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Program and Abstracts for the fourth meeting of the

Clinical Neuroscience Bern

19th November 2008

University Hospital
of Psychiatry, Bern

Conference location: Waldau

http://www.kas.unibe.ch/neuro08/

Dear participants,

We are glad to welcome you to the 4th Meeting of the Clinical Neuroscience Network in Bern. About 110 researchers from all different neuroscience-related disciplines will attend the meeting this year. There will be three main lectures and six short presentations in the morning. The main lectures will give an overview about the new possibilities for investigating cerebral functions provided by the positron production initiative at the Inselspital, which open unique potentials for investigating the brain under normal conditions and in neuropsychiatric diseases. During the extended lunch there will be an unguided postersession, however we would appreciate if one of the authors would be available at the poster during the session. In the afternoon four interesting parallel workshops are offered. This year again, we will be happy to offer three poster awards due to a generous grant by the University Hospital of Neurology.

The meeting reflects the wide spectrum of research in clinical neuroscience in Bern and we hope it will further stimulate new joint research initiatives and provide an opportunity to have a fruitful and interesting discussion of ongoing projects. We are convinced that the now fourth consecutive meeting will further strengthen the interfacultary Clinical Neuroscience Network and provide an excellent occasion for a lively and interesting exchange of study results, experience, and knowledge as well as offer the basis for the development of new interesting projects. We are looking forward to seeing you in „Waldau“ and wish you a stimulating an enriching meeting.

Prof. Dr. Thomas Dierks Prof. Dr. René Müri

Organization:

Lilo Badertscher (Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry Bern)
Thomas Dierks (Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry Bern)
Pascal Wurtz (Dept. of Neurology, Inselspital Bern)

Sponsors:
University Hospital of Psychiatry, Bern
University Hospital of Neurology, Inselspital, Bern

Program 19.11.2008

08:00 – 09:00 **Poster attaching**

09:00 – 09:15 **Opening Adresses**

- Prof. Dr. Werner Strik, University Hospital of Psychiatry, Bern
- Prof. Dr. Christian W. Hess, Clinical Neuroscience, Bern
- Prof. Dr. Urs Würgler, Rector, University of Bern

09:15 – 10:15 **Main Lectures:** Relevance of the Isotopproduction at the Inselspital for the Clinical Neuroscience in Bern

- Clinical Aspects: Prof. Dr. Thomas Krause (Head of the Department of Nuclear Medicine, Inselspital)
- Scientific Aspects: Dr. Richard Zimmermann (IBA Molecular, Gif sur Yvette Cedex France)
- Presentation of the Isotopen AG at Inselspital: Dr. Konrade von Bremen (Director SWANtec, Inselspital)

10:15 – 10:45 **Coffee Break**

10:45 – 12:45 **Short presentations**

- Thomas Reber: Nonconscious associative learning of conceptual associations for word pairs that were never presented
- Jaspal Patil: Endogenous angiotensinergic system in neurons of rat and human trigeminal ganglia
- Thomas Nyffeler: One Session of Repeated Parietal Theta Burst Stimulation Trains Induces Long-lasting Improvement of Visual Neglect
- Van Swam Claudia: Possible Dysregulation of Cortical Plasticity in Hallucinating Schizophrenic Patients
- Thomas Nevian: Signalling mechanisms in spike-timing dependent plasticity
- Viviani Roberto: On not thinking about bad things. A perfusion imaging study of a dissociation between response strategies in the presence of emotional information

12:45 – 14:30 **Postersession and Lunch**

14:30 – 16:15 **Workshops**

- TMS applications in Clinical Neurosciences (Chair: Prof. Dr. R. Müri)
- Methods of functional and structural Neuroimaging in Clinical Neurosciences (Chair: Dr. A. Federspiel/ Dr. R. Wiest)
- Scientific EEG and event-related potentials for dummies (Chair: PD Dr. T. König)
- Health Technology Assessment for Clinical Neurosciences: A Medical, Economic and Ethical Evaluation (Chair: Dr. K. von Bremen)

16:15 **Poster Award**

16:30 **End of the meeting**

Table of content

Abstracts by discipline

Neurophysiology (NP)

NP-01

EEG alpha band features associated with fMRI resting state networks

Kay Jann[1], Mara Kottlow[1], Boesch Chris[2], Thomas Dierks[1], Thomas Koenig[1]

[1]Dept.of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Switzerland , [2]AMSM, Dept. Clinical Research, University and Inselspital, Bern, Switzerland

Recently fMRI BOLD signal fluctuations have been observed that characterize different cerebral circuits by synchronous low-frequency oscillations - so called resting state networks (RSNs). However, it is still debatable whether they are caused by neuronal activity or some to brain function more unrelated phenomena (e.g. breathing, heart beats, etc.). Evidence for a relationship between RSNs and neuronal activity may be demonstrated by simultaneous EEG/fMRI measurements. In recent studies BOLD correlates of different EEG rhythms, especially the alpha rhythm, have been investigated. Although the timescale of the BOLD fluctuations and the EEG rhythms are quite distinct, the similarity of the networks described by either method is evident.
Currently we have performed simultaneous EEG/fMRI recordings in healthy subjects during relaxed wakefulness. For individual datasets we could demonstrate correlations between RSNs and EEG rhythms suggesting that these BOLD oscillations are related to neuronal activity.
Understanding the relationship between BOLD signal fluctuations and EEG rhythms may also play a role in revealing psychopathological mechanisms on a biological level, since several psychiatric disorders show changes in BOLD signals and/or EEG characteristics.

With the support of the Swiss National Foundation (Grant no. 320000-108321/1)

Neurophysiology (NP)
Network, fMRI, EEG

Poster

NP-02

Demonstration of an endogenous, neuronal angiotensinergic system in the rat and human heart

Silvan Stucki[1], Jaspal Patil[1], Thomas Schaffner[2], Hans Imboden[1]

[1]Institute of Cell Biology, University of Bern, Bern, Switzerland, [2]Institute of Pathology, University of Bern, Bern, Switzerland

Background:
Since coronary heart diseases and hypertension became a common clinical depiction, lots of investigations in the field were performed. Multiple lines of evidence showed that the octapeptide angiotensin II (Ang II), the active key player of the renin-angiotensin system (RAS), plays among other effects, important roles in the regulation of blood pressure and heart rate. Additionally it has been recognised that Ang II is not only associated with hypertension but also with coronary heart diseases. Treatment of heart failure patients with angiotensin-converting enzyme (ACE) inhibitors improved cardiac function in reducing mortal and morbid events. Furthermore histological studies demonstrated the presence of intracardiac ganglia in both atria in the rat and human heart. In the right atrium, the neurons of these ganglia are mainly distributed around the entries of the pulmonary veins, in the regions of the sinus node and the atrioventricular node.

Goal of this study:
The main goal of this project was to investigate a possible endogenous angiotensinergic system within these intracardiac ganglia mentioned above. As methods, we examined total RNA extracts of different parts of the heart with quantitative real time polymerase chain reaction (qRT-PCR) for different components of the RAS. To show the distribution of Ang II at the cellular level a self generated, monoclonal Ang II antibody was used for immunocytochemical investigations.

Results:
For the first time, we document here the existence of endogenous Ang II in neurons of intracardiac ganglia and their processes in the right and left atria. In addition, fibre pathways were detected in the septum, the right and left ventricle wall in both, rat and human hearts. Angiotensinogen–, ACE- and AT1/AT2-receptor-mRNA were detected by using qRT-PCR in total RNA extracts of the different heart structures mentioned above, while renin mRNA was untraceable. Cathepsin D is a protease responsible for cleavage beneath other substrates also angiotensinogen to angiotensin I. Cathepsin D mRNA was successfully detected in the different heart parts of the rat, indicating a possible alternative pathway to renin.

Conclusion:
Our findings indicate that Ang II is synthesized inside neurons of the intracardiac ganglia within both the atria and may act as an endogenous neurotransmitter locally within the heart. To support these results, in-situ hybridization experiments will be performed to localize the mRNA of the precursor protein angiotensinogen.

Neurobiology (PSB), Neurophysiology (NP)
Renin-Angiotensin-System, Angiotensin II, intracardiac ganglia

Poster

NP-03

GABAb receptors inhibit dendritic Ca2+ spikes in L5 pyramidal neurons by inhibiting L-type Ca2+ conductances.

Enrique Perez-Garci[1], Thomas Nevian[1], Matthew Larkum[1]

[1]*Dept. of Physiology, University of Bern, 3012 Bern Switzerland*

Cortical layer 5 pyramidal neurons are characterized by the presence of a Na+-Ca2+ spike initiation zone in the distal apical dendrite. We previously reported that activation of metabotropic GABAb receptors, in particular the GABAB1b isoform, inhibits these dendritic events for up to 500ms1. We also showed that such modulation acts directly on the Ca2+ conductances1. Here we investigated which Ca2+ conductances are targeted by these receptors.
Dendritic Ca2+ spikes were evoked via direct dendritic current injection with a patch pipette located 700-750 µm from the soma. We then bath applied different Ca2+ channel blockers to assess their impact on the Ca2+ spikes. We found that the block of both, T-and L-type Ca2+ conductances, with Ni2+ (25 µM) and nicardipine (5 µM) or nimodipine (20µM) respectively, reduced the Ca2+ spike by 46 % and 32 % as compared to control. Blockers for R-, P/Q- and N conductances had no significant effect.
We then sought to determine which of the Ca2+ conductances involved in the Ca2+ spikes, namely T- and/or L-, were inhibited by GABAb receptors. When the GABAb agonist baclofen (50 µM) was applied locally to the apical tuft, the amplitude and duration of the Ca2+ spike was diminished by 26%. This modulation was specifically occluded in the presence of nicardipine or nimodipine suggesting an interaction between GABAb receptors and L-type Ca2+ channels.
Two-photon Ca2+ imaging of dendritic Ca2+spikes revealed that GABAB receptors exerted their modulatory effect in dendritic shafts and spines to an equal amount.
In conclusion, whereas both T- and L- Type Ca2+ conductances contribute substantially to the current underlying dendritic Ca2+ spikes, postsynaptic GABAb receptors modulate only L-type channels curtailing the plateau of the dendritic spike which substantially alters the output of the neuron.
1 Perez-Garci et al. 2006 Neuron 18:603-16.

Neurophysiology (NP)
Dendritic Ca2+ Spike

Poster

NP-04

The Neurophysiological Signature of Habitual Prospective Memory Processes

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Background: Tasks that require remembering to realize delayed intentions at the appropriate occasion are defined as prospective memory tasks. Realizing the same prospective memory task repeatedly transfers an episodic into a habitual prospective memory task. Using event-related potentials (ERPs) the goal of the present study was to investigate whether characteristic neurophysiological episodic to habitual transition effects emerge when a prospective memory task is repeated.
Design: ERPs evoked by correctly answered prospective memory cues in the first part of the experiment were contrasted with those of the second part of the experiment under the assumption that the former rather represents episodic and the latter habitual prospective memory.
Results: Results revealed a significant episodic to habitual transition effect expressed by enhanced frontal negativity and parietal positivity in the ERP 400 – 600 ms post-stimulus, a time-window known to be crucial for retrieval of the intention and post-retrieval processes. Additionally, source localization using LORETA attributed the transition to a significantly lower activation in the anterior frontal regions while posterior parietal and occipital regions showed higher activation in the second compared to the first part of the experiment.
Conclusions: The findings indicate that episodic and habitual prospective memory tasks require different processes. While episodic prospective memory is supported by controlled retrieval processes guided by frontal structures, habitual prospective memory was found to be supported by automatic retrieval processes. The present study adverts to the importance of a conceptual distinction between episodic and habitual prospective memory tasks.

