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Program and Abstracts

7th annual meeting of the

Clinical Neuroscience Bern

November 22nd 2011

Conference location:

University Hospital of Psychiatry,

Bolligenstrasse 111, Bern

http://www.kas.unibe.ch/neuro11

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HOPITAL UNIVERSITAIRE DE BERNE
BERN UNIVERSITY HOSPITAL

Dear participants,

It is a pleasure to welcome you to the 7th meeting of the Clinical Neuroscience Network in Bern, where we once more would like to give you the opportunity to exchange all the findings, interesting ideas and projects you are engaged in. Again, about 150 researchers from all different neuroscience-related disciplines, mainly from the University of Bern, will attend this year.

We are pleased to announce that Prof. Dr. Anthony A. Grace, Department of Neuroscience, University of Pittsburgh will present the key note lecture entitled “Dopamine System Dysregulation by the Hippocampus and the Pathophysiology of Schizophrenia”. Dr. Grace's research interests lie at the interface of neurobiology and psychiatry. His experiments combine in vivo and in vitro electrophysiological recordings of neurons with behavioral and neuroanatomical techniques to study central dopaminergic systems, with the ultimate goal of determining the neurobiological correlates of mental disorders and the modes of action of psychotherapeutic drugs. Besides the main lecture, there will be six selected oral presentations in the morning. During the extended lunch break, an unguided poster session will take place. However, we would appreciate if one of the authors is available at the poster during the session. In the afternoon, four interesting parallel workshops are offered. This year again, due to a generous grant by the University Hospital of Neurology, we will be able to award three poster prices. Furthermore the Graduate School of Health Science of the University of Bern has supported the meeting substantially.

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 have confidence that the continuation of the series of meetings will further strengthen the interfacultary clinical neuroscience network and provide an excellent occasion for a lively and interesting exchange of study results, experiences and knowledge as well as offer the basis for the development of new and interesting projects. Finally we would like to express our gratitude to Lilo Badertscher and Matthias Grieder for their important contributions in the organization of this year’s meeting.

We are looking forward to seeing you at the University Hospital of Psychiatry and wish you a stimulating and 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)
Matthias Grieder (Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry, Bern)

Sponsors:
University Hospital of Psychiatry, Bern
University Hospital of Neurology, Inselspital, Bern
Graduate School for Health Sciences, University of Bern

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Program 22.11.2011

08:00 – 09.00 **Poster attaching**

09:00 – 09:15 **Opening Addresses**

- Regula Mader, CEO of the University Psychiatric Services (UPD), Bern
- Prof. Dr. Christian W. Hess, Chairman of the Clinical Neuroscience Bern
- Prof. Dr. Werner Strik, Director of the University Hospital of Psychiatry, Bern

09:15 – 10:00 **Key Note Lecture**

- *Prof. Dr. Anthony A. Grace*, Department of Neuroscience, University of Pittsburgh
  Dopamine System Dysregulation by the Hippocampus and the Pathophysiology of Schizophrenia
  Chair: Werner Strik

10:00 – 10:30 **Coffee Break**

10:30 – 12:00 **Short presentations** (6 selected abstracts à 15 minutes)
Chair: Hans-Rudolf Lüscher

- *Christine Bolliger* (Dept. of Clinical Research, University of Bern), Chris Boesch, Roland Kreis:
  Optimizing Two-dimensional Magnetic Resonance Spectroscopy Experiments for the Quantification of GABA and Other Metabolites in Human Brain
- *Christian Rummel* (Institute of Diagnostic and Interventional Neuroradiology, University of Bern), Martinus Hauf, Heidemarie Gast, Roland Wiest, Kaspar Schindler:
  Does multivariate analysis of nonlinear EEG interrelation help delineate ictogenic brain tissue?
- *Andreina Schoeberlein* (Laboratory for Prenatal Medicine, Department of Clinical Research, University of Bern), Martin Müller, Ursula Reinhart, Marianne Messerli, Ruth Sager, Daniel V. Surbek:
  Intracerebroventricular Transplantation of Human Placenta-Derived Mesenchymal Stem Cells for the Neuroregeneration in a Rat Perinatal Brain Injury Model
- *Rogier Min* (Department of Physiology, University of Bern), Thomas Nevian:
  Neocortical spike timing-dependent depression requires astrocyte mediated retrograde signaling
- *Sebastian Walther* (University Hospital of Psychiatry, University of Bern), Helge Horn, Oliver Höfle, Andrea Federspiel, Roland Wiest, Werner Strik, Thomas Müller:
  Prefrontal white matter integrity predicts treatment response after 4 weeks in major depression
- *Thomas Reber* (Department of Psychology, University of Bern), Roger Luechinger, Peter Boesiger, Katharina Henke:
  Unconscious Relational Inference Recruits the Hippocampus

