of the interictally reduced VEP habituation (from +3.2% to -10.8%, p=0.01).

Conclusions

These findings suggest that ketogenic diet may exert its prophylactic effect in migraine by influencing the processing of information at the cortical level. KD may be a promising therapeutic option as migraine prevention.
CORTICAL EXCITABILITY IN MIGRAINE: NEW EVIDENCE BY SOUND-INDUCED FLASH ILLUSIONS AND TRANSCRANIAL DIRECT CURRENT STIMULATION OF VISUAL CORTEX

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Question

“Sound-induced flash illusion” are a powerful example of cross-modal illusion highlighting the role of modulation and interaction of sensory modalities [1]. When a single flash is accompanied by two auditory beeps, the single flash is perceived as two flashes (‘fission’ illusion), on the other hand a “fusion” illusion occurs when a single beep causes the fusion of a double flash stimulus. Mechanisms underpinning such illusory perception are yet unknown, but through transcranial direct current stimulation (tDCS), they have been shown to critically depend on excitability of visual and temporal cortices: indeed anodal activating tDCS over occipital cortex and cathodal inhibitory tDCS of temporal cortex can disrupt the illusion[2]. In a previous study we observed that patients with migraine (with and without aura) examined both during attack and interictally show reduced ability to perceive the illusions and we interpreted this as due to visual hyperexcitability. If so, we expect that reducing cortical excitability through cathodal tDCS should normalize illusory perception in migraineurs.

Methods

18 Patients(14 F; mean age 32.11 ± 11.65 years) migraine patients [9 without aura (MWO) and 9 with aura (MWA)] were examined in the interictal phase and compared with 24 neurologically unimpaired, age and sex matched participants. The experimental paradigm for studying the illusion consisted of 1-to-4 white filled circles presented in the center of a black screen in isolation, or preceded by 1 to 4 beeps in different combinations [2]. It was performed in baseline and after real and sham cathodal tDCS stimulation with the following parameters: site: occipital cortex; intensity: 2 mA; duration: 10 min.

Results

MWO and MWA patients showed significantly less illusions with respect to healthy controls in baseline; after real cathodal but not sham occipital tDCS, a significant increase of illusory phenomena was observed in MWA but not in MWO patients.

Conclusion

MWA and MWO patients perceive less illusions, similarly to what observed by Bolognini et al [2], after increasing visual cortical excitability (through anodal tDCS) in healthy controls. Cross modal illusion can be restored in MWA patient reducing excitability by cathodal tDCS. Taken together these findings suggest a condition of increased ictal and interictal visual cortical excitability in migraine that could be reverted by cathodal tDCS, at least in MWA.
P908
CHANGES IN GLUTAMATERGIC NEUROTRANSMISSION WITHIN THE MIGRAINE CYCLE: EVIDENCE BY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS)

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Question
Although some neurophysiological studies have showed cortical excitability changes during different phases of the migraine cycle, the pathophysiological mechanisms underlying attacks recurrence remain unknown. Here we evaluated the response of the migraine motor-cortex to brief trains of 5-Hz rTMS in order to study, indirectly, presynaptic mechanisms of glutamatergic neurotransmission across the different phases of the migraine cycle.

Methods
50 migraine with aura(MwA), 50 migraine without aura(MwoA), 10 chronic migraine(CM) patients and 20 healthy subjects underwent suprathreshold (120% of the resting motor threshold) brief trains of 5-Hz-rTMS to the motor-cortex, recording Motor Evoked Potentials (MEPs) at each train stimulus. Patients with episodic migraine were studied whatever the phase of the migraine cycle: interictal, preictal, ictal or postictal.

Results
In the interictal phase, both in MwA and MwoA patients, MEPs responses changed according to attack frequency showing: increased facilitation in patients with a lower attack frequency and paradoxical inhibitory response in those with higher attack frequency, as compared to controls. A significant greater inhibitory response was recorded during the ictal and post-ictal phase as well as in CM patients. Conversely, in the pre-ictal phase, we observed a facilitatory response to the trains similar to that of normal subjects. No significant differences were recorded between MwA and MwoA patients.

Conclusions
Our results support the hypothesis that in migraine a transient increase in the threshold for inhibitory homeostatic mechanisms could favor the onset of a migraine attack. The strong activation of inhibitory homeostatic mechanisms of glutamate release could be involved, in patients with episodic migraine, in the resolution of the migraine attack and in preventing further attacks. In CM patients these mechanisms could become ineffective due to an excessive lowering in the attack threshold.
Can early neurophysiological findings be used as prognostic tools in anterior horn disease?

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Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disorder that compromises both mobility and respiration defects, leading to supportive respiration and death. Several studies have supported the notion that sporadic ALS patients with prominent upper motor neuron (UMN) symptoms, (Primary lateral sclerosis (PLS)) have a milder course of disease and relatively better prognosis compared with typical ALS (consisting of lower and upper motor neuron sings). In this retrograde study, we reevaluated the first neurological and EMG examination of 27 patients referred for ALS (12 F/15 M, mean age: 61.5). We monitored their clinical features (spasticity, hyperreflexia, pyramidal sings, bulbar sings, muscular atrophy), and their neurophysiological findings (CV, DML, CMAP, SNAP, F-min, F-mean, F occurrence, M amplitude/ F amplitude, active- chronic dennervation on EMG). The patients were followed for 4-10 years, subdividing them into two groups, i.e. patients with prominent UMN sings (PLS) and typical ALS. We monitored time to GPEG implementation, time of initiating respiratory support and total survival time from the beginning of symptoms. The aim of our study was to determine early prognostic EMG features and to correlate them with patients' clinical profile and course of disease. In our study PLS patients revealed fewer sites of active dennervation, greater F wave occurrence and increased M amp/ F amp ratio.
P910

Sensory Polyneuropathy in ALS

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Question

This retrospective research study aimed to evaluate disorders of the sensory nerve conduction studies in patients with ALS.

Methods

The results of the sensory nerve conduction studies of the median, ulnar, superficial peroneal und sural nerve of 102 patients with clinically definitive or probable ALS (El Escorial classification criteria) were compared to the results of age-matched controls suffering from low back pain (n= 85) and myopathy or myasthenia gravis (n=91). The patients were classified in two subgroups: one with normal values or with abnormal findings in only one nerve (group A) and a second one with abnormal findings in two or more nerves (group B). Patients having known secondary reasons for a sensory polyneuropathy were excluded from this study.

Results

15.7% (mean age 67.3 ± 9.5) of the ALS patients belonged to group B, compared to 11.8% (mean age 63.0 ± 13.4) and 12.1% (mean age 64.0 ± 14.6) of the low back pain and the myopathy/myasthenia patients correspondingly.

There was no statistically significant difference in the percentage of pathological electrophysiological findings in the ALS patients versus the low back pain and the myopathy/myasthenia patients (Chi square= 0.6, p=0.44).

Conclusion

A significant higher percentage of abnormal sensory nerve conduction studies in ALS patients could not be proved in this study. The percentage of the abnormal values in ALS can be compared to the known percentage of polyneuropathy in older patients.
P911

Ultrasonographic evaluation of the peripheral nerves in patients with spinal and bulbar muscular atrophy

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Question

Is the ultrasonographic evaluation able to detect the peripheral nerve atrophy in patients with spinal and bulbar muscular atrophy (SBMA)?

Methods

The participants of this study were 7 patients with SBMA and 7 healthy controls who matched age, gender and BMI with subjects. Seven patients with amyotrophic lateral sclerosis (ALS) were also enrolled in this study as a disease control. Their peripheral nerves underwent high-frequency ultrasonographic measurement of the cross-sectional area (CSA) using a 13-18 MHz linear array transducer at the following sites; median and ulnar nerves at the middle point of upper arm, tibial nerve at the ankle, and sural nerve at the calf (10 cm proximal to lateral malleolus).

Results

The CSAs of median and ulnar nerves were statistically smaller in SBMA than healthy controls (median nerve: 5.0 mm² vs. 9.0 mm², ulnar nerve: 3.6 mm² vs. 7.1mm², respectively p< 0.01). The CSA of ulnar nerve was also smaller in SBMA than ALS (3.6 mm² vs. 5.4 mm², p < 0.05). The tibial and sural nerves had no difference among the CSA of three groups (SBMA vs. controls vs. ALS: tibial nerve; 5.6mm² vs. 8.0mm² vs. 8.8mm², sural nerve; 1.9mm² vs. 2.4mm² vs. 2.0mm²).

Conclusions

The CSAs of median and ulnar nerves reflected peripheral nerve atrophy whereas the CSAs of tibial and sural nerves did not. Ultrasonographic evaluation was then able to detect the atrophy of median and ulnar nerves in patients with SBMA. Further analysis might be needed whether the peripheral nerves were more atrophic in SBMA than ALS.
P912
Muscle ultrasound as a diagnostic tool in amyotrophic lateral sclerosis - comparison to electromyography

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Background

High resolution muscle ultrasound facilitates the detection of neurogenic pathology; its ability to reliably detect lower motor neurone disturbance in amyotrophic lateral sclerosis (ALS), however, is as yet not quite clear.

Objective

We aimed to determine the role of muscle ultrasound in diagnosing patients with ALS comparing it to myography. DRKS00004322

Methods

60 patients with ALS at different stages of disease were compared to 20 patients with other neuromuscular diseases, which initially were suspected of developing ALS, and 30 healthy controls. All patients received clinical neurological examinations, muscle ultrasound and electromyography; controls did not receive EMG. Ultrasonic muscle echogenicity, fasciculations and fibrillations were evaluated in bulbar, cervical, thoracic, and lumbar regions.

Results

90% of ALS-patients showed a significant increase of echotexture (semiquantitatively graded in 4 grades) in all investigated muscles compared to patients with other neuromuscular diseases and to normal controls (mean grade 2.0-2.6 in different muscles vs. 1.0-1.2 in control, p<0.01 and mean 1.5-2.0 in ALS-mimics, p=0.015 in lower extremity and thoracic region and p=0.084-0.143 in upper extremity). Fasciculations were easily detected by ultrasound in different anatomical regions in ALS as well as in other neuromuscular diseases, but also - less frequently - in a small number of healthy controls. Fibrillations were only seen in patients. Ultrasound was more sensitive than EMG in detecting fasciculations (up to 30% higher in ultrasound), whereas fibrillations and positive sharp waves were more sensitive in EMG. Most prominent differences were in the tongue and the thoracic muscles, where ultrasound was very sensitive comparing to EMG (e.g. 20.6% vs. 7.9% in the tongue). The combination of pathologic echogenicity and fasciculation or fibrillation was interpreted as affection of 2. motoneuron. According to Awaji-Shima Criteria none of the healthy controls fulfilled criteria of affected lower motor neurons in more than 2 regions. Sensitivity to detecting lower motor neuron affection in more than 2 regions was increased from 62% using EMG alone to 90.4% using ultrasound and EMG.

Conclusions

The ultrasonic evaluation of echotexture and spontaneous activity such as fasciculations and fibrillations can serve as an add-on tool to EMG to increase detection of generalized lower motor neuron disease. A prospective study should determine its ability to shorten the diagnostic delay in ALS.
P913

NON LINEAR ANALYSIS OF HEART RATE VARIABILITY IN PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS

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Question

Is non linear analysis of heart rate variability useful in assessing autonomic cardiac dysfunction in patients with amyotrophic lateral sclerosis (ALS)?

Methods

Fifty five patients with sporadic ALS were compared to 30 healthy controls. Poincare’ Plot Analysis (SD1-standard deviation of the projection to the negative line of identity, SD2-standard deviation of the projection to the line of identity, SD1/SD2 ratio) and Detrended Fluctuation Analysis (DFA) were performed on a 10-minute ECG recording at rest. DFA was performed on linear (DFA1) and quadratic trend (DFA2) and the scaling exponent α was determined. HR correlations were also defined for short-term (<11 beats) and longer-term (>11 beats) R-R interval data (α1and α2). Measures of randomness of R-R interval time series included approximate entropy (ApEn), sample entropy (SampEn) and multiscale entropy (MSE). pNN50 was also determined.

Results

Poincare’ Plot Analysis revealed a highly significant reduction of SD1 and SD2 in ALS patients in comparison to controls (p=0.000). SD1/ SD2 ratio was also significantly reduced in ALS patients (p=0.04). In both DFA1 and DFA2, α1 was highly significantly increased in ALS patients (p=0.01 and p=0.000 respectively). α was significantly increased in ALS patients only in DFA2. Values of ApEn, sampEn and MSE were highly significantly reduced in ALS patients (p=0.000) in relation to controls.

Conclusion

Our study shows break down of fractal scaling and loss of long-range correlations of heart rate fluctuations in ALS patients. Loss of complexity is consistent with loss of autonomic neurons as part of the neurodegenerative process.
Abstracts of Poster Presentations – Poster Session 52 – Motor neuron disorders/ALS 2

P914
Tracking disease progression in Amyotrophic Lateral Sclerosis (ALS) patients using mune and macro-EMG

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Question
Amyotrophic Lateral Sclerosis (ALS) is a fatal adult-onset neurodegenerative disease characterized by the death of upper and lower motor neurons. Clinical neurophysiology plays a role both in diagnosis and assessment of its severity and progression. This study was aimed to assess ALS progression using Motor Unit Number Estimation (MUNE) and Macro-electromyography (macro-EMG).

Methods
Both techniques were applied to 61 patients, basally (T0) and after 4 (T1), 8 (T2), and 12 (T3) months. Twenty-two patients had a bulbar and thirty-nine a spinal form of disease; forty were in treatment with riluzole (Rilutek®). Thirty-three healthy volunteers served as controls. Macro Motor Unit Potentials (macro MUPs) were derived from Biceps Brachii (BB) muscle; MUNE was performed both in BB and Abductor Digiti Minimi (ADM) of the same side.

Results
MUs number decreased in both muscles throughout the entire follow up and the rate of MU decrease was similar in both muscles, but steeper distally (p<0.05). Macro-MUPs area progressively increased at T1, T2 and T3 in respect to T0 in either ALS form (p<0.005). Fiber density (FD) at T3 decreased a bit lower than T2.

Conclusions
MUNE and Macro-EMG simultaneously performed in ALS allowed to identify a trends in denervation/re-innervation rate in earlier and later stages useful to assess disease progression. Moreover the combined use of both MUNE and Macro EMG techniques in ALS patients, that are reproducible, low-cost, and relatively easy-to-perform, represent a potentially tool to effectively track and quantify over time MU number and feature’s changes, even if much work needs to be still done in scoring disease evolution.
Metal concentrations in cerebrospinal fluid and blood plasma from patients with neurodegenerative disorders

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A slow but steady increase in neurodegenerative disorders has been noted in recent decades. Degenerations in the nervous system are found in Alzheimer’s disease (AD), Parkinson’s disease (PD) and motor neuron disease (MND). In MND spinal neurons degenerate causing muscle atrophy invariably leading to death from respiratory failure. What is causing this degeneration? No consistent explanation has been presented despite intense scientific efforts. Some indications point toward metallotoxic etiologies. MND clusters have been observed in regions with elevated metal concentrations in water and soil. Several studies show increased MND frequency in certain occupations. MND-like conditions are found in animals and animal metal exposure experiments show specific spinal cord accumulations of metals. To address possible metal contributions in MND causation we measured concentrations of 22 metals in cerebrospinal fluid (CSF) from 17 MND patients and 10 controls. Ethical approval was received. Statistically significantly increased concentrations were found for manganese (Mn), aluminum, cadmium, cobalt, copper, zinc, lead, vanadium and uranium (Tab 1). Most of the detected metals are well known neurotoxicants. Manganese showed the most prominent differences between cases (median 5.67 mg/L) and controls (median 2.08 mg/L) (Fig1). Simultaneous sampling from plasma however did not show elevated concentrations, indicating metal accumulations in MND CSF. These data were presented in a thesis (http://hdl.handle.net/10616/41419) at the Karolinska Institutet Stockholm in May 2013. In AD and PD CSF metal data are scarce, but point towards metals as a contributing factor in disease causation. An overview covering existing metal data in neurodegenerative disorders will be given and properties of barrier systems between blood and brain discussed. The possibility of metal accumulations and/or multimetal toxicity as a factor contributing to neurodegenerative disorders will be introduced.

**figure 1**

**Table 1. Summary of metals found in CSF from patients with ALS in statistically significantly elevated concentrations compared to controls.** Metals present in concentrations 1SD or more above the mean for the combined cases and controls are marked with a small circle (•). Metals with known neurotoxic properties, also present in concentrations at or above 1SD, are marked with a larger triangle (▼).
**Figure 1.** Boxplots showing median concentrations of Mn in CSF and blood plasma from ALS patients and controls. The whiskers represent the 25th and 75th percentiles, circles represents outliers in the 1.5*I* interquartile range.
Fasciculations in human hereditary disease

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Objectives

Fasciculations are a frequent finding in motor neuron diseases (amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), bulbospinal muscular atrophy (BSMA)) and other lesions of the peripheral nerves but have been also reported in other neurological conditions. Fasciculations occur in genetic disorders and non-genetic disorders. Aim of the present study was to find out in which hereditary disorders fasciculations are part of the phenotypic expression.

Results

Among genetic disorders fasciculations have been reported in familial ALS due to mutations in the SOD1 gene, the TARDBP gene, in SMA due to mutations in the SMN1, SMN2, and VAPB genes, and BSMA, which is due to mutations in the androgen-receptor gene. Among the hereditary neuropathies fasciculations were reported in association with mutations in the PMP22, MNF2, TKF, TTR and gelsolin genes. Among the spinocerebellar ataxias (SCAs) fasciculations were reported in SCA2, SCA3 (Machado Joseph disease), SCA7, and SCA36 due to ATXN2, ATXN3, ATCN7, and NOP56 mutations respectively and in ataxia and oculomotor apraxia type 1 due to APTX mutations. Additionally, fasciculations can be found in Huntington’s disease, Rett syndrome, Fabry’s disease, Gerstmann Sträussler syndrome, GM2-gangliosidosis and mutations in the L1CAM gene. Among myopathies fasciculations can be observed in mitochondrial disorders and calpainopathy.

Conclusions

Fasciculations are not restricted to sporadic or hereditary motor neuron disease but occur also in hereditary neuropathies, spinocerebellar ataxias, primary myopathies, and more rare hereditary neurological conditions. All these conditions should be considered as potential causes of fasciculations.
P918
Diagnostic accuracy of electrically elicited multiplet discharges in patients with motor neuron disease

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Question

Registration of multiplet discharges (MDs) evoked by electrical stimulation of a motor nerve has been introduced recently as an approach to study distal excitability changes in such a nerve. Electrically elicited MDs in patients with motor neuron disease (MND) are thought to result from the same pathophysiological mechanism as fasciculations of distal origin. However, fasciculations may also arise at the soma, and spontaneous activity of the soma, whether in the form of fasciculations or MDs, is relatively common even in normal conditions. Hence, we hypothesized that electrically evoked MDs are more specific for MND than fasciculations. The aim of the present study was, therefore, to assess and compare the diagnostic accuracy of MDs and fasciculations in MND patients.

Methods

Patients were eligible for this study when they were referred for an EMG examination and had MND in their differential diagnosis. High-density surface EMG of the thenar muscles was performed on the same day as the standard electromyographic examination. The high-density recordings were analysed for presence of MDs, and the needle EMG of any muscle investigated in the cervical region for presence of fasciculation potentials.

Results

Of the 61 patients enrolled in this diagnostic study, 24 patients were clinically diagnosed with amyotrophic lateral sclerosis (ALS) and 12 patients with progressive muscular atrophy (PMA). Twentyfive patients received another diagnosis. Sixteen patients in whom MDs were detected were later diagnosed with either ALS (n = 11) or PMA (n = 5) (sensitivity = 45.7%, PPV = 94%). In only one patient with another diagnosis (MMN) MDs were detected (specificity = 96%). Sensitivity, specificity, and PPV for fasciculations were 48.7%, 79.2%, and 78.3%, respectively.

Conclusions

Electrically evoked MD are highly specific for ALS and PMA, more so than fasciculations. The presence of electrically evoked MDs is an early sign of lower motor neuron dysfunction.
P919
Proteomic analysis of muscle tissue from patients with motorneuron disease and controls
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QUESTION
Is there a difference in muscle proteome in patients with ALS compared to controls when analysed with mass spectroscopy (MS) and can that difference be used as a biomarker?

METHODS
A muscle biopsy was taken from the anterior tibial muscle in 10 ALS-patients and 10 controls without neurological disease. Three controls with other neurological diseases with denervation were also analysed in order get a picture of proteomic change due to denervation. Muscle biopsies were homogenized and the proteins were extracted with detergent lysis buffer. Extracted proteins were on-filter digested with trypsin. Dimethyl isotope labels were used to globally label the tryptic peptides for relative quantification. Individually labelled peptides from patients and controls were combined and analysed by reversed phase nanoliquid chromatography and mass spectroscopy. The same procedure was repeated but with different labels for patients, controls and denervation controls.

RESULTS
The abundance of eleven proteins was significantly different between patients and healthy controls. Of these proteins the most interesting were Cytochrome C oxidase and Valocin containing protein (VCP). Analyses including controls with denervation due to other neurological diseases, did not show the same changes for the eleven proteins, suggesting that the differences found between ALS-patients and healthy controls were not only due to denervation.

CONCLUSIONS
Muscle proteome analysed with MS is different in patients with ALS as compared to controls. This difference does not seem to be due to denervation solely. Proteomic analysis of muscle tissue might be used as a biomarker for the disease.
Abstracts of Poster Presentations – Poster Session 52 – Motor neuron disorders/ALS 2

P920
Sonographic assessment of nerve and root atrophy in ALS

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Objective

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease mainly affecting the upper and lower motor neurons. Because reinnervation may preserve muscle strength and a motor action potential until its late stage, a sensitive measure to reflect the axon loss is needed for early diagnosis and follow-up. Therefore, the aim of the study was to assess the degeneration of the nerve roots in ALS by ultrasonography.

Material and methods

Thirty-five patients (20 men, 58.0 ± 11 years) who met the diagnostic criteria of ALS (Revised El Escorial with Awaji electrodiagnostic criteria) and 37 normal control individuals (13 men, 55.3 ± 8 years) received sonographic evaluation of the right C5, C6, and C7 roots and right median and ulnar nerves at the wrist. The fascicle diameters (FDs) and some of the cross-sectional areas (CSAs) were evaluated and compared.

Results

The data from the control individuals showed that the age or gender had no significant effects on the sonographic parameters. There was significant reduction of the FDs and CSAs in the ALS patients than the control individuals in all the parameters (P < 0.01). The receiver operating curve analysis showed the areas under the curves (AUCs) were greater in the cervical roots (0.74-0.87) than the peripheral nerves (0.66-0.76). The C6 FD had the greatest AUC.

Discussion

The present data revealed the sonographic evidence of atrophy of the cervical nerve roots and peripheral nerves in ALS that likely represents axonal degeneration. Although the present data were similar to the previous presentation assessing the peripheral nerve (Cartwright, et al) in ALS, the evaluation of the nerve root can further utilize the ultrasonographic assessment of the motor nerves that innervate the proximal musculature. The sonographic evaluation of the peripheral nervous system can become a useful measure for diagnosis and progression of ALS.

figure 1
ALS Dysphagia: Different BoNT/A Response for Different Pathophysiology

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**Background**

dysphagia is a very common and troublesome complication in Amyotrophic Lateral Sclerosis (ALS) that may be due to upper and/or lower motor neuron (UMN/LMN) involvement. So far, no pharmacological treatment has provided to be successful in ALS-associated dysphagia.

**Aims**

This study looked at the effect of botulinum neurotoxin type A (BoNT/A) in ALS patients with dysphagia due to isolated UMN involvement or combined UMN/ LMN impairment associated with oral phase and/or oropharyngeal muscles involvement. Establishing whether different pathophysiological mechanisms underlie different responses to BoNT/A treatment may have important patient management implications.

**Patients and Methods**

thirty-five sporadic ALS patients with dysphagia were screened. Twenty-out-of-35 with upper esophageal sphincter (UES) hyperactivity were included in the study. Based on the presence or absence of LMN impairment, the 20 patients were divided into 2 groups. Irrespective of the groups, all 20 patients were treated with BoNT/A into the UES. The study outcome was dysphagia severity scored using the Penetration Aspiration Scale (PAS), measured before and 2, 4 and 20 weeks after injection. **Results:** significant mean PAS reduction at week 2 and 4. The botulinum-dependent PAS reduction was entirely associated to the variability showed by the group of patients with no sign of LMN impairment (group 2) and was not observed in group 1.

**Conclusions**

The significant improvement observed in patients with isolated UES dysfunction suggests that different pathophysiology of ALS dysphagia predisposes patients to different response to treatment with BoNT/A. This treatment may represent an alternative treatment to PEG or prolong PEG-free time.
Comparative detection of fasciculations with ultrasonography and surface electromyography in amyotrophic lateral sclerosis patients

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Since Awaji criteria in 2008 (1), fasciculations are of particular importance in the diagnosis of amyotrophic lateral sclerosis (ALS) to assess lower motor neuron involvement. Both surface EMG and ultrasonography (US) are non invasive and painful methods that have demonstrated accuracy for detection of fasciculations in comparison to clinical and electrophysiological examination (2).

The objective of this study was to compare detection of fasciculations with surface EMG and US in ALS patients and its contribution to the diagnosis.

This study prospectively enrolled 18 patients who were referred to our EMG clinic for early diagnosis of ALS. All patients were classified according clinical and electrophysiological examinations using Awaji algorithm. We performed US and EMG examinations in 15 muscles for only one (tongue, paraspinalis T10, abdominal) or both sides (deltoid, flexor carpi ulnaris, first dorsal interosseus, vastus medialis, tibialis anterior, gastrocnemius). Using 13-6 mHz linear array transducer and surface electrodes, each muscle was screened during 30 seconds to determine presence or absence of fasciculations.

11 males and 6 females were included. Fasciculations were detected in 64.6 % of 270 muscles with surface EMG whereas 62.4 % (p=0.64) with US, and only 35.1% according to clinical examination and 50 % to electromyography. Frequencies of fasciculations were higher in limbs muscle using surface EMG and for axial muscle using ultrasonography. Proportion of the patients with the definite category of the awaji criteria increased from 22% using only EMG to 56 % with US and 38,8 % with EMG (p=0,5).

These results confirm help for diagnostic of both non invasive methods. US was more sensitive for detection of fasciculations in axial and deep muscles and it was easier to use and less liable to artefacts. Both techniques weren't much more sensitive for tongue like in Misawa study(2).

Surface EMG and US improve detection rate of fasciculations. US can be a useful tool to increase Awaji algorithm sensitivity in ALS.


Complex fasciculation potentials and survival in amyotrophic lateral sclerosis

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Question

Our aim was to investigate the relationship between distribution of fasciculation potentials (FPs) and clinical features, and the correlation between FPs and survival in patients with amyotrophic lateral sclerosis (ALS).

Methods

In 85 patients with sporadic ALS, we prospectively performed needle EMG in five to seven muscles of each patient. The shape of the detected FPs was analyzed by inspection, and FPs with > 4 phases were judged as complex FPs. We followed the patients until the endpoint (death, tracheostomy, or ventilator use), and analyzed the correlation between complex FPs and survival period using the Cox proportional hazard model.

Results

Complex FPs were observed in 47 patients (55.3%) in at least one muscle, more frequently in the muscles with normal strength or mild weakness. The presence of complex FPs was associated with shorter survival (hazard ratio 3.055; 95% CI 1.417-7.406; p = 0.004). The median survival times after the disease onset were 3.1 and 1.5 years for patients without and with complex FPs, respectively (p = 0.0017). The greater the number of muscles with complex FPs, the shorter the survival and the faster the progression speed.

Conclusions

Wide distribution of complex FPs is associated with shorter survival in ALS. Axonal membrane instability and resultant spontaneous firing of distal motor axons might be directly associated with the extension of motor neuron degeneration.
Phrenic nerve motor responses and survival in amyotrophic lateral sclerosis

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Question

The aim of the study was to investigate the relationship between phrenic nerve motor responses and respiratory function, and survival prognosis in patients with amyotrophic lateral sclerosis (ALS).

Methods

In 84 patients with sporadic ALS, we performed peripheral electrical stimulation of the phrenic nerves at the posterior edge of the sternocleidomastoid muscle. Diaphragm motor responses were recorded from the disk electrodes placed on the xiphoid process (active) and on the costal margin of the mid-clavicle sagittal line (inactive). Peak-to-trough amplitudes of diaphragm M waves (Damp) were measured. We evaluated forced vital capacity (%FVC) as respiratory function. Endpoints were set at the time of death, tracheostomy, or ventilator use, and the survival periods were calculated from the time of examination to the endpoints. We analyzed the correlation between the phrenic response size and respiratory function test, and survival periods.

Results

%FVC was 65.1% (mean) (SD 29.3), and Damp was 0.44 mV (0.28). There was a weak significant correlation between the values of %FVC and Damp ($R^2 = 0.097; p = 0.008$). The significant difference in survival rate was noted between the patients with Damp ≥ and < 0.4 mV (Cox model, hazard ratio 3.009; $p = 0.003$). Multivariate analysis showed that Damp was one of the independent predictive factors for survival after the examination.

Conclusions

Phrenic nerve motor responses reflect respiratory function and predict survival prognosis after the examination. The amplitude size < 0.4 mV may lead us to consider further respiratory support including non-invasive ventilation for ALS patients.
Electromyographic evidence for repair of motor neurons in patients with ALS

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Question

Amyotrophic lateral sclerosis (ALS) is a fatal disorder characterized by the degeneration of both upper and lower motor neurons. Repair of motor neurons has not been observed in patients with ALS so far; collateral sprouting frequently is found, it causes the polyphasic motor unit action potentials (MUAPs) in concentric needle electromyograms (CNEMG) recorded from patients with ALS. Axonal growth would yield small, instable, polyphasic, so called nascent MUAPs. To detect neural repair, we screened for nascent MUAPs in patients with ALS.

Methods

11 patients with definite ALS according to the El Escorial criteria were studied. Four patients were in a compassionate use treatment program with s.c. rec-hu-G-CSF. CNEMG recordings from hypothenar muscles of at least 50 seconds duration were analyzed independently by two of the authors, WSM and CB, with particular respect to nascent MUAPs. CB was fully blinded throughout his analysis.

Results

Nascent MUAPs were consistently found in all patients treated with G-CSF and in one of the other patients. In one other patient nascent MUAPs were found only by CB. The difference between treated and untreated patients was statistically significant (Fisher’s exact test).

Conclusions

The presence of nascent MUAPs indicates that repair of motor neurons may occur in ALS patients spontaneously. The higher incidence of signs of repair in patients treated with G-CSF is encouraging. Moreover it is in line with the findings of Pitzer et al. (JNC 2010) and Henriques et al (Mol. Therapy 2011) who described identical phenomena in an SOD1 G93A experimental ALS mouse model. Therefore it may be worthwhile to further elucidate these repair mechanisms ALS.
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Somatosensory evoked potential (SEP) modulation by quadripulse transcranial magnetic stimulation (QPS) in benign myoclonus epilepsy patients
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Object
Quadripulse transcranial magnetic stimulation (QPS) applied over primary motor cortex (M1) induces powerful bidirectional long-lasting effects on somatosensory cortex (S1) as well as M1. The purpose of this study is to investigate QPS effects on S1 in myoclonus epilepsy (ME) patients.

Method
Eleven normal volunteers and 6 ME-patients participated in this study. QPS was applied with different interstimulus intervals (ISIs) of 5, 30, 50, 100, 500 and 1250 ms on the left M1 for 30 minutes. We measured the N20 to P25 (N20p-P25) and P25 to N33 (P25-N33) amplitudes of the ipsilateral median nerve somatosensory evoked potential (SEP), and compared their time courses between normal subjects and the patients.

Results
In normal subjects, the P25-N33 amplitude was enhanced by QPS-5 (ISI = 5 ms) and suppressed by QPS-50 (ISI = 50 ms), QPS-100 (ISI = 100 ms), QPS-500 (ISI = 500 ms) and QPS-1250 (ISI = 1250 ms), QPS-30 (ISI = 30 ms) and sham stimulation showed no significant effects upon it. The N20p-P25 amplitude was not affected by any QPSs. In ME-patients, in contrast, the P25-N33 amplitude was enhanced by QPS-5, QPS-30, QPS-50 and QPS-100, but not affected by either QPS-500 or QPS-1250. Furthermore, N20p-P25 amplitude was also enlarged by QPS-5, QPS-30 and QPS-50, but not altered by QPS-100, QPS-500 and QPS-1250.

Conclusions
In normal subjects, QPS on M1 with different ISIs showed bidirectional effects on S1, which was compatible with the Bienenstock-Cooper-Munro curve. On the contrary, in ME-patients, the QPS on M1 unidirectionally potentiated S1, which suggested heterotopic hyper-excitabile connection between M1 and S1.
On the neurophysiology of myoclonus-dystonia and why it stands apart from other primary dystonia

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Question

Myoclonus-dystonia (M-D) is a clinical syndrome characterized by a combination of myoclonic jerks and mild to moderate dystonia and is mostly due to SGCE mutations. It is not clear whether the M-D phenotype in SGCE mutated patients reflect a primary dysfunction of the cerebello-thalamo-cortical pathway or of the striato-pallido-thalamo-cortical pathway. The exact role of an additional cortical dysfunction in M-D pathogenesis is also unknown. The aim of this study was to clarify the neurophysiological characteristics of M-D, thereby gaining further insight into the pathophysiology of the disease. Based on our findings, we discuss whether myoclonus dystonia due to SGCE deficiency stands apart from other primary dystonia.

Methods

We studied 12 M-D patients from 11 unrelated families with a proven mutation or deletion of the SGCE gene. We performed clinical evaluation using UMRS and BFM clinical scale. The resting and active motor thresholds, short-interval intracortical inhibition, and short-interval intracortical facilitation were measured as well as responsiveness of the motor cortex to rapid paired-associative stimulation. Cerebellar functioning was also tested by the means of classical eye blink conditioning.

Results

We found both abnormal membrane excitability of the cortico-cortical axons and normal intracortical gabaergic inhibition, contrasting with what has been described in other forms of primary dystonia. M-D patients also shared some common pathophysiological features of dystonia, including increased plasticity of the motor cortex and cerebellar dysfunction.

Conclusions

Our findings indicate that specific underlying dysfunctions are associated with the very particular clinical phenotype of M-D, and make it a unique entity that stands apart from other primary dystonia.
Tremor resetting by multi-focal single and paired transcranial magnetic stimulation in Parkinson's disease and essential tremor

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Objective

The pathogenesis of tremor in Parkinson’s disease (PD) and essential tremor (ET) is still not fully understood. Dysfunction in the cerebellothalamocortical circuit is thought to play an important role. This study tested the role of three motor-related cortical areas, the primary motor cortex (M1), the supplementary motor area (SMA) and the cerebellar cortex, on PD and ET tremor by single and paired transcranial magnetic stimulation (TMS).

Methods

Ten PD patients (age 62.7±11.4 years) with significant resting tremor and ten ET patients (age 64.3±13.2 years) with prominent postural tremor were studied. All patients received brain imaging and surface electromyography (SEMG) examinations to verify the clinical diagnosis prior to the TMS investigation. Resting motor threshold (RMT), TMS intensity to elicit a motor evoked potential (MEP) response around 1mV and paired TMS intensity to evoke a significant long-interval intracortical inhibition (LICI) (~50% reduction of the non-conditioned test MEP; LICI₅₀⁰, interstimulus interval 200ms) were determined at the M1 contralateral to the recording site where maximal tremor activity was detected by SEMG. LICI is mediated through GABA₉ receptors and supposed to be involved in tremor pathogenesis. A figure-of-eight coil was used for M1 stimulation, and a double cone coil for SMA and cerebellar stimulation. Tremor reset for the target hand muscle was evaluated by calculating a tremor reset index according to Pascual-Leone et al. Muscle Nerve 1994;17:800-7, and Ni et al. Ann Neurol 2010;68:816-24.

Results

For PD and ET, significant tremor resetting occurred by single and paired TMS of M1, and by single TMS of SMA. There was no significant tremor resetting by cerebellar TMS either by single or paired stimulation. RmANOVA revealed a significant main effect of stimulation site (F₂,₃₆=22.63, p<0.001) and a significant interaction between stimulation protocol (single and paired stimulation) and stimulation site (F₂,₃₆=4.24, p=0.032). Post hoc analyses showed that M1 stimulation, both single and paired, induced a more significant tremor resetting phenomenon compared to SMA and cerebellar stimulation.

Conclusions

Findings suggest that M1 and SMA are involved in the pathogenesis of the resting tremor in PD and the postural tremor in ET. Paired TMS, which may activate GABA₉ mediated inhibition reset tremor in M1 but not in SMA, suggesting an anatomical and circuit-specific neuromodulation in both tremor patterns.
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Sense of Agency in Motor Control: An EEG Study

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Objective

The SA is a person’s feeling that his action has been generated by himself. The neural substrates of SA were investigated in many neuroimaging studies, but the functional connectivity of identified regions has only infrequently been investigated.

Methods

We examined the cortical network relating to SA modulation with the power spectrum and phase coherence of EEG in sixteen right-handed, healthy volunteers.

Results

In power spectrum analysis, the most profound desynchronization of EEG was observed in alpha and beta bands over SA modulation. In the alpha band, the significant, relative power changes were seen on the nearly all the recording electrodes. The phase coherence of alpha band was most clearly directly related to changes in SA. The functional connectivity was lower as the participants felt themselves to adjust their own movements better. The electrodes (FP1, FP2, F7, F8, F3, FZ) in the anterior frontal lobe were functionally connected to the middle central, parietal, temporal, and occipital lobes in the right hemisphere during SA modulation.

Conclusions

Alpha oscillation connecting the fronto-central area to several other brain regions appears most directly related to the sense of SA. Alpha oscillation may have a major functional role in SA processing.

*Some of this data were presented at the MDS 16th International Congress of Parkinson's Disease and Movement Disorders in 2012.
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MYOCLONUS IN IDIOPATHIC PARKINSON'S DISEASE

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Introduction

Myoclonus comprises a heterogeneous group of rapid, involuntary jerky movement disorders originating from any localization between cortex and peripheral nerve. Extrapyramidal diseases are among causes. Being more common in corticobasal degeneration (CBD), other possible extrapyramidal disorders are Parkinson's disease (PD), multiple system atrophy, progressive supranuclear palsy, Huntington's disease, dentatorubral-pallidoluysian atrophy, Lewy body dementia. Presences of giant evoked potentials and C-reflex suggest cortical origin of myoclonus in CBD. Here, we aimed to systematically analyze presence and characteristics of myoclonus in PD.

Patients and method

We included 17 PD patients with myoclonus (M/F: 9/8, 65.3±9.3) and 16 PD patients without myoclonus (M/F: 6/10, 63.6±10.2) who were examined between January 2010 and June 2011. Clinical characteristics were noted. We performed surface electromyography over biceps brachii, forearm flexor and extensor muscles and abductor pollicis brevis and recorded reflex responses over these muscles after median nerve stimulation.

Results

Myoclonus was 35-100 ms in duration (mean: 61.9±18.9). Rest tremor was less frequently observed in myoclonus positive group (62.5% vs 21.4, p=0.033). Only one PD patient who also had myoclonus exhibited long latency reflex (LLR) during rest. LLRs during active movement were present in 11 PD patients without myoclonus (68.8%) compared to 10 patients in myoclonus positive group (58.8%) (p=0.554). However, LLR amplitudes were significantly higher in the myoclonus positive group (386.8 µV vs 1055.1 µV, p=0.024).