Neurophysiology (NP)
prospective memory; habitual prospective memory; event-related potentials; transition

Poster

NP-05

5-HT2 receptors activation increases the number of intrinsically spiking cells in spinal cord cultures

Antonny Czarnecki[1], Vincent Magloire[1], Jürg Streit[1]

[1]*Department of Physiology, University of Bern, 3012 Bern, Switzerland"*

The vertebrate spinal cord is equipped with a number of neuronal networks, the central pattern generators (CPGs) that underlie repetitive patterns of behavior like locomotion. Activity in such networks is mediated by intrinsic cellular properties as well as by the synaptic coupling through neurotransmitters and neuromodulators. Indeed, 5-HT stabilizes fictive locomotion induced by NMDA. The current challenge is to understand the mechanisms underlying rhythm generation in more detail. In this study, we focused on the modulation of the intrinsic activity by 5-HT in spinal cord cultures (E14 rats). We investigated theses cultures (slices and dissociated cells) on the network level using multielectrode arrays (MEAs) and on the cellular level using whole cell patch clamp. All cultures form networks in vitro and showed bursting network activity, which is based on repetitive recruitment of the neurons by intrinsically spiking cells through recurrent excitation. Surprisingly, when we studied the intrinsic properties of neurons that were pharmacologically isolated with bicuculline, strychnine, CNQX and APV, 5-HT had not an effect on the activity of intrinsically spiking cells. However, a percentage of the cells that were not intrinsically spiking under these conditions were transformed into intrinsically spiking cells by 5-HT (34% of the cells). We have then tested the hypothesis that 5-HT acts via modulation of the persistent sodium currents INaP in these neurons. It appeared that 5-HT increased the amplitude of INaP specifically in the non intrinsic spiking cells and thus switched these cells into intrinsically spiking cells via activation of 5-HT2-R. We concluded from these findings that serotoninergic modulation can turn silent into spontaneously spiking neurons and thus activate new sources for rhythm generation in spinal networks.

This work was supported by the Swiss National Science Foundation (SNF Grant N°3100-107641/1)

Neurophysiology (NP)
5-HT2 receptors, Sodium persistent current, Intrinsic activity, spinal network

Poster

NP-06

Possible Dysregulation of Cortical Plasticity in Hallucinating Schizophrenic Patients

Claudia van Swam[1], Andrea Federspiel[1], Daniela Hubl[4], Roland Kreis[2], Peter Vermathen[2], Chris Boesch[2], Roland Wiest[3], Werner Strik[4], Thomas Dierks[1]

[1]Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern/Switzerland, [2]Magnetic Resonance Spectroscopy and Methodology - Department of Clinical Research - University of Bern/Switzerland, [3]Dept. of Neuroradiology, University of Bern, Switzerland, [4]University-Hospital of Psychiatry Bern, Switzerland

Background: Functional and structural studies have substantially increased our knowledge regarding the neurobiological mechanisms of auditory verbal hallucinations (AVH). In this context functional and structural alterations in areas important for language-production and perception including the primary auditory cortex repeatedly have been discussed. However, especially investigations of gray matter in the context of AVH have reported conflicting results. Cortical thickness analysis is a method to investigate subtle structural changes in brain gray matter.
Objective: Using cortical thickness analysis the present study aimed to investigate changes in cortical thickness specific to AVH in schizophrenic patients.
Methods: Anatomical data from 10 patients with chronic schizophrenia suffering from persistent AVH and 10 patients with chronic schizophrenia who never have experienced AVH were acquired. Based on comparison of the cortical thickness of the left hemisphere (speech dominant) between the two patients groups, brain regions with changes being specific for the patients of the hallucinating group were identified.
Results: AH patients demonstrated cortical thinning in regions responsible for sensory processing (parietal operculum, heschl's gyrus and postcentral gyrus) rather than areas related to motor and speech production (premotor cortex and dorsolateral inferior frontal gyrus) in the speech dominant hemisphere.
Conclusions: The results suggest that AVH arise from a complex interplay of slow changing rather enduring structural changes in white and gray matter and faster dynamic functional conditions.

Neurophysiology (NP)
Schizophrenia, Hallucinations, MRI, Cortical Thickness

Talk, Poster

NP-07

Signalling mechanisms in spike-timing dependent plasticity

Thomas Nevian[1]

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Spike-timing dependent plasticity is a plausible mechanism for experience-dependent modifications of synaptic efficacy as the basis of memory formation. The signaling cascades that transform near coincident electrical activity of the pre- and postsynaptic neurons into a change in synaptic strength are quite diverse and yet not fully understood. The initially required step in this sequence is a rise in postsynaptic calcium. We investigated the calcium transients in spines of layer 2/3 pyramidal neurons for spike-timing dependent plasticity protocols by two-photon fluorescence microscopy. The volume averaged calcium transients were uncorrelated to the direction of the change in synaptic efficacy because several pairing protocols evoked similar spine calcium transients but resulted either in long-term potentiation or long-term depression. Thus calcium is not a unique determinant of spike-timing dependent plasticity. We found that the activation of a metabotropic glutamate receptor (mGluR) coupled signaling cascade following calcium influx through voltage-dependent calcium channels is required for the induction of long-term depression whereas long-term potentiation only required a large calcium influx mediated by the activation of NMDA receptors. We conclude that the volume-averaged peak elevation in calcium in spines of layer 2/3 pyramidal neurons determines the magnitude of the long term changes in synaptic efficacy to some degree. The direction of the change is controlled, however, via a mGluR-coupled signaling cascade. mGluRs act in conjunction with phospholipase C as sequence-sensitive coincidence detectors when postsynaptic precede presynaptic action potentials to induce long-term depression. Thus two different coincidence detectors control the induction of spike-timing dependent plasticity.

Neurophysiology (NP)
synaptic plasticity, ltp, ltd, memory, calcium, two-photon microscopy

Talk, Poster

NP-08

Maximal excitation of the brachial plexus by percutaneous monopolar stimulation

Lea Firmin[1], Sebastian Humpert[1], Kai Michael Rösler[1]

[1]*Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland*

Objective: To demonstrate that percutaneous transthoracical stimulation of the brachial plexus at Erb's point reliably elicits maximal muscle responses without provoking adverse effects.
Methods: We retrospectively analysed brachial plexus stimulation results from 1004 consecutive examinations of normal subjects and patients. Transthoracal plexus stimuli were applied as described by Roth and Magistris (1987). Compound muscle action potentials to stimulation at Erb's point (CMAPErb) were compared with CMAPs stimulation of the ulnar and median nerve at the wrist (CMAPwrist).
Results: No adverse effects due to plexus stimulation were observed. In normal subjects, mean CMAP amplitude ratio (CMAPErb / CMAPwrist recorded from ADM) was 0.86 (SD 0.054) and mean CMAP area ratio was 0.94 (SD 0.036). The incidence of low amplitude and area ratios in patients with peripheral neuropathy was significantly higher than in normal subjects.
Conclusion: Transthoracal stimulation at Erb's point is safe and reliably allows supramaximal stimulation of the brachial plexus.

Neurophysiology (NP)
Brachial plexus, transthoracic stimulation, Erb's point, temporal dispersion, amplitude decay, area decay

Poster

NP-09

A method to measure the distribution of central motor conduction times in man

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[1]Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland, [2]School of Mathematics and Statistics F07, University of Sydney, NSW 2006, Australia

Objective: To establish a method to measure the intra-individual distribution of cortico-motoneuronal conduction times (CMCTs) in healthy subjects and patients with multiple sclerosis (MS) using transcranial magnetic stimulation.
Method: We used the triple stimulation technique (TST) to quantify the proportion of excited spinal motor neurons supplying the abductor digiti minimi muscle in response to a maximal magnetic brain stimulus (Magistris et al., 1998). By manipulating the TST delay systematically, it was possible to quantify the contribution of central motor tract portions with submaximal CMCTs to the TST amplitude.
Results: Our method allowed the establishment of an intra-individual CMCT distribution for each of the 25 examined healthy subjects and 16 patients with MS. The density functions derived from the individual CMCT distribution functions showed two peaks in most subjects. The first (second) peak appeared at a CMCT that was 2.7 ms (7.6 ms) longer on average than the individual minimal CMCT (CMCTmin) in healthy subjects. In patients with MS, it appeared at a CMCT that was 5.1 ms (11.4 ms) longer on average than the intra-individual CMCTmin. The mean individual prolongations of the CMCTs at the peaks compared to individual CMCTmin differed significantly between healthy subjects and patients with MS. In addition, we determined the CMCT prolongations at the 25%, 50% and 75% quantiles of the intra-individual CMCT distribution functions as a parameter of distribution width. Mean CMCT prolongations were significantly longer at all quantiles in patients with MS than in healthy subjects.
Discussion: Differing conduction velocities of axons within the pyramidal tract are the most likely factor to cause the observed CMCT distribution. Therefore, the bimodal shape of most intra-individual CMCT distributions suggests a fast and a slow subgroup of pyramidal tract fibres in man, as previously described in animal studies. Slowly conducting central motor fibres contribute more to central motor conduction in patients with MS than they do in healthy subjects.

Neurophysiology (NP)
transcranial magnetic stimulation, motor evoked potentials, triple stimulation technique, multiple sclerosis, central motor conduction time

Poster

NP-10

The suicidal brain: First results of an fMRI pilot-study

Thomas Reisch[1], Erich Seifritz[2], Fabrizio Esposito[3], Roland Wiest[4], Konrad Michel[1]

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Attempted suicide is the main risk factor for suicide. The concept of the suicidal mode suggests that the suicide attempt is a trial to reduce unbearable mental pain. As a consequence a suicide action plan is stored as a contingency plan in the neuronal circuitry and will be re-activated by future experiences of mental pain. We hypothesized that fmri-imaging would allow to better understand the neural correlates of the suicidal mode in comparison to neutral situations, using the technique of autobiographical recall. We further hypothesized that there would be a difference in neural activation between sequences of mental pain preceding suicidal behaviour and sequences of suicide action.
Eight patients who had recently attempted suicide were interviewed with a narrative interviewing technique. Interviews were video-recorded and fully transcribed. Sequences of mental pain related to suicidal behaviour were identified. MRI scanning was done in a 1.5 Tesla Magnetom, using autobiographical recall of three conditions: mental pain, suicide action, and neutral situations. Sequences were applied in a block design, with 25 sec. of relaxation interspersed.
First results of this pilot study will be presented, and their implications discussed.

Neurophysiology (NP), Neuropsychology/ Psychiatry (PSP)
fMRI, mental pain, suicidal behaviour

Poster

NP-11

Congruent music and affective attitude influence the anticipation and perception of emotional events – a sLORETA study on healthy subjects with low depression scores

Mara Kottlow[1], Rahel Willi[2], Thomas Baumgartner[3], Thomas Koenig[1], Lutz Jancke[2]

[1]Department of Psychiatric Neurophysiology, University Hospital of Psychiatry Bern, University of Bern , [2]Department of Neuropsychology, Institute of Psychology, University of Zurich, [3]Institute for Empirical Research in Economics, University of Zurich

Recent studies have shown the influence of music on the experience of emotion intensity. In this study, we replicated the results, additionally analyzing the cued expectation of the emotional stimuli.
17 female subjects with low depressiveness scores participated in this EEG study expecting and afterwards processing blocks of sad or happy pictures with or without congruent music. Peripheral psychophysiology and psychometrical ratings were collected. Alpha frequency band power, inversely related to neural activity, was analyzed with sLORETA (standardized low resolution brain electromagnetic tomography).
A significant increase in brain activity was visible during the announced expectation of happy emotional pictures with music vs. without music in anterior cingulate and inferior parietal regions. During the presentation of conditions with vs. without music, we found significantly higher activations in emotion relevant brain regions, supported by increased empathy ratings and HR during happy conditions with music. Happy compared with sad conditions resulted in activity within emotion relevant areas, whereas sad conditions activated rather visual and auditory perception areas.
Our results show intensity related anticipation and processing of emotional events, presumably influenced by the positive affective attitude of subjects. Definitive argumentations require the outstanding comparison with healthy subjects with high depressiveness scores.