12:00 – 14:00 **Poster Session and Lunch**

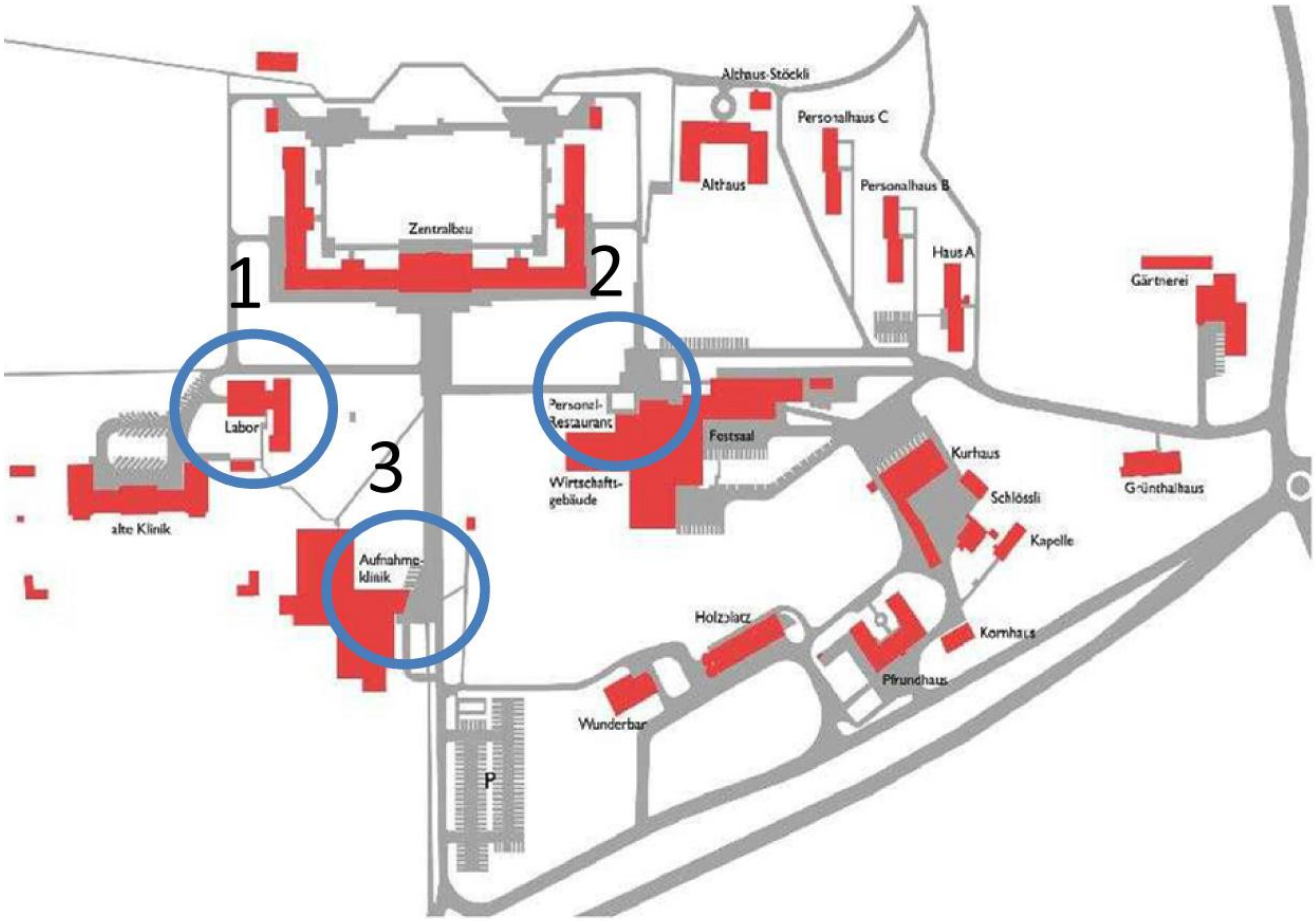
14:00 – 16:30 **Workshops**

- Workshop 1: **Deep brain stimulation as a treatment for obsessive/compulsive disorder: What animal models tell us about mechanisms**
  Chair: *Anthony A. Grace*
- Workshop 2: **Sleep**
  Chair: *Johannes Mathis / Katrin Henke*
- Workshop 3: **Optogenetics**
  Chair: *Thomas Nevian*
- Workshop 4: **Clinical Neurogenetics**
  Chair: *Jean-Marc Burgunder*

16:30 – 17:00 **Poster Awards**

17:00 **End of the meeting**

Site Map



1 Labor:
Workshop (upper level: room 309)

2 Wirtschaftsgebäude:
Posters / Lunch (basement: room 419)
Workshops (basement: rooms 412, 416, 418)

3 Aufnahmeklinik:
Registration
Welcome addresses, key note lecture, short presentations, coffee break (Auditorium Wölfli)

Key Note Lecture

Dopamine System Dysregulation by the Hippocampus and the Pathophysiology of Schizophrenia

Anthony A. Grace

University of Pittsburgh

Schizophrenia is a complex disorder in which patients exhibit psychotic symptoms (hallucinations and delusions) as well as cognitive impairments and deficits in social interactions. Despite substantial research over decades into this disorder, the pathophysiology has only recently become more apparent. In particular, a focus on the dopamine system has been prevalent, given that drugs that release dopamine exacerbate psychosis, drugs that treat schizophrenia block dopamine, and human imaging studies show that schizophrenia patients release more dopamine in response to amphetamine, with the increased release proportionate to the exacerbation of psychosis produced. One hindrance to the advancement of knowledge about this disorder is the lack of effective animal models. Nonetheless, recent work has shown that disruptions of early brain development can lead to models that effectively mimic many of the