Conclusions

Our results clearly show that myoclonus of cortical origin is common in PD. Myoclonus in PD is unrelated to presence of tremor. LLRs during active contraction are normally obtained in healthy individuals. However, high amplitude LLRs, as in our myoclonus positive group, are known to reflect cortical hyperexcitability. Therefore, we may suggest that there exists a cortical hyperexcitability in PD patients with myoclonus.
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Reproducibility and validation of Standardized handwriting tasks

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Question

Are standardized handwriting tasks reproducible in healthy participants?

Methods

36 healthy adult participants of different ages were included. Participants performed circle, spiral, star and zigzag tracing tasks and a modified Fitts’ task twice with one week in between. Pen tip trajectories were recorded. Additionally, motor skill was assessed by the Purdue peg board test (PEG). Movement time was compared between the first and second measurement for the tracing tasks. Results were analysed for reproducibility using intra class correlation coefficients (ICC).

Results

The 36 participants were divided in three age-groups (each N=12; Group 1: 20-29 years (8 male), Group 2: 30-50 years (7 male) and Group 3: 51-75 years (7 male)). Results show high agreement between the first and second measurement for the tracing tasks (all ICC > 0.80). The modified Fitts’ task consisted of 8 different conditions and showed medium to high agreement between the first and second measurement (ICC = 0.67 - 0.83). The scores on the PEG test showed high agreement between the first and second measurement (ICC &gt; 0.85).

Conclusions

Although a high agreement was seen in the tracing tasks between the two measurements, movement time at the second measurement generally decreased compared to the first measurement, which indicates a learning effect. To test whether these handwriting tasks are suitable to monitor disease progression, the tests should be repeated with a longer time interval to investigate the duration of the learning effect. To conclude, this study shows that standardized handwriting tasks are reproducible in healthy participants.
P931
Efficacy and safety of botulinum toxin in different kind of drug-resistant tremors

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Question
Botulinum toxin (BT) is an effective treatment for dystonia, spasticity, and other movement disorders. We report the single centre experience with its use in 22 patients with tremors refractory to medical treatment.

Methods
Twenty-two patients affected by different kind of drug - refractory tremors of limbs or head and treated with BT type A, were retrospectively evaluated. The etiological subtypes were idiopathic tremor (7), patients affected by multiple sclerosis (7), post traumatic tremor (5), Parkinson Disease (2) and spino-cerebellar ataxia (1). Tremor involved upper limbs in 19 cases and head in 2 cases. Clinical and instrumental (EMG) assessment of each patient identified tremor-related muscular involvement.

Thirteen patients were treated with EMG-guided BT injection. All sessions of treatment were separated by a mean interval of 3-6 months.

Results
There was a significant clinical improvement after treatment in 14 patients. Of the eight unsatisfied patients, three received only one treatment and seven were treated without the use of EMG-guided procedures. Two patients became resistant to treatment and were switched to different A or B toxin type. Three patients affected by multiple sclerosis reported weakness managed by a toxin dose decrease, but no major side effects were reported.

Conclusions
BT injections are an effective and safe treatment for drug-resistant tremors of different origin/type. Weakness seems a dose-dependent side effect, particularly in patients with previous strength impairment. We highlight the utility of a correct evaluation of clinical and electrophysiological pattern of tremor, eventually followed by EMG-guided injection in clinically complex cases.
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PALMARIS BREVIS SPASM. A REPORT OF 11 CASES

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Question

The Palmaris Brevis (PB) spasm is a rare and benign condition of localized muscular hyperactivity. Describe the neurophysiological findings of PB spasm and also determine its origin (idiopathic or in the context of a Ulnar nerve injury) is the propose of this report.

Methods

Retrospective chart review of 11 patients with PB spasm including history, patient’s occupation , Ulnar nerve injury associated and PB spasm EMG findings.

Results

EMG findings in all cases were abnormal spontaneous activity of single MUPs and/or myokymia with a visible dimpling of the hypothenar eminence. Also it is noted that in 4 cases diffuse or focal demyelinating Ulnar nerve injury was detected, alone or in the context of a Demyelinating Neuropathy (Multifocal Motor Neuropathy, Mononeuritis Multiplex) with conduction blocks. In 1 case CTS surgery was the cause and in the rest no cause was detected (Compression of superficial Ulnar nerve branch in the wrist like an occupational syndrome?)

Conclusion

PB spasm is an involuntary and visible dimpling of hypothenar eminence corresponding with an abnormal spontaneous activity of single MUPs and/or myokymia in PB muscle. This spasm could be idiopathic (probably due to compression of superficial ulnar nerve branch in the wrist like an occupational syndrome) or associated with diffuse or focal demyelinating Ulnar nerve injury, isolated or in the context of Demyelinating Neuropathy (Multifocal Motor Neuropathy, Mononeuritis Multiplex with conduction blocks).
P933
Quantification of movement disorders symptoms employing attitude sensors

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Question

The diagnosis of movement disorders is a time intensive process in which the patient is interviewed and the symptoms are evaluated. However, even the most common types of movement disorders have a high percentage of misdiagnosis (depending on the clinical context, up to 30-50% for essential tremor¹ and 25% for Parkinson’s disease²). To increase diagnostic accuracy, attitude sensors can be placed on the patient during evaluation. They combine different signals to obtain their own orientation. The goal is to use these sensors to quantify characteristic features of the movement disorder (e.g. tremor, bradykinesia, ataxia) and determine the added value to current diagnostic evaluation techniques.

Methods

During movement disorders evaluation, sensors are placed on the affected limbs of the patient. A computer model and algorithms have been developed to derive quantitative parameters from instantaneous device orientations resulting in movement speeds, frequencies, joint angles and distances travelled by the limbs. Sensors accuracy is determined by comparison against 3D optical tracking. Also, the possibility to extend the recordings outside the clinic is evaluated.

Results

Results obtained from patients with tremor and bradykinetic Parkinson’s patients are compared against clinical evaluation (polymyography and UPDRS).

Conclusions

Attitude sensors may have added value for the diagnosis of movement disorders in the clinic and open up the possibility of remote measurements of movement disorder symptoms outside the clinic.

References

LONG TERM EFFECTIVE THALAMIC DBS FOR NEUROPATHIC TREMOR IN PATIENTS WITH HEREDITARY MOTOR-SENSORY POLINEUROPATHY

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Question

Charcot Marie-Tooth disease (CMT) is an inherited disorder of the peripheral nervous system with many clinical and hereditary variants. Many CMT2 patients are affected by a type of tremor syndrome, very disabling, and which pathophysiology remains unclear. Deep brain stimulation (DBS) has been successfully applied to treat most types of tremors by implanting electrodes in the ventral intermedium nucleus of the thalamus (VIM)

Methods

We present two patients with CMT who, during the course of the disease, developed a drug-resistant disabling neuropathic tremor. Genetics, clinical scales and neurophysiologic studies are presented. Due to the lack of response to pharmacological treatment, they were considered good candidates to treatment with DBS of the VIM.

Results

Both patients responded positively to stimulation, with a significatively reduction of the disability scales, and with an improvement of their quality of life.

Conclusion

DBS of the VIM is an established treatment for tremors of central origin. We presented two cases of tremors with a peripheral cause which responded well to this treatment.
P935
Distinguishing essential tremor from parkinsonian tremor: differences in spatiotemporal parameters in a 3D tremor analysis

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Objective

To determine differences in the spatiotemporal characteristics of postural tremor between patients with essential tremor (ET) and patients with Parkinson's disease (PD).

Background

The differential diagnosis of tremor is mainly based on clinical criteria. Electrophysiological studies can be a useful diagnostic tool, but there is an appreciable overlap between tremor-dominant PD and advanced ET with regard to basic tremor parameters like amplitude, frequency, activation pattern or phase deviation of different affected muscles.

Methods

Postural hand tremor was measured using an ultrasound-based three-dimensional (3D) real time motion analysis system (CMS 70P, Zebris, Isny, Germany). Different spatiotemporal parameters of tremor like 3D amplitude, frequency and vector angles of hand tremor movement in the transversal plane through the metacarpal joints as well as the variation and dispersion of these parameters throughout two recorded sequences of 60s each were calculated. Statistical analysis used Student's T-Test for unpaired samples.

Results

A total of n=45 Patients (mean age+/-SD 67+/-11 years) with considerable postural tremor (score >=2 on UPDRS III item 21), diagnosed according to usual clinical criteria either with ET (n=22) or PD (only tremor type I; n=23), were included in the study. Mean tremor frequency was slightly but not significantly higher in the ET group (5.7+/-0.8Hz vs. 5.3+/-0.7Hz; p=0.084). However, both the variation of the 3D tremor amplitude over time (see Fig. 1A for examples in a single ET and PD patient) as well as the dispersion of the vector angle of the tremor beats in the metacarpal plane (Fig. 1B) were significantly higher in the PD group (p>0.05). In 20 out of 23 PD patients characteristic oscillations of the tremor amplitude could be observed (see Fig. 1A, tremor beats 150-300 in the PD example), but only in 6 out of 22 patients with ET.

Conclusions

The analysis of particular spatiotemporal 3D parameters of tremor like the variation of tremor amplitude over time or the dispersion of the 3D vector angle of the tremor movement might be an additional diagnostic tool for the differentiation of patients with tremor-dominant PD from advanced ET.
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figure 1

A

PD

ET

B

PD

ET

vector angle [°]
% of tremor beats

vector angle [°]
% of tremor beats
Electrophysiological evaluation of patients with truncal myoclonus

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**Question**

What kind of electrophysiological features do patients with truncal myoclonus show, and how useful are comprehensive electrophysiological examinations in classifying myoclonus into cortical, subcortical, and spinal, based on the pathophysiological mechanisms?

**Methods**

We investigated 2 patients with myoclonus of the trunk. Patient 1 was a 50-year-old male who had been suffering from abdominal myoclonus at rest without stimulus sensitivity for 5 years. Patient 2 was a 48-year-old female with myoclonus of the neck and shoulders at rest in the last 3 months, which was sensitive to stimulus especially to sounds. Both patients showed no abnormal neurological findings besides myoclonus. Brain and spinal MRI were unremarkable. In both patients, we performed electroencephalography (EEG) - surface electromyography (EMG) polygraph recording during both awake and sleep, Jerk-locked back averaging (JLA) triggered by the EMG of involved muscles, and somatosensory evoked potentials (SEPs) to evaluate giant SEPs and C-reflex elicited by median nerve stimulation.

**Results**

Both patients showed relatively long duration of myoclonic bursts for more than 200 ms. In Patient 1, the onset of myoclonic activity of upper rectus abdominis muscle preceded that of lower rectus abdominis by about 30 ms. The EMG of abdominal myoclonus was recorded not only in awake but also in sleep. In Patient 2, the onset of myoclonic activity of the left trapezius muscle preceded that of the right by about 10-30 ms. Auditory stimulus induced exaggerated startle response shown by masseter EMG and subsequent augmentation of the habitual myoclonus. No myoclonic activity was recorded during sleep. In both patients, there was no finding suggestive of cortical hyperexcitability by EEG, JLA, or SEPs. We diagnosed Patient 1 as propriospinal myoclonus and Patient 2 as subcortical myoclonus.

**Conclusion**

Comprehensive electrophysiological studies including EEG-EMG polygraph during sleep are useful to classify myoclonus involving trunk.
Essential tremor (ET) is the most common tremor disorder. It is characterized by a postural and kinetic tremor. It has been repeatedly shown that the cerebellum is involved in ET (1). The olivocerebellar system, consisting of the inferior olive nucleus (ION), dentate nucleus (DN) and cerebellar cortex, is important for timing of movement. It has been suggested that timing is altered in ET patients (2). To study functional aspects of rhythmic motor function in ET we set out to investigate olivocerebellar activations during a finger tapping task. We hypothesized changes in olivocerebellar activations, especially decreased cerebellar cortical activity in ET, during a task involving motor timing.

Methods
Thirty propranolol sensitive ET patients with familial upper limb tremor and 30 healthy controls were included. T2*-weighted EPI sequences (180 volumes, TR: 2s, voxel size: 3.5x3.5x3.5mm) were acquired on a 3T MRI scanner. The fMRI task consisted of alternating rest and finger tapping (at a rate of 2Hz) blocks. Analysis was performed in SPM8, and included realignment, coregistration and first-level analysis. Normalization of the contrast images was performed using the spatially unbiased infra-tentorial template (SUIT). Subsequently, contrast images were smoothed (4mm kernel). Between group random-effects analysis was performed and functional activation of the left ION was determined in a conjunction analysis of patients and controls, applying small-volume correction.

Results
Within-group analysis showed activations in the cerebellum, red nucleus, basal ganglia and primary motor cortices in both groups. Between-group analysis at whole-brain level did not show any significant differences. Region-of-interest analysis of the left ION showed significantly higher activations in controls compared to ET patients (peak voxel level: p = 0.013 (FWE and small-volume corrected), see figure 1).

Conclusions
Exploratory analysis suggests altered ION activity in ET patients compared to controls. Further analysis of the cerebellar cortex and DN, and connectivity within this network is necessary to draw further conclusions on this result. Understanding the pathophysiology of the olivocerebellar system in ET patients is of great importance for unraveling the mechanism of tremorgenesis in ET.

References
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P938
Corticomuscular coherence in essential tremor during motor and cognitive tasks

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Question
Corticomuscular coherence (CMC) is present in essential tremor (Raethjen et al., 2007; Schnitzler et al., 2009) but has a yet unexplained intermittent character showing changes in coherences around tremor frequency (Raethjen et al., 2007). CMC might be influenced by several factors, including mental and motor tasks. The current study investigates the effect of different tasks on CMC in essential tremor. Furthermore, it investigates differences in CMC across the efferent motor (C3) and the afferent sensory areas (P3). This knowledge will give more insight in the role of cortical oscillatory activity in essential tremor.

Methods
Twelve essential tremor patients were included (age 58.9 ±16.2; off medication) for EEG-EMG recordings. Tasks, each with a duration of 1 minute and designed to induce tremor, included keeping right arm outstretched against gravity, with and without a mental loading math task, and keeping arms outstretched bilaterally. The 64-channel EEG and 8-channel bipolar EMG recorded from the upper were segmented into 4-s long epochs. Coherences between rectified EMG signals of the wrist extensors and the EEG signals from sensory and motor cortex (P3 and C3; Hjorth derivation) were calculated around the tremor frequency (tremor band = 4-9 Hz). Outcome measures are CMC for the different tasks, variation in CMC using standard deviation of 20 seconds moving window (time resolution 4 seconds), and relative EMG power. Between task variation was statistically tested with a one way ANOVA.

Results
Preliminary results show CMC around the tremor frequency in all patients. Between tasks, the CMC showed no significant differences (figure 1). Coherences were not present continuously but intermittently, in contrast to relatively consistent EMG power. The variation in coherence was less profound in sensory areas (P3) contralateral to the tremor during the mental loading task, but not significantly different from the other tasks.

Conclusions
We confirm CMC with intermittent cortical involvement in essential tremor. In addition, the intermittent coupling with motor areas and tremor seems to be independent from the task, whereas sensory input might be influenced by cognitive loading. This supports the hypothesis that the intermittent nature of cortical involvement of motor areas is a characteristic of essential tremor and possibly indicating a switch in cortical and subcortical oscillating systems.

Schnitzler et al. Mov Disord 2009

figure 1

Figure 1: EEG/EMG coherence of a typical essential tremor patient over 1 minute (4-s long epochs) during both arm outstretched, right arm outstretched and during right arm outstretched mental task.
Altered auditory startle reflex pattern in functional movement disorders: a new diagnostic tool?

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Question

Is the auditory startle reflex pattern altered in patients with functional jerky movement disorders compared to healthy volunteers and can it be used as diagnostic tool?

Methods

Between 2011 and 2013 the auditory startle response was assessed in patients with functional jerky movement disorders (n=16) and healthy gender- and age-matched control subjects (n=15). The auditory startle reflex was studied using a well validated paradigm [Bakker et al. 2009]. Trials of 8 auditory stimuli (loudness 104 dB, onset 200 Hz, duration 50 ms) were binaurally presented with a time interval varying from 1.5 to 3 minutes whilst surface electromyography (EMG) was recorded of 7 muscles. Auditory stimuli triggers were stored synchronously with the EMG data. Responses were manually marked according to predefined criteria for two different time windows, the first auditory motor response (20-220 ms) and the late, orienting response (100-1000 ms). The mean and range of onset latencies of the EMG responses were calculated. Response probability, defined as the chance(%) of a muscle to respond following stimulation, was determined for each muscle separately as well as for all muscles together. Response probabilities were analyzed using a linear mixed-model analysis (repeated measures ANOVA) with fixed effects. Group differences in onset latencies were tested using the Mann-Whitney U test.

Results

Preliminary data show a higher total response probability of the late, orienting motor response in the patient group. Total response probability of the early auditory motor startle response did not differ, although a trend suggests an increase in patients. No difference in mean latency was found between groups.

Conclusions

Results imply an increased second orienting startle response in patients with jerky functional movement disorders. The distinction between two different time windows in particular, a method which our research group pioneered [Bakker et al. 2013], could make the startle response a useful measurement in neuropsychiatric disorders. Further investigation could help provide an objective diagnostic measure in this challenging disorder.

Reference List


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P1096
Probing ipsilateral connectivity between dorsal premotor and primary motor cortex in healthy subjects and patients with Parkinson’s disease with dual-site TMS

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Question

Studies in primates provided evidence for direct connections from ipsilateral dorsal premotor cortex (PMd) to primary motor cortex (M1). Little is known about these intrahemispheric premotor-to-motor networks in elderly subjects and patients with Parkinson’s disease (PD). Here we used high-focal dual-site TMS to tap into effective connectivity between PMd and M1 in the intact human brain. Diffusion tensor imaging (DTI) was used to examine whether effective premotor-to-motor connectivity correlates with the microstructure of white matter underlying the stimulated areas in the studied groups.

Methods

13 young healthy subjects (age 25±6), 13 elderly healthy subjects (52±7) and 12 patients with PD (66.7±7,H&Y=2.5±0.8) were included in this study. PD patients were tested in two sessions (ON and OFF dopaminergic condition). Using two highly focal minicoils, dual-site TMS was given to the left M1 and PMd. The paired-pulse paradigm consisted of a first suprathreshold to M1 and a second subthreshold PMd stimulus which was given at interstimulus intervals ranging from 0.8- to 2 ms, 0.4 ms steps. Pulses were applied in a choice-reaction time task (CRTT) given at 125 ms after presentation of the instruction cue. To tap into the structural connectivity of the connection we acquired DTI images (3 acquisitions of 32 directions b=1000 and 5 b0 images) with a 3T MRI scanner from all participants.

Results

Premotor-to-motor facilitation was time, effector- and group specific. At an interstimulus interval of 1.2 ms, paired stimulation of the M1 and PMd facilitated mean MEP amplitudes relative to single-pulse of M1 in healthy young subjects. This facilitation was abolished in elderly healthy subjects and PD patients in medication ON condition. PD patients in the OFF condition presented the premotor-to-motor facilitation. Individual differences in functional connectivity during CRTT show highly specific correlations with parameters of microstructural integrity in localized regions of white-matter in the premotor cortex as showed by DTI.

Conclusion

Our results show an ipsilateral facilitatory premotor-to-motor pathway that is transiently activated during CRTT which decreases with normal aging. In PD patients the cortico-cortical connectivity was dependant on dopaminergic medication. In PD patients, a compensatory upregulation of premotor-to-motor facilitation might compensate for the nigrostriatal dopaminergic dysfunction and motor deficits in PD patients in the medication OFF condition, counteracting normal aging.
Simultaneous rTMS and piano playing improve hand dexterity and induce changes in cortical excitability in a professional pianist affected by multiple sclerosis: a case report.

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Introduction

Motor learning is a fundamental process of neurorehabilitation. One of its neurophysiological substrates - modulation cortex excitability - provides the rationale for non invasive brain stimulation techniques, such as repetitive transcranial stimulation (rTMS). Therefore, association of neuromotor rehabilitation and rTMS may be more effective than their use alone.

Methods

A 39 y.o. pianist affected by multiple sclerosis with a bimanual (L>R) sensory-motor impairment due to 3 cervical relapses in the previous 3-12 months (the last at C4 level) underwent 3-weeks neurorehabilitation sessions (twice a day, 5 days a week) together with treatment sessions of H-coil rTMS (10 Hz, bilateral fronto-parietal cortex, 90%MT) simultaneously to piano exercises. Before (T0) and at the end (T1) of the study, functional (Nine-Hole-Peg-Test, Pinch, Jamar, piano MIDI sequencing) and neurophysiological tests (focal cortical mapping at 115% MT) were performed. Nine hole peg test-NHPT and MIDI sequencing were also collected before and after each rTMS-piano session.

Results

At T1, the patient improved at NHPT in both hands (Right: 27.1” vs 15.45” ; Left 49.5” vs 36.4”) and in piano performance. We found a decrease of MT and of cortical map motor area in both hemispheres. Improvement of these parameters occurring within single sessions was more evident in the first week of treatment, due to progressive improvement of baseline values.

Conclusion

Neurorehabilitation combined with simultaneous association of complex hand motor training and rTMS could improve hand motor performance and modulate motor cortical excitability. Placebo-controlled studies are needed to quantify the hypothetical synergic effect of rTMS and motor training.

figure 1
Bimanual Sequence Learning in Musicians

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Question

Due to their lifelong musical training, musicians show improved sensorimotor performance compared to non-musicians. In the present study, we used a bimanual Serial Reaction Time Task to investigate the effect of switching between hands within a motor learning task by comparing professional musicians (n=20) to non-musicians (n=20). Previous studies showed a reduced interhemispheric inhibition in musicians. Therefore, when investigating the effects of switching between hands during the task, we expected less “switch costs” in musicians compared to the control group.

Methods

Participants performed the bimanual SRTT on two training days, which were separated by one week. They were asked to use their index- and middelfingers of both hands to respond to a visually displayed sequence of letters. We analyzed the performance of the two groups on global sequence learning, which was defined as the total time needed to complete the 15-letter sequence, as well as on the effect of switching between both hands during the trial.

Results

Both groups showed a significant decline in response time in the learning sequence over time, with faster response times in the musicians group. However, the groups did not differ in their amount of sequence learning over time. During the performance of the bimanual SRTT, response times increased in both groups during a between hand switch. Those switch costs were reduced over the time course of learning. However, professional musicians already showed less switch costs at the start of the experiment and a faster reduction of those switch costs than the control group.

Conclusions

In the present study we provide indirect proof that bimanual motor sequence learning is dependent on interhemispheric inhibition between both primary motor cortices by comparing the performance of professional musicians to non-musicians.
Question

Listening to music moves our minds and moods, thus stirring interest in its neural underpinnings. How the multitude of compositional features making up for the appeal of natural music (where a composer's opus is not manipulated for analytic purposes) engages a listener's brain has been addressed only recently also through invasive electrocorticography (ECoG) which offers a unique blend of high spatial and temporal resolution.

The goal of the present analysis was to explore whether features of music that relate to the perceptual dimensions loudness, presence of lyrics, timbre, harmony, dissonance and texture can be traced in ECoG and, eventually, how respective areas of activation compare to those which were found to be associated with the processing of sound intensity previously.

Methods

We report an in-depth analysis of two ECoG data sets obtained over the left hemisphere in ten patients during presentation of either a rock song or a read-out narrative. First, the time courses of six music features (intensity, presence/absence of vocals, spectral centroid, harmonic change, roughness, and novelty) were extracted from the audio tracks and found to correlate amongst each other to varying degree, a testimony to the artful fabric of features intrinsic to natural music. Accordingly, in a second step the specific impact of each single musical feature on ECoG high-gamma power (70-170 Hz) was uncovered by calculating partial correlations to remove the influence of the other five features.

Results

The alternating presence/absence of vocals in ongoing instrumental music and also in speech was identified as the dominant driver for ECoG high-gamma power over temporal auditory, inferior frontal and precentral areas (see Figure 1). Uniquely in the rock song, the neural processing of vocal lyrics was maintained in parallel to music-specific high-gamma activations related to measures of timbral features and harmonic change that were identified in a posterior peri-Sylvian network.

Conclusions

These distinct and robust ECoG activations by vocal speech-related content embedded in instrumental music show that the very onset of speech-related vocal content within a stream of music has a major impact on the brain response as it effects stimulus-related neural activity distributed across several distinct brain regions.
Neural entrainment to musical rhythms in the human auditory cortex, as revealed by intracerebral recordings

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**Question**

Beat and meter refers to the spontaneous perception of periodicities while listening to music, occurring within the frequency range of musical tempo (e.g., perceiving a waltz as a three-beats meter). How the brain computes this perception of periodicity from complex rhythms that are not necessarily periodic in reality remains unknown.

**Methods**

Here, using depth-electrodes implanted in the superior temporal gyrus of two patients with refractory partial epilepsy, we tested whether listening to rhythms that induce spontaneous beat and meter from the non-periodic modulation of the sound envelope induce beat- and meter-related neuronal entrainment within the auditory cortex.

**Results**

We found that in the medial part of the left and right primary auditory cortex, steady-state evoked potentials (SS-EPs) were elicited at frequencies corresponding to the rhythm envelope. Most importantly, the amplitude of the SS-EPs obtained at beat and meter frequencies were selectively enhanced, even though the acoustic energy of the eliciting sounds was not necessarily predominant at these frequencies. Furthermore, this selective enhancement was impaired by accelerating or decelerating the tempo of the rhythmic stimuli such as to move away from the range of frequencies at which beats are usually perceived. Strikingly, these neural responses were highly similar to that obtained using this approach to capture beat and meter-related activities at the level of the scalp.

**Conclusions**

Taken together, the results of this first intracerebral investigation of the neural responses to musical rhythms in humans show that beat and meter perception modulates the processing of incoming auditory input already at the level of the primary auditory cortex, probably through a top-down mechanism of dynamic attending. These observations highlight the interest of human intracerebral recording to understand beat perception in music and, more generally, how perceptual objects emerge within the human auditory system.
Mirror motor activation during music listening in professional pianists: a neurophysiological study

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Introduction

Neuroimaging studies have reported mirroring motor activation to music listening in skilled musicians. Actual corticospinal modulation, together with hand specificity of such activation remains to be clarified. We tested the dynamic functional motor cortex modulation in professional pianists while listening to well-known, predictable melodic sequences, using Transcranial Magnetic Stimulation (TMS) and electroencephalography (EEG).

Methods

Two groups of subjects were studied: professional pianists (n=10) and control naïve subjects (n=10). Participants listened to a melodic tone sequence containing the alternating repetition of a pentatonic scale in two different octaves. Participants, unaware of the scope of the study, were asked to detect a random deviant tone in the sequence, remaining still and especially not moving their arms/hands during the whole experiment. Using a circular coil on the vertex, Motor Evoked Potentials (MEP) were recorded bilaterally (abductor pollicis brevis-APB; abductor digiti minimi-ADM) at different time points, with 32 channels EEG monitoring. MEP amplitudes were expressed as percentage of that obtained in a resting condition. EEG event-related desynchronization (ERD) of the mu rhythm was assessed by comparing its spectral power during listening vs rest.

Results

A significant side x time x group interaction on MEPs amplitudes (repeated measures ANOVA, p=0.009) was found. Pianists showed a significant (post-hoc paired t p=0.001) MEP modulation of right hand muscles according to the timing of their actual activation when playing the piano sequence. This modulation was significantly higher (post-hoc unpaired t p=0.01) vs controls, who did not show significant MEP changes. Moreover, a subgroup of pianists preferring the right hand to play in the low-octave scale had a trend for left hand inhibition. Left sensori-motor frontal mu ERD to the melodic sequence played with the right hand was present in 9 pianists vs 4 control (chi-square, p=0.029).

Conclusions

Pianists display a dynamic auditory induced motor resonance to piano listening. This phenomenon, suggesting the presence of an *audio-motor mirror system* activated by piano music in professional pianists, can be related to their ability to confer a gestural meaning to well-known melodies.
P945

Pesticides as a possible triggering antigenic factor in myasthenia gravis

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Introduction
In the state of São Paulo (Brazil) it is very common application of pesticides in farming without protective equipment, with great exposure of laborers to toxic agents. The domestic use of insecticides is also very widespread. Defects of neuromuscular transmission, with myasthenia, related to organophosphate pesticides were demonstrated¹². Household use insecticides of the chemical group of pyrethrins and pyrethroids act on the nervous system of insects and humans³.

Objective
To search correlations between Myasthenia Gravis (MG) and chronic exposure to pesticides in our region.

Methods
Standard Questionnaire about exposure to pesticides was applied, in patients being from UNESP and UNIFESP Medical Services with clinical and EMG diagnosis of MG and in controls. Data were statistically analyzed by the test of association chi-square and Fisher’s exact test.

Results
From the total of 217 patients with MG, exposure to pesticides was found in 182 patients (83,8%) and patients with MG not exposed in 35 ones (16,1%). From the total of 227 controls (without MG), exposure to pesticides was found in 152 patients (66,9%) and not exposed in 75 ones (33%). Myasthenic patients were more exposed to pesticides, with p < 0.0001= highly significant).

Discussion
Insecticides, including household use ones, have loads of substance of potentially antigenic for man⁴. The present data are alarming for the great exposure of human to pesticides in our country. We think pesticides may have a possible role as antigenic trigger for Myasthenia Gravis.

References
Impairment of excitation-contraction coupling in myasthenia gravis: a new method using post-tetanic potentiation

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Question

We have reported a novel method to assess excitation-contraction (E-C) coupling in the masseter muscle in myasthenia gravis (MG). Although this method enabled to elucidate the correlation of E-C coupling time (ECCT) and bite force, it was necessary to insert a needle electrode into the mandibular notch for trigeminal nerve stimulation. Are there more simple and more sensitive methods to apply to the other muscles?

Methods

We tried to detect a post-tetanic potentiation of E-C coupling in the hand muscle using surface disc electrodes in 12 patients with MG and 24 healthy volunteers. The compound muscle action potential (CMAP) was recorded from abductor pollicis brevis muscle after a supramaximal stimulation of the median nerve at the wrist. Simultaneously, the movement related potential (MRP) was recorded using an accelerometer taped at the thumb. After the baseline recording, the median nerve was stimulated at a frequency of 10 Hz for 10 seconds. The CMAP, MRP and ECCT were recorded chronologically after tetanic stimulation.

Results

1. MRP amplitudes were significantly increased 5 and 10 sec after tetanic stimulation in controls, but not in MG.
2. ECCTs were significantly decreased 5, 10 and 30 sec after tetanic stimulation in controls, and 5 and 10 sec in MG.
3. CMAPs were not changed after tetanic stimulation in both groups.

Conclusions

The post-tetanic potentiation of E-C coupling was easy to measure in the hand muscles, and more sensitive to detect impairment of E-C coupling in MG.
P947
Repetitive Nerve Stimulation of Facial and Trapezius muscles: Relative sensitivity in the different subgroups of myasthenia gravis

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Questions

The sensitivity of repetitive nerve stimulation (RNS) in Trapezius and in facial muscles in the clinical groups of Myasthenia gravis (MG).

Methods

RNS was performed in 83 patients with MG in Orbicularis oculi (O.O.), nasalis and Trapezius. Patients were classified in three groups according to MGFA and divided in group 1 (Type I), group 2 (Type IIa, IIIa, IVa) and group 3 (Type IIb, IIIb, IVb).

Result

There were 43 male and 40 female MG patients. 19 in group 1, 35 in group 2 and 29 in group 3. RNS was abnormal in 69 patients (83.1%): In O.O. 53 patients (63.8), in Nasalis in 48 patients (57.8%) and in Trapezius in 46 (55.4%).

The sensitivity of RNS in O.O. was 57.9% in group 1, 61.8% in group 2 and 70% in group 3 (p>0.65). The sensitivity of Nasalis and Trapezius was low in group 1 (21% and 26% respectively, and significantly higher in group 2 and 3 (65%-76%) (P<0.001).

Discussion

The reported diagnostic yield of RNS in ocular MG is 30-60%. This is consistent with our findings. In MG patients type II and III (MGFA classification) RNS in Nasalis and Trapezius is recommended, while in type I O.O. must be the first muscle to be tested.
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P948
Clinical profile of myasthenia gravis patients in Turkish speaking Cypriot population

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Introduction

The aim of this study is to evaluate clinical profile of myasthenia gravis patients in turkish speaking cypriot population.

Method

A retrospective hospital based study was carried out from the year of 2004 to 2013 and included 34 patients who were diagnosed with myasthenia gravis (MG). Patients were grouped according to their age, gender, duration of illness, type of the illness, accompanying thymoma or any other autoimmune illnesses, family history of myasthenia gravis and according to their treatment.

Results

Among the patients 53% were female while 47% were male. The mean age of female patients was 49.3 and 56 for male patients. Ten patient was ocular, 23 were generalized while 1 patient was congenital myashtenia gravis. Duration of the illness was 7.8 years among women and 6.9 among male patients. Thymoma was present at seven patient but 44% had thymectomy procedure. At three patient rheumatoid arthritis, at 4 patient thyroid disease, at 1 patient diabetes mellitus, at 1 patient demyelinating disease, at one patient Behçet disease and at one patient both rheumatoid arthritis and hyperthyroidism were accompanying MG. Among the patients 20% had family history of myasthenia gravis and 17.6% had other autoimmune diseases. Nine patient (26.5%) received plasmapheresis while 13 patient (38.2%) received intravenous immunoglobulin.

Conclusion

This study, first of its kind, gives valuable information about MG patients. Family history of myasthenia gravis and accompanying other autoimmune diseases have highlighted the importance of familial autoimmunity and poly-autoimmunity in MG.

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**Question**

Studies of neuromuscular transmission in children are important for the diagnosis of myasthenia. A challenge is that the onset of congenital myasthenic syndrome often occurs when neuromuscular junctions are considered immature (0-4 years of age). Further, there is a shortage of published normal data for pediatric studies of repetitive nerve stimulation (RNS) and single fiber EMG (SFEMG).

**Methods**

We identified all examinations of RNS and/or SFEMG in children, with referring diagnosis of myasthenia, aged 0-18 years from January 2003 until October 2013 at the department of Clinical Neurophysiology, Uppsala University Hospital. A pathological decrement was defined as ≥ 10%.

**Results**

A total of 85 children were identified. Age at examination ranged from 4 days to 18 years (mean: 10.4 ± 6.2 years) and the cohort consisted of 40 girls (47%). A diagnosis of neuromuscular transmission failure was made in 14 children (9 girls; mean age: 6.8 ± 5.7 years), who were significantly younger than the remaining children (p=0.034). RNS was performed in the following muscles: abductor digiti minimi (52%), anconeus (61%), nasalis (52%) and trapezius (57%); a pathological decrement in any muscle was found in only 4 children. SFEMG in extensor digitorum communis (EDC) and/or orbicularis oculi (OO) was pathological in 10 children. Mean MCD in the myasthenic group ranged between 72-106 μs in the EDC and 67-120 μs in the OO. In the group with normal neuromuscular transmission, mean MCD ranged from 21-53 μs in the EDC (N=18) and from 21-53 μs in the OO (N=11). There was an age-dependent correlation of amplitude in all examined muscles, however decrement and jitter values showed no specific age correlation.

**Conclusion**

Although SFEMG was found to be the most sensitive examination for the diagnosis of myasthenia in children, it was performed only in 26% of cases. This large cohort adds important data to the paucity of published normal values for pediatric neuromuscular transmission.
Is the Decremental Pattern in Lambert-Eaton Syndrome Different from that in Myasthenia Gravis?

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Question

We reviewed our experience to determine if the decremental pattern during low-frequency repetitive nerve stimulation (LF-RNS) distinguishes between the Lambert-Eaton myasthenic syndrome (LEMS) and myasthenia gravis (MG).

Methods

LF-RNS studies were reviewed from 34 LEMS and 44 MG patients, 4 of whom had antibodies to muscle specific kinase (MuSK). In each train of stimuli we calculated the ratio between the early and the later decrement. Receiver-operator characteristic (ROC) curves were calculated to determine the ratio that best distinguished between LEMS and MG. Positive and negative predictive values for these conditions were calculated for this optimum ratio.

Results

The late decrement was more often greater in LEMS and the converse was true in MG, but with some overlap in values in individual patients. ROC curves showed that a late decrement more than 102% of the early decrement discriminated between LEMS and MG in 90% of studies. The decremental pattern in MG patients with MuSK antibodies resembled that in LEMS.

Conclusions

When the decrement becomes progressively greater during trains of low frequency RNS, the patient is more likely to have LEMS than MG, and in MG, is more likely to have MuSK antibodies. This finding should prompt further clinical, serological and electrodiagnostic evaluation to clarify the diagnosis.
Repetitive nerve stimulation often shows a normal decrement in acute severe generalised Myasthenia Gravis: crucial to perform CNE jitter analysis for correct diagnosis

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Question

Neuromuscular transmission is clinically assessed with repetitive nerve stimulation (RNS) and/or concentric electrode (CNE) jitter analysis. The aim of this study was to assess whether there is a different diagnostic pattern of RNS and CNE between patients with generalized myasthenia gravis (GMG) with acute onset (≤3 weeks) versus slow onset (≥4 weeks).

Methods

All consecutive examinations that established the diagnosis of GMG at the department of Clinical Neurophysiology, Uppsala University Hospital, were retrospectively analyzed from January 2012 to September 2013. Patients were separated into two groups according to disease presentation: acute onset (1-3 weeks) or slow onset (≥4 weeks). Disease duration, age and severity [Myasthenia Gravis Foundation of America (MGFA) class] were noted. A pathological decrement on RNS was defined as ≥10% and at least 3 muscles had been recorded (nasalis, trapezius, anconeus, abductor digiti minimi, deltoid). CNE jitter analysis was performed in the orbicularis oculi and/or frontalis muscle.

Results

A total of 24 patients diagnosed with GMG were identified. Six patients fulfilled the criteria of acute onset GMG (mean age 68 years; 4 women). Only one patient in the acute onset group had a pathological decrement, whereas all patients had markedly abnormal CNE jitter in either the orbicularis oculi or frontalis muscle. The slow onset group included 18 patients (mean age: 55.6 years; 8 women). All these patients had a pathological decrement. The groups did not differ in AChR antibody presence (83% versus 89%) whereas the MGFA class was higher in the first group (range: 3A-5; median: 4B) compared to the second group (2A-3B; median: 2A).

Conclusion

RNS is initially negative in many cases of acute severe GMG, including cases of myasthenic crisis. Performing CNE jitter analysis is therefore of crucial importance for making a correct early diagnosis.
N-Hexane Polyneuropathy: Clinical And Electrophysiological Review With Five Patients

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Introduction

N-Hexane is an aliphatic hydrocarbon derivative, which is widely used in industrial settings. Because of the volatile property of this substance, working in insufficiently ventilated close workplaces may cause slow progressing, sensory-motor polyneuropathy with axonal degeneration and secondary demyelination. We would like to present clinical and electrophysiological data of five cases of n-hexane neuropathy.

Methods

We evaluated five male patients who had prior n-hexane exposure with polyneuropathy. Electrophysiological examinations included nerve conduction velocities, needle EMG and in two cases evoked potentials. Three patients also had control examinations after termination of exposure.

Results

Four patients had axonal motor polyneuropathy, while one patient had sensory-motor axonal neuropathy, which affected motor fiber predominantly. We found mild prolongation of P 100 latency in one patient. Also one patient had conduction block and another patient had mild conduction slowing in fasciculus gracilis. In control examination two of three patients had deterioration clinically and electrophysiologically.