Neurophysiology (NP)
Affective Neuroscience, EEG, sLORETA

Poster

NP-12

Intrinsic activity and positive feedback in motor circuits in organoypic spinal cord slice cultures

Magloire Vincent[1], Streit Jürg[1]

[1]*Department of Physiology, University of Bern, Bühlplatz 5, CH-3012 Bern, Switzerland.*

In co-cultures of embryonic rat spinal cord slices and skeletal muscle, spinal motoneurons innervate muscle fibers and drive muscle contractions. Evidence for this finding comes from multielectrode array (MEA) recordings showing that the activity in the neuronal networks and in muscle fibers in these preparations is frequently correlated. However, besides such correlated activity, muscle contractions often appear in the absence of population activity in the spinal cord networks. Such uncorrelated muscle activity remains almost unchanged when the population bursts in the neuronal networks are blocked by un-coupling the network with the glutamatergic antagonists CNQX and d-APV showing that it is not driven by the population activity in spinal networks. On the other hand, the uncorrelated muscle activity is fully blocked by the muscular nicotinic antagonist d-tubocurarine, showing that it is driven by motoneurons. Together these findings suggest that motoneurons in this preparation are intrinsically spiking in the absence of synaptic input. Analyzing the correlated muscle activity, we found that in 15 % of the population bursts, muscle activity appears at the beginning or before neuronal activity, suggesting that motoneurons drive the population activity. The positive feedback from motoneurons to spinal networks involves nicotinic receptors, since both the total numbers of population bursts as well as the percentage of such bursts that are initiated by muscle activity are reduced by a block of cholinergic but not muscarinic receptors. All together these findings suggest that in organotypic spinal cord cultures, intrinsic firing of motoneurons drives part of the spontaneous population burst activity.

This work was supported by Swiss National Science Foundation Grants No. 3100-067048.0 and 3100A0-107641/1

Neurophysiology (NP)
motoneuron,skeletal muscle, co-cultures, curare, multielectrode arrays

Poster

NP-13

Mechanisms of spike discharge oscillations in organotypic cultures of neonatal rat cortex

Juerg Streit[1], *Ruth Rubli*[1], *Antonny Czarnecki*[1]

[1]*Dept. of Physiology, University of Bern, 3012 Bern, Switzerland*

Early network oscillations and spindle bursts are typical patterns of spontaneous rhythmic activity in cortical networks of neonatal rodents in vivo and in vitro. Later in postnatal development, oscillations in the a and ß range appear in intact animals as well as in cortical slices. The mechanisms underlying such oscillations undergo profound developmental changes in the first postnatal weeks. Their possible role in cortical development and function is not well known. We have studied spontaneous and evoked patterns of activity in organotypic cultures of slices from neonatal cortex grown on multielectrode arrays (MEAs) for several weeks. Episodes of spontaneous spike discharge oscillations at 7 - 25 Hz lasting for 0.6 - 3 seconds appeared in about half of these cultures spontaneously and could be triggered by electrical stimulation of few distinct electrodes. These oscillations usually covered only restricted areas of the slices. Besides oscillations, single population bursts that spread in a wavelike manner over the whole slice also appeared spontaneously and were triggered by electrical stimulation. In most but not all cultures, the oscillations appeared as afterdischarges of strong population bursts. Both population bursts and spike discharge oscillations required intact glutamatergic synaptic transmission since they were suppressed by the AMPA/kainate glutamate receptor antagonist CNQX. The NMDA antagonist d-APV suppressed the oscillations but not the population bursts, suggesting the involvement of NMDA receptors in the oscillations. Electrical coupling by gap junctions was however not required for the oscillations since the gap junction blocker carbenoxolone did not suppress them. In contrast, carbenoxolone facilitated oscillations in a similar way as weak disinhibition by low doses of bicuculline did. The oscillations were thus not of the neonatal type but resembled more those of later postnatal stages, suggesting an in vitro development of cortical circuits. The culture model thus allows investigating the role of rhythm generation in postnatal cortical circuit formation. Supported by SNF grant No. 3100A0-107641/1.

Neurophysiology (NP)
rhythm generation, development

Poster

NP-14

Blockade of activity in the lower layers of the cortex leads to anomalous increases in local field potentials in the upper layers

Tobias Bock[1], Masanori Murayama[1], Matthew Larkum[1]

[1]*Institute of Physiology, University of Berne, 3010 Berne, Switzerland*

Local field potentials can be recorded non-invasively over long periods of time and present an attractive way to measure cortical activity in both human patients and animal experiments. These signals are conventionally interpreted as representing the flow of bulk current in the tissue mostly due to synaptic currents. Beyond this, however, it is often impossible to make firm conclusions about the physical mechanisms underlying these signals. Recently it has been shown in animal experiments that dendrites not only have receptor channels that carry current but also active dendritic spikes that can dominate the local currents. In principle, these currents should also be observable in the extra cellular field potential. We present a study investing the possible influence of calcium spikes in the dendrites of layer 5 neocortical pyramidal neurons. We took advantage of a recent finding using optical recordings of intracellular Ca^{2+} transients in dendrites of layer V (L5) pyramidal neurons which showed that pharmacological block of neuronal activity with tetrodotoxin (TTX) in layer V induces an anomalous increase of dendritic calcium spikes. The study showed that these effects arose from the inhibition of Martinotti cells in layer V which normally suppress these calcium spikes.
We repeated the experiments with TTX in L5 while recording LFPs with a 16-channel linear electrical probe (Michigan Probe) vertically introduced into the hind limb area of the somatosensory cortex of the rat. Under control conditions, hind limb stimuli lead to LFPs in all layers. Using current source density analysis (CSD) we could identify a strong sink in L4/L5 as well as individual action potentials in the LFP recording. Application of TTX to layer 5 lead to a substantial decrease of spikes in this layer and to a disproportionate increases in LFP signals in the upper layers. Since TTX blocks activity, it is hard to interpret these signals as increases in synaptic currents. Our interpretation, consistent with the optical recordings implies that the LFP signal was influenced by the increase in calcium spike activity due to a block of feedback inhibition by L5 interneurons.

Neurophysiology (NP)
extracellular field potentials, dendritic activity, TTX

Poster

NP-15

Time dependent effects of levodopa / benserazide and pramipexole on periodic leg movements (PLM) in patients with idiopathic restless legs syndrome (RLS)

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Objective: To compare time dependent treatment effects of the dopamine agonist pramipexole (PPX; SIFROLâ) with a half-duration (t1/2) of 8-12 hours with dual-release levodopa/benserazide (L/B, MADOPAR DRâ) (t1/2 = 3-4 hours) on periodic limb movements (PLM) in patients with idiopathic restless legs syndrome (RLS).
Methods: Post-hoc analysis of the PLM-indices of the first to eight hour in bed at baseline and under treatment with PPX or L/B obtained from 46 patients in the double-blind, randomized, Swiss multicenter, comparative crossover trial in 2006* (submitted for publication).
Results: Under baseline conditions the PLM index was significantly larger in the first four hours compared to the second part of the night and both drugs showed a statistically significant reduction of the median PLM-index under treatment compared to baseline which was significantly larger in the first four hours compared to the second part of the night. L/B reduced the median PLM-index from 32.2 to 11.0 in the first four hours of bedtime and from 21.8 to 13.1 in the second part, whereas PPX decreased this index from 35.8 to 9.0 in the first four hours and from 15.7 to 7.4 in the second part. Statistical analysis of the PLM reduction under treatment demonstrated no significant difference between the two drugs, neither in the first four hours of bedtime ($p = 0.207$), nor in the second part ($p = 0.831$).
Conclusion: Both drugs L/B and PPX significantly reduce the PLM index not only in the first four hours, but also in the second part of the night. The absence of any difference between the drugs supports the value of PPX as an alternative to the standard medication L/B in the treatment of RLS patients. On the other hand the equal effect of both drugs in the second part of the night underlines the positive effects of the dual-release formulation in Madopar DR® despite its shorter half-duration.

* The Swiss multicenter RLS Study 2006 was sponsored by Boehringer-Ingelheim

Neurophysiology (NP)
periodic leg movements (PLM), Restless Legs Syndrome, Pramipexole, Levodopa

Poster

NP-16

Learning in populations of spiking neurons: how to find strength in numbers.

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It is widely believed that the aggregation of many individual neurons into a population is a key mechanism for achieving robust information processing in the brain. Thanks to averaging, fluctuations present in the single neurons have only little influence on the population response. However, in the context of reinforcement learning, this averaging has its flip side. Since the single neuron performance is only loosely related to the population response, a global reinforcement signal based on the population response can only unreliably assess the performance of any single neuron. Reinforcement feedback is therefore difficult to be interpreted at the level of the single neuron (or even the single synapse) and, for standard reinforcement algorithms, slows down dramatically with increasing population size. We suggest a novel, biologically realistic form of synaptic plasticity, which combines the reward feedback with the population feedback, and which overcomes the degradation of learning with increasing population size.

Neurophysiology (NP)
computational neuroscience, reinforcement learning, synaptic plasticity

Poster

NP-17

Hierarchical novelty-familiarity representation in the visual cortex

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The roles for top-down signals in visual processing have been intensively studied experimentally in the last few years and have also been modeled theoretically. In particular, predictive coding, where feedback from higher cortical areas carries expectations of lower level activity and the feedforward signal carries the error in those expectations, has been shown to explain the emergence of extra-classical receptive field effects (Rao and Ballard, 1999).

Since top-down predictions cannot be independent of the bottom-up input, the interpretation of a visual scene must be an iterative process in which the initial activation pattern relaxes to a solution matching expectation with sensory experience. However, in models, such as the one of Rao and Ballard, where top-down effects propagate over all layers of the visual hierarchy, the relaxation times are too slow compared to the time scale of visual processing.

Our starting point is the observation that predictive coding results in each higher layer performing principal component analysis of the activity in the preceding lower layer. Importantly, this is done in an unsupervised setting, with limited receptive fields, and without propagating top-down effects through the entire visual hierarchy. In our model, not only the top-down connectivity, but also the effective resulting feedback is confined to proximal layers, yielding fast relaxation.

We study our model's performance after allowing it to learn the synaptic efficacies of two visual processing stages on a set of 1000 natural images (Van Hateren and van der Schaaf, 1998). Despite a compression factor of 4 for each stage, the image reconstruction quality is quite good and very strongly outperforms local averaging, indicating nontrivial principal component extraction beyond the mean. Indeed, the effective receptive fields after learning show neurons specialized for edge detection, simple-like cells, and other, more complex structures.

We have also tested the generalization ability of our model on a set of 200 natural images to which the network had not been exposed during learning. The reconstruction quality was, on average, as good as that on the 1000 familiar images, implying that the learning had resulted in the proper extraction of visual features characteristic of the entire set of natural images as a whole. Thus, hierarchical predictive coding suggests an effective way for the visual system to square the need for fast processing and different abstraction levels with the integration of top-down clues.

Neurophysiology (NP)
computational neuroscience, visual system

Poster

Neurobiology (PSB)

PSB-01

Endogenous angiotensinergic system in neurons of rat and human trigeminal ganglia

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To clarify the role of Angiotensin II (Ang II) in the sensory system and especially in the trigeminal ganglia, we studied the expression of angiotensinogen (Ang-N)-, renin-,
angiotensin converting enzyme (ACE)- and cathepsin D-mRNA, and the presence of Ang II and substance P in the rat and human trigeminal ganglia. The rat trigeminal ganglia expressed substantial amounts of Ang-N and ACE mRNA as determined by quantitative real time PCR. Renin mRNA was untraceable in rat samples. Cathepsin D was detected in the rat trigeminal ganglia indicating the possibility of existence of pathways alternative to renin for Ang II
formation. In situ hybridization in rat trigeminal ganglia revealed expression of Ang-N mRNA in the cytoplasm of numerous neurons. A number of neurons and their processes in
both the rat and human trigeminal ganglia were stained for Ang II. Post in situ hybridization immunocytochemistry reveals that in the rat trigeminal ganglia some, but not all Ang-N mRNA-positive neurons stain for Ang II. In conclusion, these results suggest that Ang II could be produced locally in the neurons of rat trigeminal ganglia. In some neurons Substance P was found colocalized with Ang II. The number of Substance P immunopositive neurons
appears lower than that of those positive for Ang II. The localization and colocalization of neuronal Ang II with Substance P in the trigeminal ganglia neurons may be the basis for a participation and function of Ang II in the regulation of nociception and migraine pathology.