characteristics of this disorder. We have used prenatal administration of a mitotoxin, methylazoxymethanol acetate (MAM) to pregnant rats and examining the offspring as adults. These rats show deficits in neuroanatomy, sensory gating, executive function, and exacerbation by drugs consistent with what has been observed in human schizophrenia patients. We have found that these rats show a unique activation of dopamine neuron firing in the midbrain, with an aberrant increase in the “gain” of the dopamine signal to stimuli. This hyper-reactivity is apparently driven by a loss of interneuron function within the hippocampus - a pathology also present in the hippocampus of schizophrenia patients. This dopaminergic overactivity can be partially reversed by administration of antipsychotic agents; however, these drugs appear to work several steps downstream from the hippocampal deficit. We have found that a drug that specifically targets the limbic hippocampus, i.e. a GABA A alpha 5 positive allosteric modulator, is effective at directly reversing dopamine system hyperactivity by acting at the source of the pathology. Moreover, recent work suggests that the pathophysiological change itself may be prevented by peripubertal intervention, suggesting a potential route to prevention of conversion to psychosis in susceptible individuals. Therefore, the use of this animal model has provided key insights into the pathophysiology of schizophrenia, which has led to the evolution of drugs that target the sites of deficit and that may be more effective therapeutic agents.

Abstracts by discipline

Methodology (MT)

MT-01

Antiviral effect of siRNA against Langat virus in cell culture and organotypic hippocampal rat brain slices

Carola Maffioli[1], Stephen Leib[1], Olivier Engler[2]

[1]*Institute of Infectious Diseases, University of Bern,* [2]*Spiez laboratoy, Spiez*