Conclusions

N-hexane usually causes axonal sensory-motor polyneuropathy but motor neuropathy is not rare. We found electrophysiological abnormalities mostly involving motor nerves. It could be deduced that motor involvement precedes sensory abnormalities in some cases. The deterioration after discontinuation of exposure is described as “coasting”. It is frequently seen and become maximal within two-three months. Also evoked potential studies can be useful showing that subclinical involvement.
Objective: In myasthenia gravis (MG), exercise exacerbates decremental response at the low-rate stimulation (LRS) in the repetitive nerve stimulation test (RNS). This phenomenon is known as post-exercise exhaustion by decrement (PEE-D). To find the best duration of exercise for post-exercise exhaustion by decrement (PEE-D) in myasthenia gravis (MG).

Materials and methods: The diagnosis of MG was made on the basis of fluctuating muscle weakness with at least one of the following four tests being abnormal: acetylcholine receptor antibody (AChR-Ab), muscle specific kinase antibody (MuSK-Ab), RNS test, and single-fiber electromyography (SFEMG). In 24 (75%) patients, AChR-Ab was positive. In 32 tests in 32 MG patients, the repetitive nerve stimulation test was performed in the abductor digiti quinti muscle. 3-Hz responses for 2 s were obtained with the supramaximal stimulation at rest, immediately after (PE0), 30 s after (PE30s), and at 1 m, 2 m, 3 m, and 4 m after 10-s, 30-s, and 1-m exercises.

Results:
1. At rest in 32 MG patients, mean CMAP amplitude was normal (9.722 mV ± 3.712) and mean decremental response was 16.0%. An abnormal decrement (≥ 8%) was observed in 21 (67%) patients at rest and in 11 additional patients with exercise.
2. There was not any post-exercise facilitation (PEF-A) or exhaustion (PEE-A) by amplitude in MG.
3. With regard to mean decremental responses, there was an improvement from that at rest with all three exercise durations at PE0, indicating that there is post-exercise facilitation by decrement (PEF-D).
4. Compared with the decrement at rest, a significantly worse decrement was found at PE2m and PE3m after 30-s exercise, and at PE2m, PE3m and PE4m after 1-m exercise. In 11 patients who showed a decremental response only with exercise, PEE-D was observed in five after 30-s exercise and in eight after 1-m exercise.

Conclusion: One minute exercise is the best for evaluation of PEE-D in MG.

Table. Serial decremental responses (-) after exercise (N=32)

<table>
<thead>
<tr>
<th>Exercise duration</th>
<th>10-s</th>
<th>30-s</th>
<th>1-m</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest</td>
<td>-16.0±16.2</td>
<td>-16.0±16.2</td>
<td>-16.0±16.2</td>
</tr>
<tr>
<td>PE0</td>
<td>-4.6±9.0‡</td>
<td>-7.8±11.4‡</td>
<td>-10.7±15.3‡</td>
</tr>
<tr>
<td>PE30s</td>
<td>-13.6±14.3</td>
<td>-13.5±15.9</td>
<td>-17.0±16.7</td>
</tr>
<tr>
<td>PE1m</td>
<td>-17.2±17.4</td>
<td>-19.1±17.7*</td>
<td>-20.7±17.2‡</td>
</tr>
<tr>
<td>PE2m</td>
<td>-18.8±18.1</td>
<td>-21.3±19.5‡</td>
<td>-22.7±21.0‡</td>
</tr>
<tr>
<td>PE3m</td>
<td>-17.2±16.5</td>
<td>-21.6±18.4‡</td>
<td>-23.7±20.8‡</td>
</tr>
<tr>
<td>PE4m</td>
<td>-16.7±16.5</td>
<td>-18.4±14.6</td>
<td>-22.6±19.6‡</td>
</tr>
</tbody>
</table>

* P<0.04 ‡ P<0.004
Abstracts of Poster Presentations – Poster Session 56 – Neuropathies 3

LP54
Myasthenia onset in the senior age group

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Introduction

Myasthenia often develops between the age of 15 and 30. However, past decades have seen the increase in the disease among the senior age group.

Aim of research

The paper aims to examine peculiarities of myasthenia onset and its clinical implications among people of elderly and senile age.

Resources and methods

We conducted a retrospective clinical neurodiagnostics of patients with myasthenia, compiled symptoms characteristics during the disease onset and accessed their development during the first year among the senior age group individuals. Our research indicates 109 patients have developed the late-onset disease in the last 15 years (487 patients). Myasthenia developed at the age of 60 or later was regarded as the late-onset myasthenia.

Results and consideration

The age group under examination comprised 46 men and 63 women. Ophthalmic disorders were myasthenia onset symptoms in 70.6% of cases, while 29.4% had bulbar disorders, weakness in limbs and fewer cases of myasthenic crisis. In the first 2-3 months 49 patients progressed to generalized myasthenia. A full-scaled picture of myasthenia is observed in 96 cases within the first year. In the first 6 months 67 patients progressed to generalized myasthenia, while in 12 month the number increased to 77. Consequently, generalized myasthenia among senior patients progressed more intensively during the first 6 months. In the first year 32 patients suffer such localized types of myasthenia as ophthalmic, a more rare pharyngo-facial and musculoskeletal disorders . Thymoma was observed during the first year in 7 cases. Myasthenia among senior patients was confounded by a wide range of associated somatic diseases, such as: diseases of the cardiovascular system, circulatory encephalopathy, thyroid diseases, diabetes, consequences of cerebral circulation disorder, oncological diseases.

Conclusion

The last 15 years have seen the increase in the disease among the senior age group. In most cases ophthalmic disorders such as ptosis or diplopia were the symptoms of myasthenia onset. Generalized myasthenia developed more intensively in the first 6 months. Myasthenia course was severely confounded by a wide range of associated somatic diseases.
Mixed-type polyneuropathy in Wilson's Disease

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Introduction
Wilson's Disease (WD) is an autosomal recessive disorder of abnormal copper metabolism which predominantly affects the central nervous system and the liver. Peripheral nervous system involvement is rarely reported in the context of WD and not well characterized.

Objectives
To report a WD patient with peripheral neuropathy.

Design
Case report

Setting
Neurology Diagnostic Unit, P.O. San Martino, Oristano, Italy

Methods
A 58-year-old male suffering from WD on therapy with trientine referred to our center because of mild distal limb weakness with hypoesthesia. Clinical evaluation showed mild leg weakness with foot drop and hyporeflexia. A nerve conduction study was performed using standard techniques (Medtronic Keypoint v5.09). Distal motor latency, F-wave latency, motor nerve conduction velocity and CMAP were evaluated in the deep peroneal, posterior tibial, median and ulnar nerves; sensory nerve conduction velocity and SAP were measured in the sural, superficial peroneal, median, ulnar and radial nerve. Analysing his anamnestic and laboratoristic data no other cause of polyneuropathy was found.

Results
Electroneurography findings suggested an asymmetric length-dependent sensory-motor neuropathy of mixed type.

Conclusion
We confirmed peripheral nervous system involvement in WD. According to the literature, also our findings showed both myelin and axonal damage. Polyneuropathy may appear despite therapy, although a iatrogenic contribution cannot be excluded.

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Ronald F. Pfeiffer, M.D. Wilson’s Disease, Semin Neurol. 2007 April;27(2):123-132
P958
Uncommon axonal neuropathies at the intensive care unit (ICU)

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Question

Differential diagnostic questions of acute and subacute polyneuropathies causes difficulties.

Methods

Two cases of acute/subacute polyneuropathies were chosen from the 10-12 patients treated yearly on our ICU. Electroneurography/electromyography (ENG/EMG) was done in our electrophysiological laboratory on Keypoint machine.

Results

The first patient was a 19-year old female. One month before admission left sided mild paresis and increased deep tendon reflexes occurred during low blood-sugar level, which recovered after glucose therapy. Two weeks afterwards, she was operated with suspicion of appendicitis not proven. Meanwhile, ascending type of hypotonic tetraparesis with decreased deep tendon reflexes developed. Routine laboratory parameters were normal, bacterial and viral infections were excluded. ENG showed severe axonal motor nerve neuropathy. Porphyrin and protoporphyrin from blood proved acute intermittent porphyria. Neurological symptoms recovered after hemin infusion.

The second patient was a 17-year old female, admitted with ascending type of tetraparesis, without fever, or bacterial viral infection. After some days, urinary retention developed. Intracranial and spinal MRI were negative. On admission ENG showed moderate axonal motor and sensory neuropathy in the lower limbs. After clinical progression, severe sensory predominant sensomotor polyneuropathy with the suspicion of radiculopathy in all limbs was detected. Immunological tests (pANCA, cANCA, anti-gangliozid, anti-nuclear antibodies), serology were negative. The amount of B-type cells and IgM was higher. Sudden heart failure caused death. Autopsy and histology showed no signs of inflammation. The final diagnosis was thought to be acute motor-sensory axonal neuropathy.

Conclusion

ENG/EMG helps us to more precise, fast diagnosis and follow-up, in order to start the appropriate therapy.
P959
Clinical and neurophysiological spectrum of peripheral neurotoxicity in patients with CD30-positive malignancies, treated with Brentuximab Vedotin.

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OBJECTIVE
To describe the clinical and neurophysiological spectrum of neurotoxic peripheral motor involvement in patients treated with Brentuximab Vedotin.

BACKGROUND
Brentuximab Vedotin is an antibody-drug conjugate composed by the anti-CD30 chimeric IgG1 monoclonal antibody cAC10 and the antimicrotubule drug monomethylauristatin E. Brentuximab vedotin is effective as a single-agent therapy for the treatment of relapsed or refractory CD30-positive malignancies such as classical Hodgkin lymphoma (HL) and anaplastic large cell lymphoma (ALCL).

Peripheral sensory neuropathy, grade 1 or 2 in severity, seems to be one of the most frequent adverse events. Grade 3 motor neuropathy is believed to be present only in a minority of patients. Discontinuation of treatment may be followed by improvement of the neurologic symptoms, but complete regression of the neuropathy is not the rule.

CASE REPORTS
We studied 7 patients treated with Brentuximab Vedotin for HL who developed a sensory-motor neuropathy. The degree of motor involvement varied from mild hyposthenia prevalent in distal muscles of the limbs to severe upper limb diplegia, mimicking motor neuron disease. The sensory-motor conduction study show principally a reduction of sensory-motor conduction velocities, with SAP and cMAP amplitudes reduced. Some patients, however, developed severe reduction of the amplitudes of proximal cMAPs resembling motor conduction blocks. The needle EMG study showed acute denervation in weak muscles, with high amplitude, polyphasic MUPs producing a less-than-full interference pattern. The discontinuation of the treatment and repeated plasmapheresis have been followed in our patients by progressive improvement of muscle strength.

CONCLUSIONS
Peripheral nerve neurotoxicity is a well known event in patients treated with antimicrotubule drugs and motor involvement is also possible, with severe impact on patients’ quality of life. More studies are needed to assess the incidence of peripheral neurotoxicity, the clinical and neurophysiological pattern of the neuropathy, the rate of reversibility and the presence of risk factors for grade 3-4 neurotoxicity.
Case Report: Post herpetic motor plexopathy in a patient suffering for multiple myeloma

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Case report of a 59 year old in treatment for multiple myeloma, that suffered a severe herpes zoster infection in the left brachial plexus territory. 3 weeks after symptoms onset he developed severe weakness of muscles in the shoulder girdle as well as sensory symptoms like paresthesiae in both hands and forearms.

NCS and EMG examination was undertaken.

Nerve conduction tests showed increased distal motor and sensory latencies in the median nerves. There was no reproducible motor response from biceps when stimulating the left musculocutaneous nerve, and the response from Deltoid when stimulating the left axillary nerve was very low in amplitude. The contralateral motor responses were normal. EMG showed a severe pattern of acute denervation without volitional activity in the left biceps brachii muscle. Left Deltoid and Infraspinatus showed also signs of acute denervation but some volitional activity was preserved. Left Upper Trapezius, Triceps and pronator teres showed largely normal EMG features.

After extensive questioning the patient admitted to sensory symptoms in his hands prior to the herpetic infection. However, there were no other factors to explain the acute neurogenic changes in the left C5-C6 territory, so the diagnosis was of a post herpetic motor plexopathy affecting the C5-C6 roots, with a marked emphasis in the left musculocutaneous nerve territory. Although this condition has been previously reported in previously healthy subjects, Our experience suggests that previous health conditions might increase the risk of developing acute motor symptoms in the course of the herpes zoster infection.
Intraoperative monitoring of brachial plexus neurofibroma and treatment of postsurgical neuropathic pain in allergy to conventional drugs. Case report.

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**Introduction**

Benign tumors arising from brachial plexus are infrequent. There is little experience in the diagnosis and surgical treatment of them as well as in the identification of nerve roots by intraoperative monitoring (IOM). The most common side effect of the surgery is the appearance of neuropathic pain which is a really disabling pathology and whose treatment is mainly based on two drugs: gabapentine and pregabaline.

**Case report**

We review a patient with a neurofibroma of upper trunk of brachial plexus not associated with neurofibromatosis and a documented allergy to Gabapentine and Pregabaline. The patient underwent surgery with the help of IOM. During the surgery the brachial plexus around the tumor was identified what allowed a complete resection without any neurological deficit. However the patient continued with neuropathic pain after surgery. Due to his allergy it was necessary the use of analgesic agents associated to Lacosamide (Vimpat®) which has allowed the patient remain asymptomatic till these days.

**Conclusion**

Brachial plexus is a quite uncommon location for tumors. For this reason it should be explored and operated by a team of experienced specialists in order to optimize the clinical prognosis. The use of IOM during the surgery is essential since thanks to it we can minimize the risks and increase the surgical success. For postsurgical neuropathic pain Lacosamide has proved to be a really effective and safe drug with very few side effects.
P963
The application values of short-segment nerve conduction studies in the cubital tunnel syndrome

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Objective To evaluate the value of the short-segment nerve conduction studies (SSCSs, inching test) in the diagnosis and localization of cubital tunnel syndrome (CubTS). Methods The clinical and electrophysiological data in 46 patients (92 limbs from 32 men and 14 women, aged from 19 to 59 years, with average age of 41.20 years) with CubTS were collected. Forty-one patients had unilateral symptomatic arms, 5 patients had bilateral symptomatic arms. There were 35 left sides and 16 right sides in the symptomatic arms and 41 asymptomatic arms in the 46 patients. Short-segment nerve conduction studies were performed in both arms in all 46 patients. Sixty ulnar nerves were studied in 30 healthy control subjects using inching studies. Results The 51 symptomatic arms with CubTS were abnormal in long segment motor nerve conduction studies. There were abnormal 68 arms (51 symptomatic arms, 17 asymptomatic arms) in the inching studies. The lesions were located 2 cm proximal to the elbow - the elbow segment (AE2-E) in 41 arms (44.6%), the elbow - 2 cm distal to the elbow segment (E-BE2) in 23 arms (25%), 4 cm proximal to the elbow - 2 cm proximal to the elbow segment (AE4-AE2) in 18 arms (19.6%), 6 cm proximal to the elbow - 4 cm proximal to the elbow segment (AE6-AE4) in 9 arms (9.8%), 2 cm distal to the elbow - 4 cm distal to the elbow segment (BE2-BE4) in 8 arms (8.6%) and 4 cm distal to the elbow - 6 cm distal to the elbow segment (BE4-BE6) in 6 arms (6.5%) respectively. Conclusion The SSCSs are more sensitive significantly in detecting CubTS than the conventional long segmental motor conduction studies; it could localize the entrapment lesions precisely in the patients with CubTS. It is a useful tool for the detection of ulnar mononeuropathy at the elbow, especially in diagnosing the patients with CubTS who have no clinical features or a normal long segmental nerve conduction findings.
P964
VEMP in longitudinal follow-up of vestibular neuritis

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Objective

The aim of this study was to evaluate recovery of vestibular nerve function after vestibular neuritis (VN).

Methods

Twenty-six patients with the diagnosis of VN were included in this study. Following parameters were collected: nystagmus, Fukuda test, brain MRI and ocular VEMP (oVEMP) and cervical VEMP (cVEMP) recordings at baseline and VEMP were repeated one year later. Clinical recovery was defined as the absence of symptoms and normal neurological examination. Improvement of oVEMP results was estimated according to the asymmetry ratio (AS).

Results

Out of 26 patients, 15 patients (58%) showed clinical recovery, while 11 (41%) did not show complete recovery. On the other hand, 7 patients showed improvement and 19 showed worsening on oVEMP AS after one year follow-up. There was no correlation between clinical recovery and oVEMP AS recovery between groups (p=4.24). Chronic white matter supratentorial lesions present on brain MRI negatively correlated with clinical recovery (Phi coefficient -0.637, p= 0.001). Concerning oVEMP AS, there was no statistically significant difference between groups (improvement and worsening) in the AS at the onset of symptoms, but there is statistically significant difference between two groups at one year follow-up (11% versus 60%, p<0.00, respectively). In both groups there was statistically significant difference between ocular AS at the onset of the symptoms and at one-year follow-up (51% vrs. 11%, p=0.002 and 37% vrs. 60%, p=0.003, respectively).

Conclusion

This study has shown that clinical recovery of VN is a result of central compensatory mechanisms, rather than recovery of vestibular nerve function.
Correlation of nerve ultrasound, electrophysiological and clinical findings in chronic inflammatory demyelinating polyneuropathy

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**Question**

We present the nerve ultrasound findings in chronic inflammatory demyelinating polyneuropathy (CIDP) and examine their correlation with electrophysiology and functional disability.

**Methods**

75 healthy controls and 48 CIDP patients underwent clinical, sonographic and electrophysiological evaluation a mean of 3.9 years (SD +/- 2.7) after disease onset. Functional disability was documented using the Medical Research Council (MRC) sum score, Rasch-built Overall Disability Scale (R-ODS) (¹) and the modified Rasch-built fatigue severity scale (²).

**Results**

The CIDP patients showed a mean MRC Sum score of 20 (SD +/- 3.6), R-ODS score of 24.8 (SD +/- 9.2), modified Rasch-built fatigue severity scale of 18.2 (SD +/- 4.1). Nerve ultrasound revealed statistically significant higher cross sectional area (CSA) values of the median (p<0.0001), ulnar (p<0.0001), radial (p<0.0001), tibial (p<0.0001), fibular nerve (p<0.0001) in most of the anatomic sites and brachial plexus (p<0.0001) when compared to controls. The electroneurography documented signs of permanent axonal loss in the majority of peripheral nerves. A correlation between sonographic and electrophysiological findings was found only between the motor conduction velocity and CSA of the tibial nerve at the ankle (r= -0.451, p=0.007). Neither nerve sonography nor electrophysiology correlated with functional disability.

**Discussion**

CIDP seems to show inhomogenous CSA enlargement in brachial plexus and peripheral nerves, with weak correlation to electrophysiological findings. Neither nerve sonography nor electrophysiology correlated with functional disability in CIDP patients.

**References**


P966
Motor unit number estimation in patients with inflammatory demyelinating Polyneuropathies

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\textsuperscript{2}Aarhus University Hospital, Department of Neurology, Aarhus, Denmark

Question
Can Motor Unit Number Estimation (MUNE) methods quantify the degree of axonal loss and reinnervation in patients with acute- and chronic inflammatory demyelinating polyneuropathies (AIDP, CIDP) compared with control subjects?

Methods
Seven AIDP patients (mean age 47.4, range 23-73) and six CIDP patients (mean age 67.8, range 55-76), were prospectively included. Sensory and motor nerve conduction studies and Multipoint Stimulation (MPS) and Motor Unit Number Index (MUNIX) examinations on Abductor Pollicis Brevis (APB) by stimulating the median nerve were conducted in all patients. Additionally, motor unit size was calculated as surface motor unit potential (sMUP) and Motor Unit Size Index (MUSIX). AIDP patients were examined 2-3 weeks after symptom onset. CIDP patients have had the diagnosis 1-12 years. The results were compared with twenty healthy controls (mean age 46.7, range 23-67).

Results
In AIDP patients MUNIX (mean 84, range 39-148) and MPS (mean 117, range 65-182) were significantly lower than control MUNIX (mean 215, range 131-391) and MPS (mean 329, range 165-503) (p<0.01). Similarly in CIDP patients both MUNIX (mean 64, range 19-139) and MPS (mean 98, range 15-223) were lower than controls (p<0.01). In CIDP patients MUSIX (mean 90, range 61-136) and sMUP (mean 50, range 29-69) were significantly higher than control MUSIX (mean 58, range: 40-89) and sMUP (mean 35, range 22-61) (p<0.05). In contrast, no significant difference was found for MUSIX (mean 65, range 48-104) and sMUP (mean 40,range 18-58) in AIDP patients compared to controls (p>0.05). When AIDP and CIDP groups were combined a sensitivity of 84.62% for MPS and 69.23% for MUNIX were estimated.

Conclusions
Decreased MPS and MUNIX suggest presence of axonal loss both in AIDP and CIDP. Increased motor unit size in CIDP patients indicates compensatory reinnervation. Moreover, MPS is shown to be a more sensitive MUNE method than MUNIX in inflammatory demyelinating neuropathies.
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**Figure 1**

N. Medianus - APB

Multiple point stimulation (MUNE)

- Controls
- AIDP
- CIDP

Figures 1 and 2 show data distributions for N. Medianus - APB with controls, AIDP, and CIDP groups. The graphs display multiple point stimulation (MUNE) and motor unit number index (MUNIX) with mean values and standard deviations.

**Figure 2**

N. Medianus - APB

Motor unit number index (MUNIX)

- Controls
- AIDP
- CIDP

Figures 1 and 2 illustrate the comparison of N. Medianus - APB in different conditions, highlighting the differences between controls, AIDP, and CIDP.
P967

Two novel HSJ1 mutations in a cohort of distal hereditary motor neuropathy patients

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Distal hereditary motor neuropathies (dHMN) form a rare group of hereditary neuropathies characterized by distal motor symptoms. HSJ1 was recently found as the causative gene of a recessive dHMN in a Moroccan Jewish kindred.

In this study, we undertook genetic testing for mutations in the HSJ1 gene in a cohort of dHMN patients from Germany and Austria. We found four patients, two each in two families, with HSJ1 mutations. Both HSJ1 mutations were novel and homozygous. One mutation was a splice-site-, the other a missense-mutation. The splice-site mutation was shown to lead to inclusion of an intron into the transcript, causing reduced expression of HSJ1 protein in patient fibroblast cultures. Patients showed distal-symmetric pareses of the legs and the hands. Nerve conduction studies showed axonal neuropathy with signs of acute and chronic denervation in electromyography. In one family, there was mild sensory involvement in clinical and electrophysiological testing.

Taken together, we show a low frequency of HSJ1 mutations and present two novel mutations in our cohort of dHMN patients.
Motor Unit Number Estimation in Diabetes Mellitus patients with and without polyneuropathy

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Question

What is the utility of Motor Unit Number Estimation (MUNE) methods in quantifying the degree of axonal loss in Diabetes Mellitus patients with and without polyneuropathy?

Methods

Twenty-two Type I and Type II diabetic patients were prospectively included. Patients were divided into neuropathic (10) (mean age:66, range:47-78) and non-neuropathic group (12) (mean age:64, range:41-78), based on clinical examination and nerve conduction studies in dominant median motor and sensory, bilateral peroneal and tibial motor and bilateral sural nerves. Multipoint Stimulation MUNE (MPS) and Motor Unit Number Index (MUNIX) examinations on Abductor Pollicis Brevis by stimulating the median nerve were conducted. Motor unit size was calculated as surface motor unit potential (sMUP) and Motor unit size index (Musix). The results were compared with twenty untrained healthy control subjects (mean age:46.7, range:23-67).

Results

In neuropathic patients MUNIX (mean:122, range:34-308) and MPS were (mean:100, range:63-262) significantly lower than control MUNIX (mean:215, range:131-391) and MPS (mean:329, range:162-503) (p<0.05). Similarly, in non-neuropathic diabetic patients, MUNIX (mean:147, range:65-306) and MPS (mean:147, range:61-304) were lower than controls (p<0.01). sMUP was significantly higher both in neuropathic (mean:71, range:38-120 ) and non-neuropathic (mean:64, range:39-130) patients than controls (mean:35, range:22-61) (p<0.05). In contrast, there was no difference in Musix between controls (mean:58, range:40-89) and neuropathic (mean:67, range:34-122) or non-neuropathic (mean:65, range:43-112) diabetic patients (p>0.05).

Conclusions

Decreased MPS and Munix values together with increased sMUP suggest presence of axonal loss not only in neuropathic but also in non-neuropathic diabetic patients which probably could not be determined by routine NCSs due to compensatory reinnervation. However, further studies should be conducted with larger patient groups and older control subjects.
New Evidence Suggesting High Fasting Glycemia as A Cause of Peripheral Neuropathy in Non-Diabetic Subjects

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Question

Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) have been referred to as “pre-diabetes” and represent an increased risk for diabetes. Although several groups have mentioned the necessity of evaluation of patients with IGT for neuropathy, IFG patients have not been studied yet. Microvascular inflammation is one of the major pathogenetic mechanisms in diabetic peripheral neuropathy (DPN). However, the relationship between inflammation and nerve conduction studies (NCS) abnormalities has not been studied extensively. We aimed to investigate the associations between the serum biomarkers of inflammation and endothelial dysfunction and the most distal sensory NCSs in the very early phases of diabetes, namely IFG and IGT.

Methods

NCSs including sural, medial dorsal cutaneous (MDC), dorsal sural (DS) and medial plantar (MP) sensory nerves, were performed on 44 controls, 25 IFG and 25 IGT patients. Symptoms and examination were scored using Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS). Serum vWF and sE-selectin levels were analyzed for endothelial dysfunction, inflammation was assessed through an IL-6 assay.

Results

Compared with controls, IL-6 levels were higher in IFG and IGT; vWF and sE-selectin levels were higher in IGT (p<0.001). Compared with IFG patients, levels of all biomarkers were higher in IGT (p<0.05). Increase in IL-6 levels was related to increase in NSS and NDS. Both IFG and IGT patients showed significant abnormalities in MDC, DS and MP sensory NCSs, even in patients with preserved sural NCSs. Increase in biomarkers of inflammation and endothelial dysfunction were correlated with various NCS abnormalities in MDC, DS, and MP sensory NCSs (p<0.05).

Conclusions

Our results indicate that neuropathy might begin in individuals as early as IFG stage. This is confirmed by both clinically, through increased NSS and NDS, and electrophysiologically, through impaired NCSs of the most distal sensory nerves. Besides, the marked elevation in IL-6 indicates the on-going inflammation process in IFG patients. Abnormalities in the most distal sensory NCSs were associated with biomarkers of inflammation and endothelial dysfunction. Our findings highlight the importance of evaluating individuals with IFG, as well as IGT, in terms of peripheral neuropathy.
P970
Distinctive Patterns of Sonographic Nerve Enlargement in Charcot-Marie-Tooth type 1A and Hereditary Neuropathy with Pressure Palsies.

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OBJECTIVE
We systematically investigated main arm and leg nerves in CMT-1A and HNPP patients to determine whether nerve sonography is able to discriminate between HNPP and CMT-1A.

BACKGROUND
Sonographic detection of morphologic abnormalities in polyneuropathies is a relatively new research area. The most prominently encountered pathological features are nerve enlargement, increased fascicle size, hypo-echogenicity and intraneural vascularization. There are only a few case reports and case series, mentioning nerve enlargement in CMT and HNPP patients. However, no systematic investigation has been performed yet.

METHODS
We recruited 9 patients fulfilling the international criteria on CMT-1A and 9 with DNA proven HNPP. Medical Research Council sum-score was determined. A standardized sonographic protocol was applied. We evaluated nerve size and vascularization in median, ulnar, fibular and posterior tibial nerves as well as brachial plexus were bilaterally. We also quantitatively assessed fascicle size and echogenicity.

RESULTS
All 18 patients demonstrated nerve enlargement, but no increased vascularization. HNPP demonstrated larger nerves than CMT-1A at sites of entrapment (median nerve at the carpal tunnel p = 0.049 and ulnar nerve at the sulcus p < 0.001). CMT-1A revealed larger nerves than HNPP, proximal to sites of entrapment (median and fibular nerve, brachial plexus p < 0.001). Nerve fascicles where larger (p < 0.001) and also more hypo-echogetic in CMT-1A than in HNPP. Nerve and fascicle size, as well as echogenicity did not correlate with age, gender or MRC sum-score. The swelling ratio of HNPP was greater in HNPP than CMT-1 at median (p < 0.001), ulnar (p = 0.02) and fibular nerve (p < 0.001).

CONCLUSIONS
In CMT-1A enlargement of nerves and fascicles is multifocal among multiple nerves, whereas in HNPP it is restricted to sites of entrapment. The swelling ratio is able to discriminate between HNPP and CMT-1A.
NEUROLOGICAL OUTCOMES FOLLOWING CHEMOTHERAPY TREATMENT: ASSESSMENT OF FUNCTIONAL IMPAIRMENT, PRECISION GRIP AND NERVE FUNCTION

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**Question**

Chemotherapy-induced peripheral neuropathy (CIPN) is a common, dose-limiting side effect of cancer treatment. However, little is known about the relative sensitivity of different outcome measures to assess the functional impact of CIPN on patients.

**Methods**

We compared neurophysiological parameters (routine nerve conduction studies, nerve excitability profile), psychophysical tests, assessments of hand function (pegboard tasks, grip-lift tasks), patient questionnaires (FACT-NTX) and neuropathy grading scales (Total neuropathy score-TNS) in 12 oxaliplatin-treated patients assessed 4.4 ±1.2 months following completion and compared with age-appropriate healthy controls (N=7).

**Results**

At follow-up, 42% patients reported ‘quite a bit’ to ‘very much’ tingling and numbness, and 50% reported mild persisting tingling and numbness. Patients demonstrated impaired performance on pegboard tasks (CIPN 89.7±8.3sec; HC 62± 5.9sec; P≤.05) and elevated thresholds in sensory perception tasks (Grating orientation task CIPN 5.2±.8mm; HC 2.6±.8mm; P≤.05). Patients also demonstrated significantly elevated peak grip force (CIPN 13.1 ±0.9N; HC 9.6± 0.8N; P≤.05) and static grip force (CIPN 12.5± 1N; HC 8.5±0.5N; P≤.05). Sensory nerve excitability profile abnormalities correlated to clinical severity of neuropathy assessed by the TNS (Hyperpolarizing threshold electrotonus 90-100ms;r= -.85; P≤.005) and patient questionnaires (Superexcitability;r=-.89; P≤.005). Patient self-report of functional deficits in fine motor skills was correlated with performance on pegboard (r = -.748; P≤.01) and sensory perception tasks (r=-.813; P≤.05). Additionally, self-report of neuropathic symptoms was correlated with sensory nerve excitability profile (Superexcitability;r=-.723; P≤.05 ).

**Conclusions**

CIPN produces lasting impairments in tactile sensitivity, precision grip and nerve function. Assessment of hand function and precision grip may be useful to quantify functional abnormalities in patients with CIPN.
P972
Na\textsubscript{v}1.8 channel dysfunction in demyelinating Charcot-Marie-Tooth disease - insights from mice heterozygously deficient for the myelin protein P\textsubscript{0} gene

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Question

In demyelinating Charcot-Marie-Tooth disease (CMT1), apart for nerve conduction slowing, a common neurophysiological abnormality is the increased threshold for electrical nerve stimulation. The aim of this study was to investigate the relationship between progression of neuropathy and impaired excitability in a CMT1 mouse model.

Methods

We investigated the neuropathy of mice heterozygously deficient for the myelin protein P\textsubscript{0} gene (P\textsubscript{0}+/−) at 3, 7, 12 and 20 months of age with particular emphasis on motor function. Investigations were carried out by combining nerve conduction studies, rotor-rod motor performance tests, and classical histomorphology with nerve excitability testing by “threshold-tracking”. The expression and function of voltage-gated Na\textsuperscript{+} channels (VGSC) was distinguished by teased-fiber immunohistochemistry as well as genetic and pharmacologic manipulations.

Results

P\textsubscript{0}+/− developed a slowly progressively demyelinating neuropathy with conduction slowing phenotypically similar with CMT1. Apart from an increased rheobase, other measures of excitability of the tibial motor axons were impaired in P\textsubscript{0}+/− as compared to P\textsubscript{0}+/+ littermates at all investigated time-points. Among those, the P\textsubscript{0}+/− had larger threshold changes during hyperpolarizing threshold electrotonus and smaller threshold changes during depolarizing threshold electrotonus. In apparent contrast to neuropathy progression, the magnitude of these differences in excitability appeared to decrease with age. This time-course reflected the increased ectopic Na\textsubscript{v}1.8 VGSC isoform expression at the nodes of Ranvier of motor axons in P\textsubscript{0}+/− and in old P\textsubscript{0}+/+. 

Conclusion

Our data suggest that in P\textsubscript{0}+/− mice the decreased motor excitability reflects, at least in part, a VGSC dysfunction with increased Na\textsubscript{v}1.8 isoform expression. This raises hope that subtype-selective VGSC blockers may be used to improve motor function in CMT1.
P973
H reflex of flexor carpi radialis is affected in C7, not C6 radiculopathies

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Introduction

The H reflex of the flexor carpi radialis (FCR H-reflex) has not been commonly used for the diagnosis of cervical radiculopathy, in comparison with the routinely tested soleus H reflex, which is selectively related to S1 nerve root function clinically, although both S1 and S2 roots innervate soleus. FCR is innervated by C7 and C6 nerve roots, but few studies reported if the attenuation of FCR H reflex is caused by lesions affecting C7 or C6 nerve roots, or both. It was reported that FCR H reflex became absent after total C7 nerve transaction in human (Lu, Zhu et al, 2001). We aimed to study if abnormal FCR H-reflex is related to C7 radiculopathy.

Methods

FCR H reflex was studied in 41 healthy subjects (control group, 22 to 62 years old, F 21, M 20) , in 51 patients ( 25 to 61 years old, F 23, M 28 ) with surgery confirmed single level unilateral C7 radiculopathy and 54 patients (21 to 54 years old, F 17, M 27) with C6 radiculopathy. FCR H-reflexes were recorded by a concentric needle electrode with stimulation (1.0 ms in duration) of the median nerve at above the elbow. Abnormal FCR H reflex was defined as the absence of the H reflex or the side to side difference of the H latency was over 1.5 ms, based on the normal side to side difference of H reflex latency of 16.9 ms (SD 1.7 ms), results from our control group. Conventional NCS and EMG were performed, and patients with disorders of peripheral and central nervous system were excluded.

Results

- In C7 radiculopathy: FCR H reflexes were abnormal in 45 patients (88.2%). H-reflex was absent in 16 cases and with prolonged latency in 29 cases. The abnormal side to side difference of latency varied from 1.5 to 2.8 ms.
- In C6 radiculopathy: FCR H reflexes were abnormal in 2 patients (3.7%), which showed prolonged latency on the involved side.

Conclusions

The highly selective involvement of FCR H-reflex in C7 radiculopathy, but not in C6 radiculopathy, would suggest a more common application of this test in the diagnosis of cervical radiculopathies.
Background

Physicians have recognized the association between diabetes mellitus (DM) and several conditions of the hand. The most commonly recognized are trigger finger, tenosynovitis, Dupuytren's disease (DD), carpal tunnel syndrome (CTS), and limited joint mobility (LJM). However, there is a paucity of data regarding the presence of a possible relation between those soft tissue lesions and diabetic autonomic neuropathy.

Aim

To investigate the relation between sympathetic dysfunction and soft tissue rheumatisms of the hand in diabetics.

Patients

The study included 3 groups. Group 1: 20 diabetic patients with one or more of the previously mentioned soft tissue lesions. Group 2: 20 diabetic patients without any hand pathology and 20 healthy controls.

Methods

Patients were thoroughly evaluated assessed for the presence of diabetic autonomic neuropathy (DAN) using tilt table test before proceeding to the electrophysiological tests. Electrodiagnostic techniques included (1) sensory conduction of median, ulnar, and superficial radial nerves. (2) Motor conduction of median and ulnar nerves. (3) Sympathetic skin response (SSR).

Results

5 patients had trigger finger, 2 had tenosynovitis, 1 had Dupuytren's contracture, 6 had CTS, and 2 had LJM. In addition, 4 patients had combined CTS and trigger finger. Abnormal SSR was detected in 10 patients in group 1 and in 11 patients in group 2 (in the form of absent response or delayed latencies). There was no statistically significant difference between group 1 and 2 regarding the frequency of SSR abnormalities. There was a statistically significant relationship between the presence of CTS in group 1 patients and abnormal SSR results. There was statistically significant relationship between positive tilt table test results in group 1 patients and abnormal SSR in the same group.

Conclusions

Diabetic patients with CTS tend to have prolonged SSR of the hand. Further studies are recommended to study other factors responsible for the occurrence of diabetic soft tissue lesions.

References

P975
Pitfalls of the palmar mixed method.

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Questions

A number of sensitive comparison methods in nerve conduction studies have been proposed for diagnosing CTS. The palmar mixed method to compare the latencies of mixed nerve conduction from palm to wrist between median and ulnar nerves is one of such tests, and has been selected as one of 5 practice standards in the practice parameter proposed by American Association of Electrodiagnostic Medicine (AAEM). This method is also adopted for the combined sensory index (CSI), the sum of three latency differences, median-ulnar across the palm (palmdiff), median-ulnar to the ring finger (ringdiff), and median-radial to the thumb (thumbdiff). However, a possible pitfall of this method that the activated branches might differ depending on the stimulus intensity has been suggested, with no actual documentation. In this study, we aimed to investigate this pitfall of the palmar mixed method.

Methods

Subjects consisted of 3 healthy subjects, 2 healthy subjects with subclinical CTS, and 1 patient with clinical CTS. The median or ulnar nerve was stimulated 8 cm distal to the recording electrode for each nerve. The median nerve was stimulated at various sites from radial to ulnar side and at various intensities.

Results

Selective stimulation of the median nerve branch at the second web space between the second and third metacarpal bones was achieved in 4 of 6 subjects using a stimulus current of around 10 mA. Supramaximal stimulation spreading to neighboring median nerve branches was achieved at 20-50 mA, when the sensory nerve action potential (SNAP) was 1.7-3.7 times higher than that obtained by the selective stimulation. In a subject with subclinical CTS, the median-ulnar latency difference in the palmar mixed method (palmdiff) at the second web space was within normal limit (0.36 ms), whereas palmdiff at the third web space (0.68 ms) and ringdiff (0.72 ms) were definitely abnormal. In a clinical CTS patient, palmdiff was normal (0.16 ms), whereas thumdiff (1.10ms) and ringdiff (0.46ms) were abnormal.

Conclusions

In the palmar mixed method, the stimulation may easily spread to neighboring branches, which may cause a problem for amplitude evaluation. Furthermore, the sensitivity of the palmar mixed method may be lower than other sensitive comparison methods.
Clinical and electrophysiological evaluation of neutral wrist nocturnalsplinting in patients with carpal tunnel syndrome

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Question

To assess prospectively the effectiveness of neutral wrist nocturnal splinting in patients with CTS by clinical scores and nerve conduction studies, and to explore their correlations.

Methods

There were 41 patients who met the inclusion criteria enrolled. The enrolled subjects were clinically evaluated by symptom severity scale and functional status scale and electrophysiologically evaluated by conventional NCS; distal motor latency (wrist-abductor pollicis brevis), sensory conduction velocity (wrist-digit2 and wrist-digit4), and sensory latency difference between median and ulnar nerve (ΔDSL) were measured. Eligible subjects were treated with wrist splinting, patients who had no improvement of symptoms were treated with local steroid injection, others continued to wear splints. SSS, FSS and NCS were also evaluated after splinting for 3.03±1.16 months.