Neurobiology (PSB)
Angiotensin II, Substance P, Pain, Sensory system

Talk, Poster

PSB-02

Cultured midbrain dopaminergic neurons transiently co-expressed serotonergic marker in vitro but not after transplantation in vivo.

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Comprehensive knowledge of the development of neuronal subpopulations in the ventral mesencephalon (VM) is essential for cell replacement strategies in Parkinson's disease. Importantly, it has been reported that several neurons in the VM of adult rats co-express the neurotransmitters dopamine and GABA. Furthermore, co-localization of the dopaminergic marker tyrosine hydroxylase (TH) with GABA and choline acetyl transferase has been described in cultured neuroblasts. In our previous study, we demonstrated that about one third of TH-immunoreactive (-ir) neurons also expressed serotonin (5-HT) in dissociated fetal rat VM cultures. This colocalization was found to be dependent on plating density and culture time. In addition, we observed that treatment with brain derived neurotrophic factor significantly reduced colocalization rate indicating the importance of growth factors for emerging phenotype of TH-ir neurons. In the present study, we now demonstrate by means of double-immunofluorescence, that 5-HT and TH was also co-expressed in neurons from organotypic VM cultures and in expended and differentiated VM precursor cells therefore further corroborating our findings of co-expression of both neurotransmitters in VM cells. As it has been suggested that 5-HT neurons are involved in graft induced dyskinesias in cell replacement approache in Parkinson's disease, we initiated an in vivo study. 6-hydroxydopamine-lesioned rats were intrastriatally implanted with VM tissue grafts and immunohistochemically inverstigated for possible colocalization of TH and 5-HT. Preliminary data showed that one month after transplantation none of the TH-ir neurons in the grafts also contained 5-HT. Taken together, our findings demonstrate that subpopulations of cultured midbrain dopaminergic neurons also express serotonin, an observation which may have impact for studies investigating generation of dopaminergic neurons from neuronal precursors / progenitors. Moreover, grafted VM precursors cells seem to find appropriate environment support after transplantation to follow a specific pattern of differentiation / maturation.

Neurobiology (PSB)
ventral mesencephalon, dopaminergic neurons, serotonergic neurons, transplantation

Poster

PSB-03

Expression pattern of Trefoil factor 1 in the developing and adult rat midbrain

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Trefoil factor 1 (TFF1) belongs to a peptide family (TFF1-3) most distinctly expressed in the gastrointestinal tract, where they play essential roles in the composition and function of the mucosal protective barrier at several discrete levels. TFF peptides have been shown to influence precursor cell migration and epithelial restitution and furthermore to protect cells against apoptosis. TFF1 was first discovered in a human breast cancer cell line, and it has been shown to stimulate the migration of breast cancer cells. Recent years' research has revealed that TFFs also are neuropeptides expressed in some areas of the central nervous system but expression of TFF1 in the CNS is poorly described and in few studies only. In the present study we investigated the expression pattern of TFF1 in the developing and adult rat brain by means of immunohistochemistry. In addition, we studied the effects of a 6-hydroxydopamine (6-OHDA) lesion on the distribution of TFF1-immunoreactive (ir) cells. We detected TFF1-ir cells predominantly distributed in the substantia nigra pars compacta (SNC) and the ventral tegmental area. Phenotypical characterization of TFF1-ir cells in the ventral mesencephalon showed that a great number of TFF1-ir cells in the SNC also expressed tyrosine hydroxylase (TH) whereas co-localization was less pronounced in the ventral tegmental area. TFF1 expression was found almost exclusively in neurons but not in glial cells based on their morphological appearance. Interestingly, we observed that the number of TFF1-ir neurons in the SNC was significantly higher in the early postnatal period as compared to the adult brain suggesting that TFF1 may play a role in the development and/or maturation of dopaminergic neurons. Preliminary data revealed that striatal expression pattern and number of TFF1-ir neurons in the SNC did not differ between 6-OHDA lesioned and control animals hinting to the idea that these cells are not projection neurons. Identifying subpopulation of nigral neurons is of special interest in relation to Parkinson's disease, a neurodegenerative disease characterized by a progressive loss of dopaminergic neurons particularly in the SNC. As a result it is important to achieve detailed knowledge on the biology of these midbrain dopaminergic neurons.
In sum, our study demonstrates that distinct populations of dopaminergic as well as non-dopaminergic midbrain neurons express TFF1 likely developmentally regulated.

Neurobiology (PSB)
dopaminergic neurons, Parkinsons disease, substantia nigra

Poster

PSB-04

Evaluation of Neuronal Stem/Progenitor Cells in Hippocampal Slice Culture for Regenerative Therapies in Bacterial Meningitis

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Background: Bacterial meningitis causes life-long disabilities in up to 50% of the survivors. Brain injury caused by bacterial meningitis prominently affects the hippocampus a brain region involved in learning and memory function. In experimental bacterial meningitis hippocampal injury is characterized by apoptosis of cells in the subgranular zone of the dentate gyrus (DG). In the DG neurogenesis occurs lifelong and this brain structure is therefore potentially well equipped for brain repair. Multipotency and the capacity for continuous self-renewal make embryonic stem cells attractive candidates for cell-replacement studies.
Aim: To investigate tissue repair mechanisms by stem/progenitors cells grafted into organotypic hippocampal slice cultures.
Method: An in vitro co-culture model combining long-term hippocampal slice cultures from postnatal rats (P4/5) with embryonic stem/progenitor cells from the subventricular zone (E14-17) was established to assess whether the stem/progenitors cells survive and integrate into the host tissue. To this end, we expanded stem/progenitor cells from the subventricular zone of embryonic day 14 to 17 rats as neurospheres in vitro. To track the fate of transplanted cells in the host tissue, cells were either labelled chemically or cells were isolated from transgenic rats expressing green fluorescent protein (GFP). Chemically labelled as well as GFP-expressing cells were then grafted into organotypic hippocampal slices in the hilus region of the DG. Cells were allowed to grow in co-culture conditions with the addition of epidermal (EGF) and basic fibroblast growth factor (bFGF). The survival and integration of grafted cells was examined on cryosections of organotypic slice cultures and the differentiation stage was assessed by immunohistochemistry.
Results: Histomorphologic analysis revealed migration and neurite outgrowth of both types of cells into the DG at day 7 after engraftment. In the presence of bFGF and EGF both chemically labelled and GFP-expressing neurosphere cells were able to differentiate and to mature into neurons.
Conclusion: Embryonic derived stem/progenitor cells grafted into organotypic slice cultures survive, migrate, proliferate, differentiate and integrate into the host tissue. The transplantation of neurosphere derived stem/progenitor cells may hold promise for regenerative therapies aimed at repair of apoptotic brain damage in the hippocampus of patients suffering from neurofunctional sequelae after bacterial meningitis.

Neurobiology (PSB)
bacterial meningitis, apoptosis, organotypic hippocampal cultures, neuronal stem/progenitor cells, brain repair mechanism

Poster

PSB-05

Adjuvant glycerol in bacterial meningitis: Anti-inflammatory effect but no neuroptotection in an infant rat model

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Objectives: A clinical study published in October 2007, demonstrated beneficial effects of adjuvant glycerol in children suffering from bacterial meningitis. The study indicates that glycerol significantly reduces severe neurological sequelae. We initiated a study in infant rat pneumococcal meningitis to investigate the mechanisms underlying the beneficial effect of glycerol.
Methods: Eleven days old rats were infected intracisternally with 10 µL saline containing Streptococcus pneumoniae (6.15 log10 cfu/ml, n = 34) or mock-infected with the same amount of sterile saline (n = 8). All animals were treated with ceftriaxone (100 mg/kg body weight s.c., n = 42). Then both groups were randomized to receive either 50 µl glycerol p.o. (1.5 mg/kg body weight, n = 21, i.e. 17 infected and 4 mock-infected animals) or an equal amount of carboxymethylcellulose 2% p.o. (n = 21, i.e. 17 infected and 4 mock-infected animals). At 24 h and 40 h after infection, cerebrospinal fluid (CSF) was obtained by intracisternal puncture. At 40 hours after infection, all animals were sacrificed and the brains dissected. Brain weight and water replacement was determined to assess the density of brain tissue as an index for brain edema formation. Subsequently, the brains were immersion fixed in PFA 4% in PBS followed by sucrose 18% in PBS. Brain sections (45 µm thick) were stained using cresyl violet to determine apoptosis in the hippocampal dentate gyrus and the extent of cortical brain damage. CSF was analyzed for myeloperoxidase (MPO) activity and the concentrations of matrix metalloproteinase (MMP) - 2 and MMP-9.
Results: All parameters were statistically tested to compare infected animals receiving glycerol vs. infected animals receiving carboxymethylcellulose. No significant effect was seen on brain density, brain damage, MMP-2 and MMP-9 concentration at 24 hours after infection. The MPO activity at both time points and the MMP concentrations at 40 hours after infection were significantly reduced by glycerol.
Conclusions: In the present study no reduction of brain damage by glycerol was observed. Nevertheless, our study revealed potential mechanisms underlying a neuroprotective effect of glycerol. The reduced activity of MPO at both time points indicates that less inflammatory cells i.e. neutrophils invaded the CSF. A large body of evidence indicates that MMPs contribute to the development of brain injury in bacterial meningitis. Thus, the decrease of MMP-2 and MMP-9 at 40 h after infection suggests a potential neuroprotective effect of adjuvant glycerol, as found in the clinical study, and may be due to its anti-inflammatory effect.

Neurobiology (PSB)
neuroinfectiology, meningitis, glycerol, neuroprotection, anti-inflammatory

Poster

MR-Methodology (PSM)

PSM-01

Feasability data on a functional magnetic resonance imaging (fMRI) study of the lateral geniculate nucleus: comparison of different sequence types

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Introduction: *After acute demyelinating optic neuritis, recovery to near normal visual acuity is common, despite the frequent persistence of conduction abnormalities detected by the visual evoked potential (VEP). Central adaptation may contribute to the recovery. Cortical reorganization is well described, but adaption is unknown for the first nucleus of the visual pathway, the lateral geniculate nucleus (LGN): This is a small structure which is located where spatial and signal intensity distortions during functional magnetic classical echo planar imaging (EPI) blood oxygenation level dependent (BOLD) sequences are common. Steady state free precession (SSFP) sequences have been used for fMRI and may offer higher resolution without distortion.*

Aim: *To compare EPI with SSFP sequences for functional imaging of the LGN, for further use in a study of optic neuritis.*

Methods: *fMRI with visual stimulation was performed on healthy volunteers with both EPI and SSFP sequences.*

Results: *fMRI with EPI BOLD sequences reliably detected LGN activation. Higher resolution and absence of distortions was confirmed for the SSFP sequences, but with current parameters, functional sensitivity was considerably lower.*

Conclusion: *Activation of the LGN by visual stimulation can be reliably detected with classical EPI BOLD sequences. The SSFP sequences require further optimization regarding functional sensitivity.*

MR-Methodology (PSM)

Poster

PSM-02

Simultaneous eye tracking and functional Magnetic Resonance Imaging: Neuronal mechanisms underlying visual exploration

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The analysis of visual exploration is important for the understanding of strategies used by human subjects during task solving. Eye movements are known to change with task demand. We have previously shown that increasing the task demand results in a subsequent increase of neuronal activity. In the current study the amount of fixations were recorded simultaneously with neuronal activity when subjects performed a visuospatial task of increasing difficulty. Our aim was to examine the relationship between eye-movements and strength of neural activity in the human brain.
Methods: 13 healthy young subjects participated in the study. The paradigm consisted of schematised clock images manipulated to reach different difficulty levels. Functional activity was measured in a 3 Tesla Magnetic Resonance Imaging (MRI) system. Eye-movements (number of fixations) were recorded with a MR compatible infrared camera. We used an extended general linear model, modelling the dependency of the Blood Oxygenation Level Dependent (BOLD) signal on the subjects'visual exploration, to investigate task demand dependent signal changes and to generate statistical parametric maps (SPMs) using t-statistic.
Results: A significant linear relationship was found between BOLD signal amplitude and amount of fixations in the superior parietal lobe and the eye fields in the frontal and parietal regions.
Conclusions: Increasing task demand leads to more visual exploration, which is related to an augmented use of brain resources, especially in regions responsible for visuospatial functions and eye-movement control. Simultaneous recording of eye-movement parameters with fMRI may provide deeper insights into the neuronal mechanism underlying visual exploration in humans.