Tick borne encephalitis virus (TBEV) is the causative agent of tick borne encephalitis (TBE), a potentially fatal neurological infection affecting humans in Europe and Asia. TBEV, which belongs to the mammalian group of tick-borne flaviviruses, is transmitted by the bite of infected ticks and despite the availability of a vaccine, approximately 2000 infections occur every year in Europe. To date there is no effective antiviral therapy for TBE. The antiviral effect of RNA mediated interference (RNAi) by small interfering RNA (siRNA) was evaluated in cell culture and organotypic rat hippocampal cultures (OHC). Langat virus (LGT), a naturally attenuated flavivirus strain closely related to TBEV exhibits a low-pathogenicity for humans but retains neurovirulence for rodents. LGT was used herein for the establishment of an in vitro model of TBE. LGT productively infected both, dissociated HeLa cells and 400 µm-thick organotypic tissue slices of rat hippocampus cultured on a porous membrane. Once infection was established, we analyzed the efficacy of 19 different siRNA sequences targeting defined regions of the Langat genome to inhibit virus replication in the 2 in vitro systems.
The most efficient suppression of virus replication in both in vitro systems was achieved by siRNA sequences targeting genes within the envelope and the 3' untranslated region (UTR). When siRNA was administered to HeLa cells before infection with LGT, a 1000-fold reduction of infectious virus particles was observed while delayed treatment after infection decreased the viral replication by 90%. In OHC the replication of LGT was reduced by up to 97% in the pretreatment paradigm compared to OHC transfected with non-targeting siRNA used as controls.
Conclusion: Organotypic rat hippocampal cultures represent a suitable in vitro model to investigate neuronal infection mechanisms and treatment strategies in preserved three-dimensional tissue- and cyto-architecture and cellular composition of the brain. Our results demonstrate that siRNA is an efficient approach to limit LGT virus replication in vitro.

methodology, neurobiology

Poster

MT-02

Does multivariate analysis of nonlinear EEG interrelation help delineate ictogenic brain tissue?

Christian Rummel[1], Martinus Hauf[1], Heidemarie Gast[2], Roland Wiest[1], Kaspar Schindler[2]

[1]*Institute of Diagnostic and Interventional Neuroradiology, Inselspital, Bern,* [2]*Department of Neurology, Inselspital, Bern*

Purpose
Ictogenic brain tissue can be characterized by altered EEG interrelation as measured during pre-surgical evaluation. Very recently, bivariate interrelation measures were found to lateralize the seizure onset zone to one cerebral hemisphere in inter-ictal stereo-EEG of patients suffering from mesial temporal lobe epilepsy [1]. Surrogate corrected nonlinear interrelation outperformed linear and nonlinear bivariate measures alone. We here conducted a similar study, subjecting bivariate estimates for significant linear interrelation (SLI, i.e. interrelation that cannot be explained by random effects) and significantly nonlinear interrelation (SNI, i.e. interrelation that cannot be explained by linear correlation) to multivariate analysis.

Methods
From 20 consecutive patients undergoing intracranial EEG (iEEG) monitoring in the epilepsy surgery program of the Inselspital Bern those with excellent (N=8) and negative (N=4) outcome were selected. For each included patient peri-ictal epochs of multi-channel iEEG were analyzed retrospectively. Equal-time cross-correlation and mutual information were used as linear and nonlinear interrelation measures. The null hypotheses of purely random correlation [2,3] and entirely linear interrelation [3] were tested separately for all electrode pairs using ensembles of independent and multivariate surrogate time series. Matrices quantifying SLI and SNI separately element-wise were analyzed in multivariate manner. Patterns of SLI and SNI were correlated with surgical outcome.
Results
SLI and SNI showed distinct spatio-temporal dynamics. The seizure onset zone (SOZ) and brain tissue that was later surgically removed differed from conserved tissue with respect to its degree of localized SNI, which cannot be explained by linear correlation alone. SNI was higher during seizure than inter-ictally.
Conclusions
Our results indicate that distinction of SLI and SNI [1,3] may be helpful to better delineate ictogenic brain tissue.

Supported by Schweizerischer Nationalfonds.