Results

(1)The follow-up was completed in 20 patients (31 wrists) with splinting. Compared with those before splinting, SSS (t=5.956, P=0.000) and FSS (t=5.452, P=0.000) decreased; DML(t=2.431, P=0.021) shortened and ΔDSL (t=2.978, P=0.006) decreased significantly after splinting. (2) There was significant correlation between SSS and DML (r=0.420, P= 0.019), SCV of wrist-digit2 (r=-0.425, P=0.017), SCV of wrist-digit4 (r= -0.519, P=0.003), no correlation between SSS and ΔDSL (P>0.05); and there was no correlation between FSS and the parameters of NCS (P>0.05).

Conclusions

Neutral wrist nocturnal splinting is effective at least in the short-term in CTS. There is little correlation between clinical scores and NCS, which suggests that utilizing both approaches to assess the therapeutic effect of treatment on CTS is of more significance.
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P977
Motor nerve conduction study and muscle strength in newly diagnosed POEMS syndrome

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Introduction

Mixed demyelination and axonal loss were electrophysiological features of POEMS syndrome. It is unclear whether the demyelination and axonal loss happened concurrently or one after another.

Methods

EMG was performed in 37 patients with newly diagnosed POEMS syndrome. Compound muscle action potential (CMAP) amplitude, distal motor latency, motor nerve conduction velocity (MCV), spontaneous activities were collected. Muscle strength was measured according to Medical Research Council (MRC) scale.

Results

A total of 192 nerves were evaluated. MCV, CMAP amplitude, and MRC were significantly decreased in nerves of upper limbs than lower limbs (\(P<0.01\)); while there was no difference between median nerve and ulnar nerve in MCV, CMAP amplitude and MRC (\(P>0.05\)), the same between tibial and peroneal nerve. No CMAP response was evoked in almost half of nerves in lower limbs, which was significantly higher than upper limbs (\(P<0.01\)). MCV decreased in all nerves with decreased CMAP amplitude or decreased MRC, in 93% nerves with normal amplitude and in 95% nerves with normal MRC. CMAP amplitude decreased in 67% nerves with normal MRC, and in 96% nerves with decreased MRC. Abnormal SA was presented in 32.4% muscles of upper limbs, 94.6% of lower limbs. Conventional needle EMG showed that abnormal spontaneous activity (SA) presented in 32.4% muscles in upper limbs, in 94.6% muscles of lower limbs. EMG was followed up in 3 patients. All showed that decreased MCV was the earliest change in motor NCS.

Conclusion

decreased MCV is the earliest change in motor NCS, demyelinating changes happen earlier than axonal loss, and the damage of the nerves happen earlier and more severe in lower limb than upper limb. Recognition of these features can lead to early diagnosis of POEMS syndrome, and give some clues for better understanding the mechanism and pathophysiology of POEMS neuropathy.
Peripheral Neuropathy Based on Electroneurography in Nasopharyngeal Carcinoma Patients Treated with Cisplatin

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Background

The majority of cancer patients will experience neuropathy. Neuropathic symptoms arising from chemotherapy can inhibit the therapeutic process. Cisplatin is the most widely used chemotherapy in the treatment of nasopharyngeal cancer (NPC) and the many causes of peripheral neuropathy.

Objective

This study aims to describe the neuropathy using electroneurography examination in NPC patients who received cisplatin in Cipto Mangunkusumo Hospital, Indonesia and the factors that related to it.

Method

The study subjects were NPC patients with cisplatin less than 6 months before the examination, whether single, as kemoadjuvant or in combination with other chemotherapy. Diabetes Mellitus and patients with previous neurological disorders excluded from the study. Anamnesis, neurological physical examination, and electroneurography (ENG) were done. The study was conducted using a cross-sectional design. The data was collected between February and May 2013.

Results

A total of 100 study subjects consisted of 81 male subjects and 19 female subjects were included in this study. Age of study subjects ranged from 30-60 years. There were 76% of the subjects had neuropathy, 51 subjects had neuropathy based on ENG. There were 82.89% had sensory neuropathy. Most (89.47%) had axonal degeneration and none suffered pure demyelination. There is a statistically significant relationship between age and dose with the incidence of clinical neuropathy (each p <0.05).

Conclusion

The prevalence of neuropathy in cisplatin chemotherapy in NPC patients in Cipto Mangunkusumo was as high as 76%. Older age and greater total doses are all factors that influence the neuropathy in NPC patients receiving cisplatin chemotherapy.

Keyword

Neuropathy, cisplatin, nasopharyngeal cancer
P979
Value of latency difference of the second lumbrical-interossei as a predictor of carpal tunnel syndrome in uremic patients

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BACKGROUND

Routine electrophysiological parameters for diagnosing carpal tunnel syndrome do not detect median neuropathy at wrist in cases with concomitant severe peripheral neuropathy whatever its cause. Uremic patients on dialysis may have hand symptoms that may be because of peripheral neuropathy, carpal tunnel syndrome, or both.

OBJECTIVE

The authors aimed to assess the significance of the second lumbrical-interosseus (2L-INT) latency difference as a predictor of carpal tunnel syndrome in uremic patients on dialysis.

METHODS

Fifty-four consecutive cases (108 hands) of end-stage renal failure on dialysis (hemo or peritoneal) were subjected to routine electrophysiological studies for carpal tunnel syndrome. 2L-INT latency difference was measured in all cases.

RESULTS

The cases (94.3%) had abnormal electrophysiological studies. Routine tests revealed carpal tunnel syndrome in 54 hands, and all of these had prolonged 2L-INT latency difference. Peripheral neuropathy was found in another 42.9% hands, but 75.6% of these had prolonged 2L-INT latency difference, suggesting a concomitant carpal tunnel syndrome, whereas on using the routine neurophysiological studies, only 13.3% were diagnosed as carpal tunnel syndrome. Overall, the frequency of carpal tunnel syndrome in uremic patients on maintenance dialysis using standard nerve conduction parameters was 51.4%; however, the frequency increased substantially to 83.8% if 2L-INT latency difference is included in the criteria for the diagnosis.

CONCLUSIONS

Carpal tunnel syndrome is common in patients with end-stage renal failure on dialysis. 2L-INT latency difference is a sensitive test to predict median neuropathy at wrist in presence of peripheral neuropathy.
P980

Nerve Conduction in Polyneuropathy complicating Multiple Mononeuropathy, Associated to Disturbances in the Iron Metabolic Profile.

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Question

Nerve Conduction (NC) was performed to find most affected nerves, and their sensory/motor tendencies, in patients with a Polyneuropathy complicating Multiple Mononeuropathy (MM), due to Disturbed Iron Metabolic Profile (DIMP).

Methods

Distal sensory and motor latencies were obtained from Median and Ulnar nerves, distal sensory latency for the Sural nerve and motor velocity in Common Peroneal. Sample consisted of 67 patients suffering Paresthesiae etc, when examined showing: glove/stocking signs, diminished OT reflexes, all from 87 patients qualifying as MM. Inclusion required at least 2 cranial or peripheral altered nerves. Also required for inclusion, was abnormality of at least one of the six items of the routine Iron Metabolic Profile: serum iron, % saturation, TIBC, Ferritin and Transferrin. Cases came from Neurological departments at the Rehabilitation Center and Universidad Central del Este. Tests were performed with a Sierra Cadwell electromyographer, using minimal variations on parameters published by DeLisa. Excluded were 33 cases having no DIMP, but serving as epidemiological controls.

Results

Most affected nerve was Sural with latencies averaging 4.1 ms, while abnormal Median and Ulnar latencies were down to 3.6 ms; also abnormal. Median motor latency occurred at 3.9 ms versus Ulnar nerve motor latency, normal at 3.15 ms. Common Peroneal motor nerve velocity was abnormal at 45.5 mts/sec. NC in Controls had similar results. For clinical aspects: Neurologia Argentina 2013;5:164-170.

Conclusion

Polyneuropathy complicating Multiple Mononeuropathy associated to diminished Iron Metabolic Profile Items is mainly sensory, affecting all 3 sensory nerves; only 2/3 motor nerves.
**P981**

**Electrodiagnosis in carpal tunnel syndrome, contribution of nerve conduction study of the first digit median nerve**

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**Introduction and Objective**

Carpal tunnel syndrome is one of the most frequent entrapment neuropathy and affects around 3-8% of the population of working adults. The aim of this study is to evaluate the contribution of nerve conduction branch to the first finger of the median nerve in the early diagnosis of mild to severe forms of this neuropathy.

**Materials and Methods**

64 participants (81.3 females), mean age of 44.9 years-old (± 12.6), 26 with complaints of neck pain and 38 with complaints of pain in the hands. Study was made of the sensory nerve conduction by antidromic and orthodromic stimulation technique of palm-wrist and motor, based on anatomical parameters as using the second wrist fold over the palm and fingers-hand, electromyography electrode bipolar concentric coaxial needle.

**Results**

Linear regression analyses showed significant impact on STC of the following parameters: Latency of the Finger III (t= 2.32, p=.026), Speed of the Finger 1 (t=-.3461, p=.001), Speed of Palmar-wrist (t=-2.710 p=.010), Amplitude Finger I (t=-2.376 p=.024) and Amplitude of Palmar-wrist (t=-2.646 p=.013). Among these parameters Speed of Finger I and Speed of Palmar-wrist seems to present the strongest effect. The covariate Age was only correlated (Person correlation analyses) to the parameters Latency of Finger I (r=.286, p=.024) and Speed of Finger IV (r=-.302 p=.015) meaning that how older the patient bigger is the latency of Finger I and faster is the firing of the nerve fibers of the Finger IV.

**Conclusion**

Taking all the parameters into account, it’s possible to propose that The Finger I can add important information into the STC investigation. The branch of the Finger I is one of the first to be affected, manifesting itself most prominently through prolongation of latencies and reduced sensory conduction velocity, while other branches show minor changes even with the patient's symptoms (pain in hands, fingers, forearm and shoulder).


LP55
Extending the knowledge of the hereditary neuropathy with liability to pressure palsies: a clinical and electrophysiological study.

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Hereditary Neuropathy with Liability to Pressure Palsies (HNPP) is an autossomal dominant disorder usually characterized by episodes of recurrent and painless focal motor and sensory peripheral mononeuropathy. Its diagnosis can be somewhat challenging due to clinical and neurophysiological superposition to other diseases.

Question: To evaluate the clinical and the electrophysiological characteristics of a group of genetically proven HNPP patients, searching for particularities that may help diagnosis.

Methods: We retrospectively reviewed clinical and electrophysiological features of 39 patients with HNPP harboring the typical PMP22 deletion on chromosome 17p11.2.

Results: Family history was absent in 16/39 (41%). The first spontaneous complaint was a localized muscular weakness in 24 patients (61%). Interestingly, pain was the first complaint in 6 patients and other 3 complained of pain at some point of their disease. Sensory deficit was the first sign in 5 patients and paresthesias in 4 patients. According to the physical examination, 26 patients manifested a multiple mononeuropathy pattern, 7 presented an isolated mononeuropathy, 4 had a chronic sensorimotor polyneuropathy, 1 developed a predominant sensory polyneuropathy and 1 patient presented a unilateral brachial plexopathy. Despite the clinical presentation, nerve conduction studies showed a pattern of sensory and motor neuropathy with focal conduction slowing in 38 patients, only one had an isolated mononeuropathy. The most frequently involved nerves were the ulnar motor and sensory, median motor and sensory and peroneal nerves. Reduction in conduction velocity characterized the involvement of the ulnar (motor and sensory) and median (sensory) nerve studies; prolonged distal latencies and F-waves characterized the involvement of the fibular nerves; and prolonged distal latencies (out of proportion to the reduction in forearm CV) was a characteristic of the median motor nerve. The most frequent focal slowing was that of the ulnar nerve segment at the elbow. Temporal dispersion was observed in some sensory and motor nerves. Conduction block was infrequent.

Conclusions: Although most HNPP patients have a long history of sensory manifestations, including transitory paresthesias and disesthesias, the most frequent active complaints are motor weakness and pain. NCV are particularly important, characterizing an asymmetrical sensory and motor neuropathy with focal slowing of NCV.
Contralateral Reinnervation in Patients with Facial Nerve Palsy

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We present a series of nine patients with facial nerve palsy whose facial muscles were electrophysiologically proven to be reinnervated by the contralateral facial nerve. The duration from symptom onset spanned from 3 to 114 months. All subjects had moderate to severe facial palsy initially. Contralateral reinnervation was observed in both traumatic and idiopathic etiologies; also in both complete and incomplete palsies. Cross-innervation is more frequently reported in muscles near the midline; however, this is the first report demonstrating evidence of cross-innervation in muscles far from the midline - the frontalis, the orbicularis oculi, and the zygomaticus. Although contralateral reinnervation after facial nerve palsy is a common observation, it has not gained appropriate attention. Without recognition of this phenomenon, misinterpretation of the electromyography may mislead the proper timing of nerve repair or reanimation procedure. Therefore, routine examination of motor action potential by contralateral stimulation during electromyography, especially in patients with moderate to severe palsy, would provide accurate assessment of the injured nerves and would help in appropriate decision making for further treatment.

Fig. 1. Typical CMAP responses which are recorded with a needle electrode placed in the paralyzed left frontalis (patient no. 1). The needle electrode was located halfway between the hairline and eyebrow on a line passing vertically through the patient's pupil.

Fig. 2. A scatter diagram of the onset latency versus duration from symptom onset in the nasalis muscle. There is a significant tendency of the onset latency in the nasalis to decrease when the duration from symptom onset increased ($p = 0.045$, $R^2 = 0.412$).

figure 1

figure 2
Electrodiagnostic and sonographic findings determining the long term prognosis in common fibular neuropathy

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Question
What is the natural history of common fibular (CF) neuropathy and what are the predictive prognostic factors of a CF neuropathy?

Methods
We re-evaluated 69 patients with a CF neuropathy. Primary outcome was the recovery reported by the patients and secondary outcome was improvement of muscle strength at clinical examination at follow-up. Baseline characteristics were used to compare between the patients who reported complete recovery and the patients who did not and between the patients with clinical improvement and the patients without clinical improvement.

Results
Weakness reported by the patients and MRC score of the peroneus longus, extensor hallucis longus and tibialis anterior at neurological examination improved significantly. Complete recovery was reported by 29 (42%) patients. The absence of the distal compound muscle action potential (CMAP) amplitude of the extensor digitorum brevis (EDB) was significantly more common in patients who did not report complete recovery ($p = 0.002$). Clinical improvement of muscle strength occurred in 49 (71%) patients. The group without improvement was significant older, a greater proportion had an absent distal CMAP or very low CMAP amplitude of the EDB (< 2 mV) and the mean cross sectional area of the CF nerve at the level of the fibular head (FH) was significant larger.

Conclusion
The absence of the distal CMAP amplitude of the EDB is a predictive factor associated with less reported recovery and less clinical improvement. A larger CF nerve at the level of the FH is associated with less clinical improvement.
Neurography, QST and CHEP in the diagnosis of neuropathic complications after laser and fibrovein treatment of varicose veins

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Question

Incidence and type of neuropathic complications after laser or laser-fibrovein treatment for varicose veins, using neurophysiologic, psychophysical and structured clinical sensory examination.

Methods

24 patients were studied before and after laser (N= 9), laser-fibrovein (N= 14) and only fibrovein (N= 1) treatment of varicose veins. Subjective symptoms were assessed with a symptom chart. Clinical sensory tests were done at saphenous, sural, and superficial peroneal nerve distributions bilaterally; included sharp-blunt and warm/cold discrimination, quantitative sensory testing, tactile and mechanical pain detection thresholds with Semmes-Weinstein monofilaments and thermal detection thresholds. Pain wind-up was tested with monofilaments. CHEP recordings (Contact heat evoked potential) were done at superficial peroneal and saphenous distributions bilaterally. Sensory neurography was studied bilaterally from all 3 nerve distributions.

Results

Three patients (12,5%) reported subjective pain symptoms after treatment, two (14%) after laser-fibrovein treatment, one (4%) after laser treatment. Patient 1 got reversible partial sural nerve lesion verified with neurography, warm/cold and sharp-blunt discrimination after laser-fibrovein treatment, on the fibrovein treated area. CHEP were unrecordable already at preoperative point. Patient 2 got reversible pain at fibrovein treated saphenus area, verified with thermal thresholds and CHEPs. Laser treated patient 3 got reversible pain only on the punctated area at medial malleol site, verified with CHEPs.

Conclusion

Laser treatment alone seems to be a safe method to treat varicose veins, irreversible heat induced nerve lesions were not seen. Laser-fibrovein treatment may lead to reversible focal small fiber hypofunction as well as more severe direct nerve lesions and neuropathic pain, probably due to the fibrovein.
P1001
An fMRI preliminary study in patients with diabetes mellitus by contact heat stimuli

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Objective

To compare the difference of activation in different cerebral regions evoked by A delta and C fiber nociceptors which excited by different contact heat stimulus intensity between diabetes mellitus (DM) patients and normal subjects, and probe into the change of pain-related network, and analyze the underlying causes of pain in patients with DM

Methods

10 clinically diagnosed diabetic patients and 10 healthy volunteers ((control group), after informed consent and approved by Medical Ethics Review Committee, were included in this study. Each subject was asked to accept synchronous fMRI scanning and 41°C or 51°C contact heat stimulus. SPM8 was used to pre-process fMRI data and statistical analysis. The pre-processing consists of slice timing, realign, normalization and smooth. Two-sample t-test was used to extract the voxel in the areas of the brain (AALtemplate)and its coordinates with statistical significance (P < 0.005), and record the response intensity of activated area, and analyze the differences between two groups in the temperature of 41 and 51 degree.

Results

(1) Compared with control group at 41°C, the response of activations in DM group was lower in bilateral superior temporal gyrus, ipsilateral insula, ipsilateral postcentral, ipsilateral cuneus and ipsilateral calcarine (P < 0.005 ), but higher in ipsilateral middle frontal gyrus and ipsilateral superior temporal gyrus (P < 0.005 ). (2) Compared with control group at 51°C, the response of activations in DM group was lower in ipsilateral superior frontal gyrus, contralateral calcarine, bilateral cuneus, bilateral middle and posterior cingulum gyrus, bilateral cerebelum, ipsilateral middle frontal gyrus and ipsilateral anterior cingulum gyrus (P < 0.005 ), but higher in contralateral brainstem, ipsilatera lingual, bilateral thalamus, contralateral inferior frontal gyrus, bilateral superior and middle frontal gyrus, bilateral precentral and bilateral paracentral lobule (P < 0.005 ).

Conclusions

There exist a series of pain-related cerebral areas, which consist of pain-related networks in the brain. Contact heat stimulus may be hopefully a preferred tool in the study of pain-related network. The pain-related network in the brains of patients with DM had changed: some areas became more active, but some areas became less active. This may mean that the pain-related network in the brain has experienced reconstructed or changed at the connection level. But whether this phenomenon is associated with pain in the patients with DM deserves further study
P1002
Modulation of intracortical inhibition and spatial somatosensory discrimination of the affected hand in patients with CRPS type I by using cutaneous anesthesia of the forearm

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CRPS is characterized by decreased somatosensory and motor impairment besides other symptoms like signs of inflammation and chronic neuropathic pain in the affected limb. With respect to neurophysiology a decreased short intracortical inhibition (SICI) and smaller representation distance in the primary somatosensory cortex between the thumb and the pinky have been reported when investigating the affected hand these patients. Anaesthesia of the forearm skin is capable to modulate both SICI and spatial tactile resolution (STR) of the fingers. We thought that this intervention would be perfectly suited to investigate changes in neurophysiology and sensorimotor performance in patients with CRPS I. We here present a protocol for testing patients with CRPS I using double pulse TMS and spatial high resolution fMRI for the somatosensory cortex.
DIFFERENTIAL GENE EXPRESSION IN TWO DIFFERENT EXPERIMENTAL MODELS OF NEUROPATHIC PAIN

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Background

Neuropathic pain has a major impact on health worldwide. Diverse subtypes of neuropathic pain have shown different responses to pharmacological treatment. Progressive tactile hypersensitivity (PTH) manifesting after sciatic nerve crush and spared nerve injury (SNI) are two distinct rodent experimental models of neuropathic pain. Microarray gene analysis on central nervous system tissues holds great promise for discovering novel targets for persistent pain modulation.

Question

What are the differences in gene expression at the ipsilateral dorsal root ganglia (DRG) between an animal model of stimulus-induced neuropathic pain (PTH) and another model of spontaneous neuropathic pain, both generated after sciatic nerve lesions?

Methods

Rat models of sciatic nerve crush (group I) and spared nerve injury (group II) were used for these studies. 36 male rats were randomly assigned to three groups including a control group. The development of mechanical alodinia and PTH was evaluated using von Frey monofilaments. The global gene expression in DRG was measured at 16 weeks after surgery using the Affymetrix GeneChip® Rat Expression Set 230 (Santa Clara, CA). Ant colony optimization algorithms were used to analyse the data. The candidate genes were classified according to their function.

Results

The rats in group I developed PTH 10 weeks after surgery while the rats in group II developed mechanical alodinia in the first week. Significant differences in DRG gene expression between the two neuropathic pain models were found. There was little overlap between genes altered in each injury model, suggesting that they produce distinct peripheral mechanisms mediating the observed mechanical alodinia or the PTH.

Conclusions

These two models of persistent neuropathic pain produce different hypersensitivity outcomes and differential gene expression. These results suggest that diverging mechanisms lead different behavioral outcomes in these pain models.

Significance

These distinct pathophysiologic mechanisms present in the evaluated models may implicate unique drug or gene therapies for these subtypes of chronic neuropathic pain syndromes.
Allodynic evoked potentials with Air-puff evoked potentials? A preliminary study in 23 patients with neuropathic pain.

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Question

To determine whether the allodynic sensation elicited by air-puff stimuli is associated or not with a specific scalp evoked-potential (EP).

Material and methods

Twenty-three patients with confirmed neuropathic pain and dynamic allodynia to air-puff stimuli were included. EPs to air-puff were recorded after stimulation of a control area on which air-puff was not painful according to the technique described in Condé et al., 2013. The same air-puff stimulations applied on the painful area induced an allodynic sensation (mean VAS= 4/10). Temperature of air-puff was either ambient in 14 patients, or cold in 9 patients. Two series of 20 stimulations were applied on the control area and on the allodynic area.

Results

Air-puff stimulation reproduced the allodynic sensation of the patients in 10/14 at ambient temperature and in 9/9 patients at cold temperature. On average (grand mean) there was no significant difference in the amplitude of N2P2 between the control and the allodynic areas (10.4 µV ± 6.9 vs 10.6 µV ± 6.5, p=0.975 for ambient temperature, and 1.03 µV ± 4.2 vs 8.8 µV ± 6, p=0.374 for cold temperature). However, at individual levels, there are very different patterns of air-puff EPs. 50% of patients had lower amplitude of EPs on the allodynic area as compared to the control area and, as previously observed with other EPs, including laser EPs. 50% of patients had a higher amplitude of EPs on the allodynic area as compared to the control area and, for a small proportion of them, this difference was significant, suggesting that allodynic sensation could be associated not only with a response reflecting a deficit of sensory systems but also with an amplification systems leading to amplified air-puff EPs.

Conclusion

For the first time, an allodynic sensation may be associated not only with the marker of somatosensory deficit (decreased EPs) but it can also be associated with increased amplitude of the EPs.
Are there mirror neurons for pain in the human insula?

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The aim of this study was to detect whether the insular cortex, which encodes pain stimuli, does also respond to images of other's pain using direct recordings of evoked potentials through depth electrodes implanted in the insula.

Images depicting pain and no pain situations were presented during 100 ms, and immediately masked to thirteen patients in whom intracortical electrodes had been implanted in the insular cortex before epilepsy surgery. Patients, who were not instructed of any cognitive task other than looking at the stimulus, were unable in such conditions to consciously perceive whether the presented images were or not “painful”. Evoked potentials (EPs) to painful and non-painful images were averaged separately over an analysis time window of 1.5 sec after the onset of image presentation.

Results showed that EPs to painful and non-painful images were different in shape and amplitude. This difference began 200 ms and ended 600 ms after the image presentation in the posterior insula. In the anterior insular cortex this difference lasted between 250 and 500 ms. Painful EPs showed a large negative component culminating around 300 ms after the onset of the image presentation as compared to the non-painful EPs in the posterior insula and around 400 ms in the anterior insular cortex.

These specific responses to images depicting other's pain scenes are likely to reflect an implicit pre-conscious response triggered by the observation of other's pain in the human insula. This area was shown by our previous intracortical recordings to be responsive to skin Laser pain stimuli. This finding suggests that mirror pain neurons are present in the insular cortex and involved in the process of human pain empathy.
CRPS: Neglect-like symptoms in a clinical setting - a methodical approach

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Complex regional pain syndrome (CRPS) consists of peripheral and central symptoms. Some neurocognitive symptoms are referred to as “neglect-like”. 44 patients with CRPS of the upper limb and 25 healthy controls were examined to address these “neglect-like symptoms”. Limb laterality test: We presented 40 pictures of right and left upper limbs via Recognise®- Software. Task was to identify the laterality of the pictured limb as quickly and accurately as possible. Subjective visual midline: Patients were seated in a dark room in front of a screen, where an illuminated vertical rod could be moved laterally. Patients were asked to verbally direct the rod to their perceived visual midline. The arithmetic mean from ten trials was calculated. Questionnaires: subjective neglect-like symptoms questionnaire (Frettloh), HADS (hospital anxiety and depression scale). Results: Reaction- times and accuracy of the limb-laterality-test for pictures of the affected and unaffected limb were not significantly different. Healthy controls had faster reaction times in the limb-laterality test (median: controls: 1.9s; patients 2.4 s; p<0.05). No significant difference could be found either between the perception of the subjective midline of patients and controls. Neglect-like symptoms questionnaire correlated significantly with HADS subscores A (r=.543, p<.001), D(r=.598,p<.001) and HADS in general (r=.594,p<.001). We could not reproduce described results of smaller studies in a clinical routine setting. The limb-laterality test shows a global but not a limb-specific problem in laterality recognition. Scoring in neglect-like symptoms was predicted by psychic state but not by findings indicative for cortical neglect.
P1008
Analgesic effects of navigated motor cortex rTMS in patients with chronic neuropathic pain

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Introduction

In the management of chronic neuropathic pain, repetitive transcranial magnetic stimulation (rTMS) is known to produce significant analgesic effects when administered at high frequency over the precentral cortex controlaterally to the painful side. The conventional method of TMS positioning relies on the determination of motor “hot spot”. However, this method is not optimal and recent research has suggested that more effective target corresponds to an anatomical location adjacent to the motor hotspot. Therefore, anatomical information provided by MRI seems important to ensure precise TMS targeting. Thus, we decided to use navigated TMS (nTMS) and compare the efficacy of stimulating the anatomical M1 location, by MRI-guided rTMS, with stimulation of the classical motor hotspot by rTMS.

Methods

We enrolled 66 adult patients with unilateral or asymmetrical chronic neuropathic pain from central or peripheral origin. Pain was located at the face, the hemibody, upper limb or lower limb. Each patient received three stimulation sessions with an inter session interval of more than 3 weeks: first and second sessions were non navigated sham and active sessions, respectively; rTMS was targeted to the motor hotspot of the hand muscles on the painful side. The third session was navigated and targeted to the anatomical representation of the painful zone on the anterior lip of the central sulcus. TMS effects were assessed by using visual analogous scale (VAS).

Results

Both anatomically-navigated therapy and motor hot spot-targeted therapy showed efficacy, sham stimulation had no effect during the week of assessment. At 2-3 days post-stimulation, anatomically-navigated therapy resulting in 17.4% reduction in pain on VAS and motor hot spot-targeted therapy in 12.2% reduction in the whole series of patients.

According to pain location, we observed no analgesic effect from any method in hemibody pain; significant analgesic effect for both active stimulation conditions on lower limb pain; significant analgesic effect for both active stimulation conditions on upper limb pain, with anatomically-navigated therapy being more effective than motor hot spot-targeted therapy (23.3 vs. 17.4%).

Conclusion

MRI guided stimulation shows higher efficacy in pain control than classical, motor hot spot-targeted stimulation. This superiority was more pronounced in pain of facial, and especially, upper limb origin. In order to validate the MRI-navigated stimulation method, the results of this first study need to be replicated.
P1009
Relation between the sensory abnormalities and the treatment response in patients with complex regional pain syndrome of the upper extremity

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Question
The complex regional pain syndrome (CRPS) is a disabling disease, which leads often to invalidity due to limited treatment options [1]. There are no longitudinal studies on the sensory changes in course of the disease and on their relation to the treatment success.

Methods
24 patients with CRPS were examined by Quantitative Sensory Testing (QST) using the DFNS-protocol [3] on the affected hand and contralateral at baseline (T1) and 6 months later (T2). Somatosensory evoked potentials after single and paired-pulse simulation of the median nerve were performed to assess the paired-pulse suppression (PPS, n=19) [3]. Additionally, pain intensity and hand function were assessed. Treatment response: pain relief >30% on T2. Statistics: z-transformation [4], Wilcoxon test, Pearson correlation.

Results
At follow-up we found an abnormally decreased pressure pain threshold (PPT) and an increased pain response to repeated pinprick stimuli, while the detection thresholds were on average within the normal range. At baseline the sensory profiles of the later treatment responders (TR) were similar to those of the later non-responders (NR). In the TR-group (n=17, pain intensity (NRS 0-10), T2: 2.1±1.7) we found a reduction of the pressure hyperalgesia at T2. In the NR-group (n=7, pain intensity (NRS 0-10), T2: 5.7±2.7) the pressure hyperalgesia remained at T2; pinprick hyperalgesia has additionally developed. There was a correlation between PPS and PPT (z-value) at T2 (r=0.49; p<0.05) as well as between the difference (T1-T2) of both (r=0.65; p<0.01), whereas a low PPT was associated with an impaired PPS.

Conclusion
In patients with CRPS the sensory profile remained nearly unchanged within 6 months. The most distinct finding in CRPS was the pressure hyperalgesia [5], but successful treatment led to its normalisation. Thus, PPT could be a promising outcome criterion in pharmacological studies on CRPS. A further hint for its clinical relevance was the association with impaired PPS in the course of the disease, which was suggested to represent maladaptive central nervous changes in CRPS [3].

Reference
Question

Thalamic pain is a notoriously treatment-resistant type of central post stroke pain (CPSP) that may develop after thalamic stroke [1]. Lesion mapping recently demonstrated crucial areas in the pathogenesis of thalamic pain [2], but the development of pain cannot be accurately predicted by lesion location only.

Spinothalamocortical tract damage is crucial for development of CPSP. Thalamic pain patients consistently exhibit deficits of temperature and pain discrimination, suggesting spinothalamic dysfunction, and to a lesser degree, symptoms of lemniscal dysfunction. The integrity of the spinothalamic and lemniscal tracts can be objectively studied with laser-evoked potentials (LEPs, [3]) and somatosensory evoked potentials (SEPs).

In this study, we combined thalamic lesion localization, sensory examination, and LEP/SEP recordings in a group of thalamic stroke patients. By combining these three measures, we aimed to predict the patients' susceptibility to CPSP.

Methods

We have so far examined 35 thalamic stroke patients (23 with pain) with sensory symptoms in one half of the body. Sensory examination included testing of lemniscal function, tactile discrimination and thresholds for laser heat/pain. The affected nuclei were defined by superimposing MRIs onto the Morel [4] thalamic atlas. LEPs/SEPs were recorded to stimulation of affected and healthy limbs.

Results

Lemniscal function, tactile and laser pain thresholds were more disturbed in patients with pain than in pain-free patients. While involvement of ventral posterior nucleus did not discriminate patients with or without pain (78% vs 67%), the anterior pulvinar nucleus was significantly more affected in patients with pain (89% vs 11%) and the lateral posterior nucleus was mostly affected in painless cases (67% vs 22%). The latencies of LEP peaks N2 and P2 to stimulation of the affected limb were significantly delayed in patients with pain vs pain-free patients. Single-trial analysis in individual patients suggests higher jittering of individual responses to consecutive trials in pain patients.

Discussion

The observed differences in sensory characteristics, lesion location and electrophysiological properties between patient groups suggest that combining the three axes of analysis is a powerful tool to detect those thalamic patients at increased risk to develop thalamic pain.

References

P1011
Abdominal acupuncture reduces laser-evoked potentials and laser pain perception in healthy subjects

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Question
Acupuncture is known to reduce clinical pain, although the exact mechanism is unknown. The aim of the study is to evaluate whether abdominal acupuncture is able to modify pain perception.

Methods
10 healthy subjects underwent a protocol in which laser-evoked potentials (LEPs) and laser pain perception were collected before the test (baseline), during abdominal acupuncture and 15 minutes after needle removal. The same subjects underwent also a similar protocol, in which, however, sham acupuncture without any needle penetration was used.

Results
During real acupuncture, the N2/P2 amplitude reduction, as compared to baseline, was significantly higher than during sham acupuncture (p<0.001). While during real acupuncture the N2/P2 amplitude reduction lasted up to 15 minutes after needle removal, no after-effect was observed during sham acupuncture. Laser pain perception was reduced during real acupuncture, but not during sham acupuncture. In conclusion, our results show that abdominal acupuncture reduces LEP amplitude and laser pain perception in healthy subjects.

Conclusions
Our study provides objective evidence that abdominal acupuncture reduces the brain response to cutaneous painful stimuli in healthy subjects. Therefore, the use of abdominal acupuncture as therapeutic approach in the treatment of pain condition is supported by the present results.
P1012
ANTIDROMIC AND ORTHODROMIC NEUROPHYSIOLOGICAL RESPONSES DURING SPINAL CORD STIMULATION

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Spinal Cord Stimulation (SCS) is largely used for the treatment of patients with chronic pain refractory to pharmacological therapy. Despite this large diffusion, its efficacy is variable and inconstant, probably because its antalgic mechanisms remain largely unknown. In this context, any adjunctive information on SCS functioning can be useful to better manage the patients treated with SCS.

Aim of the study was to verify the real possibility to record orthodromic (cortical) and antidromic (peripheral) neurophysiological responses during SCS.

We reviewed all the neurophysiological recordings we performed in patients with SCS for both clinical and research purposes. In particular, we focalized on cortical and peripheral responses. The first were recorded with needle scalp electrodes (Cz’ - Fz), the second were detected with needle electrodes percutaneously positioned close to a peripheral sensory nerve. In total we analyzed 37 recordings from 24 patients.

The results showed that during SCS it is possible to constantly record evoked responses from the cortex and from the peripheral sensory nerves.

In conclusion, neurophysiological responses evoked by SCS can be obtained from cortex and peripheral sensory nerves. These recordings could be useful for the clinical management of patients with chronic pain treated with SCS, at least in case of doubts about the integrity of the lemniscal system, indispensable condition for the antalgic effect of the SCS. Further studies on larger populations are warranted.
P1097
Assessment of therapeutic effects of repetitive transcranial magnetic stimulation in radiculopathic pain

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Background

Cervical radiculopathy (CR) is largely a clinical diagnosis and cortical stimulation has emerged as an effective and promising modality in the investigation of novel approaches for pain relief.

Objective

The aim of this work is to investigate whether high and low frequencies of repetitive transcranial magnetic stimulation (rTMS) have a pain relieving effect in patients with radicular pain assessed by different pain scales and if these effects are prolonged or only short lasting.

Subjects & Methods

This study was carried out on 20 patients, 10 received 20 hertz rTMS protocol and the others received 1hertz rTMS protocol. Pain scales: visual analogue scale (VAS), brief pain inventory (BPI): pain severity score (PSS) and pain interference score (PIS) used to assess the clinical efficacy of rTMS sessions on pain.

Results

There was a highly statistically significant reduction of pain scores (VAS, PSS, PIS) after treatment compared to before treatment (pConclusion: rTMS can be used as a noninvasive therapeutic test for patients with drug-resistant chronic pain with more reduction of pain scales ratings in the high frequency group.
P982
ALLODYNA-RELATED EXCITABILITY CHANGES AT THE BRAINSTEM AND CORTEX IN PRIMARY HEADACHES

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Question

Our aims were to assess the excitability of motor cortex and trigeminal structures in patients with primary headaches experiencing allodynia and to investigate the alterations in interictal allodynia and blink reflex (BR) excitability after repetitive transcranial magnetic stimulation (rTMS).

Methods

Patients with lateralized primary headaches were included and Allodynia Symptom Checklist was used to detect allodynia. Paired TMS and BR recovery studies were performed on both sides. 10Hz or sham rTMS was applied on the motor cortex in patients with interictal allodynia. Allodynic symptoms were registered quantitatively and BR study was repeated after these trials.

Results

Seventeen of 34 patients with headache described allodynia. Our findings showed bilateral hyperexcitability of cortical and trigeminal structures in the allodynic group. Interictal allodynia, detected in 13 allodynic patients, improved after rTMS as compared to sham stimulation and this effect appeared to be more evident in the late period.

Conclusions

Bilateral increases in the cortical and trigeminal excitability were shown in allodynic patients and rTMS was effective for reducing clinical allodynia. We suggest that allodynic condition of the patients should be taken into account in the planning and evaluation of electrophysiological studies and rTMS may be considered as a treatment alternative for troublesome allodynia.
P983
Auditory and Visual AlphaStimulation reduces Behavioural and Electrophysiological Pain Ratings in Healthy Volunteers

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It has previously been established that our brain oscillatory alpha power (8-12Hz) is reduced when we experience pain (Huber et al 2006). There appears to be a negative correlation between alpha power and the acute pain response (Nir et al 2010). Increasing alpha power could hence reverse this relationship to reduce pain. Oscillatory frequencies can be modulated by auditory and visual entrainment, where brainwave frequencies adapt to the rhythm at which they are being stimulated.

The aim of this study was to determine whether 10 minutes of visual or auditory entrainment at 8 Hz, 10Hz and 12Hz using flashing LED goggles (visual) or binary beats (auditory), will affect the volunteers’ pain perception of the acute heat laser stimulus, compared to the 1Hz visual or white noise auditory control.

We recruited 47 healthy (23 male), right handed subjects with a mean age of 22.25 ± 2.00. 32 Subjects were placed in the visual entrainment group and 15 in the auditory (recruitment on-going). Volunteers were subjected to four different visual or auditory stimulations, each lasting 10 minutes: 1 Hz (visual control)/White Noise (auditory control), 8Hz (low-alpha), 10Hz (mid-alpha), 12Hz (high-alpha). After each session volunteers were asked to rate 20 heat laser pulses at their pre-determined level 7.

Ten minutes of visual or auditory alpha stimulation was enough to increase alpha power, with the largest effect at 10Hz.

After visual entrainment ERPs and behavioural pain ratings reduced significantly with the largest effect at 10Hz, followed by 8Hz. A significant decrease in ERPs and behavioural pain ratings was found after all three auditory alpha stimulations, with no different between frequencies.

Increased oscillatory alpha power has been associated with a meditative state. Previous results suggest laser-heat induced pain is perceived as less painful by meditators (Brown et al. 2010).

The reduction in pain may not be due to increased alpha power disrupting the neural encoding of pain, but rather due to the associated increased state of relaxation.

Whether these effects are due to the neural encoding of pain being disrupted, or other side effects of alpha entrainment, is still unknown.