MR-Methodology (PSM), Neurophysiology (NP), Neuropsychology/ Psychiatry (PSP)

Poster

PSM-03

Signal Reliability Testing of in vivo ^{1}H-SVS-MRS Signals

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Introduction and Purpose
In order to make SV-MRS more clinically viable, assessment of signal-quality and signal-reliability of the data should preferably be handled automatically by the MR-scanner system rather than by medical staff. Signal quality is determined by the line-width, and line-shape and can be estimated by the CramÉr-Rao minimum variance bound. The spectral reliability indicates whether the data can be trusted and can be determined by statistical tests for Gaussiannes of separately stored MRS data-acquisitions. In this contribution, we devise, apply, and test two statistical methods that can be used for fully automated data-reliability-and quality-assessment.

Materials and Methods
The SV-MRS signal reliability of the data is most affected by patient motion during acquisition. In order to assess the reliability of SV-MR-data, it is essential to store the data of each signal acquisition separately, rather than averaging the data of all acquisitions irreversibly prior to storage. For these separately stored data, we have devised, applied and tested two statistical methods:
a) Statistical normality tests of the signal noise applied on these separately stored signals,
b) Application of special type of reconstructive order-statistics filtering (median-filtering), if tests under a) fail

Results
We demonstrate the method on an in vivo proton brain case recorded at 3T with and without patient motion. The estimated skewness and kurtosis MRS-signals (3rd and 4th moment about the mean) are sensitive parameters for detecting signal unreliabble MRS-signals. Median filtering is applied on non-reliable spectra before quantification in order to minimize signal artifacts due to outlier signals.

Conclusion
Combination of statistical tests with median filtering can provide user-free reliability and quality assessment and will help to improve the value of SV-MRS in clinical diagnostics.

MR-Methodology (PSM)
Magnetic Resonance Spectroscopy, reliability assessment, quality assessment

Poster

PSM-04

Use of imputation techniques for the reconstruction of virtual parametric maps of segmented brains: With a case study of ADC map changes in schizophrenia

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Introduction
In structural imaging, the signal in each voxel is often a mixture arising from different tissues (grey, white matter, or CSF). This phenomenon, which goes under the name of partial volume effect (PVE), constitutes a potential confound in statistical analysis of images using the statistical parametric mapping approach. The elimination of voxels in which PVEs occur is fraught with difficulties, since they do not occur in the same position across subjects. Here, we explore the use of a statistical technique, imputation, to overcome this problem.

Methods
Imputation consists in replacing missing data (in this case, voxels contaminated by PVEs) with randomly generated data having the distribution of the observed data (in this case, voxels without or low PVEs). A preliminary segmentation procedure provides here estimates of the existence of PVEs in each voxels. Statistical inference must take into account the replacement of data through imputation.

Results
We present imputed parametric maps of apparent diffusion coefficients (ADC) in white matter constituting a virtual reconstruction of this segment from data with low PVEs. Further, we apply this technique to a comparison sample of schizophrenic subjects, carrying out two separate comparisons, one for gray and one for white matter. We show that most of the changes demonstrable in the schizophrenic sample with ADC maps arise from the gray matter compartment.

MR-Methodology (PSM), Neuropsychology/ Psychiatry (PSP)
diffusion-weighted imaging, schizophrenia

Poster

PSM-05

Histidine transport dynamics across blood brain barrier: Initial magnetic resonance spectroscopy measurement

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Introduction:
In this work, we will present our initial findings on histidine transport dynamics across blood brain barrier.

Method:
The study involves blood histidine level (HL) and brain HL measurement after a single dose of 400mg/kg body weight of histidine. The blood HL is measured ex vivo with mass spectroscopy, and brain HL via in vivo with magnetic resonance spectroscopy (MRS) [1]. The healthy volunteers receive an initial blood test and MRS measurement. They are then given the histidine orally with 180mg zinc tablet supplements, and followed up with multiple sessions of MRS measurement and blood test for 12 hours. The MRS voxel is located immediately above the lateral ventricle in the medial part of the brain. This location is chosen for the large 65x45x20mm3 MRS voxel size in a relatively uniform volume of the brain (no contribution from ventricles or skull) The size is necessary because of the low intrinsic concentration of histidine in normal human brain.

Result:
Brain HL reaches a peak around 5 hours after ingestion, preceded by a maximum HL concentration in blood of about 4500umol/L around 3 hours after intake. While blood HL decreases after the peak, brain histidine concentration reaches a ceiling and remains at that level for many hours for some volunteers. Between subjects, large inter-individual differences have been found. Brain HL quoted is relative to normal HL (before histidine loading); absolute quantifications of brain histidine concentration are in progress. To date we have scanned a total of 8 volunteers.

Discussion/Conclusion:
There are some intriguing observations in this study. Firstly, the histidine uptake curve for blood (approximately 40 times more than normal range at peak level) is different among volunteers. This is not expected as the volunteers have same diet and the histidine was given in powdered form for fast uptake. Secondly, the brain HL should have the same but delayed dynamics as blood HL, but this is only true for some volunteers. Further analysis is necessary for understanding the histidine transport dynamics.

[1] P. Vermathen et al. Magn Reson Med, 43(5):665–75, 2000.

MR-Methodology (PSM)
histidine, MRS

Poster

PSM-06

Breaking language: A paradigm that dissociates semantic and phonological functions in left posterior temporal and parietal brain regions

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Previous functional Magnet-Resonance-Imaging (fMRI) findings suggest a dissociation of language (i.e., phonology and semantic) functions in posterior temporal and parietal brain areas. However, this assumption is mostly derived from group analyses that compare activations patterns across different stimuli and subjects groups. Here, we present results of a simple block-design paradigm that localises language functions connected to left posterior brain areas in group and single subject analyses by demanding semantic and phonological judgements to the same word-stimuli. The subjects (10 males) judged words according to semantic (living?, yes/no) and phonological (2 syllables, yes/no) features via button press. The left angular gyrus (BA39), a multimodal brain areas thought to sub-serve semantic retrieval, was less deactivated for semantic compared to phonological judgements. During phonological judgements we observed enhanced activation compared to semantic decisions in a left parieto-frontal network, comprising the intraparietal region. These areas are associated with the phonological working memory loop and the mirror neuron system. Our results confirm previous findings. Hence, the present paradigm constitutes a research tool that dissociates distinct language functions and corresponding brain regions.

MR-Methodology (PSM), Neuropsychology/ Psychiatry (PSP)

Poster

Neurology (PSN)

PSN-01

Long-term Follow-up with Diffusion Q-Ball Imaging after Ischemic Stroke in Childhood – a Clinical Outlook

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Introduction
The remarkable flexibility of the maturing brain to recover after an injury is a longstanding discussion in neuroscience. However, literature is still lacking details as to what extent injuries in specific areas impact other brain regions. Moreover, the time lapse of structural changes is largely unknown. This unsatisfying situation makes planning of adequate and specific therapeutic interventions difficult. Therefore, the aim of the present study is to obtain objective records of individual cerebral reorganisation processes during sensitive periods after ischemic strokes in childhood.

Subjects and Methods
Children underwent Diffusion Q-Ball imaging (QBI) examination three times within one year post-stroke. The examinations took place one month, three months and one year after occurrence of the arterial ischemic stroke. The diffusion sequence was a twice-refocused balanced echo planar sequence used along with house-internal modifications concerning the number and distribution of the calculated gradient directions. All experiments were performed on a TIM-Trio 3.0T scanner (Siemens). Generalized fractional anisotropy and ADC maps were calculated in order to detect degeneration and to investigate potential changes in reorganization.

Results
The comparison of intra-individual data of the different time slots show axonal changes over time. Structural changes have been detected near the lesion as well as in remote areas. Variances in the distribution of the axonal fibres have been observed in homotopic areas of the injured tissue as well as in functionally connected regions. Furthermore, the analysis showed that even very circumscribed lesions may have extensive impact on reorganisation processes in the maturing brain.

Conclusion
QBI provides a unique insight into the dimensions of neuroplasticity after ischemic stroke. Its non-invasive character allows individual analysis of the extent of structural changes over time. This method may thus be an excellent instrument to assess the severity of ischemic brain insult. In the future it may also help evaluate therapeutic interventions and may provide another benchmark for the effectiveness of rehabilitation after stroke.

MR-Methodology (PSM), Neurology (PSN), Rehabilitation (PSR)
Pediatrics, Ischemic stroke, Diffusion Q-Ball Imaging, Neuronal reorganisation

Poster

PSN-02

Scene exploration with central field loss

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We evaluated the impact of central scotomata on eye movements during a binocular search task on natural scene images in eight patients with age-related macular degeneration and four patients with Stargardt disease.

Patients' search performance and eye movements were compared with controls' data under two experimental conditions, with focused and blurred images. Blurred images were used to simulate a reduced visual acuity in controls.

AMD patients' performance and eye movement measures were dissimilar to those obtained in both control conditions. Their performance was reduced and they made shorter fixations. In contrast, Stargardt patients' results differed from controls in the focused condition but were similar to those of controls in the blurred condition.

This suggests that Stargardt patients are better adapted to their visual field defect than AMD patients, as their compensation strategies rely on a broader exploration of images. Similarly to previous results obtained in normally-sighted individuals, fixation distribution was inhomogeneous in patients, revealing a tendency to make more frequent and longer fixations in the central part of the images.

Neurology (PSN)
eye movements, visual exploration, age-related macular degeneration, central field loss, eccentric fixation

Poster

PSN-03

Erythropoietin Improves Hearing Loss and Neuronal Regeneration after Experimental Pneumococcal Meningitis

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Background: Up to half of patients surviving pneumococcal meningitis suffer from neurologic sequelae including hearing loss, memory and learning difficulties. In experimental pneumococcal meningitis, these functional deficits are associated with loss of neurons in the cochlea for hearing loss and in the dente gyrus of the hippocampus for learning deficits, respectively. Erythropoietin (EPO) has been shown to act neuroprotective in paradigms of brain injury including ischemia, hypoxia, and encephalitis. Here, the effects of EPO were evaluated in an infant rat model of pneumococcal meningitis.
Material and Methods: Pneumococcal meningitis was induced in 11 day old Wistar rats by intracisternal injection of Streptococcus pneumoniae. Control littermates were injected with saline. Eighteen hours after infection, antibiotic therapy (ceftriaxone, 100 mg/kg s.c. bid) was initiated. Animals were randomized for treatment with EPO (500 U/30 g) or an identical volume (150 µL) of saline for 5 consecutive days after infection. In order to label dividing cells, bromodeoxyuridine (BrdU) was administrated for 3 consecutive days, directly after the infection or 3 weeks later. Hearing capacity was tested in both ears assessing auditory brainstem response 3 weeks after infection and animals were sacrificed subsequently for histomorphometry. BrdU cell density was determined in the dentate gyrus of the hippocampus.
Results: Hearing loss assessed 3 weeks after infection was significantly attenuated upon EPO treatment. While hearing threshold in infected, saline treated, animals was 81.1±17.1 dB (n=26), this threshold was reduced to 69.8±20.6 dB in infected, EPO-treated animals (p=0.04, t-test). In the hippocampus, EPO significantly (p=0.04, t test) increased the rate of cell proliferation in the dentate gyrus 3 weeks after infection (262±123 BrdU positive cells/mm2, n=5) when compared with infected animals treated with saline only (148±21 cells/mm2, n=7).
Conclusion: In experimental pneumococcal meningitis EPO attenuates hearing loss and increases cell proliferation in the neurogenic zone of the hippocampus. Ongoing studies will clarify whether the mechanism underlying this pleiotropic effect is due to a neuroprotective effect during the acute disease or an effect supporting regeneration in the inner ear and the hippocampus respectively.