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(3) C. Rummel, E. Abela, M. Müller, M. Hauf, O. Scheidegger, R. Wiest, K. Schindler, Phys. Rev. E 83:066215 (2011)

methodology
epilepsy; pre-surgical evaluation

Talk

MT-03

Measurement of Driving-relevant Cognitive Performance with a Focus on Older Age Groups

Rahel Bieri[1], Michael Jäger[1], Tobias Nef[1,2], René Müri[1,3], Urs P. Mosimann[1,4]

[1]Gerontechnology & Rehabilitation Group, University of Bern , [2]ARTORG Center for Biomedical Engineering Research, University of Bern, [3]Division of Cognitive and Restorative Neurology, Department of Neurology, Inselspital, University of Bern , [4]Department of Old Age Psychiatry, University Hospital of Psychiatry, University of Bern

Introduction. A number of specific cognitive skills are fundamental for the ability to drive safely. Therefore, especially for older age groups an objective, reliable and valid assessment of these skills is necessary.
Method. A newly developed screening tool that consisted of six subtests (maximum duration 2 min.) was used to assess the following driving-relevant cognitive skills: selective and divided attention, eye-hand coordination, executive functions, regulation of distance and velocity, and extrapolation of distance and velocity. The tests were presented on a computer screen and the reactions of the participants were registered with a commercially available steering-wheel and foot pedal. To assess feasibility, clarity, usability, and differences in cognitive performance, the tests have been administered to 14 younger (mean age = 28.5 years, SD = 3.5) and 5 older (mean age = 68.6 years, SD = 11.4) healthy subjects.
Results. In this pre-study we could show that the six subtests of the screening tool discriminated between the two age groups in the expected direction. The two groups did no differ regarding the ease of understanding the instructions and operating the test hardware. Results indicated that the chosen difficulty level was too easy for some tests and could not capture the whole range of performance levels, which led to ceiling effects. There were no differences between the two groups in subjective ratings of the tests' clarity and usability.
Discussion & Outlook. Preliminary results show that a newly developed computer-based screening tool discriminates between groups with different performance levels. On the basis of these results the specifications of the tests have been adapted in order to achieve the optimal difficulty level. Furthermore, the tests proved to be equally suitable for different age groups and subjects with different experience with computers. In a next step, we will investigate the correlation between the performance in the adapted screening tool and different performance variables in simulated driving in a larger sample.

methodology, psychiatry, psychology

cognition

Poster

MT-04

Localization of transient EEG gamma synchronization with help from the BOLD signal: Finding a face integration network

Mara Kottlow[1], Kay Jann[1], Thomas Dierks[1], Thomas Koenig[1]

[1]*Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Bern*

Previous animal studies have reported gamma zero-lag phase synchronization as marker for visual binding. These common-phase gamma oscillations have not been analyzed with EEG. Some EEG studies analyzed the so-called phase locking factor measuring the consistency of phase shift across trials or the induced gamma amplitude to study visual binding. In contrast here, we introduce a method for the identification of networks oscillating with zero-lag phase synchronization measured with simultaneously acquired EEG and fMRI from healthy human subjects during an exemplary face binding task. Subjects were presented with parts of a schematic face (eyes, pupils, mouth) moving in an unpredictable manner (NOFACE condition) and during some periods producing a unitary face (FACE condition). Zero-lag phase synchronization was measured by means of the global field synchronization (GFS). GFS is a global measure of instantaneous functional connectivity providing information on the amount of zero-lag phase synchronization in specific frequency bands throughout the brain under a specific condition. For matter of localization, single-trial values of gamma GFS were correlated with the simultaneously acquired BOLD responses.As predicted, we found increased gamma phase synchronization during the FACE condition. The GFS-BOLD correlates involved face specific regions transiently synchronized during face integration. Taking the integration of face parts to a unitary percept as example for visual binding, we present a method for localizing transiently synchronized regions. These regions formed part of different levels of visual hierarchy. We therefore suggest that zero-lag phase synchronization in the gamma range may exist between remote regions of the visual system. A further analysis will follow the relationship between the functional connectivity represented by GFS-BOLD correlates and structural connectivity as measured with diffusion tensor imaging.

methodology, physiology
EEG/fMRI, gamma phase synchronization, face, binding

Poster

MT-05

Do DTI white matter tracts between regions of face recognition correlate with the amount of EEG gamma phase synchronisation during a face binding task?