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Question

Despite concerted efforts from pharmacologic research into pain, many patients fail to achieve sufficient pain relief with the currently available drug. N-Acetyl-cysteine (NAC), an old and safe drug used as a mucolytic agent, enhances the endogenous activation of presynaptic metabotropic glutamate receptors type 2 and inhibits neurotransmitter release, thus possibly negatively modulating nociceptive pathway function. In this study we verified whether 1200 mg of oral NAC inhibits nociceptive pathway function by investigating how this drug modulates pain related responses in animals and humans.

Methods

We have investigated the NAC-induced changes in tail flick evoked by heat stimulation in 6 mice; then in 10 healthy subjects we measured changes induced by NAC on thermal-pain perceptive thresholds as assessed by quantitative sensory testing and laser evoked potentials, according to a cross over, double-blind placebo-controlled design.

Results

In mice, NAC caused a tail flick delay, reverted by a single injection of the mGlu2/3 receptor antagonist (LY341495). In humans, NAC did not change the thermal-pain perceptive thresholds as assessed by quantitative sensory testing (P > 0.08), but reduced the laser pain ratings and the amplitude of laser evoked potentials (P < 0.05).

Conclusions

Our data, showing that NAC delays the tail flick response and reduces the laser pain ratings and the amplitude of laser-evoked potentials, indicate that NAC inhibits nociceptive pathway function. These findings suggest that this drug is worthy of being tested in a clinical trial in patients with pain.
Diabetic small fibre neuropathy diagnosis: a comparison between the diagnostic accuracy of skin biopsy and laser evoked potentials.

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**Introduction**

Small fibre neuropathy related to diabetes is a condition characterized by a selective involvement of nociceptive fibres. Since small nerve fibres cannot be investigated by means of the standard electrophysiological tests, the only methods for assessing small fibre impairment are the skin biopsy, considered as the gold standard, and laser evoked potential recordings. Whereas LEPs are a suitable tool for assessing the Ad fibre function, the skin biopsy is successfully employed to test the C-fibres.

**Question**

The purpose of this study is to compare the accuracy of LEPs and that of skin biopsy in the diagnosis of diabetic SFN.

**Methods**

We screened 100 diabetic patients with distal sensory disturbances and, on the bases of clinical examination and standard nerve conduction study, they were divided in for subgroups: patients with small fibre neuropathy, pure large fibre neuropathy, mixed neuropathy and without neuropathy. The first group of patient underwent LEPs and skin biopsy, to test the sensibility and specificity of LEP in comparison with the gold standard.

**Results**

Assuming the skin biopsy as the Gold Standard, we found a LEPs sensitivity of 92.31% and a specificity of 75%.

**Conclusion**

Our data suggest that LEPs have a diagnostic efficiency comparable to that of skin biopsy in the detection of small fibre neuropathy.
Paroxysmal pain is mediated by non-nociceptive large myelinated fibres. A neurophysiological study in normal humans.

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Question

We aimed at verifying whether high-frequency, low-intensity electrical stimulation, selectively activating non-nociceptive large myelinated fibres, can induce a painful paroxysmal sensation resembling the electrical shock-like pains that may occur in neuropathic pain conditions.

Methods

We investigated five patients with typical Trigeminal Neuralgia (TN) by delivering a train of stimuli at their fifth digit using various frequencies (50-200 Hz), durations (0.2-2 s) and intensities lower than pain threshold when delivered in single pulses, to ascertain which kind of stimulus mostly approached the painful paroxysm resembling the TN electrical-shock-like sensation that the patients were accustomed to perceive in their face. According to patient's report, the train most resembling their painful attacks was a 100-Hz train of at least 1 s, although all patients said that their paroxysms lasted more. Thereafter we delivered a 1-s, 100-Hz, low-intensity train of stimuli to the fifth finger of 10 healthy subjects, and collected their pain score on a 0-10 NRS. We also assessed thermal and pinprick threshold and recorded laser evoked potentials (LEPs) in their ulnar territory of the hand. Then we performed a ropivacaine block of the ulnar nerve at the wrist and measured again thermal and pinprick thresholds and recorded LEPs. Once we obtained the complete absence of sensations and evoked potentials related to small-diameter fibres (Aδ and C), we again delivered to the 5th finger the same train of stimuli performed before block.

Results

We found that the NRS did not change before and during complete block of small fibres (5.9 ±0.8 and 5.5 ±1.3; P> 0.20).

Conclusions

We propose that, in contrast with common notion, electrical-shock-like sensations are mediated by large myelinated fibres. This finding is supported by clinical data showing that in patients with various neurological diseases paroxysmal pain is associated with large myelinated fibre dysfunction.
**P988**

**Shifting attention between the space of the body and external space. Electrophysiological correlates of visual-nociceptive crossmodal spatial attention.**

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**Question**

The study tested whether nociceptive stimuli applied to a body limb can orient spatial attention in external space toward visual stimuli delivered close to that limb.

**Methods**

Nociceptive stimuli were applied to either the left or the right hand. 800 ms later, task-relevant visual stimuli were delivered at the location adjacent to the stimulated hand (70% valid trials) or adjacent to the other hand (30% invalid trials). Participants were instructed to respond as fast as possible to the infrequent occurrence of a target visual stimulus.

**Results**

Visual stimuli were discriminated with shorter reaction times and elicited ERPs of greater magnitude in the valid as compared to the invalid trials. This enhancement affected the N1 component, suggesting that the location of the nociceptive cue modifies visual processing through a modulation of neural activity in the visual cortex.

**Conclusions**

We hypothesize the existence of a common frame of reference able to coordinate the mapping of physical threats both on the space of the body and in external space.
Patients with unilateral widespread chronic pain, associated with recurrent herpes simplex virus (HSV) infections, show functional and structural changes in the insula, anterior cingulate cortex and thalamus, suggesting central dysfunction of the pain system in these patients. We aimed to clarify whether the observed deficient activation of these areas to acute nociceptive stimuli is due to a lesion at a lower level of pain processing pathways. Therefore we explored the functional integrity of the ascending nociceptive pathways by recording the cortical evoked responses to noxious laser stimulation using magnetoencephalography (MEG) and electroencephalography (EEG) in eight patients (age 41-51 years, mean 46) with recurrent HSV infections and a history of chronic, spontaneous, and unilateral pain, and in nine age-matched healthy control subjects. The cortical evoked fields of the HSV patients, originating from the secondary somatosensory and posterior parietal cortices, as well as the evoked potentials recorded from the midline, did not differ from those of the control subjects, indicating functionally intact ascending nociceptive pathways.

The present results show that our patients with chronic unilateral pain do not show signs of spinothalamic tract lesion. This indicates normal processing of sensory aspects of painful stimuli, while higher pain processing areas may show altered activation.
P990
Uncovering the tactile aspects in sensing drops of water

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**Question**

Intraneural microstimulation has shown that tactile sensations can result from the activation of single mechanoreceptive afferents. However, in general, sensations, including those in pathological states, occur from the central integration of many inputs, e.g. the perception of wetness through activity in thermo- and mechanoreceptive afferents. We aimed to determine which mechanoreceptive afferents contribute to the perception of water droplets.

**Methods**

Single unit microneurography was performed in 8 subjects, in either the left median nerve or lateral antebrachial nerve. Unitary recordings were sought from myelinated and unmyelinated mechanoreceptive afferents. Afferent firing was recorded to 10 separate drops of water (each 0.05 ml) delivered 5 cm above the unit’s receptive field, at room temperature. Data were analysed using custom-written Matlab scripts.

**Results**

Only a Pacinian corpuscle unit and two hair units fired in response to the water droplets. All other units showed no activity to the drop stimuli, which included slowly-adapting type 1 (n=5) and type 2 (n=1), rapidly-adapting type 1 (n=2), and C-tactile (n=2) units.

**Conclusions**

We can feel tactile components of water droplets on the skin due to precise temporal encoding in mechanoreceptive afferents, which we find originates from PC and hair units. These are both highly sensitive and temporally-accurate afferents, which also respond to light blowing on the receptive field, rather than just skin indentation. It is important to understand sensations from the skin in health and pathology, including how different afferent types contribute to integrated sensations, such as dysaesthesias in neuropathic states.
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P991
Low Heart Rate Variability during sleep in patients with Juvenile Idiopathic Arthritis

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Introduction

Idiopathic juvenile arthritis (JIA) can be described as a chronic inflammatory syndrome associated with chronic pain status. Patients with JIA may have a high cardiovascular morbidity and mortality. Changes in heart rate variability (HRV) may be a great marker of less favorable healthy life in all ages. Moreover, low HRV may be an indicator of increase in cardiovascular risks, including sudden death. The aim of this protocol was performed the HRV analyses during sleep in pediatric patients with JIA.

Methods

We studied 10 patients with JIA that were compared with 10 healthy subjects matched for age, gender and Tanner stage. All subjects were monitored following one night of habituation in the sleep laboratory. Sleep analysis was performed by international criteria. The HRV Standard Time and Frequency Domain were calculated for 5-minute periods in all sleep stages. The frequency components were subdivided in low and high frequency, and the time domain analyses were calculated by determination of the ratio of the standard deviation of the RR intervals. The U-test for independent samples was used for identifying differences in HRV parameters, with a significance level set at 5%.

Results

We found that JIA patients had more arousals than controls. They also presented a reduction in NREM sleep, and they had a significantly longer total sleep time, and wake time after sleep onset (WASO). The analyses of HRV in time and Frequency Domain during sleep demonstrated the presence of significant differences between JIA patients and controls in all stages of sleep. We found changes in the standard deviation of normal-to-normal interval (SDNN) during slow wake sleep (SWS) [47.0 ±38.5 vs 94.6 ± 75.2, p=0.02], and by the total power of spectral analyses. The total power was lower in patients than in healthy controls in all sleep stages (p<0.05). Positive correlation was found between number of joints with impairment and pNN50 parameter (rs=0.45; p<0.05).

Conclusion

Patients with JIA showed sleep fragmentation and they had presented changes in their cardiovascular autonomic function during sleep. We found low HRV in patients with JIA during all sleep stages. The treatment of sleep disruption in patients with chronic pain can be a successful strategy to control their cardiovascular risk.
P992
APPROACHING THE MECHANISMS UNDERLYING ANALGESIA INDUCED BY HIGH VOLTAGE ELECTRICAL STIMULATION OF LUMBOSACRAL NERVE ROOTS

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Question

Maximal High Voltage Electrical Stimulation (HVES) of lumbosacral nerve root (4-6 stimuli, 15-20 seconds apart), delivered at the optimal stimulation site (OSS) on the vertebral column¹, produces an almost immediate, transient (few hours) but prominent, homo- and heterotopic analgesic effects²,³ (average pain reduction of 70%). The question arises whether analgesia simply represents a “counter-irritation” effect due to the local pain caused by HVES.

Objective

To approach the mechanisms of analgesia induced by root HVES.

Methods

In 10 patients with acute or chronic nociceptive or mixed pain due to shoulder or coxo-femoral arthropathies, cervical or lumbosacral radiculopathies, a strictly local, Painful Skin Stimulation (PSS) was performed at the OSS through two surface electrodes placed 2 cm apart. Five stimuli, 15-20 seconds apart, were delivered with a HVE Stimulator using a stimulus intensity eliciting a pain similar to that on average induced by root HVES (BS-11 verbal score: 6-7). The procedure was proposed as a technique “with possible analgesic effects”. The following day, root HVES was performed and proposed as “a technique similar to the previous one with possible analgesic effects”. Pain was monitored for at least 12 hour using the BS-11 verbal score.

Results

In no case PSS induced significant analgesic effects in spite of positive expectations. In all cases root HVES induced an analgesic effect of usual magnitude and showing a similar time course in spite of negative expectations due to the disappointing results of the previous procedure.

Conclusions

Our results prove that analgesia to root HVES does not simply stem from a local conditioning pain. Compelling evidence accordingly indicates that root HVES cannot achieve activation of the high-threshold, small myelinated and unmyelinated nociceptive fibres of dorsal nerve roots. This suggests that analgesia to HVES requires activation of large-diameter afferent fibres of dorsal roots.

3. Troni W et al, AAN 2013
Circadian hyperactivity of the lower limb nociceptive system in idiopathic Restless Legs Syndrome: a CO2 Laser Evoked Potential study

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Question

The idiopathic form of Restless Legs Syndrome (RLS) is a common sensorimotor disorder involving nociceptive system. Aim of the study was to assess the nociceptive system during the night and afternoon in idiopathic RLS patients, by recording the laser evoked potentials (LEPs).

Methods

We studied 11 patients (mean age 53.40±18.59 years; 6 males, 5 females) affected by idiopathic RLS. LEPs were recorded to stimulation of the right foot, hand and perioral region. LEPs were recorded at night (between 9,00 PM and 11,00 PM) and in the early afternoon (between 1,00 PM and 3,00 PM). Two consecutive averages (20 trials each) were obtained for each stimulation site. LEPs were recorded from 3 recording electrodes placed at Cz, Fz, and T3 sites of the 10-20 International System. The results were compared with 11 control subjects age and sex matched (mean age 55.3±18.7 years).

Results

In RLS patients, we found a significant increase of N1, as well as N2-P2 amplitude after foot stimulation during nighttime session (p=0.016 and p=0.003, respectively) when compared to daytime. The N1 and N2/P2 amplitude after hand and face stimulation was not significantly different comparing two sessions (p>0.05).

Conclusions

We did not find any structural impairment of the nociceptive system in RLS. However, there is a prevailing activity of the Adelta nociceptive system of lower limbs during nighttime.

These findings suggest, in idiopathic RLS, a circadian disinhibition in the central processing of the lower limb Adelta-fiber inputs.
P994

Thalamic responses to nociceptive stimuli in humans

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While the main cortical generators of laser-evoked potentials (LEPs) are well characterised now (operculo-insular cortex and mid-anterior cingulate), those of the thalamus have been scarcely studied. We report LEPs to nociceptive stimuli recorded in four thalamic nuclei. These results were obtained in 17 epileptic patients implanted with intracranial electrodes, who received laser stimuli slightly above nociceptive threshold.

Local early responses (onset 110-150 ms) were consistently recorded in the ventro postero lateral nucleus (VPL), the anterior pulvinar (PuA) and the central lateral nucleus (CL). They occurred in the same latency range than that of the posterior insula and their amplitude was twice smaller than that of the cortical response. Contrasting with these 3 ‘early responding’ nuclei, the responses in the medial pulvinar (PuM) nucleus did not develop until 100 ms later and their morphology more desynchronized. EEG coherence of the four thalamic nuclei with cortical areas was analyzed: the coherence of VPL and PuA with cortical areas was spatially limited, while that of CL and PuM was extensive.

Early responses from VPL, CL and PuA appear to reflect direct post-synaptic responses to spinothalamic projections. Conversely, the delayed response of the PuM -an associative thalamic nucleus- may reflect cortico-subcortical interactions subserving communication between cortical associative areas. The different levels of EEG coherence of the 4 nuclei with cortical areas, spatially limited for VPL and PuA and extensive for CL and PuM is in accordance with their functional connectivity with the cortex.
Effect of one night of total sleep deprivation on the electrophysiological response to radiant heat stimuli - a laser-evoked potential (LEP) study

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Question/Aim

To investigate the effect of one night of total sleep deprivation (TSD) on pain perception and the electrophysiological response to radiant heat stimuli.

Methods

Twelve young healthy non-smoking students (age 23 ± 3.8 ys, 5 female, 7 male) with good sleep quality (Pittsburgh Sleep Quality Index < 5) were included in the study. Laser-evoked potentials (LEP’s) were recorded after a night of habitual sleep (HS) and after TSD in a cross-over design. In females, the time-points of investigation were adjusted to the menstrual cycle. Laser stimuli were applied to the dorsa of both hands under three different conditions: 1) focusing (discrimination of two different laser energies), 2) distraction (mental arithmetic), 3) neutral condition. EEG data (62 Ag-AgCl-electrodes, band-pass 0.15-500Hz, sample rate 1000 Hz) were analyzed with respect to the vertex potential (N2P2) recorded at Fz, Cz and Pz (reference: ipsilateral earlobe). “Pain intensity” and “Unpleasantness” after HS and TSD were assessed according to a Visual Analogue Scale (VAS, 0-100).

Results

“Pain Intensity” and “Unpleasantness” were significantly increased after TSD (p < 0.01). While TSD had no effect on the latency of the vertex potential, the P2 amplitude of the N2P2 complex was significantly reduced under the conditions “focusing” (p< 0.01) and “neutral” (p< 0.05). TSD had no significant effect on the P2 amplitude when subjects were distracted (p= 0.3). To evaluate this attention-dependent reduction of the P2-amplitude after TSD, habituation (expressed as percentage amplitude decrease to repetitive stimuli) was analyzed. After TSD, habituation was significantly enhanced under the conditions "neutral" (p< 0.01) and "focusing" (p< 0.05) but not under “distraction” (p=0.7).

Conclusion

TSD induces hypersensitivity to radiant heat stimuli and modifies the P2-amplitude of LEP’s. The attention-dependent amplitude reduction of the P2 component may at least in part be explained by enhanced habituation to repeated laser stimuli after TSD.
P996
CORTICAL, SUBJECTIVE AND SYMPATHETIC RESPONSES TO NOCICEPTIVE LASER STIMULI. A CORRELATIONAL STUDY

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The galvanic skin response (GSR) and heart rate are two sympathetic indexes reflecting an autonomic arousal. The GSR can be triggered by a wide variety of external and internal stimuli and particularly by pain and its amplitude correlates with subjective pain ratings and the amplitude of the vertex response obtained in response to painful stimulation (Chapman et al. 2001). Similarly, heart rate (HR) correlates with subjective pain ratings of pain delivered by a thermode (Moeltner et al. 1989). Since the amplitude of cortical responses to laser pulses is also known to correlate with the subjective pain sensation, in this study we investigated the relationships between fluctuations in sympathetic response amplitude, amplitude of laser evoked potentials (LEPs) and simultaneous subjective pain ratings.

Twelve healthy adults participated to the experiment (7 women; 21 to 52 years old). A-delta specific stimuli were delivered at nociceptive threshold using a Nd:YAP laser over the dorsum of the hands and feet. Four consecutive runs of 10 trials each were delivered. Pain ratings were asked after each stimulation. LEPs were recorded on frontal, central and parietal electrodes and were analyzed on an epoch of 1000ms. GSR was measured by changes in the conductivity of the palms of both hands. Heart rate was measured by two electrodes, one on the back of each hand.

GSR amplitude and heart rate increase to painful laser stimulation correlated very significantly with both subjective pain ratings (respectively: r = 0.43, p<0.0001 and r = 0.15, p= 0.004) and N2-P2 amplitude (r= 0.36, p<0.0001 and r = 0.18, p= 0.0016). Similarly N2P2 amplitude is significantly correlated with subjective ratings (r=0.5, p<0.0001). Such correlations are, however, attenuated because of intrinsic oscillations of each of the variables (LEPs, GSR, HR) within the series of stimulations and these oscillations were not in phase.

Galvanic skin response amplitude and N2-P2 amplitude are the best indicators of subjective pain perception as compared to the heart rate. The strength of correlation between GSR amplitude and N2-P2 amplitude increasing during a series of 10 stimulations, it seems to be better to wait the end of a series to study such correlations once the system has stabilized.
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P997
The role of pain catastrophising in the distorting effect of negative expectancy on pain-positive messages
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Background and aim
In our previous work, we were able to experimentally prove a clinical phenomenon in which prior negative expectancies about a given positive suggestion will reduce its efficiency. We also found that this effect was positively correlated with paincatastrophisingscores, i.e., pain ratings in the prior negative expectancy condition were positively correlated with scores on the paincatastrophisingscale. Paincatastrophising may be the mechanism in which prior negative expectancy has its distorting effect on positive messages.

In our current study, we aim to explore this relation further, by investigating to what extent catastrophising influences the effect of prior negative expectancy cues on a given pain stimulus.

Methods
Thirty-three healthy participants were divided into two groups of pain catastrophisers (high vs. low) based on an initial screening on Pain catastrophising scale. In the first part of the experiment, participants received laser stimuli under two main conditions. During each trial, subjects were presented with anticipation cues, followed by a laser pulse. Condition 1 was a positive expectancy condition in which a single cue predicted a non-painful stimulus. Condition 2 was a prior negative expectancy condition in which the first pain cue predicted ‘high’, while the second cue predicted a non-painful stimulus. In the second part of the study, the same conditions were repeated again but with a pain catastrophising manipulation task just after the cue and prior to the stimulus. In both conditions, two-thirds of the stimuli were predicted correctly by the cue just preceding the stimulus, while one-third of the trials actually used ‘medium’ stimuli. Only the latter, however, were used for analysis. An EEG recording was obtained during the experiment.

Results
EEG results: In the low-pain catastrophising group there was no difference between the two conditions before and after the task, while in the high-pain catastrophising group there was a reduction in the LEP peak ($n^2$), particularly in the prior negative expectancy condition after applying the pain catastrophising manipulation task.

figure 1
P998
Excitability changes at brainstem and cortical levels in patients diagnosed with migraine and cluster headache

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Question

Previous studies reported altered excitability of the central nervous system (CNS) in patients with primary headaches, however their results are controversial. The aim of this study was to assess the interictal excitability of motor cortex and trigeminal structures in patients diagnosed with migraine or cluster headache.

Methods

Twelve patients with migraine without aura (MoA), 8 migraineurs with aura (MA) and 14 patients with cluster headache (CH) diagnosed according to the criteria of International Headache Society (2004) were included in this study, all patients had lateralized headaches. Paired pulse transcranial magnetic stimulation was delivered bilaterally on primary motor cortex to assess short intracortical inhibition (SICI) and intracortical facilitation (ICF) periods of cortical excitability. Moreover, blink reflex recovery was studied at 200, 300, 500 and 800ms interstimulus intervals (ISIs) to investigate the excitability of trigeminal structures in the patient groups and 16 control subjects.

Results

ICF was significantly higher at the symptomatic side only in patients with MA compared to control subjects (p=0.001). There was no significant difference for the SICI between patient and control groups. Furthermore, blink reflex excitability was found to be increased bilaterally in patients with MoA, MA and CH in comparison to controls at different ISIs.

Conclusions

Our findings suggested that patients with lateralized primary headaches had bilateral hyperexcitability at the trigeminal level whereas only patients with MA displayed unilateral cortical excitability changes interictally, implicating some common but also diverse pathophysiological mechanisms for these primary headaches.
P999
Sensitivity of infrared thermography imaging in the evaluation of the accuracy of nerve root and sympathetic nerve blocks

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Question
In chronic pain patients diagnostic nerve root and sympathetic nerve blocks play an important role for pain management. To evaluate the accuracy of the blocks infrared thermography (IRT) can be used. To our knowledge the diagnostic value of IRT in this field is unclear. A retrospective analysis of all IRT’s taken in diagnostic nerve root and sympathetic nerve blocks within a 12 month period was performed to assess the value of IRT.

Methods
In our daily routine IRT is taken 15 minutes before and after diagnostic nerve root and sympathetic nerve blocks. Interventions are done under fluoroscopy using lidocaine or chirocaine. A positive IRT is considered if an increase of temperature for at least 1°C occurs. A significant improvement in pain is considered when at least 50% pain improvement is achieved 30 minutes post intervention.

Results
278 nerve root and 21 sympathetic nerve blocks were evaluated. The ratios (in percentages) for positive IRT / significant pain improvement / both positive IRT and significant pain improvement were: cervical 20/57/14, thoracic 6/42/3, lumbar 32/53/21 resp. sacral 42/52/26. The ratios for L5 blocks were 52/56/33 and for S1 blocks 50/53/32 respectively. In sympathetic nerve blocks the following ratios were found: cervical 100/33/33 and lumbar 71/79/50.

Conclusion
In diagnostic nerve root blocks IRT does not contribute to assess the technical quality of the intervention, except for L5 and S1 intervention were IRT might be helpful. In cervical and lumbar sympathetic nerve blockades IRT may contribute to assess the quality of the intervention.
Transcranial magnetic stimulation enhances the potential of rehabilitative multidisciplinary treatment in chronic pain patients.

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Background

Chronic pain is a frequent, disabling condition, often resistant to pharmacological treatment, which constitutes a challenge for physicians. The feed-forward interactions between physical and emotional pain and the consequences of pain in altering emotional and psychological status, require a broader, multidisciplinary approach in understanding and treating such a condition.

Recent studies have shown that, despite the origin and the site of pain, plasticity changes occur in several regions of the brain as a result of a deranged “alert system”, with a consequence reduced cerebral gray matter volume and density and a change in cortical excitability.

Among the differently involved brain areas, the prefrontal region seems to be responsible for the top-down control over pain and cognitive reappraisal of pain. In chronic pain condition prefrontal cortical excitability is reduced.

We propose a study through standard repetitive transcranial magnetic stimulation (rTMS) -a non-invasive technique used to modulate cortical excitability- to interrupt the chronic pain processing in the brain.

Methods

Ten patients with mixed chronic pain types (i.e. lumbar pain, oncologic pain, post-stroke pain, phantom-limb pain) were assigned into two groups. The first group received the standard rehabilitative approach, while the second group underwent 9 session (3 times a week) of rTMS for 15 minutes, together with a pain-centered multidisciplinary rehabilitative approach (physiotherapy, massage, neuropsychological support).

Outcome measures were changes in the visual analogue scale (VAS) for pain and cortical excitability parameters (resting motor threshold, suprathreshold motor-evoked potentials, short intracortical inhibition, and intracortical facilitation) Data on depression, anxiety (Beck, Hamilton scale) and quality of life scales (SF-36) were recorded as secondary outcomes.

Results

A variable clinical outcome, but an improvement in cortical excitability parameters is evident at the end of the 3-weeks rTMS treatment in comparison to the only standard rehabilitative treatment. Follow-up is ongoing. All patients well-tolerated the stimulation.

Conclusions

rTMS may enhance the possibility that a multidisciplinary approach in the rehabilitative setting provides pain relief in chronic pain patients.
**LP58**

**A hidden mesencephalic variant of central pain**

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**Background**

Central post-stroke pain (CPSP) can occur after lesions located anywhere in the somatosensory pathways. The most common lesions affecting the spinothalamic tract concern the spinal cord, the lateral medulla (Wallenberg syndrome), the posterior thalamus and the opercular-insular area.

**Cases**

We describe five patients who developed CPSP following a limited lesion in the posterior midbrain. All patients felt initial sensory loss predominant for spinothalamic modalities, then they progressively suffered from pain mostly described as burning and/or cooling, combining spontaneous and provoked pain. The lesion was secondary to minor cranial trauma in three patients and to spontaneous haemorrhage in two. Contralateral thermal deficits were constant and could be objectively demonstrated in all cases using laser-evoked potentials (LEP). Normal somatosensory evoked potentials (SEP) attested that lemniscal pathway was spared in three patients. The two patients with associated lemniscal involvement had less intense pain than the three others, even though the spinothalamic abnormalities were similar. In three cases, standard MRI failed to identify the lesion that evidenced only with thin contiguous slices performed on the basis of objective abnormalities of LEP recording.

**Discussion and conclusions**

These five cases emphasize that minute mesencephalic lesions involving the spinothalamic tract may induce neuropathic pain. An associated involvement of lemniscal pathway preserved from intense pain. A complete lesion on somatosensory pathways may induce a more severe deafferentation but less pain. An alternative explanation would be that the extension of the lesion to the periaqueductal gray matter could induce analgesia. CPSP secondary to small midbrain lesions may be difficult to diagnose even with MRI. The condition can be misdiagnosed as malingering or psychogenic pain and the frequency of such lesions is probably underestimated. Dissociated sensory signs with spinothalamic predominance should prompt electrophysiological testing with SEPs and LEPs, to objectify and quantify abnormal sensory transmission.
Heterotopical hyperalgesia induced by high frequency electrical stimulation: characterizing the respective contribution of heat-sensitive Aδ and C fiber afferents.

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Question

High frequency electrical stimulation (HFS) of the human skin induces increased pain sensitivity in the surrounding unconditioned skin. The aim of the present study was to characterize the relative contribution of heat-sensitive Aδ- and C-fiber afferents to the heterotopical hyperalgesia induced by HFS.

Methods

In healthy volunteers we applied HFS to the ventral forearm. In a first experiment, brief and intense CO₂ laser stimuli were used to concomitantly activate heat-sensitive Aδ- and C-fiber nociceptive afferents. These stimuli were detected with reaction times compatible with the conduction velocity of Aδ-fibers. In a second experiment, temperature-controlled laser stimulation was used to activate low-threshold C-fiber afferents without concomitantly activating Aδ-fiber afferents. These stimuli were detected with reaction times compatible with the conduction velocity of C-fibers. The intensity of perception and event-related brain potentials (ERPs) elicited by the two types of thermonociceptive stimuli delivered to the surrounding unconditioned skin were recorded before and after HFS. Mechanical hyperalgesia following HFS was confirmed by measuring the changes in the intensity of perception elicited by mechanical punctate stimuli.

Results

HFS enhanced the perception to mechanical punctate stimuli and thermonociceptive stimuli co-activating Aδ- and C-fibers. HFS did not enhance the perception to thermonociceptive stimuli selectively activating C-fibers. The ERPs elicited by concomitantly activating Aδ-fiber and C-fibers afferents were not enhanced after HFS. Similarly, ERPs elicited by selectively activated C-fibers were also not enhanced following HFS.

Conclusion

Our results clearly show that HFS induces heterotopical heat hyperalgesia to thermonociceptive stimuli activating both Aδ- and C-fibers. However, the heat hyperalgesia was not accompanied by an enhancement of the ERPs, probably indicating that the heat-sensitive Aδ-fiber afferents (Type II AMH) do not contribute to this heterotopical heat hyperalgesia. Likewise, HFS does not appear to exert an effect on the responses elicited by the transient activation of heat-sensitive C-fiber afferents.
P1013
ABOUT THE PATHOGENESIS OF ROMBERG´S SYNDROME. I - ELECTROMYOGRAPHICAL FINDINGS IN PATIENTS WITH LOCALIZED SCLERODERMA. Financial support by the FAPESP, process number 2011/02605-1.

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Objective
Romberg´s syndrome has clinical interface or superposition with Localized Scleroderma (LS). This study was performed to evaluate patients with LS by electromyography (EMG) in the muscles beneath sclerodermic lesions.

Methods
Routine conduction studies were performed and patients underwent EMG with co-axial electrode placed into the muscles beneath cutaneous lesions. Homologous muscle of the contralateral side was used as control. Electrical activity at rest, mild and maximal voluntary effort was studied. In the recent months it was possible to perform quantitative electromyography (QEMG) of several patients.

Results
To this moment 17 patients were studied. All patients were aged between 15 and 46 years. Conduction nerve studies (latencies, amplitudes and velocities) were normal. Myopathic pattern was seen in 10, neurogenic pattern was found in 6, and normal findings in 1.

Discussion
Our results suggest that LS is a heterogenous syndrome, the findings could be myopathic, neurogenic or normal [1,2,3]. The etiology and pathogenesis remain uncertain, but studies with EMG are needed to investigate a similar disease, the Romberg syndrome (or progressive facial hemiatrophy).

References

Fig1-Examples of LS on the head.
Fig2-Examples of LS on limbs with simmetrical sites for QEMG.
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figure 1

figure 2
ABOUT THE PATHOGENESIS OF THE ROMBERG’S SYNDROME. II - EXPERIMENTAL STUDY AND ELECTROMYOGRAPHICAL FINDINGS IN HUMAN PATIENTS. Financial support by the FAPESP, process number 2011/02605-1.

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Introduction

Romberg syndrome, or progressive facial hemiatrophy or Parry-Romberg syndrome is a rare condition. It was described in 1846, and 167 years after the original descriptions, etiology, pathogenesis and treatment remain uncertain [1,2]. This work describes overview of experimental studies and electromyographical (EMG) data of 9 patients.

Methods

Experimental study on different species - clinical follow-up for several years after unilateral cervical sympathectomy of the superior cervical sympathetic ganglion. Descriptive clinical study and EMG data of 9 patients with Romberg syndrome.

Results

Sympathectomy induced progressive hemifacial atrophy in cats. Romberg’s syndrome was diagnosed in 12 patients, use of concentric needle electrodes were authorized in 7 (6 women, 1 male). EMG examination showed neurogenic pattern in 3, in patients with skin changes suggesting localized scleroderma. Myopathic pattern was found in 1, and normal findings were observed in 3 (patients with pulsatile headache ipsilateral to the hemifacial atrophy). QEMG showed increased RMS on the muscles of the hemifacial atrophic side.

Discussion

Based on clinical and EMG findings, experimental data and literature review, the authors consider the Romberg syndrome heterogeneous, and believe that EMG is useful to classify the Romberg’s syndrome into 2 types: a) Scleroderma type - patients with neurogenic or myopathic EMG; b) Sympathetic type - patients with normal EMG.

References


Legends

Fig1-Findings from the experimental study, including hemifacial atrophy in cats.

Fig2-Patients with neurogenic (A,B,C), myopathic (D,E,F) or normal EMG pattern (G,H,I).
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figure 1

figure 2
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P1015
Source localization and propagation of periodic complexes in Subacute Sclerosing Pan Encephalitis (SSPE) using MEG-EEG: A Novel approach towards understanding subcortical myoclonus

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Objective

To study the genesis and propagation patterns of periodic complexes (PCs) during myoclonic jerks in Subacute Sclerosing Pan Encephalitis (SSPE) using Magneto encephalography (MEG) and Electroencephalography (EEG).

Methodology

Simultaneous MEG (306 channels) and EEG (64 channels) in five patients of SSPE (M: F= 3:2; age: 10.8±3.2 years; duration: 6.2±10 months) was carried out using Neuromag-Triux system. Qualitative analysis of 150 PCs/patient was performed. Fifty classical PCs of similar morphology and significant field topography were analysed, at the ‘onset’ and ‘earliest significant peak’ of the burst by discrete and distributed source imaging methods for MEG & EEG independently.

Results

MEG background was asymmetrical in 2 and slow in 3 patients. PCs were periodic (3) or quasi-periodic (2), occurring every 4-16 seconds and monomorphic in a patient but varied in morphology across patients. Major source localization of the onset of bursts by Magnetic Source Imaging (MSI) was in thalami (43%) & peri-central sulci (33%) while by Electric Source Imaging (ESI) it was in orbito/inferior frontal (35%) & peri-central (34%) regions. Major source localization of the earliest significant burst peak by MSI was in parietai (40%) and anterior/inferior frontal (42%) regions while by ESI it was in orbito/inferior frontal (45%), pre-central (28%) regions. With ESI 6-20% of activities were smeared/non-focal. Further analysis revealed that PCs were generated in thalami and propagated to posterior cingulate and to motor-sensory cortex in 3 patients.

Conclusions

This is first ever study of simultaneous MEG-EEG recording of periodic complexes. It has provided insight into the understanding of subcortical myoclonus and generator and propagation of PCs in SSPE.
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figure 1

(A) At the onset of Periodic complex using Discrete Source Modelling

Cluster of dipole sources in Thalamus with Propagation.

(B) At the onset of Periodic complex using Distributed Source Modelling (CLARA)

Volume distribution in Thalamus
Vol. distribution in Insula/Thalamus

figure 2

(C) Source waveform in Periodic Complexes at the peak and all the possible sources were analyzed with (with no assumption on number of sources)

(D) Magnetic field topography (peak)

(E) At peak of periodic complexes with Discrete & Distributed source imaging methods

Peri-central activities
Anterior frontal activity
Anterior frontal activity
P1016
Electrophysiological study of distal axonopathic, proximal demyelinating polyneuropathy in a case of Addison's disease only received steroid therapy for 30 years.

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Question
What is the underlying cause of weakness of Leg and forearm muscles in a case of 36 years old male patient diagnosed as Addison's disease only received steroid therapy since aged 6 years.

Methods
Clinical and electrophysiological study involving sensory and motor conduction in lower and upper limbs, F waves, H reflex, Needle EMG, SEP, ABR and PR-VEP where performed three times during the last 10 years.

Results
The patient is presented with bilateral pes cavus, weak dorsiflexors, wasting of leg muscles feet parathesia, which progressed slowly during the last 20 years. Two month ago he experienced progressive weakness of the wrist and finger extensors on both sides. MRI study of the brain and spinal cord was unremarkable.

Nerve conduction study and needle EMG revealed findings consistent with distal axonopathic peripheral neuropathy involving distal segments of the sensory and motor fibers of the common peroneal, posterior tibial and radial nerves but demyelinating neuropathy involving both Femoral and axillary nerves with significant delay of the F waves and H reflex. The study revealed normal SEP, ABR and PR-VEP.

Conclusion
Follow up electrophysiological studies during the last 10 years revealed findings of mixed distal axonopathic neuropathy associated with proximal demyelinating neuropathy with no evidence of Myelopathy or central Lesion.
Predictive mechanisms improve the vestibulo-ocular reflex in bilateral vestibular failure patients

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Patients with unilateral (UVF) or bilateral vestibular failure (BVF) suffer from blurred vision during head movements as an impaired vestibulo-ocular reflex (VOR) cannot sufficiently stabilize visual images on the fovea. In contrast to UVF, BVF patients often do not recover. The aim of this study was to test whether extravestibular mechanisms can help to improve the VOR.

Eye and head movements were recorded during predictive and non-predictive passive and active head movements (head impulse test, HIT) in patients with bilateral vestibular failure (N=31) and age-matched healthy participants (N=31).

In both groups VOR gain was higher in predictive passive HIT as well as in active HIT compared to passive non-predictive HIT. In patients predictive passive head movements elicited a VOR gain increase of 24% but this increase was significantly larger with active HIT (148%). Increase of VOR gain during predictive (4%) and active HIT (8%) was much smaller in healthy participants.

Improved eye stabilisation during active HIT is likely to be caused by non-vestibular predictive mechanisms using the efference copy of the neck and head motor command and of the proprioceptive feedback signal. This prediction probably includes the anticipation of the own gaze error in BVF providing a strong rationale for vestibular rehabilitation. The intact contralesional VOR of UVF patients with increased VOR gain during active HIT is unlikely to account for the improvement in BVF ipsilesional VOR gain, i.e. in UVF active HIT benefit from extravestibular information and not from central compensation of remaining vestibular function.
Acute idiopathic sensory neuronopathy with posterior reversible encephalopathy syndrome

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A previously healthy, 20 yr-old mother who delivered a baby six weeks earlier had progressive tingling and numbness from feet to hands in a week. Her balance was off. She was unwell and lethargic but afebrile. Her BP was 143/94 mmHg. Unsteady gait, heel to shin ataxia and generalized hyporeflexia were seen. She felt dizzy and collapsed in next 24 hours. There was a brief period of unresponsiveness. Her BP was 71/41 mmHg.

Investigations were made for a possible GBS. CSF studies were normal. EMG/NCS were obtained 10 days after symptoms onset. Sural, peroneal, tibial medial plantar sensory NCS are normal while median, ulnar, and radial SNAPs are low in amplitude. Motor nerve conduction studies are normal. A sensory neuronopathy diagnosis was made. Various immunological tests were done and none were revealing.

On 6th day of admission patient had multiple generalized tonic clonic seizures with loss of consciousness. EEG revealed encephalopathy with occipital area attenuation. MRI brain scan is consistent with posterior reversible encephalopathy syndrome (PRES).

NCS were repeated nine days, 7 weeks and a year later. She was treated with IV IgG and she went home two weeks later.