Neurology (PSN)

Poster

PSN-04

One Session of Repeated Parietal Theta Burst Stimulation Trains Induces Long-lasting Improvement of Visual Neglect

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Visual neglect is a frequent disability in stroke and adversely affects mobility, discharge destination and the length of hospital stay. It is assumed that its severity is enhanced by a released interhemispheric inhibition from the unaffected towards the affected hemisphere. We aimed to test whether parietal inhibitory theta burst transcranial magnetic stimulation (TBS) over the unaffected hemisphere can induce a long lasting improvement of visual neglect by reducing the interhemispheric inhibition.
Eleven patients with left-sided visual neglect due to subacute right hemispheric stroke were included in the study. Four conditions were tested: 1) two trains of TBS over the left contralesional posterior parietal cortex (PPC); 2) four trains of TBS over the contralesional PPC; 3) sham stimulation over the contralesional PPC; 4) control condition without any intervention. The TBS effect on visual neglect improvement was evaluated with PVT, a subtask of the Vienna Test System. The primary outcome was the number of perceived left and right visual targets. After a baseline testing, stimulation was applied and the performance was evaluated at 1 hour, 3 hours, 8 hours, 24 hours, 32 hours, and 96 hours after stimulation.
Two trains of TBS over the contralesional PPC significantly increased the number of perceived left visual targets for up to 8 hours as compared to the baseline testing. No significant improvement was found with sham stimulation and in the control condition without any intervention.
The application of four trains of TBS disproportionately prolonged the stimulation effect: a significant increase of perceived left visual targets was found for up to 32 hours after stimulation.
Inhibitory TBS over the unaffected PPC improved visual neglect suggesting a reduction of interhemispheric inhibition. The disproportionate prolongation of the stimulation effect following repeated TBS trains within one session suggests long-term potentiation like mechanisms on cortical synapses. Future studies will have to examine whether TBS can improve neglect also on the level of daily activity and thus may have a therapeutic potential.

Neurology (PSN), Neuropsychology/ Psychiatry (PSP), Rehabilitation (PSR)
Visual neglect

Talk, Poster

PSN-05

Failure of muscular blood flow regulation in chronic inflammatory demyelinating polyneuropathy as measured by BOLD-MRI

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Objective:
We applied functional magnetic resonance imaging (fMRI) using blood oxygen level dependent (BOLD) endogenous contrast to assess the response of human skeletal muscle to exercise.

Methods:
Supramaximal repetitive electrical stimulation of the peroneal nerve was applied at 20 Hz during 2 minutes. Series of BOLD echo planar images (EPI) of the corresponding leg muscles were acquired before and after the electrically imposed exercise. For this preliminary evaluation, a patient with chronic inflammatory demyelinating polyneuropathy was compared to a healthy subject with and without complete block of the distal ischiadic nerve (induced by injection of a local anaesthetic proximal to the stimulation site).

Results:
In the control subject, the muscle fMRI response (BOLD signal intensity increase) after imposed exercise was limited to the corresponding leg muscles compared to pre-exercise values. This signal intensity-ratio (pre- to post-exercise) did not change after application of the complete nerve block. In the patient, no change in singal intensity was noticed after the exercise.

Conclusion:
Our preliminary data shows a possible failure of autoregulation of regional blood flow to exercised muscles in patients with CIDP. This is possibly due to constant vasoconstriction because of autonomic hypersensitivity as a result of chronic co-affection of the corresponding autonomic fibres, as the changes of BOLD signal in the control subject did not change in the presence of an acute complete proximal nerve block.

MR-Methodology (PSM), Neurology (PSN), Neurophysiology (NP)
fMRI

Poster

Neuropsychology / Psychiatry (PSP)

PSP-01

Cognitive functioning during methadone and buprenorphine treatment

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Abstract:
Cognitive impairment in drug-dependent patients receiving methadone maintenance treatment has been reported previously. We assessed cognitive functioning after at least 14 days of stable substitution treatment with buprenorphine or methadone and after 8 to 10 weeks. We performed a randomized, non-blinded clinical trial in 59 drug-dependent patients receiving either buprenorphine (BUP) or methadone (MMP) maintenance treatment and healthy normal controls (n=24) matched for gender, age and educational level. Thirteen patients dropped out of the study before the second testing was performed (BUP, n=22; MMP, n=24). A neuropsychological test battery was used to measure selective attention, verbal memory, motor/cognitive speed and cognitive flexibility. In addition, subjective perceived stress was assessed with a questionnaire. Patients in both treatment groups performed equally well in all of the cognitive domains tested. Both BUP and MMP patients showed significantly improved concentration and executive functions after 8 to 10 weeks of stable substitution treatment. The control group achieved better results than the BUP and MMP groups in most cognitive domains, indicating cognitive impairment in the patients. Perceived stress did not show any significant change after 8 to 10 weeks of treatment and no major differences were detected between the three groups. No effects of perceived stress on cognitive function were found.
Our results indicate a cognitive impairment in patients receiving maintenance treatment with buprenorphine or methadone compared to healthy controls. Selective attention improved in both patient groups during treatment. We propose that the improvement of attention may facilitate rehabilitation of drug-dependent patients.

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Neuropsychology/ Psychiatry (PSP)
cognitive function, opioid dependence, substitution treatment, methadone, buprenorphine

Poster

PSP-02

Unconscious learning of new conceptual associations between masked stimuli is possible within one trial

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Prominent models of human long-term memory systems do not account for an unconscious form of rapid associative learning, which is the form of learning required for episodic memory. Nor do these models envision a role for the hippocampus in any form of unconscious learning. Recent functional magnetic resonance imaging experiments suggest that it is humanly possible to form and later retrieve new semantic associations in just one trial without conscious awareness of encoding or retrieval. The associative priming effects reported in these previous studies were small and based on group statistics. For single subject use (e.g., assessment of patients), a masked associative priming test needs to be developed that yields effects on a single subjects basis. Here, we present a new masking paradigm which pushes effect size and yields masked associative priming effects in long-term memory.

Neuropsychology/ Psychiatry (PSP)
long-term memory, unconscious learning, conceptual associations, hippocampus

Poster

PSP-03

Nonconscious associative learning of conceptual associations for word pairs that were never presented

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The distinction between conscious and nonconscious forms of memory has a long held tradition in psychology. Here, we provide with evidence against this distinction by demonstrating a form nonconscious long-term memory that suffices the criteria of associative conceputuality and flexibility, which in the past have been reserved soley for (conscious) declarative memory (see e.g. Smith & Squire, 2005). Our previous work (Henke et al., 2003) suggested that learning and storing new conceptual face-word associations are possible with a single learning trial even without conscious stimulus perception at encoding due to stimulus masking. These associative priming effects were small and manifested only in reaction latencies. Here, we used stimulus masking in a new word-word learning paradigm which yielded effects of nonconscious conceptual associative learning reflected in response accuracy. These accuracy effects were dependent on a previous familiarization with task procedures (Exp. 1) and on participants insight in the relation between study and test items during this supraliminal familiarization with the task (Exp.2). Remarkably, these associative priming effects manifested for word pairs that had never been presented but were merely related to nonconsciously encoded conceptual word-word associations. Thus, we present evidence that semantic associations to unconsciously encoded word pairs are activated and remain powerful enough to influence conscious decision making at test. Further, we tested for transitive inference to occur for subliminally encoded premise (word-) pairs (Exp. 3). By this, it is shown that this form of nonconscious learning not only leads to conceptual associations but also flexible representations of the subliminally encoded items.

Neuropsychology/ Psychiatry (PSP)
nonconscious memory

Talk, Poster

PSP-04

Negative and positive priming effects in patients suffering from Parkinson's disease

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The present study investigated inhibitory mechanisms assessed by negative priming (NP) in patients suffering from Parkinson's disease (PD). Previous studies yielded highly ambiguous results. Therefore, it was examined whether uncontrolled effects of anti-Parkinsonian drugs may account for the heterogeneity of previous outcomes. Identity and location negative (NP) and positive priming (PP) effects in twenty medicated PD patients and 20 PD patients after drug withdrawal were compared to NP and PP effects in 20 sex- and age-matched healthy controls. While location NP was not affected by PD, identity NP was reduced in medicated PD patients compared to non-medicated PD patients and healthy controls. When controlled for general slowing, identity and location PP did not differ between PD patients and healthy controls. The results endorsed the notion that uncontrolled effects of anti-Parkinsonian drugs may have contributed to the heterogeneity of previous results on NP effects in PD patients. Furthermore, our findings lead to the conclusion that dopaminergic medication dispensed to relieve PD related motor symptoms can have adverse effects on cognitive functions.

Neuropsychology/ Psychiatry (PSP)
Parkinson's disease, negative priming, dopaminergic drug effects

Poster

PSP-05

Selective modulation of illusion processing using rTMS: Having a look at the Brentano Illusion

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In the Brentano version of the Müller-Lyer illusion, one half of the line looks longer than the other. Previous research suggests, that illusion strength depends on activity in bilateral occipital and right parietal cortex. Recently, it has been shown that different versions of the Müller-Lyer illusion do not only affect manual bisection performance but also eye movements. The aim of the present study was to test whether manual and oculomotor illusion effects can be altered by interfering directly with cortical processing by means of theta burst stimulation rather than changing characteristics of the illusion itself. Subjects bisected Brentano illusions following occipital, parietal or no stimulation. We found that manual and oculomotor illusion strength can be altered by theta burst stimulation. Specifically stimulation over the occipital cortex markedly reduced illusion effects, while stimulation over the right parietal cortex had a smaller effect on illusion size compared to the control condition. These findings suggest that the Brentano illusion depends on a balance between early occipital (bottom-up) and subsequent parietal (top-down) processing of visual input. A balance that can selectively be shifted by theta burst stimulation

Neurology (PSN), Neuropsychology/ Psychiatry (PSP)
Length illusion, rTMS, Eye Movements,

Poster

PSP-06

Why do boys suffering from Duchenne muscular dystrophy have heterogeneous cognitive abilities?

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Background:
Duchenne muscular dystrophy (DMD) is a hereditary xp21-linked recessive disorder that is clinically characterized by a severe, progressive and irreversible loss of muscular function and strength. Over time, patients suffering from DMD exhibit deterioration of skeletal muscles eventually leading to death. Approximately one in 3300 live male births are affected, making it the most prevalent of muscular dystrophic disorders and the second most occurring genetically inherited human disease. DMD has long been recognized as a cause of mental retardation. However, there is tremendous individual variation in intellectual functioning across affected boys.

Aim:
A comprehensive neuropsychological assessment has been conducted to emphasize possible cognitive impairments and strengths among these patients. Moreover, a genetic evaluation has been accomplished to detect gene deletions.

Methods and Subjects:
A group of 16 boys with DMD aged 6 to 20 years (mean age 12 years 1 month, SD 4 years 4 months) received a battery measuring besides general intellectual abilities a broad range of specific neuropsychological functions. The battery included tests to assess skills in following domains: Intellectual ability, information processing speed, different aspects of attention and distractibility, perception, verbal/auditory and visuo-spatial performances, arithmetic/mathematics, problem solving and executive functions, verbal fluency and very important different aspects of memory skills. Furthermore, the performance of the DMD group has been contrasted with normative data of the healthy population and compared with the site of the gene deletion.

Results:
As anticipated, in the present cross-section study mental impairments of the boys suffering from DMD did correlate neither with age nor with the stage of the muscle disease. General cognitive abilities showed a mean IQ of 86 with broad individual variation (IQ between 52 and 120). Verbal IQ was not significantly lower than performance IQ, whereas most patients performed poorly on specific attention tasks, arithmetic and digit span tests.

Conclusion:
DMD provides an unique opportunity to investigate neuropsychological impairments caused by a single gene mutation. Moreover, it is possible to analyze the impact of a protein on cognitive development. It seems that auditory short-term memory is most likely impaired in patients suffering from DMD. Nevertheless, it has to be stressed that a very broad range of intellectual abilities with individual cognitive strengths and weaknesses seems to characterize DMD, making it probable that specific dystrophin isoforms have different impacts on brain functions.