Mara Kottlow[1], Tobias Bracht[1], Kay Jann[1], Lester Melie-Garcia[2], Thomas Dierks[1], Thomas Koenig[1]

[1]*Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, 3000 Bern 60, Switzerland ,* [2]*Neuroinformatics Department, Cuban Neuroscience Center, Havana 15202, Cuba*

EEG gamma phase synchronization is a measure of transient functional brain connectivity and has been found to be a representative marker for visual binding. The purpose of this study is to verify the assumption that structural connectivity builds the basis for transient synchronization phenomena in the brain. In a previous study, we had measured simultaneous EEG and fMRI on 14 healthy subjects during a face binding task. We found positive correlations between a quantification of EEG gamma phase synchronization (global field synchronization; GFS) and BOLD responses in 14 cortical regions. Additionally, we had recorded a diffusion tensor imaging (DTI) sequence on the same subjects. 11 of the mentioned cortical regions, including the right middle fusiform gyrus, lay within the borders of this DTI sequence. Those regions have been defined as regions of interest (ROI). We applied a probabilistic fibre tracking approach in order to extract the most probable anatomical pathways connecting these ROIs. Our first hypothesis is that gamma phase synchronization may occur between regions connected through

white matter tracts. We therefore assume that white matter tracts build the hard wire basis for gamma GFS. Our second hypothesis is more experimental: Both, the ability for binding/expression of gamma phase synchronization and the quantification of white matter tracts vary between subjects. Hence, we suppose that there may be a correlation between the structural connectivity of white matter tracts on one hand, as measured by the probability of connectivity between the regions of visual binding and the mean functional anisotropy (FA) of these fibre tracts, and the amount of gamma phase synchronization during a visual binding task on the other hand. The findings of this study may lead to insights into the relationship of structural and functional connectivity as measured with EEG. Further, the results may add to the understanding of inter-individual differences in the ability of the brain to produce gamma GFS, which is important for the investigation of aberrant gamma synchronization known to be altered in different psychiatric disorders.

methodology, physiology
DTI, EEG/fMRI, face, gamma, binding

Poster

MT-06

Optimizing Two-dimensional Magnetic Resonance Spectroscopy Experiments for the Quantification of GABA and Other Metabolites in Human Brain

Christine Sandra Bolliger[1], Chris Boesch[1], Roland Kreis[1]

[1]*DRNN/DKF, Inselspital/University of Bern*

Introduction
Magnetic Resonance Spectroscopy (MRS) can be used for non-invasive quantification of metabolite concentrations in vivo. Metabolites give rise to characteristic ^{1}H MR spectra, depending on the position of the hydrogen atoms in the molecular structure and the pulse sequence applied. The contribution of the metabolite spectrum to the total spectrum depends linearly on the concentration of the metabolite in question.
Fitting a parameterized model function to the total spectrum allows for the quantification of metabolite contents. The error of the fitted parameters, in particular the concentrations, is evaluated using the so-called Cramer Rao Minimum Variance Bounds (CRBs) [1].
However, quantification of brain metabolites from ^{1}H MR spectra is difficult due to considerable overlap between metabolite spectra, e.g. the GABA spectrum is overlaid by resonances of creatine, glutamate, glutamine, and N-acetyl-aspartate and macromolecules, which is reflected in large CRBs.
Therefore, it can be beneficial to acquire not only one spectrum but a series of spectra with different pulse sequences and to fit all these spectra simultaneously. An example for such a two-dimensional experiment is 2DJ spectroscopy [2], where a series of PRESS scans is acquired by incrementing the echo time (TE) from one scan to the next by a fixed step size. We call a similar experiment *generalized 2DJ* when arbitrary TEs are allowed.
For a given experiment we can estimate expected CRBs without actually acquiring spectra, but based on simulated metabolite spectra, literature values for the parameters and an assumed noise level. In order to determine optimal experiments, a large set of experiments is considered and for each of them expected CRBs are estimated. Experiments yielding minimal CRBs for the metabolites of interest are considered to be optimal.
Methods
All generalized 2DJ experiments consisting of 8 PRESS scans are considered, where selected TEs range from 22ms in steps of 8ms up to 142 ms (16 TEs). Spectra for 15 brain metabolites were simulated in gava [3] using quantum mechanical principles and concentrations from the literature [4]. They were used as model functions for all experiments. The data was assumed to be fitted as a 2D array using linear combinations of model functions and prior knowledge in both dimensions [5]. Optimal experiments with minimal CRB for GABA, glutamate, glutamine and glutathione were identified.
Results
The best generalized 2DJ experiment for GABA quantification found was {4x22ms,4x94ms}, for which the CRB could be reduced to 88.5% compared to ordinary 2DJ with {22,38,54,70,86,102,118,134} ms. Glutamate CRB could be reduced to 68.3% using the generalized experiment {6x22ms,1x54ms,1x142ms}, glutamine to 81.5% using {6x22ms,2x94ms}, and glutathione to 85.6% using {7x22ms,1x118ms}. Optimal experiments for all metabolites show scarce population of the TE space with heavy weighting of the shortest TE. The specific optima depend on the choice of fit parameters, the macromolecular baseline model, prior knowledge constraints, as well as expected metabolite levels.
References