This is a case of acute sensory neuronopathy of idiopathic nature with PRES in a six weeks post-partum patient. This is a first case report of such combination. Follow up NCS revealed losses of SNAPs appeared in arms followed by legs. Peroneal nerves are affected before sural nerves. Despite the clinical improvement, NCS failed to reveal the parallel changes.
There are extensive areas of white matter T2 hyperintensity predominantly bi-parietal regions with scattered frontal and occipital lobes involvement.

Suggestive of vasogenic oedema.

Features are typical of posterior reversible encephalopathy syndrome.
P1021
Thoracic outlet syndrome - the proposition of new diagnostic procedures

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**Question**

Thoracic outlet syndrome (TOS) is a rare disorder affecting the lower trunk of the brachial plexus and subclavian vessels between the neck and axilla. Several types of TOS are distinguished: vascular (venous or arterial) and neurogenic (true or non-specific). The diagnosis of TOS is based on the clinical examination (including vascular tests) as well as on results of electroneurophysiological tests, angiography, classical radiology, MRI and USG-D.

**Methods and results**

We present a history of 30-year-old-woman with confirmed arterial TOS who was complaining of the pain and the weakness in the right upper extremity. On clinical examination we found only reduced tendon reflexes of the right upper limb and positive vascular tests. The electroneurography (ENeG) of the brachial plexus showed only the reduced conduction volume between the Erb point and the armpit during the ulnar conduction test. The electromyography (EMG) of the upper limb muscles showed no denervation and reinervation. The F wave in normal position of the right hand and in during Addson, Allen test showed no difference. The laser evoked potentials evaluated the proper functions of small fibres’ sensory pathways. The contralateral test were also conducted.

**Conclusion**

According to our clinical and neurophysiologiacal examination we did not find any evidence concerning the neurogenic lesion of the brachial plexus.

**Key words**

thoracic outlet syndrome, electroneurography, electromyography, laser evoked potentials
Increased cortical excitability in patients with stiff person syndrome assessed by paired-pulse transcranial magnetic stimulation. A case study of two patients.

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Question

Stiff person syndrome (SPS) is a rare neurological condition characterized by stiffness and spasms of the axial and limb muscles. Cortical and spinal hyperexcitabilities are thought to be important pathophysiological mechanisms. We describe intracortical inhibitory and excitatory balance in two patients with the SPS diagnosis.

Methods

The function of intracortical inhibitory and excitatory interneurons was studied by using paired-pulse transcranial magnetic stimulation (ppTMS). Motor threshold (MT) was determined and thereafter baseline motor evoked potentials (MEPs) were recorded from the abductor pollicis brevis muscle using single-pulses and 120% MT intensity. Short-interval intracortical inhibition (SICI) was assessed using ppTMS with interstimulus interval (ISI) of 3 ms (pulse intensities 80% and 120% MT). Intracortical facilitation (ICF) was studied using 13 ms ISI (90% and 120% MT pulse intensities). Silent period recordings were also conducted using single pulses (120% MT pulse intensity).

Results

Patient 1 had pronounced ICF (MEP increase 400% when compared to baseline MEP) and decreased cortical inhibition (ppMEP amplitude 92% of the baseline MEP). The silent period was found to be abnormally long (158 ms). MT was normal.

Patient 2 demonstrated pronounced ICF (ppMEP amplitude three times higher than baseline MEP) and absent SICI (ppMEP amplitude same as baseline MEP amplitude). The silent period and MT were normal.

Conclusions

SPS patients showed signs of decreased SICI and increased ICF in ppTMS-study. TMS is a promising tool in diagnosing stiff person syndrome.
P1023
CLINICAL AND ELECTROPHYSIOLOGIC FINDINGS IN SCHWARTZ-JAMPEL SYNDROME

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Question

Schwartz-Jampel syndrome (SJS) is a rare autosomal recessive disorder characterized by generalized myotonic myopathy, joint contractures, skeletal anomalies, and short stature, caused by mutations in the HSPG2 gene encoding perlecan. The aim of this study is to present the electrophysiologic manifestations and underline the clinical heterogeneity of patients with SJS.

Method

We presented clinical features, immunohistochemical, molecular and electromyographic (EMG) findings of six patients with SJS.

Result

Clinical diagnosis was mainly based on dysmorphic features and concentric needle EMG changes showing spontaneous, continuous high frequency myotonic and/or complex repetitive discharges. The study group comprised 3 males and 3 females with a diagnosis of SJS, aged between 2 and 7 years. All except one had consanguineous parents. Physical examination revealed generalized muscle hypertrophy in four cases, in addition to muscle stiffness, joint contractures, orthopedic problems of varying severity and typical facial features like blepharophimosis, pursed lips, and microstomia, observed in all cases. All patients except one had short stature. In one patient molecular analysis confirmed homozygosity for p.R1550C mutation in exon 37 of the perlacan gene. Analysis of perlecan expression by fibroblast cells revealed deficiency of perlecan mRNA and reduced perlecan immunstaining in two patients. We considered 2 cases who had metaphyseal dysplasia from birth and were more severely affected corresponded to SJS-type 1b and the others corresponded to SJS type 1a. A needle EMG examination in all the patients showed continuous spontaneous activity including myotonia and complex repetitive discharges. In two patients, the myotonia was responsive to carbamazepine and in one, to phenytoin.

Conclusion

Clinical features of SJS may vary from mild myotonia with subtle radiological signs to severe myotonia with contractures. Although the diagnosis is mainly clinical and confirmed by immunohistochemical and molecular studies, EMG examination supports the diagnosis.
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P1024
Ocular motor and vestibular findings in Niemann-Pick type C disease: a case report

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Question
To assess the function of vestibular and ocular motor system in one patient with genetic diagnosed Niemann-Pick Type C disease (NPC), which is characterized by progressive neurological and cognitive impairment due to the pathological lipid storage, particularly in brainstem, leading to supranuclear vertical saccade palsy, as well as in cerebellum. The 51-years old female patient, with at the age of 49 genetic diagnosed NPC disease due to the mutation in the NPC1 gene presented discrete cerebellar ataxia, mild cognitive impairment and discrete splenomegaly.

Methods
The standardized neurootological battery, including neuroophthalmological examination, ocular and cervical vestibular evoked myogenic potentials (VEMP), video-assisted head-impulse test and videooculography (VOG), was performed.

Results
Ocular motor testing revealed a vertical saccade palsy with in particular downward saccades impairment, and horizontal oscillations as an expression of compensation by horizontal saccade system. The o- and cVEMP findings (oVEMP: mean latency 9,7 ms, mean amplitude 33,3 µV, cVEMP: mean latency of 26,3 ms, mean amplitude of 128,15 µV) demonstrated a good function of the peripheral as well as central otolith pathways. The video-assisted head impulse evaluating the vestibulo-ocular reflex revealed a normal gain of 1. The VOG showed normal parameters of horizontal saccades (mean maximal velocity 395,8 °/s, mean amplitude 12,94 ° by stimulus of 17 °, and mean latency of 155 ms), vertical saccades were not detectable. The smooth pursuit was horizontal as well as vertical borderline (gain of 0,69 horizontal, 0,7 vertical by 0,1 Hz). The peak slow phase velocity of optokinetic nystagmus was 3,65 °/s, horizontal, 3,1°/s vertical.

Conclusions
Ocular motor systems, incl. smooth pursuit, horizontal saccades, and optokinetic nystagmus, but the vertical saccades, showed fair to good function. Vestibulo-ocular reflex seems to be unaffected, too. Graviceptive pathways, tested by the VEMP examination, seem to be intact suggesting the sparing of this system in NPC disease.
**P1025**
Progression of balance disturbances in premanifest and symptomatic SCA1 and SCA2 gene carriers

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**QUESTION**
The autosomal dominant inherited spinocerebellar ataxias (SCA) are so far non curable neurodegenerative disorders. Balance disturbances are usually the first signs of SCA. Does one year follow up reveal any differences in balance alterations between healthy people, premanifest SCA gene carriers (RISCA) and SCA patients? Are there any clinical or posturographic parameters that predict manifestation or deterioration of the disease?

**METHODS**
36 genetically confirmed SCA1 and SCA2 subjects (19 RISCA in mean age 27.1±5.6y, 17 symptomatic SCA patients aged 40.7±13.9 with average disease duration 6.4±6.9 y) and 14 healthy volunteers (C) aged 35.4±13.6 underwent static posturography twice in one year interval. The trajectory of the center of feet pressure (COP) during quiet standing with eyes open (EO) and closed (EC) was analyzed by use of: mean radius (R), developed surface area (A) and mean velocity of COP movements (V). Neurological examination was performed with the Scale for Assessment and Rating of Ataxia (SARA) and Inventory of Non-Ataxia Signs (INAS). The volumetric MRI images of the cerebellum and cervical spinal cord were analyzed.

**RESULTS**
Five RISCA patients became clinically symptomatic (RISCA-S) after one year. Statistically significant changes in the 2nd posturographic examination were seen in SCA, RISCA-S and C for EO, but only in RISCA-S for EC. The highest rises of sways measured by R were: ΔR_{EO}= 3.7±1.7mm and ΔR_{EC}= 7.52±3.8mm for RISCA-S, despite that mean SARA in the follow up visit was 7.1±2.1 versus SCA, where ΔR_{EO}= 2.5±3.4mm, ΔR_{EC}= 0.17±6.2mm and SARA=12.1±3.8. Four of five RISCA-S had had SARA>1.5 during the first examination, however the COP measurements had not revealed any differences between future RISCA-S and RISCA.

**CONCLUSIONS**
The study confirms the high sensitivity of both posturography and SARA. The COP movements in SCA group were more sensitive in EO than in EC probably because patients were adapted to the disequilibrium. The same explanation might be for the lower increase of R in SCA than in RISCA-S. Further observations of RISCA are needed to estimate if 2 points of SARA is an appropriate moment to start preventive rehabilitation. Our results suggest, that posturography is the useful, objective method for balance assessment and can serve as the objective measure of disease progression.

The research was supported by grant 674N-RISCA/2010 from Polish Ministry of Science and Higher Education.
Hirayama disease is a sporadic disorder characterized by a juvenile-onset of upper limb distal muscular atrophy. The pathogenesis of this sporadic disease has not yet fully clarified: neuroimaging studies suggest that cervical flexion myelopathy with mechanical ischemic damage of spinal motoneurons could be the most likely hypothesis. A 19-year-old man presented with a 4-years history of progressive right distal upper extremity weakness. The disorder was characterized by an insidious onset and neurologic examination showed a tremor of the right hand, weakness and atrophy in the right C7-T1 myotomes and normal sensory findings. Electrophysiological studies revealed neurogenic changes in the C7-T1 myotomes. Magnetic resonance imaging showed a mild atrophy in the right anterior horn cell region at C7-C8 level. According to Hirayama et al. the dynamic changes induced by neck flexion could be due to a disproportionate growth between the vertebral column and the content of the spinal cord during the adolescence growth spurt. In this view, we think that our case indirectly supports the hypothesis that a spinal growth disproportion could predispose to the subsequent development of a juvenile amyotrophy of the upper limb.

The 49,XXXXY chromosomal constitution is a rare syndrome described by Fraccaro in 1960 (only one hundred cases in literature). We describe a 38-old male who arrive our observation for a clinical picture of vertigo. The patient presented a tetra X-syndrome diagnosed at the Pediatric Hospital of Florence when he was 5 years old. Cranial TC showed the presence of cortical atrophy with a non-communicating hydrocephaly and an ischemic small lesion in periventricular left anterior area. In spite of patient limited collaboration we carried out a neurophysiological examination which has not been reported previously. SEP, MEP and SSR were normal and equally the VCM, M response amplitude and F waves latency. Instead there was a light increase of P100 latency of PEV and an increase of I wave latency of BAEPs, with normal central conduction time. Also VCS were slightly reduced with normal SAP amplitude. No denervation or myopathic alterations were present; we recorded only un increase in polyphasic motor units and a 5.5-6.0 postural tremor. EEG showed aspecific diffuse alterations.
P1027
Neurophysiological findings in patients with ceroidlipofuscinosis due to CLN6 mutations.


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**Question**

To describe the neurophysiological pattern of patients with neuronal ceroid lipofuscinosis (NCL) associated with CLN6 mutations.

**Methods**

We reviewed clinical features, EEG patterns and evoked potentials performed in ten NCL patients with CLN6 mutation.

**Results**

Patients were separated in two groups depending on the onset age: eight presented at 5±1.6 years with psychomotor regression, while two presented with myoclonus epilepsy at ages 16 and 28 years.

In the first group, clinical features included progressive motor impairment, visual defect and seizures, as expected for the late childhood NCL form. In the two late-onset patients, the phenotype fitted typical Kufs’ disease; vision was unaffected.

The earliest neurophysiological evaluation was performed in the first group at 6.1±2.7 years. The EEG showed slow background and spontaneous 2.5 Hz spike and wave in six; six patients showed photosensitivity. One patient had myoclonic jerks at the onset, but other three developed multifocal myoclonus later. The electroretinogram (ERG) was attenuated in four, while flash-induced visual evoked potentials showed attenuated main P2 and increased P1 components. In all, somatosensory evoked potentials (SEP) were significantly enlarged.

In the two Kufs’ patients, EEG background was normal and included bilateral posterior spikes powerfully enhanced by light stimulation. In both action myoclonus was severe. ERG was normal, visually evoked potentials were difficult to evaluate due to EMG artifacts and SEP were enlarged.

**Conclusions**

Though different clinical presentations ranging from the late infantile to adulthood forms, some neurophysiological aspects were similar, including remarkable photosensitivity and increased SEP amplitude. Multifocal myoclonus occurred in both patients with late infantile form and in the two adults with Kufs’ disease.
Abstracts of Poster Presentations – Poster Session 58 – Rare neurological diseases

P1028
Source localization and propagation of periodic complexes in Subacute Sclerosing Pan Encephalitis (SSPE) using MEG-EEG: A Novel approach towards understanding subcortical myoclonus

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Objective

To study the genesis and propagation patterns of periodic complexes(PCs) during myoclonic jerks in Subacute Sclerosing Pan Encephalitis(SSPE) using Magneto encephalography(MEG) and Electroencephalography(EEG).

Methodology

Simultaneous MEG (306 channels) and EEG (64 channels) in five patients of SSPE (M: F= 3:2; age: 10.8±3.2 years; duration: 6.2±10 months) was carried out using Neuromag-Triux system. Qualitative analysis of 150 PCs/patient was performed. Fifty classical PCs of similar morphology and significant field topography were analysed, at the ‘onset’ and ‘earliest significant peak’ of the burst by discrete and distributed source imaging methods for MEG&EEG independently.

Results

MEG background was asymmetrical in 2 and slow in 3patients. PCs were periodic (3) or quasi-periodic (2), occurring every 4-16 seconds and monomorphic in a patient but varied in morphology across patients. Major source localization of the onset of bursts by Magnetic Source Imaging(MSI) was in thalami (43%) & peri-central sulci (33%) while by Electric Source Imaging(ESI) it was in orbito/inferior frontal (35%) & peri-central(34%) regions. Major source localization of the earliest significant burst peak by MSI was in parietal (40%) and anterior/inferior frontal (42%) regions while by ESI it was in orbito/inferior frontal (45%), pre-central (28%) regions. With ESI 6-20% of activities were smeared/non-focal. Further analysis revealed that PCs were generated in thalami and propagated to posterior cingulate and to motor-sensory cortex in 3 patients.

Conclusions

This is first ever study of simultaneous MEG-EEG recording of periodic complexes. It has provided insight into the understanding of subcortical myoclonus and generator and propagation of PCs in SSPE.
Primary Skull Base Chondrosarcoma: cerebrospinal fluid otorrhea after Postoperative radiotherapy

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Objective

To Discusses the preoperative diagnosis, treatment, postoperative radiotherapy complications of Primary Skull Base Chondrosarcoma.

Methods

Observe and analyze the case of primary skull base chondrosarcoma patients clinical diagnosis and treatment process in detail.

Results

Postoperative patients with cerebrospinal fluid leakage, intracranial infection.

Conclusions

The Skull Base Chondrosarcoma is a very rare, slow-growth and local invasive low-grade malignant tumor, clinical manifestations and imaging the lack of specificity, preoperative diagnosis is very difficult, and at the same time is very important, Postoperative radiotherapy treatment has an important effect, but there may appear leakage of cerebrospinal fluid, which in turn to intracranial infection, which will caused great trouble to the patient.so clinical diagnosis and treatment should be alert to whether it will be merged cerebrospinal fluid leakage after radiotherapy, and then advance to take precautions to avoid some of the postoperative radiotherapy complications.
P1030
Clinical and electrophysiological follow-up study of a patient with congenital myasthenic syndrome (CMS) associated with mutations in the gene of the agrin (AGRN)

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²Institute of Biomedical Research of Vigo (IBIV), Dept of Neurosciences, Vigo, Spain
³UC Davis Medical Center, Sacramento, United States

Question

We describe the clinical and electrophysiological findings of a severe form of congenital myasthenic syndrome (CMS) caused by two heteroallelic mutations in the gene encoding agrin (AGRN) (Maselli et al 2012.).

Patient and Methods

A 43 year-old-man, born after a normal pregnancy and delivery at term, presented with generalized hypotonia in the first months of life. He walked at 12 months but then progressively developed ptosis, neck and truncal muscles weakness and progressed slowly over time. There was arreflexia with flexor plantar responses. He never complained of sensory symptoms. Parents were normal; an older brother with a similar condition died when he was 15 years.

Electrophysiological investigations were performed on many occasions; complete blood count and metabolic panel of serum and CSF were always normal. Antibodies against AChR, MuSK, and P/Q voltage-gated were negative.

Results

Motor and sensory nerve conduction studies were normal. RNS of the median nerve at 3 Hz showed a 40% decrement of the 4th CMAP that improved slightly after exercise and after 2 mg of Neostigmine (IM). CNEMG was myopathic and SFEMG showed increased jitter and blocking. Only 2 mg Salbutamol produce some improvement.

Ultrastructure of end-plates from a deltoid muscle biopsy showed small nerve terminals, simplified postsynaptic folds, and disruption of their architecture. Genetic analysis revealed a nonsense and a missence mutations in the gene encoding agrin (AGRN).

Conclusion

These findings demonstrate that the AGRN mutations can cause a profound disruption of the architecture of the neuromuscular junction that results in a severe CMS.
Multifocal Visual Evoked Potential in idiopathic Intracranial Hypertension

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**Purpose**

to assess the multifocal visual evoked potential changes in idiopathic intracranial hypertension patients and to compare conventional visual evoked potential and multifocal visual evoked potential methods in detecting optic pathway affection in idiopathic intracranial hypertension patients.

**Methods**

multifocal visual evoked potentials and conventional visual evoked potentials were recorded during the same session in 30 eyes of idiopathic intracranial hypertension patients with an active electrode at Oz to Fz (Oz-Fz) for the conventional visual evoked potential and the active electrodes of the multifocal visual evoked potential at the inion in the form of cross electrode fixed around the inion and the ground at Fz.

**Results**

19 eyes (63.3%) of the examined 30 eyes had abnormal conventional visual evoked potential responses; while 11 eyes (36.7%) had normal responses. 28 eyes (93.3 %) of the examined 30 eyes had an abnormal multifocal visual evoked potential responses, while only 2 eyes (6.7%) had normal responses.

**Conclusion**

multifocal visual evoked potentials is superior to the conventional visual evoked potentials in detecting local damage to the optic nerve in idiopathic intracranial hypertension patients; however there was an agreement between results of both tests.
Features of immune disorders in the acute period of traumatic brain injury

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The aim of this work was to study an influence of moderate traumatic brain injury on cytokines and the cellular immunity in early traumatic period.

Material
Survey of 28 patients aged 21 to 70 years in acute period of moderate TBI (study group), 26 men and 2 women. Control group - 20 donors, matched by sex and age with the patients of the main group.

Methods
Investigation of immune status was performed on the 2nd-3rd day after receiving TBI in terms of cellular immunity in peripheral blood
Examined the level of serum cytokines (IL-1β; IL-4; IL-6; α-TNF, γ-IFN) by using enzyme immunoassay systems.
Phenotypic characterization of lymphocyte subpopulations was performed using monoclonal antibodies in the indirect immunofluorescence test. We used the following monoclonal antibodies: CD -3 - for the determination of T- lymphocytes, CD -4 - for the determination of T-helper cells, CD -8 - for the determination of T- suppressor - cytotoxic lymphocytes, CD -16 - for the determination of natural killer cells; CD -20 - for the determination of B- lymphocytes. Obtained from the patients' blood mononuclear cells were labeled with monoclonal antibodies.

Results
The level of secretion of IL-1, TNF, IL-6, IL-4 and IFN in acute period of moderate TBI patients differs from that of healthy donors. Statistically detect increased levels of proinflammatory cytokines IL-1, TNF-alpha and IL-6, IFN and increased anti-inflammatory cytokine IL-4.
These data suggest that the immune response during moderate TBI accompanied by activation as the synthesis of pro-and anti-inflammatory cytokine with a large shift towards proinflammatory.
Study of cellular immunity in acute TBI showed decreased levels of T-lymphocytes (CD-4 +) positive cells and T-helper cells, while the level of killer cells, CD-8 lymphocytes and B-lymphocytes was increased.
Thus, TBI affects the cellular immune response, causes a decrease or increase in the level of certain subpopulations of lymphocytes, suggesting multidirectional suppressive factors stimulating effect on the immune injury.

Conclusion
1. At primary moderate and severe TBI happens suppression of T-cell immunity that manifested by reduced blood levels of T-helper cells, and (SD-4 +) positive cells and the activation of B-cell level and natural-killer lymphocyte subpopulations
2. Revealed differences in the composition of major lymphocyte subsets point to unequal participation in the pathogenesis of traumatic brain disease. Moderate TBI process involves both T-cell and B cell-dependent humoral immune responses producing autoantibody.
Abstracts of Poster Presentations – Poster Session 58 – Rare neurological diseases

**figure 1**

<table>
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<tr>
<th>Groups</th>
<th>N</th>
<th>CD3</th>
<th>CD4</th>
<th>CD8</th>
<th>CD16</th>
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<td>28</td>
<td>31,6±1,4 (P&lt;0,001)</td>
<td>18,7±1 (P&lt;0,001)</td>
<td>14,3±0,8 (P&lt;0,01)</td>
<td>16,3±1 (P&lt;0,001)</td>
<td>18,8±0,8 (P&lt;0,02)</td>
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<tr>
<td>Control</td>
<td>20</td>
<td>40,5±1,3</td>
<td>32±0,9</td>
<td>11,8±0,4</td>
<td>5±0,2*</td>
<td>16±0,9</td>
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</table>

**figure 2**

<table>
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<tr>
<th>Indicator</th>
<th>Acute period of TBI N=28</th>
<th>Control group N=20</th>
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<tr>
<td>IL-1α</td>
<td>7,6±1</td>
<td>3,3±0,4 (P&lt;0,001)</td>
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<tr>
<td>IL-4</td>
<td>3,4±1</td>
<td>1,3±0,2 (P&lt;0,001)</td>
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<tr>
<td>IL-6</td>
<td>13,7±2,3</td>
<td>3±0,4 (P&lt;0,001)</td>
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<tr>
<td>IFN</td>
<td>63,7±5,3</td>
<td>9,2±0,5 (P&lt;0,001)</td>
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<tr>
<td>TFN alpha</td>
<td>6,8±1,5</td>
<td>2,6±0,35 (P&lt;0,001)</td>
</tr>
</tbody>
</table>
P1031
A simple novel quantitative analysis of circadian rest-activity rhythm in Alzheimer’s disease

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Objective: To quantitatively examine the rest-activity rhythm in patients with Alzheimer’s disease (AD).

Design: Case-control study

Setting: Hospital-based study

Participants: Sixty-three AD patients and fifty-six non-demented participants

Measurements: All participants wore wrist actigraph devices for five to seven days. Collected actigraphy data were processed to assess sleep parameters including total sleep time, sleep efficiency, activity score during day and night time, as well as fragmentation index (FI) and its day/night ratio. Sleep diaries were provided by family or study subjects. Multiple logistic regression models were used to compare the rest and activity parameters for the entire day between control and AD patients. All analyses were adjusted for demographics, medications and comorbidities.

Results: As compared to non-demented controls, AD patients have (1) shorter wakeup and moving times during the daytime (all p&lt;0.05), (2) higher activity scores during the night time (p=0.02), and (3) less diurnal difference in sleep patterns with decreased day/night FI ratio (p=0.03). There was a significant decrease noted in the difference of diurnal activity patterns in moderate to severe AD patients.

Conclusions: AD patients have significantly disturbed diurnal rest-activity rhythms which can be quantitatively measured by a novel index of day/night FI ratio.
Study of Sleep Microstructure in patients of Migraine without Aura

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Background
Sleep disturbances in migraine are well recognized, however, data on its microstructure are sparse.

Objective
To study and compare microstructural polysomnographic (PSG) characteristics in patients of ‘migraine without aura’ with controls.

Methods
Thirty patients of ‘migraine without aura’ and thirty age matched healthy controls were subjected to overnight Polysomnography. There was a female preponderance among migraineurs (80%). Cyclic alternating pattern (CAP) analysis was performed, as per the criteria provided by Terzano et al (2002). CAP parameters were compared among the 2 groups using the Mann-Whitney U-test (p≤0.005).

Results
The numbers of Arousals, as well as, the Arousal indices were comparable between the 2 groups, both during NREM (p=0.451) and REM (p=0.143) sleep. The CAP duration in N1 (p<0.001), N2 (p<0.001) and N3 (p=0.007), and the CAP rate in N1 and N2 was higher (p<0.001) in patients. However, the overall CAP rate was not different (p=0.174). The number of CAP cycles (p=0.029) was higher among controls. The mean phase A duration (p<0.001) was higher in cases, and conversely, the mean phase B duration (p=0.006) was higher in controls. The mean A2 duration (p<0.001) was higher in patients. In contrast, the number of A2 periods & A2 indices were higher (p<0.001) in controls.

Conclusions
This study showed higher CAP duration and CAP rate, decreased cycling between different phases of CAP among migraineurs. This indicates an altered arousal mechanism and might play a role in the precipitation of migraine attacks during sleep or on awakening.
INTRODUCTION

Sleep complaints in children with Bipolar Disorder (BD) and Attention Deficit and Hyperactivity Disorder (ADHD) have been widely described. Conversely, some reports point on the role of sleep disturbances in BD and ADHD physiopathology. Clinically, pediatric BD and ADHD comorbidity is not infrequent. Nocturnal Polysomnography (PSG) could be a useful tool in order to specify the sleep disorders and to establish a differential diagnosis upon these patients.

AIM

To compare sleep architectures and other PSG data in children with BD and ADHD.

MATERIALS AND METHODS

5 BD and 5 ADHD patients aged from 7 to 18 years were recruited from the Child and Adolescent Mental Health Services. International Neuropsychiatric Interview for Kids and Adolescents (MINI-Kid) was used for diagnostic purposes. BEARS Algorithm and Sleep Disturbance Scale for Children (SDSC) were applied for screening of sleep disorders. The same day of nocturnal PSG performance Child Depression Inventory (CDI), Child Mania Rating Scale (CMRS) and Parent Version of the Young Mania Rating Scale (p-YMRS) were measured, as well as 15 days sleep calendar recording was collected. PSGs were manually scored by a blinded investigator (American Academy of Sleep Medicine, 2007 criteria). NoREM and REM Sleep Latencies, Sleep Efficiency, Sleep Time in N1, N2, N3 and REM stages, duration and number of REM cycles and REM density values were analyzed.

RESULTS

Sleep architecture showed a wide diversity among individuals, regardless the belonging group. Significant differences in PSG values according to BD or ADHD conditions were not found. Only REM density showed a higher mean value on BD than on ADHD children. No correlation between scales for the assessment of mood and sleep variables was found. Correlations between sleep architecture and current medical treatments could not be established.

CONCLUSIONS

Sleep architectures in BD and ADHD children present heterogeneous patterns. REM density seems to play an important role in the differential diagnosis of BD and ADHD. PSG may be used for an early detection of sleep disturbances in pediatric psychiatric disorders.
P1035
Overnight cardiac autonomic function during sleep disturbance in peri- and postmenopausal women

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Question
To study the effect of partial sleep disturbance on heart rate variability (HRV) during sleep in peri- and postmenopausal women on and off hormone therapy (HT).

Methods
We studied peri- (PER) and postmenopausal (POST) women aged 47.8 (0.4) years (n=17) and 62.8 (0.7) years (n=18) using a prospective case-control protocol. Polysomnography (PSG) was performed over three nights: adaptation, baseline, and sleep disturbance due to frequent blood sampling. The studies were repeated after six months during which the patients were randomised to peroral HT and non-HT groups. PSG recordings were scored in 30 s epochs. Time and frequency domain and nonlinear HRV were assessed overnight from baseline and sleep deprived nights. HRV was analysed at baseline and during sleep disturbance, and the effects of sleep disturbance, time and HT were analysed between groups.

Results
At baseline, the POST group had higher power law slopes (p=0.035) and lower spectral entropy (p=0.025) than the PER group. After six months, HRV was similar between groups during baseline. No significant HRV differences were seen between the two baseline nights.

During sleep restriction, the POST group had higher maximum heart rate (p=0.022) and lower LF power (p=0.035). After six months, the only effect was an increase in minimum heart rate in the POST HT group compared to the POST non-HT group (p=0.024). When the two sleep restriction nights were compared, power law slopes decreased in both PER HT (p=0.049) and PER non-HT (p=0.028) groups over time. No change was seen in the POST non-HT group, but in the POST HT group, total power (p=0.046), VLF power (p=0.028) and power law slope (p=0.027) decreased and spectral entropy increased (p=0.028) over time. There were no group differences in the time-induced changes.

Comparison between baseline and sleep restriction showed no HRV change in the PER group. In the POST group, maximum heart rate (p=0.003) and RMSSD (p=0.034) increased. After 6 months, no sleep restriction effect was seen, nor were there group differences.

Conclusions
Postmenopausal women had an increased vulnerability to tachycardia and rapid HRV changes during partial extrinsic sleep disturbance, while perimenopausal women were practically unaffected. After 6 months, however, this difference was not seen irrespective of HT use. This suggests a high estrogen-independent capability for adaptation in the cardiovascular autonomic system even after menopause.
P1036
First night effect evaluated by cardiac autonomic function in young and midlife women

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2TYKS, Cardiology, Turku, Finland
3University of Turku, Sleep research unit, Turku, Finland
4University of Helsinki, Physiology, Helsinki, Finland
5TYKS, Gynaecology, Turku, Finland

Question
To study first night effect using overnight cardiac autonomic function parameters in young, perimenopausal, and postmenopausal women with no previous sleep laboratory experience.

Methods
We studied postmenopausal women on oral hormone therapy (HT) (n=10, aged 64,2 (1,4) years), on transdermal HT (n=6, aged 63,2 (1,0) years), and off HT (n=28, aged 63,9 (0,8) years), perimenopausal women off HT (n=17, aged 47,7 (0,5) years), and young women (n=11, aged 23,1 (0,5) years) using a prospective case-control protocol.

Polysomnography (PSG) studies were performed over two consecutive nights. Time and frequency domain and nonlinear heart rate variability (HRV) was assessed overnight from both recordings. Possible first night effect on heart rate variability (HRV) was analysed both separately in all groups and groups combined.

Results
Groups combined, the power law slope was slightly higher (p=0,029) and spectral entropy lower (p=0,037) during the first night recording in sleep laboratory. There was no significant difference between groups in first night effect.

In separate analysis of all groups, pNN50 and HF power (p=0,016 and p=0,044, respectively) were lower during the first night in the perimenopausal group, while in postmenopausal women on oral HT, the α1 correlation coefficient of detrended fluctuation analysis was lower (p=0,038) during the first night. Other groups showed no first night effect.

Conclusions
There seems to be a slight decrease in heart rate variability during the first night spent in a sleep laboratory in women. Although this change is small, it implies that the initial stress evoked by laboratory conditions may influence the cardiovascular system as well as sleep architecture especially in older subjects.
Neurophysiological evaluation of spinal excitability in patients affected by primary Restless Legs Syndrome.

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Question

Restless legs syndrome (RLS) is a frequent condition, but its pathophysiology is not completely understood. The dopaminergic system has a primary role, and some studies have highlighted a condition of spinal hyper-excitability. The aim of our study is to explore this hypothesis through the electrophysiological evaluation of patients affected by primary RLS.

METHODS

15 women affected by primary RLS and 17 age-matched females (controls) were selected. All subjects underwent nerve conduction studies (NCS) evaluation to exclude any secondary causes of lower limb paresthesias and to evaluate spinal excitability. According to a previous study, we considered two parameters, the duration of F waves (FWD) of the tibial and ulnar nerves, and the ratio between FWD and the duration of the corresponding compound muscle action potential (FWD/CMAPD).

RESULTS

None of the subjects (both RLS and controls) included in our study showed alterations in the nerve conduction velocities. Compared to the control group, significantly higher values were found in RLS patients for the mean FWD for both ulnar (p

CONCLUSIONS

The results of our study indicate a widespread spinal motoneuronal hyper-excitability. Such condition could be mainly due to an abnormal modulation within the interneuronal system. Presently, RLS diagnosis is based exclusively on clinical criteria. The FWD/CMAPD ratio can help to shed light on the pathogenesis of RLS, is easily obtainable and can represent an instrumental diagnostic tool especially in cases of evening lower leg discomfort of unclear interpretation.
P1038
Evaluation of H Reflex excitability during motor imagery in patients with the Restless Legs Syndrome and healthy individuals

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³Istanbul University Cerrahpasa Faculty of Medicine, Neurology, Istanbul, Turkey

Questions

Motor Imagery (MI) is suggested that the neural processes associated with the motor imagery are similar to the realization of that particular movement. The increase of the excitability belonging to TMS, reflexes and the cycles related with the delayed responses has been shown.

Restless Legs Syndrome (RLS) is a sleeping disorder characterized by an abnormal sensation, legs in particular. The relationship between the desire of walking and the temporary relief of patients is known. The increase of excitability through TMS and segmental reflexes at the different levels of the CNS has been reported.

In our study we aimed to investigate the difference on the excitability of the H reflex during the imagery of walking in RLS patients and healthy individuals.

Methods

11 RLS (3 M, 8 F. Average Age: 41.2) and 15 (8 M, 7 F. Average Age: 38.4) gender and age matched control, in total 26 subjects were included to the study.

HR is studied in the supine position, while 1: resting and 2: simulating of walking and the ratio of Hmax/Mmax were obtained. The Hmax/Mmax ratios of the two groups were compared.

Results

There was no difference between M responses, HR latencies and resting Hmax/Mmax ratios in the RLS patients and control subjects. The Hmax/Mmax ratio during resting period was 44.6+ 26.6 and MI Hmax/Mmax ratio was 51.9+32.7 in the control group, whereas resting Hmax/Mmax ratio was 49.4+22.5 and MI Hmax/Mmax ratio was 40.1+23.1 in the RLS group.

Conclusion

Hmax was increased during MI at the control group, whereas it was decreased at the RLS group. This finding was interpreted as the imagination of walking decreases the spinal excitability in patients with RLS.
P1039
POLYCARDIORESPIRATORY POLYGRAPHY DIAGNOSTIC ACCURACY IN MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROM

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²VALL D'HEBRON HOSPITAL, OTORHINOLARYNGOLOGIST, BARCELONA, Spain

INTRODUCTION

The gold standard in OSAHS diagnosis is the nocturnal polysomnography (PSG). Nowadays is allowed to use polycardiorespiratory polygraphy (PCR) in patients with high pretest probability of OSAHS. The PCR has some limitations that can infraestimate the AHI; impossibility to score sleep time, respiratory effort related to arousal and hypopneas related to arousal without oxygen desaturation.

OBJECTIVE

Evaluate the polycardiographic polygraphy (CRP) diagnostic accuracy in patients with mild to moderate OSAHS.

METHODS

We evaluate 96 patients with AHI<30 in PCR and compare with the conventional polysomnography (PSG).

RESULTS

We studied 96 patients 69% male 30% female with a mean age 52±12.5 years, mean body mass index (BMI) 27.7±3.6, mean Epworth sleepiness scale 7.5±4.8 and mean AHI in PCR 11.6±7.8.

PCR show a OSAHS prevalence of 26% normal, 39.6% mild and 34.4 moderate in the selected patients.

When we compare PSG with PCR we observe statistical differences in the compute the AHI (19.2±14.9 & 11.6±7.8) and RDI (22.1±14.8 & 11.6±7.8). The mean difference in AHI and RDI are 7.6±12.0 and 10.4±12.1 respectively.

When we obtain normal results with PCR we observe in PSG a 76%(IAH) or 48%(RDI) of mild to moderate OSAHS. When we obtain mild OSAHS with PCR we observe in PSG 42.1%(IAH) or 47%(RDI) moderate and 15.7%(IAH) or 21%(RDI) sever OSAHS. When we obtain moderate OSAHS with PCR we observe in PSG 21.2%(IAH) or 18%(RDI) mild and 42.5%(IAH) or 51%(RDI) sever OSAHS.

CONCLUSIONS

PCR in mild to moderate OSAHS patients can infraestimate significantly the degree of OSAHS severity.
Intracerebral study of cortical activation during dissociated arousals

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Background

Dissociated arousals are characterized by behavioural arousal and slow-waves on ElectroEncephaloGram, that suggest the persistence of sleep. Our purpose was to determine, with intracerebral recordings, the changes in electrical activity in different cortical areas (sensori-motor and non-sensori-motors areas) during dissociated arousal states, in comparison with normal arousals.

Methods

Dissociated and normal arousals were recorded in a fifteen years-old male with drug-resistant right parietal epilepsy. We analyzed the activity from non epileptic areas, recorded in: pre- and post-central gyri, middle and superior frontal gyri, cingulated gyrus, hippocampus, middle temporal gyrus, superior and inferior parietal lobes. Time-frequency analyses were performed from 2 minutes before up 2 minutes after the beginning of the arousal.

Results

Five dissociated arousals were compared with 3 normal arousals. In dissociated arousals, we observed a blockage of very low frequencies rhythms in all areas, suggesting an arousal of the whole cortex. In motor cortex, higher frequencies rhythms occurred, similarly to a normal arousal. In other areas, a synchronization around 1.8 Hz was observed during the dissociated arousal states. This synchronization was never observed in normal arousals.

Conclusion

The slow-wave sleep is interrupted in all cortical areas during dissociated arousal state. The activity of motor cortex seem to be similar to normal arousals, whereas a probably pathologic 1.8 Hz synchronization is observed in non-motor areas.
P1041
Is Home Video Telemetry-Polysomnography (HVT-P) feasible?

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Background

HVT at King's College Hospital has been successfully used in patients referred to Telemetry Unit for seizure disorders evaluation. Some of the patients referred to Telemetry unit are for assessment of Non-Respiratory Sleep Disorders (NRSDs) and can benefit from HVT-P.

Question

Can HVT-P be performed successfully at the patients' own homes?

Methods

An observational study comprising of eleven adult patients with NRSDs was carried out. Patients underwent 2-3 nights of HVT-P at their homes. Recorded data was retrieved daily for analysis. Data acquisition included Video synchronised with sleep staging parameters consisting of 27 channels (19 EEGs, 2 EOGs, 5 EMGs and 1 ECG). Conventional parameters for duration, continuity and quality of Sleep Period Time (SPT) were applied for sleep scoring. Video quality was graded according to its ability to characterise behavioural events occurring during sleep period.

Results

Duration and continuity were good in 10/11. The EEG and Chin EMG signal were good in 10/11. The EOG signal was good in 9/11 and satisfactory in 1/11. Video was good in 6/11 and satisfactory in 5/11. Audio was good in 7/11 and satisfactory in 4/11.