Neuropsychology/ Psychiatry (PSP)
Duchenne muscular dystrophy, cognitive abilities, memory

Poster

PSP-07

Horizontal and vertical dimensions of visual extinction investigated by theta burst transcranial magnetic stimulation

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Visual extinction – the impaired perception of a contralesional stimulus in the presence of a simultaneous, ipsilesional stimulus – may occur after a lesion of the posterior parietal cortex (PPC). The present study aimed to investigate weather it is possible to induce long-lasting visual extinction in healthy subjects by interfering with the neural activity of the PPC, applying theta burst transcranial magnetic stimulation (TBS). In particular, we were interested in the influence of the manipulation of horizontal and vertical eccentricity of the stimuli. Furthermore, we aimed to test the attentional model of hemispherical rivalry as possible explanatory model of visual extinction. Results showed that a single TBS train over the right PPC is able to induce a significant increase of left visual extinction for about thirty minutes. This was not the case in the control group or in the group with control stimulation over the vertex. Moreover, it was shown that left visual extinctions were more frequent when the left stimulus was presented at more eccentric position on the horizontal axis (irrespective of right stimulus position) and in the lower part of the visual field. Finally, it was shown that when a second, subsequent TBS train was applied over the left PPC, left extinction rate decreased and became not significantly different from baseline anymore. Results are discussed within the framework of previous studies and clinical observations in patients suffering from extinction and related attentional disorders such as hemispatial neglect.

Neurology (PSN), Neuropsychology/ Psychiatry (PSP)
Visual extinction

Poster

PSP-08

Deficient learned irrelevance is rather a state than a trait marker of schizophrenic psychosi

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Deficient information processing is considered as a key feature of schizophrenia and provides a basis for its heterogeneous psychopathology. Information processing deficits become apparent in the patient's inability to adequately deal with the surrounding stimuli, i.e. to selectively attend to important stimuli and to ignore irrelevant ones, which leads to stimulus overload. A convenient neuropsychological method to assess information processing is the learned irrelevance (LIrr) paradigm. LIrr refers to the retardation of associative learning that normally occurs, if the stimuli which should be associated with each other have previously been experienced as inconsequential. LIrr is closely related to latent inhibition (LI) allowing cross-comparisons between LI and LIrr studies. As LI and LIrr, respectively, have been reported to be disrupted in acute and chronic schizophrenia patients regardless of medication, we hypothesised that an LIrr deficit might be a trait marker of schizophrenia. In order to investigate this hypothesis, we have tested healthy first-degree relatives of schizophrenia patients, individuals experiencing prodromal symptoms of schizophrenia (ultra-high-risk group (UHR)) and healthy control subjects with a computerized LIrr paradigm. We found significant LIrr in the control subjects and in the UHR group, while healthy relatives showed a trend to LIrr. We concluded that LIrr disruption might be a state marker of schizophrenic psychosis rather than a trait marker of schizophrenia.

Neurobiology (PSB), Neuropsychology/ Psychiatry (PSP)
learned irrelevance, associative learning, schizophrenia

Poster

PSP-09

On not thinking about bad things. A perfusion imaging study of a dissociation between response strategies in the presence of emotional information

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When taking a decision, emotional information, if present, is integrated into cognitive processing. While not well understood, the mechanisms of this integration are relevant in two respects. The first is the fractionation of control processes that determine response. When attention is engaged, it coordinates the cognitive resources required for the task at hand. It is unclear, however, if and how components of the attentional system make use of emotional information to determine response. The second is that we would expect such an integration of emotional information to be relevant to understanding clinical states such as depression, in which a strong emotional bias appears to gain the upper hand.

In the present perfusion imaging study, we investigate the neurobiological correlates of a task designed to contrast explicitly instructed response and spontaneous reactions in the presence of emotional information. When normal subjects rearrange a set of words to form one of two possible sentences, one emotionally negative, the other positive, they spontaneously avoid the negative choice, which makes up only 30% of responses (scrambled sentences test). This avoidance tendency is known to be modulated by depressiveness. One can, however, also instruct participants explicitly to avoid the negative choice, in this case triggering standard executive attentional systems relevant to inhibition of inappropriate response. We reasoned that if, in the presence of emotional information avoidance of negative response is mediated by executive attentional mechanisms, then there should be no difference in the relevant brain areas in the spontaneous and in the instructed conditions. If, however, emotional information can determine response irrespective of the action of executive attentional mechanisms, it should recruit distinctive areas on its own. In addition, we measured individual measures in executive attentional capacity (OSPAN test) and the functional polymorphism in the MAOA and SERT genes.

The results provide two lines of evidence in support to the conclusion that emotional information co-determines response independently from executive attentional processes. First, the dorsal and parietal areas involved in executive attention are recruited less when spontaneously avoiding the negative choice, than when the avoidance is explicit. This suggests that when acting spontaneously to avoid negative sentences, one need less attentional resources. Second, differences in executive attentional capacity are not associated with the amount of avoidance, even if they explain some of the variance in the number of sentences formed (i.e., performance irrespective of emotional valence). In contrast, state depressiveness correlates with the ratio of negative sentences. This suggests that participants did not use executive attention in increasing performance in the avoidance mechanism, while they used it to form sentences. The areas that were recruited more while avoiding negative sentences were those that are normally deactivated during the execution of a cognitive task: the ventral medial prefrontal cortex, and the left temporoparietal junction. MAOA modulated activation in the limbic region.

We conclude that inhibition of the negative choice in the face of negative salience is a process that runs parallel to the central executive and discuss the role the activated regions in terms of relatively automatic processes such as those present in visual orienting.

MR-Methodology (PSM), Neurophysiology (NP), Neuropsychology/ Psychiatry (PSP)
cognitive neuroscience, emotion, executive attention

Talk, Poster

PSP-10

Unconscious Processing of Words and Non-words: An ERP-study

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A well debated issue in cognitive psychology and neuropsychology is the question to which level an unconsciously perceived linguistic input is processed. This has often been investigated with subliminal pattern masking techniques that reduce the stimuli's sensory activation strength, which has implied problems to define an objective threshold of awareness. In this event-related-potential- (ERP-) study, a new mirror-masking technique was used that does not reduce sensory activation, but assumingly reduces top-down attentional activation. Stimuli were words and non-words written in a quadratic font that were merged with their inverted counterpart mirrored at the baseline of the letters (mirror-masking). The visual result of such mirrored letter strings were unfamiliar, abstract patterns that prevented subjective awareness of the linguistic information hidden in the seemingly meaningless patterns.
Significant differences in ERPs between mirror-masked words and non-words were found in a time range from 112-160ms after stimulus-onset above right posterior areas. A Low Resolution Electromagnetic Tomography (LORETA) model localised neuronal generators of these differences between masked words and non-words in right supramarginal gyrus (BA 40) and posterior temporal lobe, suggesting that at least an automatic differentiation occurred at a sublexical, phonological level of processing.
Our results strongly indicate that subjects unconsciously and automatically extracted some linguistic information from masked words.

Neuropsychology/ Psychiatry (PSP)

Poster

PSP-11

Lethal and non-lethal suicide attempts in Bern

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Each year about 1300 persons die by suicide in Switzerland. While lethal suicides are registered by the Swiss Federal Statistical Office (FSO), suicide attempts are not recorded systematically. The goal of the presented study is to compare lethal and non-lethal suicide methods to gather basic information for suicide prevention.
In the frame of the MONSUE/WHO study (European Multicentre Study on Suicidal Behaviour and Suicide Prevention) data on non-lethal suicide attempts are collected since 2004 using standardised methods on defined catchment areas. The agglomeration of Bern represents the Swiss study region. According to the WHO definition only suicide attempt are included that reach professional medical attention (GPs, Psychiatrist, inpatient care or outpatient care). 58% of all non-lethal suicide attempts pass through the accident and emergency department of the Bern University Hospital (Inselspital). Records on FSO data on lethal suicides are currently available until 2006. Therefore, lethal and non-lethal methods can be compared for the years 2004 to 2006 for the Bern region. Furthermore, data of the Bern region are related to suicides in Switzerland.
Self-poisoning by medication and cutting are the most often used methods in non-lethal suicide attempts, whereas hanging, shooting and medication can be found in completed suicides.
Absolute numbers of suicide attempts and relative lethality in the agglomeration of Bern are related to the Swiss data. The results are part of the basics to possibilities for suicide prevention in Bern.

Neuropsychology/ Psychiatry (PSP)
Suicide Prevention, Suicide Methods and Behaviuor, Lethality

Poster

PSP-12

Differences in motor activity between schizophrenia subgroups

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Schizophrenia and associated psychotic disorders present with a variety of symptoms. Among them many psychopathological symptoms are shared in all groups. Of special importance are motor features. Researchers have addressed this issue by means of simple observation and description. We used wrist actigraphy during the wake hours of a day to compare motor features between three schizophrenia subtypes.

Continuous wrist actigraphy was applied for 24 hours in 57 inpatients of our hospital. Of these, 35 presented with the paranoid, 11 with the catatonic, and 11 with the hebephrenic subtype. All patients received treatment as usual and were on psychoactive medication during the study. Each participant was assessed with the Positive and Negative Syndrome Scale (PANSS). Actigraphy recorded with an interval of 2s. For analyses, times of sleep were removed from the data. We calculated activity level (AL: mean activity counts per hour), movement index (proportion of active periods), and the mean duration of uninterrupted immobility (pauses).

No predictor but the schizophrenia subtype had an effect on motor activity in schizophrenia. A MANOVA revealed significant differences between subtypes ($F=3.9$; $p<0.001$). Subtypes differed in each of the three quantitative motor activity variables (activity level, movement index, uninterrupted immobility). Post-hoc tests demonstrated differences between the catatonic and the paranoid subtype, where patients with catatonic schizophrenia had increased duration of immobility. Motor activity was not related to age, gender, duration of illness, or antipsychotic drug use. The findings provide first objective data on the motor activity between different schizophrenia subtypes.

Neuropsychology/ Psychiatry (PSP)
Schizophrenia

Poster

PSP-13

Neural Correlates of Sustained Attention

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Introduction: All three versions of the Rapid Visual Information Processing task (RVIP) – RVIP0, RVIP000 and RVIP3tarseq – require the participant to sustain attention over a longer period of time (16 min). Whereas the RVIP3tarseq is standardised - including higher cognitive processes such as working memory - RVIP000 and RVIP0 are especially designed to measure purer forms of sustained attention. We investigate which brain areas are recruited by these tasks and how behavioural data and activity patterns correlate with each other. We therefore apply a rapid event related paradigm in fMRI which allows us to use the tasks in their total length.
Methods: 20 right-handed, healthy volunteers performed the tasks, in which they had to respond to specific target numbers. Reaction times (RT) and the number of hits were recorded. Nullevents (i.e. black screen) were interspersed randomly in each task. Random effects GLM analyses were performed for each task, contrasting targets vs. nullevents.
Results: RVIP0 shows the most extended and highest activations followed by RVIP000 and RVIP3tarseq. They all activate the visual areas bilaterally and the medial frontal/cingulate areas. RVIP0 is the only task that activates the right dlPFC. The inferior parietal lobules bilaterally are activated in RVIP000 and RVIP3tarseq. Furthermore, RVIP3tarseq shows the most extended deactivations in the brain regions of the default mode network, whereas the same areas are only partly deactivated in RVIP000 and not deactivated in RVIP0.
Discussion: The three SA tasks differ in the behavioural data (RT and number of hits) and in the magnitude and extent of the activated and deactivated brain regions. The activation in the medial frontal gyrus, that is involved in all tasks, might reflect planning and execution of movement. We suggest that the RVIP0, taking the behavioural data into account, is the purest form of a sustained attention task, as it is the only task where the right dlPFC is activated. The default network might only become visible when highly demanding (i.e. RVIP3tarseq) but not easy (RVIP0) tasks are executed.

Neuropsychology/ Psychiatry (PSP)
sustained attention

Poster

PSP-14

Comparison of objectively measured and observed motor activity in major depression

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The use of actigraphy in depression research can help to clarify 1) the association between the observed psychopathology of depression ratings and quantitative motor activity and, 2) the impact of recurrent depression on motor acitivty.