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methodology

Talk

MT-07

Functional Connectivity in Arterial Spin Labeling data

Kay Jann[1], Ariane Orosz[1], Thomas Dierks[1], Roland Wiest[2], Danny J Wang[3], Andrea Federspiel[1]

[1]Department of Psychiatric Neurophysiology / University Hospital of Psychiatry / University of Bern, [2]University Institute for Diagnositc and Interventional Neuroradiology / Inselspital / University of Bern, [3]Department of Neurology, UCLA, Ahmanson-Lovelace Brain Mapping Center, Los Angeles,

The identification and analysis of functionally connected networks became an established technique in basic and clinical neuroscience. Such networks are identified by two main approaches: a seed based approach (SBA) and by using independent component analysis (ICA). While in SBA one region of interest is used for correlation analyses ICA is a mainly data driven approach without the need of a-priori selection of regions. Most reports used functional Magnetic Resonance (FMRI) Blood oxygenation-level dependent (BOLD) data while only a handful of studies used Arterial Spin Labeling (ASL) data, although ASL can provide absolute measures of activity while BOLD only yields relative signal changes.
In the present work we investigated the feasibility of ICA based network analysis on ASL data. This includes the reliable identification of established networks on the group and single subject level and especially the possibility to quantify the network activity. This latter characteristic of networks in ASL provides a significant extension of network analyses compared to conventional analyses relying on BOLD signal.
The characterisation and quantification of network properties is of special interest when inter-individual differences have to be assessed. This is the case especially in clinical cohorts (i.e. Schizophrenia, Dementia, Depression) where alterations of networks (spatially) or their activity might provide insight on the pathophysiological mechanism underlying the specific individual symptoms and cognitive deficits.

methodology
ASL, Functional Networks, Cerebral Blood Flow Quantification

Talk

MT-08

Delayed cerebral circulation time in intracranial stenosis might lead to underestimation of cerebral blood flow from Arterial Spin Labeling

Kay Jann[1], Martinus Hauf[2], Frauke Kellner-Weldon[2], Marwan El-Koussy[2], Claus Kiefer[2], Andrea Federspiel[1], Gerhard Schroth[2]

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The aim of the current study was to estimate to what extent a delay of bolus arrival time (BAT) will result in an underestimation of cerebral blood flow (CBF) quantified from Arterial Spin Labeling (ASL) data. This effect is caused by increased spin relaxation when the tagged blood requires more time to reach the cortical areas. Patients with steno-occlusive arterial disease (SOAD) distal to the labaling plane were evaluated for this study since they show delayed BAT on the stenotic hemisphere while BAT is assumed normal on the healthy side.