Conclusions

Previous studies indicate that that sleep staging signals are most susceptible to quality loss making sleep analysis difficult. This study shows an overall quality of 91 % for EEG/EMG signals and 82 % for EOG signals. This suggests HVT-P can successfully be performed at the patients’ home and compares favourably with laboratory based recordings.
P1042
Relation of Sleep Stages and Sleep Period to the Cortical Excitability in Parkinson’s Disease

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Question
Sleep problems are reported by up to 98% of Parkinson’s disease (PD) patients. The mechanisms of disordered sleep in PD are not fully understood. Increased cortical excitability (CE) is associated with poor sleep quality in insomniacs. As some specific alterations of CE were identified in PD, we pursued the question if CE is related to sleep also in PD.

Methods
27 PD patients (10 women, mean age 62.7 ±8.4) underwent examination of CE with transcranial magnetic stimulation (TMS), nocturnal polysomnography and examination with the motor part of the Unified Parkinson’s Disease Rating Scale (UPDRS III). Recorded CE parameters included the resting motor threshold (RMT), the motor evoked potential (MEP) and the central silent period (CSP). CE parameters were labelled as initial (ini) when recorded after the TMS of the hemisphere where the disease began and as secondary (sec) otherwise. Bayesian model choice methodology and LASSO were used to choose the best fitting linear models for the main polysomnographic parameters.

Results
The Bayesian approach and LASSO both yield the same conclusions, i.e.: The best fitting linear model for total sleep time consists of one explanatory variable, RMTsec. The best model for wake after sleep onset uses RMTsec and RMTini, whereas the amount of NREM2 was best modelled by RMTsec and UPDRSIII. Our data did not support modelling other sleep parameters with linear models using CE parameters or UPDRSIII as explanatory variables.

Conclusions
The results indicate there may be an association between sleep disorders and CE changes in PD.
**P1043**
The quality of polysomnography recording in intensive care unit and the special requirements for the recordings set by ICU environment

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Polysomnography (PSG) is used for the diagnosis of sleep related disorders. This may not only be performed in a sleep laboratory but also in challenging circumstances at a hospital ward or in an intensive care unit (ICU). In the ICU, technical PSG problems arise that are beyond those experienced in a standard PSG laboratory.

The aim of this study is to describe the quality of the PSG carried out in the ICU in cases where a trained PSG technician is not available throughout the recording process. A further aim is to describe the proportion of artifact-free signal in each of the measured traces, causes for the artifacts as well as to find out if the recordings contain sufficient amounts of artifact-free signal for reliable analyses. We also wanted to compare the efficacy of the nasal pressure cannula with the respiratory inductance plethysmography sum signal (RIP) in detection of respiratory events in adult ICU-PSG.

A total of 20 overnight PSG recordings performed at a university hospital in southern Finland were analyzed for the study. The least artifact-free signal was to be found in the EEG-recording (78.5 %) and most artifact-free in the ECG-recording (96.5 %) and in the oxygen saturation-recording \( \text{SpO}_2 \) (96.3 %). The most common sources of artifacts in the EEG-, EOG- and ECG-recordings were body movement and poor electrode contact, in the EMG-recording ECG-artifacts, in \( \text{SpO}_2 \)-recording body movement and in the thoraco-abdominal movement detection and the EMFit-signal the occasional inability of the sensors to detect respiratory movements. Over 90 minutes (which equals one sleep cycle) of completely artifact-free signal on every channel simultaneously was found in 65 % of the recordings \((fr = 13)\). Respiratory events were scored twice in each study using a nasal pressure-signal and an RIP-signal. A statistically significant difference was detectable only in the amount of apneas/h. In one recording, the difference of the two analyses was significant.

In the ICU environment, the quality of PSG recordings varies and the most disturbing artifacts last for last for a long period of time. In circumstances where a trained PSG technician is not available throughout the recording process it is reasonable to record EEG-signal on both sides in frontal, central and occipital head regions as well as to use both the tibialis-EMG-recording and EMFit-recording to detect limb-movements. Respiratory events can usually be diagnosed by using the RIP-signal in case the nasal pressure signal for some reason not usable.
P1045
Automatic sleep classification using a data-driven approach reveals six latent sleep states

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Question

Will a sleep classifier, which uses a data-driven approach, classify sleep according to the golden standard for manual sleep scoring? Which EEG/EOG characteristics will the model include in the latent sleep states?

Methods

An automatic sleep classifier, which evaluates sleep using latent sleep states, was optimized using a data-driven approach. The model used spectral EEG and EOG measures and eye correlation in three seconds windows with one second resolution. Each thirty seconds epoch was expressed as mixture of probabilities of the latent sleep states. The model was applied to four groups to test the application: control subjects and patients with periodic leg movements represented a non-neurodegenerative group and patients with idiopathic REM sleep behavior disorder and Parkinsons Disease represented a neurodegenerative group. The model was optimized using 50 subjects and validated on 73 subjects.

Results

The optimized sleep model gave a detailed description of sleep, used six latent sleep states indicating that sleep contains six diverse latent sleep states and the state transitions were expressed as continuous processes. Statistics of the latent sleep states showed accordance to the spectral EEG and EOG content as well as eye movements in the AASM stages. The sleep model performed similar across the four groups and the overall subject-specific accuracy reached (%) 68.3 ± 7.5.

Conclusions

Analysing sleep using a data-driven approach and inclusion of only EEG and EOG revealed six latent sleep states. The model is general applicable on subject groups and may contribute to the research in sleep and neurodegenerative diseases.
P1046
Data-driven modeling of sleep EEG and EOG reveals stages indicative of pre-Parkinson and Parkinson’s disease

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Question
Will unsupervised modelling of sleep EOG and sleep EEG reveal sleep characteristics indicative of pre-Parkinson and Parkinson’s disease (PD)?

Methods
Polysomnographic (PSG) data from 10 age-matched control subjects were used to develop an EOG sleep model and an EEG sleep model. The sleep models were applied on full-night PSG data from 24 additional control subjects, 26 patients with periodic leg movements (PLM), 31 patients with idiopathic REM sleep behavior disorder (iRBD) and 36 PD patients. Based on the data-driven sleep models, features reflecting sleep characteristics in the EEG and EOG activity were computed. The total amount of data was divided into a training dataset containing 16 subjects from each of the four groups, and a validation dataset containing the remaining subjects. The features derived were evaluated, and the most discriminative ones between iRBD/PD (neurodegenerative diseases (NDD) cases) and PLM/controls (motor, but non-NDD cases) were found by training a Lasso regularized Regression model using eight-fold cross-validation on the training dataset.

Results
The best classification model included four features derived from the EEG data, and the NDD patients in the validation dataset could be classified with a sensitivity of 91.4% and a specificity of 61.1%. The most discriminative features were found to be thresholded amounts and stability of EEG topics reflected to REM, N3 and N1/N2, respectively.

Conclusions
This study suggests that the amount of N3 and R and the ability to maintain NREM and REM sleep determined by a data-driven sleep model can be used as potentially early PD biomarkers.
The Diagnostic Value of Sleep EEG in Narcolepsy

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Question

Polysomnography (PSG) and full day Multiple Sleep Latency Test (MSLT) is a tedious and costly procedure for the diagnosis of narcolepsy. Previous studies have shown differences between narcoleptic subjects and controls in the EEG during the PSG, which may be exploited to diagnose narcolepsy directly from the PSG without MSLT. We aimed to identify informative parts of the PSG-EEG, and assess the diagnostic value of these.

Methods

We analyzed the PSG-EEG signals from 137 patients with narcolepsy with cataplexy and 511 controls. Features where extracted from certain sleep stages, frequency bands and normalizations and passed to a Least Squares Support Vector Machines classifier with an RBF kernel. A subset of features were chosen and the final model was validated through bootstrap optimism estimation as well as a cross validation for extra support.

Results

Preliminary tests reveal a performance of the EEG features around an accuracy of ~80 %, sensitivity of ~25 %, and specificity around 95 %. Further work is ongoing.

Conclusion

EEG from NC patients presents significant changes likely due to destabilization of sleep-wake transitions. Further evaluation for the use as a diagnostic procedure is needed.
P1048
Increased amount of reported total sleep time during 24 hours is related to the severity of sleep disturbances in ischemic stroke patients
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Question
Are self-reported short and long term sleep quality related to the severity of sleep related breathing disturbances (SRBD) in ischemic stroke patients?

Methods
In this pilot study, 23 patients with acute first-time stroke, admitted to the stroke unit, underwent overnight polygraphy during the first 72 h after admission. Nasal airflow, respiratory movements, snoring sound, oxygenation level, and ECG were recorded. The incidence of SRBD before the stroke was studied with a questionnaire regarding their sleep three months prior the stroke. The reported quality of sleep during the treatment period in stroke unit was examined with the visual scale questionnaire containing five questions. The severity of stroke was assessed with the National Institutes of Health Stroke Scale (NIHSS) and the ability to function with the Barthel Index.

Results
Increased apnea-hypopnea index (AHI) was related to the increased amount of total sleep time during 24 hours (p=0.006). No association was found between AHI and the amount of sleep time during night. Also, no correlations between AHI and VAS questions were found. Increased AHI was related with lower Barthel Index (p=0.017) but not with NIHSS.

Conclusions
SRBD as well as excessive daytime sleepiness are common findings in patients after stroke. In our study, stroke patients with increased AHI reported increased amount of sleep time during 24 h but not during night time regarding three months pre-stroke, suggesting that they are napping. SRBD negatively affect to the functional outcome after stroke. In addition, SRBD increases the risk of developing cardiovascular diseases, which in turn increases risk for stroke. It is suggested that early diagnosis and treatment of underlying SRBD improve both recovery from stroke in short term and reduce the risk of relapses in long term. Our preliminary results suggest that reported napping may be a marker for a potential SRBD in stroke patients.
P1049
Non-REM sleep microstructures and phasic REM sleep events are associated with intracranial oxygenation changes measured with NIRS

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Question

Disordered and fragmented sleep due to sleep apnea, restless legs syndrome, and insomnia are associated with an increased risk of cardio- and cerebrovascular morbidity. Autonomic activation and repetitive hypoxia are examples of possible mechanisms mediating this risk. In addition to sleep apnea episodes, non-apneic disruptions in sleep continuity are associated with transitory intracranial hypoxia measured with near-infrared spectroscopy (NIRS). Some of the K-complexes are triggered by non-waking external auditory stimuli. Phasic rapid-eye-movement (REM) sleep is associated with the activation of the autonomic nervous system and surges in systemic blood pressure. Are these sleep microstructural phenomena associated with changes in intracranial blood oxygenation?

Methods

Six healthy volunteers were measured overnight with polysomnography and NIRS for extra- and intracranial blood oxygenation changes. Sleep spindles, K-complexes, and bursts of eye movements in REM sleep were detected. Average temporal changes in oxy- and deoxyhemoglobin triggered by these sleep events were measured.

Results

K-complexes triggered short intracranial hemodynamic responses and spindels delayed and longer responses. During and after phasic events in REM sleep, there were transient changes in intracranial blood oxygenation.

Conclusions

K-complexes are associated with transient hemodynamic changes in intracranial circulation, which can mediate harmful vascular effects during poor sleep due to noisy environments. Systemic blood pressure surges during phasic REM sleep are counteracted with vasoconstriction in cerebral arteries, leading to transient cerebral hypoperfusion and hypoxia episodes during REM sleep. This could be associated with an increased risk of stroke during early mornings.
P1050
Neurophysiological testing of the upper airway in obstructive sleep apnea showing peripheral nervous lesions

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Question
Obstructive sleep apnea (OSA) is often a progressive disorder starting with habitual snoring. The cause(s) behind this progression is not known. Snoring vibrations might cause nervous lesions, leading to both muscular weakness and impaired sensory reflex activation of dilating muscles. We aimed at establishing whether such lesions are present in OSAS and to develop methodology for appropriate testing.

Methods
Concentric needle-EMG was performed in the palatoglossus muscles of 10 non-snoring controls, 22 snorers and 11 OSA-patients. Cold detection thresholds (CDT) were tested at tonsillar pillars, tip of tongue and finger in 48 non-snoring volunteers, 46 habitual snorers and 64 OSAS-patients.

Results
In EMG, 10/11 OSAS patients had typical findings indicating motor neuropathy. Mild-moderate pathological findings were present in 12/22 snorers. EMG was normal in 10/10 non-snoring subjects. In CDT, there were significant differences at the tonsillar pillars between non-snorers, snorers and OSA-patients (p<0.01 in both cases). Snorers also had lower cold thresholds than OSA-patients (p<0.05). Thresholds at other locations showed no group differences. There were significant correlations between decreased sensory function and apnea-hypopnea index, and also to anamnestic years of snoring.

Conclusions
The degree of neuropathy in the upper airway correlates with degree of obstructive sleep disorder. This supports the hypothesis of snoring vibrations as causative of OSA. Cold threshold detection testing is non-invasive and painless. It is therefore recommended as a useful clinical method to evaluate the degree of damage in snoring and OSAS.
P1051
Spontaneous Nocturnal Neck Myoclonus Assessment with Video PSG during REM and NREM Sleep. Variability of NNM Index in Different Sleep and Neurodegenerative Disorders

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QUESTION

Neck myoclonus was systematically described and quantitative assessed during REM sleep in a sample of 190 patients (Frauscher et al, 2010). NNM was present in more than 50% of patients (Index 1.0+/-2.7/h). In suspected REM parasomnia of young 26 year-old female this index was reported reaching to 89,9/h (Otto et al 2012).

The stimulus responsiveness of the various forms of sleep myoclonus has not been carefully studied, but some forms appear to be stimulus-sensitive (Snodgrass 1990).

While during daytime myoclonus was classified by their topography and generator in cortical, subcortical and propriospinal (Cassim & Houdayer 2006, Brown & Caviness 2004) no data is available to differentiate cortical or subcortical myoclonus during sleep phases.

We aimed at determining differences of NNM in REM and NREM sleep and to analyze limited to neck or generalized NNM Indexes in different sleep and neurodegenerative disorders.

METHODS

We analyzed consecutively 27 patients (8 females and 19 males aged 6-77 years, mean age 36.4, SD 24.68) grouped in 6 categories: 3 patients with Parkinson Disease, 10 patients with OSA, 6 patients with NoREM parasomnia, 2 patients with epilepsy, 3 patient with psychiatric disorder and 3 patients with developmental impairment remitted to sleep laboratory.

EEG artifact shorter than 200 ms corresponding to video PSG observed neck myoclonus, according to the method used by Frauscher et al, was analyzed. Every NM was studied at 30 and 5 seconds timeline. We performed descriptive analysis using Ginkgo (UB 2006).

RESULTS

NM was present in 16 patients of 23 (69,56%), 4 being rejected.

NM in REM (mean NM REM 2,59/h, Max 16,04/h) and NREM (mean NM NREM 0,47/h Max 12,26/h). Secondary propagation of NM in REM (mean NM REM GEN 1,89/h Max 4,63/h) and NREM (Figures 1) (mean NM NREM GEN 0,21/h Max 1,39). Max values belonged to PD group.

Frequency of NNM was observed in REM with an index interval between 0 and 3,37 NM/h (Figure 2). In NREM the interval of NNM Index highest frequency belonged to 0-0,97 NM/h.

CONCLUSIONS

NM occurred in REM more than in NREM. There were no important differences of NNM indexes and clinical features in observed groups, except PD group which showed increased NM REM up to 16,04/h.
Prospective study is needed to demonstrate if a relation exists between PD cognitive impairment and incidence of NNM.

**figure 1**

**figure 2**

**INDEX NM REM- Frequency Histogram**
P1053
SLEEP DISORDERS AND GENE POLYMORPHISM DOPAMINERGIC (DRD4, DAT) IN THE OPEN POPULATION MEN AGED 25-64 NOVOSIBIRSK

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Question
To investigate the association of gene DRD4, DAT sleep disorders in the open population of men aged 25-64 in Novosibirsk.

Methods
As part of WHO «MONICA» in 1994, surveyed a random representative sample of men aged 25-64 years (657 men). To assess the level of sleep used a questionnaire that subjects filled out on their own. It has been suggested by the question: how do you sleep? Possible answers: "very good", "good", "satisfactory", "bad" or "very bad". Statistical analysis was performed using SPSS-11, 5.

Results
In the male's population of Novosibirsk, the prevalence of sleep disorders is high - 48.3%. The most common polymorphism of the gene DRD4: genotype 4 / 4, the second largest carriers of the genotype containing the short allele 2, slightly less than the carriers of long alleles of 6 or higher. In the study population was dominated by genotype of the gene 10/10 DAT, rarely met genotype 9 / 10 and, finally, in third place - genotype 9 / 9. Since sleep disorders are associated significantly: genotype 4 / 6 of the DRD4 gene and genotype 9 / 9 gene DAT. Carriers of genotypes containing "short" allele of the DRD4 gene 2 / 4, 3 / 4 did not experience sleep disturbances, the carriers of the genotype 4 / 4 were satisfied with sleep. Carriers of allele 11 DAT gene praised his dream.

Conclusions
In the open population of men aged 25-64 in Novosibirsk sleep disorders significantly associated with polymorphisms of genes DRD4, DAT.
P1054
SLEEP FRAGMENTATION: a sleep model to better understand the Transcranial magnetic stimulation features present in the sleep disorders

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Question

Sleep loss and sleep disorders are crucial for sleep dependent plasticity. TMS studies showed that SD influences cortical inhibitionexcitability. Alterations in movement-related cortical plasticity had been demonstrated in Restless legs Syndrome (RLS), clinically characterized by markedly fragmented sleep. By means of Transcranial magnetic stimulation (TMS), we evaluated the effect of Sleep fragmentation (SF) on cortical inhibitionexcitability and on plasticity-related TMS phenomena.

Methods

In basal condition (after a full night of spontaneous sleep), and in fragmented condition (after a fragmented night of sleep), MEP amplitude, motor threshold (MT), silent period (SP), and intracortical inhibition were assessed in healthy subjects. In both conditions each subject performed, a bimanual motor. MEPs were recorded before exercise (baseline), immediately after each exercise periods of 30, 60, 90 seconds, and after 15 minutes of rest. We evaluated if post-exercise facilitation and delayed facilitation were present.

Before each session, Stanford Sleepiness Scale was completed (SSS).

Results

MT and SSS were significantly increased in SF. No significant differences for MEP amplitude or SP or intracortical inhibition were found. In both conditions MEP amplitude was larger than baseline immediately after 30s and 60s time periods, indicating the presence of post-exercise facilitation, and then again after rest, showing delayed facilitation. Comparing the two conditions at each time point we found no significant differences in MEP amplitude.

Conclusion

SF produces significant disruption of nocturnal sleep, reduces daytime alertness and increases sleepiness. Confirmatory features of this clinical behaviour could be that in the FC we observed a significant increase in the SSS and in the MT. On the other side, SF was unable to modify cortical inhibition and to influences plasticity-related parameters. These results seem in contrast to TMS alterations observed in SD and RLS. We suggest that SD and SF represent different phenomena that can depend on variously networks acting on motor cortex. We speculate that alterations in cortical excitability found in RLS are intrinsically related to the underlying disease itself and instead they are not directly associated to the sleep fragmentation presents in the RLS.

figure 1
**Figure 2**  - Paired-pulse transcranial magnetic stimulation (TMS). The average time course at different interstimulus intervals (ISI) in the different conditions. At each ISI, the size of the conditioned motor evoked potential (MEP) is expressed as a percentage of the size of the unconditioned MEP alone. Repeated ANOVA measures showed a significant effect of inter-stimulus interval in each condition.
P1055
DIFFERENTIATING PARASOMNIAS FROM NOCTURNAL SEIZURES

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INTRODUCTION

Differentiating between nocturnal seizures and NREM parasomnias can be challenging; some features supporting an epileptic etiology of paroxismal events can help to identify them, as stereotyped nature of spells, their high frequency and tendency to cluster, timing and duration of the events and age.

CASE

We present a 32 y/o woman with a past history of epilepsy during infancy, that presented with the complain of confusional arousals occurring in clusters during nocturnal and diurnal sleep, awakenig her with a feeling of dizziness and without loss of consciousness, nor motor activity.

WORKUP

Standard diurnal awake V-EEG was normal, nocturnal v-polisomnography (V-PSG) showed up five electroclinical focal seizures, 15-30 sec. duration, during N1-N2 and one in REM. Fast activity evolving in the posterior temporal region T5 and extending to the contralateral T6 was recorded before and during the confusional awakenings. focal intercritical frontal and temporal epileptiform activity was also recorded.

CONCLUSION

Although many seizures are easily distinguished from nonepileptic events on the basis of the history, this can be difficult in cases of spells occurring during sleep and resembling NREM parasomnias, V-PSG in these cases can give us the diagnosis.
P1056
Secondary narcolepsy with intermediate hypocretin level due to brain tumour - a case story.

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Question
Narcolepsy is characterized by excessive daytime sleepiness (EDS) and/or cataplexy and diagnosis is supported by polysomnography (PSG), multiple sleep latency test (MSLT) and CSV-hypocretin level (<110 pg/mL). Secondary narcolepsy can be due to brain tumours and may have sleepiness of variable severity.

We hereby present a case of possible secondary narcolepsy with intermediate hypocretin level due to brain tumour with fluctuating symptoms of sleepiness.

Case
25-year old male, BMI 27, was referred with sleep attacks, EDS and snoring. Cardio-respiratory monitoring (CRM) in August 2012 showed mild sleep apnea, AH-indeks 10/hour, and treatment attempt was performed with CPAP. During October 2012 the patient suffered rapid decline with increased sleep time, changed personality and nocturnal motor activity. CT/MRI showed obstructive hydrocephalus and brainstem glioma verified subsequently by biopsy as low grade. The tumor was located to tectum and 3. and 4. ventricle. Also changes was seen in thalamus bilaterally. Third ventriculostomi was performed. CSF hypocretin showed intermediate level 130 pg/ml (110-200 pg/ml). After surgical treatment, patient stayed on low dose prednisolone, as attempt to taper off completely lead to relapse in symptoms on intracranial pressure. 9 months later PSG and MSLT showed moderate sleep apnea AH-indeks 23/hour without CPAP and AH-indeks 0 with CPAP and normal MSLT. The patient has not experienced cataplexy.

Conclusion
Excessive daytime sleepiness and intermediate hypocretin levels may be evoked due to brainstem glioma. CPAP treatment did not relieve symptoms despite of AHI improvement. Lowered hcrt and secondary narcolepsy may be evoked by brain stem involvement.

figure 1
Abstracts of Poster Presentations – Poster Session 59 – Sleep disorders

figure 2
P1100
Event-Related Potentials in Sleep-Related Breathing Disorders and Insomnia

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Background
Since sleep may affect information processing and therefore event related potentials, an increased P300 latency and reduced amplitude are expected to be present when sleep is disrupted and shortened. Objective: To assess event related potentials (ERPs) in patients with sleep related breathing disorders (SRBDs) and insomnia, and the association between the severity of subjective and objective sleep alterations and the changes in ERPs.

Methods
Thirty patients with SRBDs and insomnia were subjected to polysomnography (PSG), visual and auditory ERPs testing twice; pre and post sleep.

Results
We found significant decrease in ERPs latencies, and increase in their amplitudes in the morning in the control group, but not in patients. Evening ERPs were not significantly different among the groups. Morning ERPs in sleep related breathing disorders had longer latencies and smaller amplitudes. Evening to morning comparison revealed the subtle ERPs abnormalities in insomnia. No significant correlation was found between the changes of ERPs in patients and their Epworth sleepiness scale scores and the PSG data.

Conclusion
Normal uninterrupted sleep greatly enhances ERPs. Multiple P300 measurements especially in the morning provide more sensitive marker for assessment of sleep effects on attention processes. The difference between evening and morning ERPs is a very sensitive parameter and can detect subtle abnormalities especially in insomnia patients. Neither subjective nor objective estimates of sleep continuity can strongly explain the changes in ERPs.
UTILITY OF VIDEO-PSG IN THE EARLY DIAGNOSIS OF TWO PATIENTS WITH FFI

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INTRODUCTION

Fatal familial insomnia (FFI) is a very rare autosomal dominant inherited prionopathy included in the Agrypnia excitata syndrome. The video-polisomnograpy (v-PSG) findings are described when the syndrome is fully established. Here we report on two patients with a final diagnosis of FFI and v-PSG studies within a month of the clinical onset.

CASE REPORT 1

A 50 year old male with a FFI family history, the D178N mutation, and a previously normal v-PSG study whilst asymptomatic. Later on, when he begins with fluctuating diplopia, a second v-PSG revealed very pathologic results, with decreased slow wave sleep (SWS) efficiency, few spindles and great motor restlessness. He died 7 months later.

CASE REPORT 2

A 53 year old male with no family history of neurological disease presented with three week duration insomnia and sleep behavior alteration, and was referred for a v-PSG with the suspected diagnosis of a REM sleep behaviour disorder. The study showed an agrypnia excitata syndrome with insomnia, great motor restlessness with dreamlike stupor and absence of SWS and stage 2 NREM sleep. Later, the genetic study was positive for the mutation, and he died 6 months later.

CONCLUSIONS

The v-PSG is a very sensitive tool for the early diagnosis of the FFI, since the agrypnia excitata findings are already present when the clinical manifestations are still subtle.
The analysis of chemosensitive structures contribution to obstructive sleep apnea development

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Experiments on animals proved attenuation of medullary chemoreceptors activity in hypercapnia if there is any pathological process in ventral surface of medulla oblongata (VSMO). In this case respiratory arrest develops despite high functional activity of vascular chemoreceptors. The effectiveness of lung ventilation in hyper- and hypocapnia, hypo- and hyperoxia depends on the functional state of namely central chemoreceptors.

**The aim**

to compare a number of key mechanisms of apnea development after functional blockade of medullary chemoreceptors in anesthetized animals with fatal emerging and recurrent obstructive sleep apnea (OSA) in humans.

**Methods**

Central chemoreceptors blockade was made with lidocaine application (50µl, 0.01, 0.1, 1.0%) on VSMO in acute experiments in rats (n=27). Subdural introduction of catheter was made through atlanto-occipital junction to VSMO. Both electromyogram of diaphragm and truncus sympathicus activity were registered. Inhalation of carbogen (5% of CO₂ and 95% of O₂) during apnea after central chemoreceptors blockade was made. Carbogen (5% of CO₂ and 95% of O₂) inhalation was applied to 29 patients with OSA to determine the threshold of CO₂ sensitivity.

**Results**

Diaphragm and sympathetic activity inhibition after lidocaine application on VSMO decreased proportionally with anesthetic dose. Apnea developed in 5-10 sec after the application of 1% lidocaine. Simultaneous carbogen inhalation reduced apnea duration. 23 of 29 patients with OSA demonstrated decrease of sensitivity to hypercapnic stimulus.

**Conclusion**

Mechanisms of respiratory arrest associated with medullary chemoreceptors activity were showed in acute experiments. The important contribution of central chemoreceptors was stated in patients with obstructive phenomena in upper airways.
Abstracts of Poster Presentations – Poster Session 60 – Transcranial magnetic stimulation

P1061
Difference in the modulation of quadripulse transcranial magnetic stimulation (QPS) effect between L-DOPA and zonisamide

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Objective
To study effects of zonisamide (ZNS) on the motor cortical long term potentiation (LTP) induced by quadripulse transcranial magnetic stimulation (QPS).

Background
Motor cortical plasticity induced by rTMS is known to be enhanced by L-DOPA. ZNS has an anti-Parkinsonian effect, but its pharmacological mechanism remains to be determined. Here, we studied its effects on M1 plasticity and compared it between ZNS and L-DOPA.

Method
Double-blinded crossover study was performed. First step, 24 healthy subjects received a single-dose of L-DOPA/carbidopa (200mg), ZNS (25mg), or placebo. Second step, 8 healthy subjects received a single-dose of L-DOPA/carbidopa (200mg) + ZNS (25mg), L-DOPA/carbidopa (200mg) or placebo.

Two hours after the drug intake, QPS at 5ms interval (QPS5) was applied over the left M1 for 30 minutes to induce LTP like effects. The intensity was set at 90% of AMT. Motor evoked potential (MEP) was recorded from the right hand muscle after single TMS applied to the left M1. We measured MEP amplitude for up to 60 min after QPS.

Result
As reported previously, L-DOPA significantly enhanced the LTP like effect induced by QPS5 (p < 0.05), while RMT and AMT were not affected. On the other hand, ZNS had no significant enhancement of LTP like effects, even though ZNS tends to increase LTP. Add on effect of ZNS in plasticity was not shown.

Conclusion
Several previous papers proposed that ZNS has anti-Parkinsonian effect mediated by dopamine synthesis enhancement, MAO-B inhibition or non-dopaminergic effects. LTP enhancement effect of ZNS may partly explain its anti-Parkinsonian effect.
Abnormal surround inhibition and cerebellar hyper-activation of functional MRI in focal hand dystonia

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Background

Clinical features of focal hand dystonia (FHD) are task specific abnormal posturing due to sustained muscle contractions interfering with the performance of the skilled motor tasks. Surround inhibition (SI) is one important inhibition in the muscle-specific modification of the cortico-spinal pathway. In dystonic patients, abnormal involuntary co-contraction of the hand muscles is associated with a disruption of SI. The aim of the study is to research the relationship with disrupted SI and function of central nervous system during motor performance using functional MRI.

Methods and patients

Seven healthy subjects (mean ages 34.7±9.1 years, all men) and seven patients with writer cramp (mean ages 53.7±17 years, 4 men and 2 women) were enrolled. According to Beck and Hallett, the experiment was done. The EMG were recorded in both right first dorsal interosseus muscle (FDI) and abductor polices brevis muscle (APB). Subjects pushed down on a small force transducer using the tip of their index finger in response to an acoustic signal. SI was tested by using single TMS which was given before signal and 100ms, 150ms and 1200ms after signal. For functional MRI, epoch-related fMRI design to map regional changes in BOLD signal under the condition of grip task and finger tapping task.

Results

FHD showed no SI in APB and increase of the ration of FDI and APB. The finding of fMRI showed hyperactivity of motor area and excessive activation in prefrontal area. And also hyperactivity is observed in both cerebellar hemispheres.

Discussion

Our findings showed the relationship with disrupted SI and cerebellar hyper activation of cerebellum in fMRI during voluntary movement.
**Abstracts of Poster Presentations – Poster Session 60 – Transcranial magnetic stimulation**

**P1063**

**EFFECTS OF BASKETBALL SHOOTING EXERCISES ON SENSORY-MOTOR INTEGRATION IN NORMAL CONTROLS AND BASKETBALL PLAYERS**

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**Question**

What is the effect of basketball shooting exercises on sensory-motor integration (SMI) in sedentary subjects and licensed players?

**Methods**

Ten sedentary subjects and 8 licensed basketball players were included. Electrical stimulation of the median nerve was followed by transcranial magnetic stimulation (TMS) of the contralateral motor cortex. Recordings were made from the thenar and flexor carpi radialis (FCR) muscles. Inter-stimulus intervals (ISI) between the electrical stimulus and TMS were 20, 35, 50, 65, 80, 100 and 200 ms. Mean sizes of the eight motor responses elicited at each ISI were divided by those of the responses evoked by TMS alone.

Sedentary subjects performed a five-day exercise with their dominant hand targeting to a standard basket. Electrophysiological studies were performed before and after the exercise on day 1 (T0, T1) and after the exercise on day 5 (T2). Basketball players attended only to T0 and T1.

**Results**

In FCR of the sedentary group (Fig 1, amplitude ratios, blu:T0, red:T1, green:T2, bars:standard deviations), there were less short latency afferent inhibition and higher facilitation at T1 (statistically significant at ISI 35 and 50 ms). This effect decreased at T2 despite the increased success rate. Basketball players did not show a facilitation as high as that found in the sedentary group.

**Conclusion**

Short term exercises lead to SMI changes which may function in the early phase of gaining the ability. Continued training provided higher success while the electrophysiological changes was decreasing, possibly by the conversion of the learning process into different mechanisms. Exercising already gained abilities do not produce similar SMI changes.
Phasic Muscle Contraction Influence upon the Quadripulse Stimulation (QPS) Aftereffects.


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**Question**

The aftereffects elicited by repetitive transcranial magnetic stimulation (rTMS), such as theta burst stimulation (TBS), paired associative stimulation (PAS), are readily influenced by voluntary contraction of the target muscle. No investigations have suited the voluntary contraction effects on the aftereffects induced by quadripulse stimulation (QPS) (a novel rTMS technique). The aim of this study is to investigate whether or not QPS aftereffects are influenced by voluntary movements after the stimulation.

**Methods**

Twelve healthy volunteers participated in this study. QPSs were applied upon the hot spot for the right first dorsal interossei (FDI) muscle (left M1). Inter stimulus intervals (ISIs) were set at 5 ms and 50 ms (QPS-5 and QPS-50) to induce strongest long term potentiation/depression (LTP/LTD) like effects, respectively. We compared three conditions; control without voluntary contraction and two contraction conditions, in which the subjects performed 60 cycles of opening-closing right hand movements (at the rate of 1 cycle per second) at immediately or 20 min after QPSs. MEPs were recorded from the right FDI 0 to 60 minutes after QPS. The time courses of MEP size were compared among the three conditions.

**Results**

In the control condition, QPS-5 potentiated and QPS-50 depressed MEPs through 60 minutes thereafter. The voluntary movements just after QPSs abolished both LTP and LTD like aftereffects completely. On the other hand, the voluntary contraction 20 min after QPS transiently weakened both LTP and LTD like effects, and both effects finally caught up with the control levels.

**Conclusions**

The aftereffects of QPS are influenced by voluntary contraction of the target muscle. The pattern of influence depends on the time when the voluntary contraction was performed.
Induction of motor associative plasticity in the posterior parietal cortex - primary motor network

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There is anatomical and functional connectivity between the ipsilateral primary motor area (M1) and posterior parietal cortex (PPC), which plays a role in sensorimotor integration. In this study, we applied corticocortical paired associative stimuli to ipsilateral PPC and M1 (parietal ccPAS) in healthy right-handed subjects to test if this procedure could modulate M1 excitability and PPC-M1 connectivity. 180 paired transcranial magnetic stimuli to the PPC and M1 at an interstimulus interval (ISI) of 8 ms were delivered at 0.2 Hz. We found left parietal ccPAS increased excitability of conditioned left M1 assessed by motor evoked potentials (MEPs) and the input-output curve. Motor behavior as assessed by the Purdue Pegboard task was unchanged compared to controls. At baseline conditioning stimuli over left PPC potentiated MEPs from left M1 when ISI was 8 ms. This interaction significantly attenuated at 60 minutes after left parietal ccPAS. Additional experiments showed that parietal ccPAS induced plasticity was timing-dependent and was absent if ISI was 100 ms, and could also be seen in the right hemisphere. Our results suggest that parietal ccPAS can both induce associative plasticity in M1 and modulate PPC-M1 connectivity. Parietal ccPAS is a new approach to modify motor excitability and sensorimotor interaction.

figure 1

![Diagram showing time course of evaluation and changes in M1 and PPC excitability after parietal ccPAS](image-url)
Movement preparation requires early activation of the dorsal premotor area

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Introduction

The human premotor cortex (PMC) is located in the center of a frontoparietal motor network. Its significance in a hierarchical motor network remains, however, elusive. The temporal pattern of local cortical activation during the performance of behavioral tasks can be studied by TMS induced virtual lesion models. Virtual lesions are understood to provide information about the functional role of cortical areas in a larger network. This study aims to identify the temporal activation pattern of the dorsal PMC during an established behavioral task demanding premotor activation.

Methods

Nine healthy volunteers participated in the experiment. Navigated TMS was used to map Brodmann areae 4 and 6 for a primary motor (M1) and premotor stimulation hotspot. Then, subjects had to manually trace a figure while TMS was randomly applied over the PMC, M1 or the dorsolateral prefrontal cortex (DLPFC) as control condition at different time intervals before direction changes in the figure occurred.

Results

NTMS over studied regions significantly affected task performance at discrete time intervals ($F_{(10,80)}=3.25$, $p=0.001$). NTMS applied over PMC 120 and 140 ms before direction changes impaired task performance significantly more than when applied over M1 ($p=0.021$ and $p=0.003$) or DLPFC ($p=0.017$ and $p<0.001$).

Discussion

We provide novel evidence that premotor activation is crucial for task performance early in the stage of motor preparation suggesting a significant role in shaping voluntary movement. This interpretation is supported by the observation of complex movements induced by direct cortical stimulation in the premotor area and higher-order motor deficits after premotor lesions.
Abstracts of Poster Presentations – Poster Session 60 – Transcranial magnetic stimulation

P1067
Continuous theta burst stimulation with monophasic pulses: effect of current direction

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Question

In a companion poster (Sommer et al.) we show that iTBS with a monophasic anterior-posterior (AP) current pulse, which differs from conventional TBS applied with biphasic pulses (Huang et al. 2005), produces reliable suppression of corticospinal excitability. Here we test the effect of applying cTBS with the same monophasic pulses.

Methods

We stimulated the dominant hand representation of the motor cortex in 15 healthy subjects, using approximately square wave pulses (see Fig 1 Peterchev et al. 2013), generated by a prototype controllable TMS machine (cTMS-3, Rogue Resolutions Ltd., Cardiff, UK), connected to a standard figure-of-eight coil with an outer diameter of each wing of 70 mm (The Magstim Co. Ltd., Dyfed, United Kingdom). cTBS was applied conventionally (200 bursts at 5 Hz burst repetition frequency, each burst consisting of 3 pulses of 80% AMT intensity repeated at 50 Hz frequency). In two separate sessions, we applied a pulse width of 75 microseconds in the posterio-anterior (PA) current direction in the brain, and of 45 microseconds in the AP direction. Before and every 5 minutes up to 30 minutes after cTBS, we monitored the modulation of motor evoked potential (MEP) amplitude from the dominant first dorsal interosseous using blocks of conventional, monophasic, suprathreshold pulses generated by a Magstim 200² stimulator, inducing PA currents in the brain, at 0.2 Hz frequency.

Results

There was a large variation in response between individuals such that a rmANOVA using data from all points failed to show any effect of AP or PA stimulation and no difference between them. However, averaging all post-cTBS time points for comparison with baseline showed a significant MEP suppression after AP (mean suppression to 80% control, paired t-test p=0.044) but not PA stimulation.

Conclusions

Monophasic AP cTBS (like iTBS) tends to suppress corticospinal excitability but individual variability is high. PA cTBS has no reliable effect.

References

Peterchev et al. (2013) Pulse width dependence of motor threshold and input-output curve characterized with controllable pulse parameter transcranial magnetic stimulation, Clin Neurophysiol

Huang et al. (2005) Theta burst stimulation of the human motor cortex, Neuron

figure 1
Motor cortical representations differ between Asperger and typical children - navigated TMS study

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Question

Motor functions are impaired in autism spectrum disorders. Our aim was to characterize Asperger’s syndrome (AS) using transcranial magnetic stimulation (TMS). Specifically, we studied cortical functions and representations of distal hand muscles using MRI-navigated TMS (nTMS).

Method

Eight boys with AS (age 8-11 years) and age-matched neurotypical controls were studied. The resting motor threshold (MT), motor evoked potentials (MEP), latency jump and motor cortex mapping on both hemispheres were measured. Fine motor function was assessed by Box and Block Test (BBT).