59 inpatients with a diagnosis of major depression (23 with a first episode, 36 with recurrent episodes) were rated with the Hamilton depression rating scale (HAMD) and wore wrist actigraphs continuously for 24 hours.

The observation of the items activities and retardation in major depressoin could be reflected with the objective means of actigraphy. However, agitation and HAMD total score did not meet the results of quantitative motor activity. Recurrent depressive episodes effectuates patients in having lower activity levels particularly in the afternoon ($t = 2.15$, df 57, $P = 0.04$). Actigraphy should be considered as a valid instrument in clinical research to measure retardation in the course of major depression.

Neuropsychology/ Psychiatry (PSP)
actigraphy, circadian rhythm, rating scales, major depression

Poster

PSP-15

Unilateral vs. bilateral vestibular patients: differences in mental rotation performance

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Vestibular information helps establishing a reliable gravitational frame of reference and contributes to adequately perceive the location of one's own body in space. Thus, vestibular patients often show impaired performance in oculomotor responses (VOR) and in perceptual tasks such as the subjective visual vertical. To date, however, still relatively little is known about the consequences vestibular loss has on higher-level cognitive tasks. In this study, we investigate whether patients with peripheral vestibular lesions show an impaired ability to mentally rotate images of bodies and body-parts. We have used these tasks in previous studies on healthy participants and found evidence for the involvement of vestibular information (Grabherr et al., 2007). 15 participants with unilateral vestibular labyrinthectomy (10 right-sided, 5 left-sided) and 8 with bilateral vestibular loss as well as 14 age-matched control participants showing no symptoms of vestibular origin were tested in three different cognitive tasks: an egocentric mental rotation task, an object-based mental rotation task and a control task requiring a laterality judgment but no mental rotation. Two types of stimuli were used: pictures of human bodies and body parts (hands). Additionally, visual perception was assessed with a computerized version of the rod and frame test that also included a subjective visual vertical task. Results from the subjective visual vertical task confirm previously reported results, indicating a bias toward the lesioned side in participants with unilateral vestibular lesions. Participants with bilateral lesions do not show such a bias in the subjective visual vertical. Interestingly, however, in the cognitive tasks a significant group effect ($F(2,34) = 5.12$, $p = .011$) was found and post-hoc tests revealed that participants with bilateral vestibular loss show significantly increased response times compared to participants with unilateral vestibular lesions ($p = .019$) and the control group ($p = .020$). No significant differences were found between the participants with unilateral vestibular lesions and the control group. Moreover, no significant differences were found between right and left-sided labyrinthectomized participants. Thus, a task requiring mental rotation abilities appears to be more challenging for participants with bilateral vestibular loss when compared to participants with partial vestibular loss or healthy controls. Participants with unilateral vestibular lesions seem to be able to fully compensate their partial loss of vestibular information whereas the chronic absence of vestibular input leads to impaired performance in mental rotation tasks. In future studies, we aim to test patients with unilateral lesions in the acute stage before and at different stages of vestibular compensation. This study was supported by the Swiss National Science Foundation, PDFM1-114406.

Neuropsychology/ Psychiatry (PSP)
Vestibular patients, Subjective visual vertical, Mental rotation, Spatial Cognition

Poster

PSP-16

Does synesthesia work bi-directionally? A TMS study

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Synesthesia is a rare condition in which the input of one sensory modality automatically triggers an additional experience. For example, the letter A written in black triggers a RED color experience. A current assumption is that in synesthesia cross-modal associations are strictly uni-directional. However recent research showed that on an implicit level synesthesia may work bi-directionally. On a neuroanatomic level, right parieto-occipital regions have been shown to be involved in spatial binding of different stimulus attributes in synesthesia. In this study, we tested whether application of TMS to these regions would suppress the synesthetic conditioning effect and therefore would provide new evidence for the implicit bidirectional nature of cross-activation in synesthesia.

Neuropsychology/ Psychiatry (PSP)
synesthesia, grapheme-color, conditioning, TMS, EDA

Poster

PSP-17

The word-frequency mirror-effect in idiopathic Parkinson's disease: contributions of familiarity and recollection to recognition memory

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Current theories postulate that recognition memory can be supported by two independent processes, recollection and familiarity. Recollection is defined as the mental reinstatement of prior experiences, associated with vivid memory for an item and its contextual details. Familiarity is a mental awareness that an event has been experienced without mental reinstatement. Empirical findings in regard to recognition memory in non-demented patients with idiopathic Parkinson's disease (PD) are disputed. PD could affect familiarity and recollection unequally, which might explain conflicting evidence of intact versus impaired recognition memory. Only few studies have separated these two processes in PD patients, therefore we aimed to further explore which process is more likely to be impaired. The consistently observed deficit in free recall in non-demented PD patients points at an impairment in recollection rather than familiarity.
A total of 14 PD patients and a healthy control group, matched in age, gender, education and handedness was tested. Participants were required to read aloud and memorize 48 words, 24 of which either low or high frequency. Following a filled delay a recognition test consisting of 48 words from the study list and 48 lures was conducted. In order to estimate the contribution of recollection and familiarity the word-frequency mirror-effect was used in combination with the remember-know paradigm. The mirror-effect occurs when hit rates are higher and false alarm rates are lower for low-frequency compared to high-frequency words. High-frequency lures are more likely to produce familiarity-based false alarms because people are unable to distinguish if their feeling of familiarity is based on recent presentation during study episode or on prior exposures. In contrast, low-frequency words are more accurately associated with the study episode and tend to be recollected because they have less contextual associations than high-frequency words and the situation specific information from their most recent presentation (i.e. study episode) will stand out. The hit rate advantage for low-frequency compared to high-frequency words reflects the increasing ability to use recollection whereas an increased false alarm rate corresponds to judgments based on familiarity. Additionally to their old-new-judgments participants had to report if they can recollect the item from the study phase ("remember" response) or if the item seems familiarly without being accompanied by a mental re-experience ("know" response). "Remember" responses are assumed to reflect conscious recollection, while "know" responses are assumed to reflect feeling of familiarity.
Both controls and patients showed the word-frequency mirror-effect: Participants made more hits and less false alarms to low- than high-frequency words, reflecting better discrimination of old and new low-frequency words. Overall, PD patients showed near normal performance. Further analyses revealed intact recollection but impaired familiarity. This deficit emerged from the reduced discrimination ability in their judgments of knowing. Probably, patients are not able to use familiarity as well as healthy controls as a recognition criterion: Recognition – caused either by recollection or familiarity – leads to judgments of remembering whereas judgments of knowing reflect mere guessing.

Neuropsychology/ Psychiatry (PSP)
Parkinson's disease, recognition memory, mirror effect

Poster

PSP-18

Comparison of rTMS over the DLPFC vs MFC: An eye movement study

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This study was aimed at investigating the effects of theta burst repetitive transcranial stimulation (rTMS) over the right dorsolateral prefrontal cortex (DLPFC) and the media frontal cortex (MFC) on eye movements during a computerized Trail Making Test (TMT) at various degrees of difficulty. Each subject performed the task twice, with and without TMS. To analyze test performance qualitatively and to observe the use of strategies “on line”, eye movements and mouse clicks were recorded simultaneously. Within subjects comparisons revealed that after rTMS over the MFC, subjects showed more regressive fixations and more anticipatory fixations, but less target fixations while processing a sequence of actions during the TMT. This was particularly pronounced in TMT-B trials. However, this viewing pattern was not observed after DLPFC stimulation, which had no effect on regressive or target fixations but reduced anticipatory fixations.

Neuropsychology/ Psychiatry (PSP)
eye movements, TMS

Poster

Rehabilitation (PSR)

PSR-01

Hearing Improvement for Subjects Using the Bone Anchored Hearing Aid (BAHA)

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Introduction
The bone anchored hearing aid (BAHA) consists of a titanium screw which is surgically implanted in the mastoid and a hearing aid actuator that can be attached to this implant [1]. The BAHA actuators generate mechanical vibrations that are transmitted by bone conduction [2] to the inner ear and stimulate the cochlea. It is a successful method of treatment for conductive hearing loss, e.g. in patients with middle ear pathologies and single sided deafness [3, 4].

Aim
The aim of this study is to determine the patient's hearing improvement after BAHA implantation as a function of different hearing impairment conditions such as unilateral hearing loss, bilateral hearing loss and single sided deafness. Our results can be used to estimate postoperative sound field hearing threshold and speech understanding before BAHA implantation.

Subjects
This retrospective study includes 92 subjects that were implanted with the BAHA at the department of ENT, Head and Neck Surgery, Inselspital, University of Bern in Switzerland. Implanted subjects were divided into three groups according to their pattern of hearing loss (unilateral and bilateral conductive hearing loss and single-sided deafness).

Methods
Correlation between the sound field hearing threshold and the averaged pure tone hearing threshold of bilateral bone and air conduction hearing threshold are analyzed. Further, the frequent dependent hearing threshold in sound field is compared to the bone conduction hearing threshold of the better ear. Improvement of speech understanding is statistically evaluated for each group and analyzed as a function of improvement of sound field hearing thresholds.

Results
Best correlation is found between sound field hearing threshold and bone conduction hearing threshold of the subject's better ear for all three subject groups. The frequent depended hearing threshold with BAHA in sound field compared to the bone conduction hearing threshold show best results for middle frequencies (1 kHz, 2 kHz). Averages on speech understanding improvements as a function of sound field hearing improvements are related for all three subject groups.

Conclusion
The prediction of hearing with BAHA is possible on preoperative audiological data for subjects with unilateral or bilateral conductive hearing loss or single-sided deafness. All three subject groups show a similar hearing improvement in sound field hearing and speech understanding.

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Rehabilitation (PSR)

Poster

Workshops

Workshop 1: TMS applications in Clinical Neurosciences (Chair: Prof. Dr. R. Müri)

Transcranial magnetic stimulation (TMS) as a tool in clinical and cognitive neuroscience has gained growing attention because it allows for interference with cortical processes. A special emphasis will be put on theta burst stimulation (TBS) protocols. Theoretical background and specific examples of up to date TMS applications will be presented and discussed.

- René Müri: TMS online/offline approaches in Clinical Neurosciences
- Thomas Nyffeler: State dependency and TBS
- Kaspar Schindler: EEG and TBS
- Silvia Chaves: fMRI and TBS

Workshop 2: Methods of functional and structural Neuroimaging in Clinical Neurosciences (Chair: Dr. A. Federspiel/ Dr. R. Wiest)

Several methods exist in the field of neurosciences that may be used to obtain specific information about the structure of the human brain and its function. The large variety of techniques used to make pictures, i.e. to visualize the structures and the functional brain regions are summarized as Neuroimaging. The quantitative extraction of relevant parameters (e.g. Blood- oxygenation-level dependent activity, gray matter density, fractional anisotropy, cortical thickness, cerebral blood flow, etc. etc.) is beside the aspect of visualization, an additional topic covered by Neuroimaging. Therefore, in the Workshop “Methods of functional and structural Neuroimaging in Clinical Neurosciences” we present in brief basic methods (the tools) that are needed in order to conduct own fMRI and/or structural measurements. We present different acquisition schemes used in fMRI, different analysis techniques applied in fMRI experiments, new concepts addressed with diffusion tensor imaging, sophisticated applications of simultaneous EEG/fMRI recordings and latest developments in the field of morphometry.
Moreover, all these methods are discussed in the context of its clinical settings and their potential benefits as to the increase of insight of different pathophysiologies.

Workshop 3: Scientific EEG and event-related potentials for dummies (Chair: PD Dr. T. König)

In this workshop, we will give an introduction on how to use and understand EEG and event-related potentials (ERPs) as a tool for neuroimaging. We outline the basics about the physiological origin of the signal, the technique to record it, its basic physical properties, and the possibility to estimate the intracrebral distribution of its generators. Furthermore, we will analyze a small series of datasets to demonstrate typical applications and findings. The workshop should enable the participants to estimate the value and feasibility of using EEG and/or ERP for their own research interests.
EEG/fMRI recordings and latest developments in the field of morphometry.

Workshop 4: Health Technology Assessment for Clinical Neurosciences: A Medical, Economic and Ethical Evaluation (Chair: Dr. K. von Bremen)

Abstract not available

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