Results

The controls demonstrated better fine motor skills (BBT; main effect of group, p=0.005). There were no significant differences in MT, MEP latency or MEP amplitude. Latency jump in abductor pollicis brevis muscle was significantly shorter when stimulating left hemisphere (1.4 ms) compared to right hemisphere stimulation (2.3 ms) in AS group (p<0.005, pairwise comparison and hand x group interaction), whereas no interhemispheric differences were seen in controls (3.1 ms vs. 2.8. ms). Furthermore, the AS children had significantly larger cortical representation area of right abductor digiti minimi muscle compared to their left ADM as well as compared to control children (p<0.05, pairwise comparison and hand x group interaction).

Conclusions

Children with AS possess alterations in motor cortex function and extent of representation area on the left hemisphere. These results may underlie some of the known motor abnormalities and impairment in manual dexterity in AS.
P1069
The size of motor representation areas of distal hand muscles enlarge with age

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Question
We wanted to characterize the motor representation areas of distal hand muscle in developing brain by studying healthy children, adolescents and young adults with MRI-navigated transcranial magnetic stimulation (nTMS) on both hemispheres.

Method
45 healthy right-handed subjects were divided into four age groups: young children (6-8 yrs, n=7), children, (9-12 yrs, n=14), adolescence (14-17 yrs, n=12) and adults (22-33 yrs, n=12). Optimal representation site for abductor pollicis brevis (APB) was located and resting motor threshold (rMT) determined using nTMS. Functional motor areas were mapped at 110% of rMT.

Results
MT decreased with age (main effect of group, p<0.000). Optimal site for APB was located in the anatomical hand knob in all age groups on and both hemispheres. However, the size of representation area of APB differed between the groups (p<0.05, linear mixed model, main effect of group). Young children had significantly smaller cortical representation area of APB compared to older children, adolescents and adults (pairwise comparison; p<0.05 in all comparisons). Furthermore, older children had smaller representation area than adolescents, whereas in adolescents, the representation areas of APB had reached maturity. Inter-hemispheric differences were not found in any age groups (p<0.05).

Conclusions
Cortical representation areas of distal hand muscles enlarge with age. The results demonstrate the development of the cerebral cortex, specifically the motor cortex.
Motor evoked potentials studied by navigated TMS during normal development -from six years to adulthood

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Question

We examined navigated transcranial magnetic stimulation (nTMS) measures (resting motor threshold (MT), motor evoked potential (MEP) latency and amplitude, active MEP latency) as possible markers of cortical maturation and correlated them with a simple fine motor skill task.

Method

NTMS was performed on both hemispheres on 46 right-handed subjects (young children: n=10, mean 7.6 yrs; children, n=12, mean 10.8 yrs; adolescents, n=12, mean 15.8 yrs and adults, n=12, 28 yrs). nTMS was targeted to the optimal representation site of abductor pollicis brevis muscle (APB). Fine motor skills were assessed by box and block test (BBT).

Results

The examination was well tolerated with no side-effects. Fine motor skills improved with age (main effect of group, p=0.000; BBT means 52, 66, 75 and 84). MT decreased with age (main effect of group, p<0.000, means: 71%, 51%, 40% and 40%). In one child from the youngest age group the MT was above the maximal stimulator output. Both resting MEP latency (main effect of group, p<0.000; means 20.5 ms, 21.2 ms, 23.0 ms 22.6 ms) and active MEP latency (main effect of group, p<0.000; means 17.0 ms,18.5 ms, 20.6 ms and 20.5 ms) increased with age, which is explained by correlation between height and MEP latency. The MEP amplitude increased with age (main effect of group, p=0.047; means 337 µV, 844 µV, 723 µV and 1106 µV). Fine motor skills showed a negative correlation with MT in both hemispheres (p<0.05) when controlled for age (1-tailed partial correlation).

Conclusions

nTMS suits well for studying of development of the cerebral motor cortex. MT seems to reach maturity in adolescence. Fine motor skills correlate negatively with MT suggesting that lower TMS threshold is associated with greater fine motor ability.
High-frequency repetitive transcranial magnetic stimulation (rTMS) of the motor cortex has repeatedly been shown to alleviate pain of neuropathic origin (Lefaucheur et al, 2011, NCCN). The mechanisms subserving this analgesic effect are however still unclear. One leading hypothesis is that rTMS relieves pain via induction of plasticity in a network of interconnected cortical and sub-cortical brain areas. While most previous efforts have concentrated on the primary sensori-motor area (e.g. Houzé et al, 2012, Cerebral Cortex), rTMS-induced plasticity of brain regions directly associated with pain has not yet been explored.

In this study, we sought to investigate the plasticity of nociceptive networks after a session of 20 Hz rTMS to the motor cortex by a) assessing spino-thalamic pathway excitability using pairs of Nd:YAP laser stimuli delivered at pain threshold on the hand dorsum, b) modelling sources of LEPs (laser-evoked potentials, acquired with 128 electrodes) and fitting them to individual anatomy (3D structural MRI) and c) assessing subjective pain intensity and unpleasantness. Healthy subjects were tested both before and 15 to 20 minutes after two sessions of rTMS, either active or placebo (sham), that were separated from each other by a month.

At base-line in ten healthy controls, the amplitude of N1 and N2-P2 LEPs components to the second of two stimuli delivered at 1Hz was significantly reduced compared to the first by 40-50% (ANOVA (Stimulus Number x Treatment), Stimulus Number: F(1,18)= 78.7, p< 0.0001). Amplitude reduction was not different between conditions before cortical stimulation (Treatment: F(1,18)= 0.16, p= 0.70; Interaction: F(1,18)= 1.05, p= 0.32), thus yielding a measure of nociceptive networks excitability. Neither amplitude of nociceptive potentials nor subjective report (pain intensity and unpleasantness) were modulated specifically by active motor cortex rTMS. However, amplitude reduction to repetition was conserved after active rTMS, while it seemed less powerful after placebo stimulation (trend: p=0.07).

These results, which need to be confirmed in more subjects, seem to point towards a slight modulation of nociceptive cortical activity by high-frequency rTMS of the motor cortex.
P1072

*Effector-specific motor resonance is modulated by the type of observed action.*

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Covert engagement of the motor system during observation of motor acts has been a topic of investigation for the last two decades. The body of evidence collected to date is vast and yet conflicting, leaving the phenomenon of motor resonance still poorly understood.

In the present study we explored corticospinal excitability during observation of pinch and grasp actions in 18 healthy right-handed participants. Single pulse transcranial magnetic stimulation was applied to the primary motor cortex (M1) while muscle evoked potentials (MEPs) were recorded from the 1DI and ADM muscles - agonists during performance of pinch and grasp respectively. All subjects were tested twice, permitting collection of data from both hands, during stimulation of either left or right M1.

In this experiment we have considered four factors, each comprising two levels: 1) recorded hand (left /right), recorded muscle (1DI /ADM), observed action (pinch /grasp) and observed hand (left /right). Firstly, we have discovered that significant interaction between observed action and recorded muscle persisted independently of observed or recorded hand laterality. This action-specific effect was strongest in the ADM muscle where facilitation during observation of grasp was consistently higher than during observation of pinch. Secondly, we observed significant interaction between recorded and observed hand, however this relationship was only present in the 1DI muscle. Left 1DI resonated significantly stronger during observation of left hand pinch and the opposite effect was revealed in the right 1DI. This effector-specific pattern was not present in the ADM muscle during observation of grasp.

We conclude that although action-specific motor resonance is present in both hands during observation of either left or right hand, the type of observed action may modulate the effector-dependent resonance. We believe that these findings contribute to our understanding of motor resonance and need to be considered if action observation is to be used in rehabilitation of the damaged motor system.
P1073
The significance of phase and current direction of transcranial magnetic stimulation to the neuronal recruitment in motor cortex

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Question

We aimed to investigate the significance of phase and current direction for neuronal recruitment in the motor cortex using transcranial magnetic stimulation.

Methods

11 healthy subjects (8 female, mean age 27.45 ± 6.19 years) underwent a motor mapping of the first dorsal interosseus (FDI) muscle of the dominant hand. Starting from a manually determined hot-spot of its representation we measured its motor evoked potentials (MEPs) at equidistant points oriented at a hexagonal grid with a side-length of 5.77 mm with 7 MEPs each using the following pulse configurations: monopolar anterior-posterior, monopolar posterior-anterior, bipolar normal, bipolar reverse. The measurements were stopped when stimulation did not evoke any discernible MEPs. A hot-spot was determined for every pulse configuration. Based on the measurements a center of gravity (CoG) was determined for each pulse configuration.

Results

There was no significant difference regarding the size of the motor representations of the FDI per pulse configuration. The locations of the x- and y-coordinates of the calculated centers of gravity for different pulse configurations did not differ significantly as well (p=0.34 for x-coordinates, p=0.55 for y-coordinates).

Discussion

We could not find a distinct effect of the pulse configuration regarding the determination of the center of gravity using TMS. While overall variability of measurements was high, manual determination of the hot-spot appeared to be relatively robust.
The role of somatosensory input in paired associative stimulation

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Question

The mechanism of LTP or LTD-like effect in paired associative stimulation (PAS) is explained on spike-timing dependent plasticity. In facilitatory PAS, however, it is not clear why one pairing of PAS similar with short-latency afferent inhibition can induce LTP-like effect. The present data aim to provide a hypothesis about this.

Methods and Results

First step: There is a hypothesis that PAS is induced by summation of network activity (Thickbroom WG, 2007). If it is true, LTP-like effect is induced similarly when interstimulus interval (ISI) is varied between “N20 peak latency+ 2” to 25 ms. Seven healthy volunteers showed LTP-like effect with ISI of 25 ms and “N20 + 2” ms. But the effect was disappeared when ISI was randomly intermingled (Figure 1). This result denies the summation of network activity.

Second Step: In animal studies the somatosensory input generates excitatory postsynaptic potentials (EPSPs) and the stimulated nerves in the motor cortex generate back-propagating action potential (BPAP). These two potentials interact with each other, leading to LTP-like effect. We hypothesized that the somatosensory input may increase the probability of two interactions. If it is true, the jitter of peak latency is less when somatosensory input comes. In thirteen healthy subjects, the MCD was less when median nerve stimulation was applied 25 ms before TMS, compared with single pulse TMS (p = 0.02, Figure 2). Thus the somatosensory input may decrease the variation of BPAP.

Third step: If it is true, the LTP-like effect may be negatively correlated with jitter in some parameter. In effect, during PAS intervention, the effect was negatively correlated with the CoV of MEP amplitude between two serial MEPs during the last pairing from 120 to 180 stimuli (r= -0.59) in 18 healthy subjects.

Conclusion

It may be plausible that the somatosensory input may play a role in increasing the probability of interaction between EPSPs by somatosensory input and back-propagating action potential.

figure 1
Abstracts of Poster Presentations – Poster Session 60 – Transcranial magnetic stimulation

figure 2
Brainstem tumors in adults. Combination of surgery, neurophysiology and tractography. Case report.

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INTRODUCTION

Brainstem tumors can occur in both, childhood and adulthood, although they are less frequent after the age of 20. The most common symptoms include cranial nerve dysfunction, impairment of motor and sensory long routes and ataxia. In most cases surgical treatment is not possible due to the infiltration of eloquent areas observed in conventional studies. Tractography is a procedure that manifests neural tracts by using magnetic resonance imaging (MRI). It is a really useful tool for guiding preoperative subcortical mapping.

CASE REPORT

We present a 31 years old patient who presented dizziness and weakness of lower limbs, difficulty in articulating words, impossibility to swallow solid food and numbness in fingertips of both hands. A cranial MRI was performed, where an intrinsic brain stem lesion was observed. The study with tractography showed a displacement of fibers without invasion. The patient underwent surgery with a suboccipital craniotomy in which the floor of IV ventricle was exposed. Mapping was performed with identification of nuclear cores of facial and IV cranial nerve. It was possible to make a complete resection. During surgery an episode of unilateral loss of motor and somatosensory evoked potentials is observed, which was recovered before the end of it. After the surgery the patient presented a transient disturbance in cranial nerves and tetraparesia which has been recovered almost completely. Imaging studies show no long-term recurrence images.

CONCLUSION

Intraoperative monitoring can be a really useful tool for surgical resection in intrinsic brainstem lesions in adults. Tractography studies may be a very helpful technique in these complex patients.
P1077
Experiment with Using of Biphasic Pulses in SICI Test

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Short latency intracortical inhibition (SICI) is considered as one of the most popular tools in neurophysiology. Pairs of monophasic pulses used in all experiments with SICI. The research objective is to study if SICI gives the same result when using biphasic pulses.

A healthy 38 years old male was tested. TMS of the left motor cortex was performed with a figure-of-eight coil and Neuro-MS/D magnetic stimulator (Neurosoft,Russia) with a biphasic current waveform. The handle of the coil pointed backwards at 45° to the midline. MEPs were recorded from right APB using EMG amplifier. Resting motor threshold was found at 43% of device maximum output (MO). The intensity eliciting MEP of 0.5 mV was 51% of device MO. Series of stimuli were sent with 1 minute interval. Each stimulus consisted of pair of pulses. First (conditioning) had intensity 43%, second (testing) - 51%. Inter-pulse interval (ISI) in first stimulus was 2 ms. It had been increasing by 1 ms after each next stimulus. Last pair was sent with 14 ms ISI.

All MEP amplitudes elicited by stimuli with ISI below 7 ms were lower than baseline. All MEP amplitudes elicited by stimuli with ISI in a range 8-14 ms were higher than baseline. Amplitude of last curve recoded with 14 ms ISI was 2.5 mV (4.75 times higher than baseline).

Conclusion: Using of pair of biphasic pulses in SICI experiment gives the same results as using of pair of monophasic pulses.
Abstracts of Poster Presentations – Poster Session 60 – Transcranial magnetic stimulation

P1078
Early Diagnostic Criteria for Parkinson Disease

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Question

Parkinson’s disease (PD) is a progressive neurological disorder. Diagnosis is based on the results of clinical assessment. From that reason early cases of PD present a diagnostic challenge.

Methods

We analyzed possibility of diagnosis in 10 “de novo” Parkinson’s disease patients, based on characteristics of the input-output curve. Input-output (IO) curve was analyzed in two ways: gain of the curve for low-level transcranial stimulation (110% and 120% of motor threshold-MT) and calculation M of the IO curve “quality”, based on the quantum Tsallis entropy $E(q)$: $M=\sum p(x_k)q^{1-(q-1)E(q)}$, where $K$ is the number of selected points of IO curve, $x_k$ are selected points of IO curve and $p$ stands for probability.

Results

Healthy subjects with MT100μV have gain in a limited interval (70%), while all PD patients have gain that is out of that interval. IO curve quality of the healthy subjects is in the limited interval, while 80% of the PD patients have quality outside of the interval. There were no difference between subject at 120% of MT.

Conclusions

A thorough understanding of the broad spectrum of clinical manifestations of PD is essential to the proper diagnosis of the disease. It seems that unhealthy subjects on the lower level of stimulation (110% of MT) have bigger increase of the MEP, which means that in the early stage of illness they have compromised inhibitive regulatory mechanisms.


Modulation of MEP amplitudes after transcranial magnetic stimulation by ongoing cortical beta- and gamma-band oscillations

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Question

The human primary motor cortex responds to transcranial magnetic stimulation (TMS) with a variable motor-evoked potential (MEP). The relation between TMS responses and the ongoing oscillatory activity of the brain is still controversial challenged by the fact that MEP amplitudes are influenced by several factors such as proprioceptive input, muscle activity and spinal oscillations. In the present study, this challenge was addressed by a combination between TMS and the brain-computer interface (BCI) technique.

Methods

We developed a BCI-based neurofeedback environment with the opportunity to provide haptic and/or visual feedback of electromyographic (EMG) and electroencephalographic (EEG) activity conditioning subjects to reproducibly activate the central motor system both with and without muscle activation. Concurrently, navigated TMS was applied to the contralateral motor cortex in order to probe MEP amplitudes during different brain-states. In experiment 1, healthy subjects performed three different tasks: movement execution (ME), movement imagery (MI), and passive movements. In experiment 2, subjects were trained to modulate either α- or β- component of the sensorymotor rhythms (SMR) by MI.

Results

In conditions of central motor system activation (ME and MI), pre-stimulus SMR correlated negatively while pre-stimulus γ-oscillations correlated positively with MEP amplitudes. Experiment 2 disentangled a negative correlation between MEP amplitudes and β- but not α- frequencies as well as a positive correlation with γ-oscillations. Furthermore, MEP amplitudes increased over the course of the experiment when TMS was applied during β- but not α- feedback training.

Conclusion

Our results indicate a frequency-specific gain modulation of MEP amplitudes by cortical β- and γ-oscillations. TMS application in combination with the BCI technology provides a powerful tool for brain-state dependent stimulation, e.g. in the context of neurorehabilitation.
Induction of late I-waves and functional connectivity within the cortical motor system

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Introduction

Different mechanisms underlie the induction of motor evoked potentials (MEP) via transcranial magnetic stimulation (TMS). Besides direct depolarization of pyramidal cells (D-waves), also monosynaptic (early I-waves) and more complex oligosynaptic input (late I-waves) on pyramidal cells contribute to the generation of MEPs [1]. However, little is known about the involved neuronal circuitry. The assessment of functional connectivity (FC) via functional magnetic resonance imaging (fMRI) allows analyzing network interactions. We hypothesized that FC within the cortical motor system is related to the induction of I-waves via TMS.

Methods

20 healthy subjects underwent fMRI and TMS recordings, performing an isometric contraction task with their right hand. TMS with different coil orientations (posterior-anterior (PA), latero-medial (LM) or anterior-posterior (AP) directed current) was applied to left M1 in order to induce different onset-latency MEPs, reflecting the recruitment of distinct I-waves [2]. Seed-based whole brain FC was computed, using the TMS motor hotspot as seed region. Finally, voxel-wise correlations between fMRI connectivity strengths and TMS-latencies were calculated.

Results

MEP-latencies were longer and more variable for AP compared to PA and LM stimulation. Interestingly, FC of the TMS stimulation site with key motor regions (M1, SMA, dorsal and ventral PMC) was inversely correlated with AP-LM but not PA-LM differences, with small AP-LM differences (indicating a relative ease of early I-wave recruitment) being associated with higher FC within the cortical motor system.

Conclusions

Late I-waves are thought to reflect activity in pathways linking M1 with SMA and PMC [3]. Our results strongly support this hypothesis linking I-wave recruitment with cortico-cortical projections from premotor areas onto M1. Furthermore, we provide evidence that the pre-activation of such pathways underlies the inter-individual variability in the response to TMS.

References

Modulation of neocortical sensory processing by theta-burst transcranial magnetic stimulation in a rat model

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Question

Recently, we could show that theta-burst stimulation (TBS) applied via transcranial magnetic stimulation (TMS) to the rat brain strongly reduced the neocortical expression of parvalbumin (PV), indicative of a reduced activity of fast-spiking inhibitory interneurons. The current study had been conducted to test how intermittent and continuous TBS (iTBS, cTBS) affect spatial and temporal integration of sensory stimuli in rat barrel cortex with special focus on forward and recurrent type inhibitory interactions.

Methods

We recorded multi-unit spiking activity from barrel cortex upper layer 4 in urethane-anesthetized rats before, between and up to three hours after five blocks of either iTBS, cTBS or sham-TBS (600 pulses each). Single or paired tactile stimuli were applied to the principal (PW) and/or directly adjacent whisker (AW). Subsequently, cortical PV, GAD67 and c-Fos expression was analysed by immunohistochemistry (IHC).

Results

In contrast to sham and cTBS, iTBS resulted in a strong enhancement of a late sensory response component (>19ms) while the very early transient response (8-18ms) was not affected. In addition, iTBS strongly weakened the suppression of the second response resulting from paired stimulation of only the PW, or first AW then PW at 20ms intervals without affecting the first response. The first cTBS block had almost no or slightly opposite effects but a weak disinhibitory effect similar to iTBS evolved after 4-5 repetitions of cTBS. IHC revealed a reduced PV and GAD67 but increased c-Fos expression after iTBS which was not evident after cTBS.

Conclusions

Considering that iTBS enhanced only late but not early response components and only the second responses in a pair, we conclude that iTBS weakened intracortical recurrent-type inhibition likely mediated by PV+ interneurons but not thalamocortical forward inhibition. It has been shown that a subset of PV+ neurons receives strong excitatory cortical input while another group receives primarily thalamic input (Staiger et al. 2009, Brain Struct Funct 214:1-13). The former likely receive strong excitation during activation of cortical axons with TMS. Recently, it has been shown that the late sensory response component is essential for stimulus awareness in rats (Sachidhanandam et al. 2013, Nat Neurosci, DOI 10.1038/nn.3532).
P1082
Investigating the mechanisms underlying Paired Associative Stimulation

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Background

While Paired Associative Stimulation (PAS) is likely mediated by spike timing dependent plasticity (STDP), it is not known why repeated stimulation that inhibits the test response (short latency afferent inhibition, SAI) leads to synaptic potentiation. Cellular studies showed that hyperpolarization of the postsynaptic cell (e.g. induced by SAI) inhibits long term potentiation (LTP) and favors long term depression-like effects. We compared the efficacy and the underlying mechanisms of PAS with TMS delivered at N20+2 and N20+6ms latency.

Methods

7 participants (more subjects are being recruited) received PAS with median nerve stimulation (MNS) and TMS delivered at N20+2ms or N20+6ms in separate sessions. Motor evoked potentials (MEPs) were recorded from the dominant hand. For PAS, TMS was adjusted to produce ~1mV MEP in the absence of MNS. Corticospinal excitability was assessed baseline and up to 45 minutes post-PAS. The influence of MNS on SICI (ISI 2ms) and SICF (ISI 1.5ms) was assessed at N20+2 and N20+6ms latency.

Results

PAS (N20+6) was more effective than PAS (N20+2) at increasing corticospinal excitability (MEP amplitudes compared to baseline were 117±12% vs. 164±20%, respectively). SAI was stronger at N20+2 compared to N20+6ms, and correlated with PAS efficacy. SICF was more facilitated and SICI more disinhibited during SAI at N20+2 compared to N20+6ms latency.

Discussion

The results suggest that PAS LTP-like effects are opposed by the inhibitory effects of SAI, and PAS was more effective at N20+6 when SAI was minimal. These effects are not due to greater activation of late I-waves or greater disinhibition of interneurons during SAI at this later interval, because at N20+6ms there was less I-wave facilitation and less disinhibition of SICI compared to N20+2ms latency. While the interaction effects and a strict adherence to STDP would predict that PAS at N20+2ms latency would be more effective, the results instead point to the dominant influence of SAI in inhibiting PAS plasticity at N20+2ms at which SAI was strong, and that when SAI has resolved at N20+6, plasticity induction becomes more effective. The likely mechanism is that associative plasticity is strongest when associative inputs can cause the cell to fire resulting in reinforcement of synapses via the back propagating action potential.
Homeostatic metaplasticity of corticospinal excitatory and inhibitory intracortical neural circuits in human motor cortex

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Question

Homeostatic metaplasticity, a fundamental principle for maintaining overall synaptic weight in the physiological range in neuronal networks, was demonstrated at the cellular and systems level predominantly for excitatory synaptic neurotransmission. Although inhibitory networks are crucial for regulating excitability, it is largely unknown to what extent homeostatic metaplasticity of inhibition also exists. Here, we employed intermittent and continuous transcranial magnetic theta burst stimulation (iTBS, cTBS) of primary motor cortex (M1) in healthy subjects for induction of long-term potentiation (LTP)-like and long-term depression (LTD)-like plasticity.

Methods

We studied metaplasticity by testing the interactions of priming TBS with LTP/D-like plasticity induced by subsequent test TBS. Changes in excitatory neurotransmission were measured by the input-output curve of motor evoked potentials (IO-MEP), and changes in GABAergic inhibitory neurotransmission by the input-output curve of short-interval intracortical inhibition (IO-SICI, 4 conditioning stimulus intensities of 70-100% active motor threshold, interstimulus interval 2.0 ms).

Results

Non-primed iTBS increased IO-MEP, while non-primed cTBS decreased IO-MEP. Pairing of identical protocols (iTBS→iTBS, cTBS→cTBS) resulted in suppression of the non-primed TBS effects on IO-MEP, and pairing of different protocols (cTBS→iTBS, iTBS→cTBS) enhanced the test TBS effects on IO-MEP. While non-primed TBS did not result in significant changes of IO-SICI, iTBS→iTBS resulted in IO-SICI decrease, and cTBS→cTBS in IO-SICI increase compared to the non-primed conditions. The changes in SICI induced by priming TBS correlated with the changes in MEP induced by test TBS.

Conclusions

Findings demonstrate that plasticity in both excitatory and inhibitory circuits in human motor cortex are regulated by homeostatic metaplasticity, and that priming effects on inhibition contribute to the homeostatic regulation of plasticity in excitatory circuits.
P1084
Motor effects of deep repetitive transcranial magnetic stimulation with H-Coil in Parkinson’s disease: a randomized, double blind, placebo-controlled study

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Objective

One limitation to the treatment of motor symptoms in Parkinson’s disease-PD is the relatively widespread diffusion of cortico-cortical circuits affected in this condition. The H-coil allows a wider and deeper stimulation field compared with coils previously applied in PD. We aimed at evaluating safety and efficacy of deep repetitive transcranial magnetic stimulation (rDTMS) performed with H-Coil as add-on treatment for motor symptoms in PD. This is a double-blind, randomized placebo-controlled study.

Patients and Methods

Sixty PD patients underwent 12 sessions over 4 weeks of 10 Hz rDTMS, after randomization into 3 groups: Group 1 (real rDTMS on primary motor-M1 and prefrontal-PF areas; Group 2 (M1 real, PF sham), Group 3 (both sham stimulations). Primary outcome was percent reduction of Unified Parkinson’s Disease Rating Scale (UPDRS) part III, OFF therapy. Secondary outcomes were: changes in UPDRS part III sub-scores; improvement in timed tests (Hand Tapping-HT, Foot Tapping-FT, Walking Time-WT at20 meters, Nine Hole Peg Test -NHPT). Statistical analysis was performed using Mann-Whitney or t test according to data distribution. Primary outcome was tested in hierarchical order, by comparing the two real groups (1-2) only if their pooled data significantly differ from sham (Mann-Whitney).

Results

No drop-outs or serious adverse effects were recorded during the study. One patient randomized to real M1/PF stimulations was excluded soon after for uncontrolled diabetes. Patients receiving real rDTMS showed a significant improvement vs. sham in UPDRS III (p=.007), tremor subscore (p=.011) and lateralized sub-scores (p=.042 and p.012 for worse and better sides respectively). Timed tests significantly improved in the real group when considering the worse side (HT p=.041, FT p=.012, NHPT p=.003). Following the hierarchical analysis, both real rDTMS groups (1 and 2) improved significantly more than sham in UPDRSIII (p.010 and p.045 respectively), while they did not significantly differ between them.

Conclusion

Repetitive deep brain stimulation with H-Coil is safe and potentially effective as add-on treatment in PD. These encouraging preliminary results need to be more deeply explored and further validated on a larger scale.
Is it possible to define the “dose” of navigated TMS in non-motor cortical areas?

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Introduction

We evaluated the theoretical factors and empirical evidence for reliable dose definition of navigated transcranial magnetic stimulation (nTMS), which is delivered outside motor areas and produces no immediate visible responses when activating cortical neurons.

Results

The clear sensitivity of single pulse TMS responses to the orientation of the coil suggests that the predominant activation mechanisms are related to the trajectories of pyramidal tract axons and their direction along the cortical columns. Theoretical calculations and physiological evidence indicate that when local neuronal population is subjected to about 60 V/m electric field, transmembrane potential changes and subsequent action potentials are evoked in normal conditions. Columnar organization is a dominant feature of the entire cortical mantle when modulated with TMS. Thus, the roughly same value, which can be individualized by measuring the electric field threshold for evoking motor evoked potentials in optimal delivery orientation, should be sufficient lower limit estimate for, e.g., therapeutic applications of nTMS. Nevertheless, when activation thresholds of the target area have been affected, the general level of cortical excitability can be verified at the motor area.

Conclusions

Physiological principles and empirical evidence imply that nTMS is most effectively applied by orienting the electric field longitudinal and orthodromic to the greatest possible number of neurons at the site of interest. When this principle is obeyed, simple theoretical calculation provides means of delivering rather uniform stimulating current and thus feasibly uniform “dose” of TMS to cortex intra- and interindividually.
DLPFC and left supramarginal gyrus increases the recognition of instrumental and functional violations in transitive action representation

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The correct outcome of transitive actions depends on an object’s use considering both the instrumental and functional features. Indeed, the representation of object-related action includes the correct/incorrect instrumental use and the congruous/incongruous functional use of the object. Objectives. The contribution of frontal (dorsolateral prefrontal cortex, DLPFC, experiment 1) and posterior (supramarginal gyrus, experiment 2) areas to process these semantic violations (instrumental vs. functional) in action semantic representation was explored.

The DLPFC and supramarginal gyrus activity was appositely modulated by tDCS (transcranial direct current stimulation). The effect of tDCS (anodal, excitatory) when subjects processed congruous/incongruous object-related actions was verified by measuring the modulation of the ERs (Error Rates) and RTs (Response Times). Forty-three subjects performed the detection task within a dynamic context (video tapes representing a sequence of four action frames ending with a congruous vs. incongruous action).

Significantly decreased RTs were observed for incongruous stimuli in the case of DLPFC stimulation compared to the sham condition. This effect was related to both the instrumental and functional semantic violations, suggesting that the activation of the DLPFC may increase the ability to analyse the semantic anomaly independently from the anomaly type, which would limit the cognitive costs. In contrast, parietal stimulation reduced RTs only in response to functional semantic violations (fig 1a and 1b).

Thus, different cortical contributions by anterior vs. posterior areas occurred in response to semantic anomalies respectively for generic expectancy violations (more frontally distributed) and specific functional violations (more frontally distributed).
INTERACTION OF NEURONAL ANISOTROPY AND MOTOR CORTEX EXCITABILITY: A NAVIGATED TMS-DTI STUDY

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Question

TMS is considered to activate neuronal bundles parallel [1] to the induced electric field (EF) and bundles having bends [2]. TMS induced activations are, however, also affected by several physiological factors [3] that might overpower the influence of neuronal organization. Our aim in this study was to evaluate whether there is a measurable connection between the neuronal anisotropy and the TMS evoked responses.

Methods

MR and diffusion tensor images (DTIs) were taken from nine healthy subjects (6 females, age range: 27-59 years). Navigated TMS was applied to the cortical representation areas of the right and the left hand FDI and the resting motor thresholds (rMTs) were measured. Next, the stimulation was given at the representation areas at intensities of 105% and 120% of the rMT while rotating the coil within ±135 degrees from the optimal coil direction. Motor evoked potentials (MEPs) were used to form our previously introduced anisotropy index (AI) [4] which is calculated from the MEP amplitudes as a function of the stimulation angle. Subject-wise fractional anisotropy (FA) values of the stimulation targets were determined in spheres (radius=2mm) centered at 8mm depth from the cortical surface of the M1 hand area.

Results

FA values did not correlate with rMT (r≤0.201, p≥0.605). On the right hemisphere, EF at an intensity of 120% of rMT correlated with FA (r=0.714, p=0.031) and FA correlated with AI (r=−0.753, p=0.019).

Conclusions

An interaction between the motor cortex excitability (EF) and organization of neurons was shown through our newly developed AI as well as through DTI-derived FA.

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P1088
TMS-EEG signatures of GABAergic neurotransmission

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Question

The combination of transcranial magnetic stimulation (TMS) and electroencephalography (EEG) constitutes a powerful tool to directly assess human brain excitability and connectivity. TMS of the primary motor cortex elicits a sequence of TMS-evoked EEG potentials (TEPs). It is thought that GABA-A receptors (GABAAR) modulate early TEPs (< 50ms after the TMS pulse), whereas inhibitory neurotransmission mediated via GABA-B receptors (GABABR) plays a role for later TEPs (at around 100ms after TMS). However, the neurophysiological underpinnings of TEPs have not been clearly elucidated yet.

Methods

We investigated the role of GABA-A and -B-ergic neurotransmission for TEPs in healthy human subjects using a pharmaco-TMS-EEG approach. In the first experiment, the effects of a single oral dose of alprazolam (a benzodiazepine acting at α1, α2, α3 and α5 subunit-containing GABAARs) and zolpidem (a positive modulator, which mainly binds at the α1 GABAAR subtype) were evaluated in a double blind, placebo controlled, crossover study. In the second experiment, we tested the influence of baclofen (a GABABR agonist) and diazepam (a classical benzodiazepine) vs. placebo on TEPs.

Results

Results showed that the two benzodiazepines alprazolam and diazepam increased the amplitude of the negative potential at 45ms after stimulation (N45) and decreased the negative component at 100ms (N100), whereas zolpidem increased only the N45 potential. Baclofen specifically augmented the amplitude of the N100 potential.

Conclusions

In summary, our results provide evidence that the N45 potential reflects activity of α1-subunit containing GABAARs, whilst GABABRs are likely involved in generation of the N100 potential. These findings may help to characterize dysfunction of inhibitory transmission in neuropsychiatric diseases.
P1089
The roles of agency and ownership in rubber hand illusion

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Objective

During voluntary movement, we sense control over the bodily action (agency) and ownership of the body part whereas externally generated movements eliminate agency but not ownership. The aim of this study was to examine whether the sense of agency is required to cancel the shift in the internal sense of hand position induced by the rubber hand illusion.

Methods

A rubber hand illusion (RHI) protocol was administered to induce a shift in the perceived hand position in six healthy subjects. We then examined the effects of three experimental protocols to dissociate agency and ownership. The internal sense of hand position was measured before and immediately after RHI induction, and after each protocol. The protocols are: (i) internally generated voluntary hand movements (VHM), externally generated movements elicited by (ii) transcranial magnetic stimulation (TMS) or (iii) ulnar nerve stimulation (UNS). In the VHM condition, subjects performed voluntary abduction of the index finger. In the TMS condition, single pulses (140% of the resting motor threshold) were used to elicit movements in the first dorsal interosseous (FDI) muscle comparable to the VHM condition. In the UNS condition, UNS intensities were adjusted to produce comparable movements in the FDI muscle. The kinematics of index finger movements were measured using an accelerometer, muscle activities were measured with surface EMG, and subjective ratings of ownership was determined through a questionnaire.

Results

RHI induced a shift in the perceived location of the hand. Only VHM recalibrated the sense of hand positions to the pre-RHI estimates, thus cancelling the illusion. The RHI-induced shift in hand position remained intact following externally generated movements in the TMS and UNS conditions.

Conclusions

These preliminary findings suggest that volitional drive associated with a sense of agency, but not movement per se, is necessary for removal of the rubber hand illusion.
Neuronal dynamic of TMS induced MEPs: a combined TMS-EEG study

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Question

The recording of motor-evoked potentials (MEPs) elicited by single pulses of transcranial magnetic stimulation (TMS) over the primary motor cortex (M1) is a widely used non-invasive technique to assess motor cortex excitability in humans. Recently, it was shown that the electroencephalogram (EEG) can be used to measure TMS-evoked brain potentials (TEPs). Following M1 stimulation, TEPs consist of early latency responses maximal over the stimulation site, followed by later responses hypothesized to originate from frontal and temporo-parietal regions. Here, we characterized the relationship between TEPs and MEPs using machine-learning techniques, with the aim of exploring the functional significance of these brain responses and their relation to M1 excitability. Furthermore, considering that M1 excitability may be expected to vary spontaneously according to intrinsic fluctuations in neuronal excitation, we also examined whether the EEG signal measured before the onset of the TMS pulse is predictive of the elicited MEPs.

Methods

The EEG was recorded using 31 scalp channels. Single pulses of TMS were delivered over the left M1 using an intensity corresponding to the resting motor threshold of the right FDI muscle. The second-order statistic (standard deviation) was calculated using moving windows of variable width (15-200 ms). Linear Discrimination Analysis (LDA) was used to classify trials with no MEPs (magnitude <0.5 µV) and trials with MEPs (magnitude >0.5 µV).

Results and Conclusion

The occurrence of MEPs was determined by both pre- and post-stimulus EEG power, indicating that M1 excitability is dependent on spontaneous fluctuations in cortical oscillatory activity. Furthermore, the relationship between EEG power and MEPs was maximal 10-35 ms after TMS onset, indicating that M1 excitability is a strong determinant of both MEPs and early-latency TEPs.
Abstracts of Poster Presentations – Poster Session 60 – Transcranial magnetic stimulation

P1101
Transient effects of transcranial magnetic quadripulses on the human motor cortex

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Question
Transcranial magnetic quadripulse stimulation (QPS) induces bidirectional long term plasticity depending on the interstimulus interval (ISI) and follows the Bienenstock-Cooper-Munro theory of synaptic plasticity. However, the exact electrophysiological mechanism determining this frequency dependent bidirectionality is not clear.

Methods
In 18 healthy subjects we investigated the effect of one burst of four monophasic TMS pulses at ISIs of 5 and 50 ms. Motor cortical excitability was evaluated by the motor evoked potential amplitude at 5 to 1000 ms after a burst.

Results
Both 5 and 50 ms bursts induced an early facilitation followed by a longer lasting inhibition. The facilitation lasted longer after the 5 ms burst, while the inhibition was more pronounced after the 50 ms burst.

Conclusions
Transsynaptic activation of pyramidal neurons by a single TMS pulse is characterized by an early facilitation and subsequent inhibition. Our results suggest a summation of both excitatory (EPSP) and inhibitory postsynaptic potentials (IPSP) by four pulses applied as one burst. The difference between the two conditions may be the frequency dependency of EPSP- or IPSP-summation. Since IPSP typically peaks at a longer latency, four pulses at 50 ms led to more pronounced summation of inhibition compared to those at 5 ms. These transient effects reflect pure electrophysiological property changes within the cell membrane or synapse and are different from the plastic changes after QPS resulting from synaptic efficacy changes based on some protein synthesis. However, this early frequency dependency may at least partly contribute to the bidirectional character of QPS plasticity.
LP64
Action perception: the mirror neuron system recognizes the temporal properties of movement

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Question

Recognition of movement might rely on both spatial (i.e., body posture) and temporal features (i.e., rhythm among the subcomponents of movement). A wealth of body of evidence suggested that body posture modulates action perception. A question remains still open related to the ability of the mirror neuron system to selectively recognize the temporal features of movement.

Methods

To elucidate this topic we choose a type of movement (execution of un-paced finger opposition movements), of which we know the spontaneous tempo and in a first set of experiments, we recorded cortical excitability by means of TMS, from hand muscles, while subjects were viewing videos showing a hand performing finger opposition movements at a rate similar to, lower or higher than the spontaneous one. Then we tested whether an observational training, consisting in watching a 10 min-video of repetitive finger movements faster than the spontaneous ones, was able to modulate motor resonance, as tested with TMS.

Results

We found that cortical excitability measured in the hand muscle was significantly enhanced when the speed of execution of the observed action was congruent to the spontaneous one than when it was lower or higher than the spontaneous one. More, observational training induced a behavioural shift of the spontaneous execution rate and a modulation in the resonance of the motor system versus the “spontaneous” rate of the observed movements.

Conclusions

Here, we demonstrated that the mirror neuron system is able to selectively recognize temporal properties of a certain movement as belonging to the personal motor repertoire and that learning of temporal characteristics may occur by observational training, in terms of changes in motor behaviour and changes in motor resonance mechanisms. These results open the possibility to either develop tailored protocols of observational training in order to restore movement timing when it is lost and change the innate temporal properties of a certain movement.
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