We used Digital Subtraction Angiography to estimate BAT and grade of stenosis in nine patients with SOAD. Regional CBF from the anterior and posterior flow territories of the middle carotid arteries (MCA) were quantified with pseudocontinuous ASL and compared between healthy and stenotic hemispheres as well as their association to BAT.
CBF in anterior and posterior MCA territories were significantly reduced on the stenotic hemisphere depending on the estimated BAT. Moreover, grade of stenosis and BAT revealed a significant positive correlation.
Thus, the more severe the stenosis, the longer was the BAT which resulted in reduced quantified CBF values. Therefore, special caution is needed when interpreting CBF values quantified in populations with altered blood flow and delayed circulation times and one might need to adjust the CBF values with regard to circulation times.

methodology
ASL, Cerebral Circulation Times, Carotid Artery Disease

Poster

MT-09

Physiological and behavioral effects of theta burst stimulation of the primary motor cortex in healthy subjects

Ariane Orosz[1], Kay Jann[1], Miranka Wirth[1,3], Roland Wiest[2], Thomas Dierks[1], Andrea Federspiel[1]

[1]Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Switzerland, [2]Department of Diagnostic and Interventional Neuroradiology, Inselspital, University of Bern, Switzerland, [3]Helen Wills Neuroscience Institute, University of California, Berkeley

Theta burst stimulation (TBS) is a novel variant of repetitive transcranial magnetic stimulation (TMS), which induces long-lasting changes in neuronal excitability. When achieved in the primary motor cortex, such physiological modulations might also produce effects on motor behavior. In the present study we applied TBS in combination with pseudo continuous arterial spin labeling (pCASL) in order to address the questions of whether TBS has an effect on cerebral blood flow (CBF) and if TBS-induced plasticity can modify motor behavior. Twelve right-handed healthy subjects were stimulated using an inhibitory continuous TBS protocol over the right motor cortex. For Sham stimulation, the stimulation coil was tilted away by 90° from the effective tangential orientation. PCASL was performed before (pre TBS/ pre Sham) and immediately after treatment (post TBS/ post Sham). During the pCASL runs, the subjects performed a fingertapping task with their left hand, sequentially opposing the thumb to index, medium, ring and little finger at individual maximum speed. The task was presented in a block design with alternating fingertapping and resting state control conditions. We found a significant increase of CBF in the primary motor cortex after TBS, but not after Sham. It is assumed that inhibitory TBS induced a “local virtual lesion” which leads to the mobilization of more neuronal resources, in order to complete the fingertapping task in equal measure. There was no TBS-specific modulation in motor behavior, which might indicate that acute changes in brain plasticity caused by TBS are immediately compensated. This compensatory reaction seems to be observable at the metabolic, but not at the behavioral level.

methodology, neurobiology, neuroradiology, physiology
theta burst stimulation, arterial spin labeling

Poster

MT-10

The Default Mode Network in patients with depression and healthy controls: insights from Arterial Spin Labeling

Orosz Ariane[1], Kay Jann[1], Oliver Höfle[2], Thomas Dierks[1], Helge Horn[2], Roland Wiest[3], Thomas Müller[2], Andrea Federspiel[1], Sebastian Walther[2]

[1]Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Switzerland, [2]University Hospital of Psychiatry, University of Bern, Switzerland, [3]Institute of Diagnostic and Interventional Neuroradiology, Inselspital, University of Bern, Switzerland

Functional connectivity analyses have identified networks with altered spatial patterns in patients compared to controls. These changes have further been attributed to inter-individual differences in the severity of specific symptoms. Up to date, network analysis is performed on fMRI BOLD signal data that provides good estimates of the spatial properties of networks, but is incapable of quantifying the level of network activity. Networks are however not only defined by their spatial constitution (i.e. the areas that participate in the network). Also the absolute level of activity of the network and its nodes might explain differences between patient and control groups as well as within the patient group. Unlike BOLD, Arterial Spin Labeling (ASL) allows quantifying network activity in terms of cerebral blood flow (CBF) in absolute units of ml/100g/min. Here, we report on the first approach of network identification and quantification in the ASL data of 22 patients with major depression and 22 healthy controls. Networks were identified with an Independent Component Analysis (ICA) and subsequent region of interest analyses were performed to compute CBF values. We focused on the default mode network (DMN), which is the most dominant resting state network. CBF values were extracted for the whole brain grey matter (GM), the DMN as well as for its subregions (ACC, PCC, right IPL, and left IPL) and were submitted to analyses. When comparing the mean CBF values of the DMN between groups, the patients with major depression have significantly lower CBF than healthy subjects. However, as CBF in the GM also differed significantly between groups ($T=6.97$, $p<.0001$), the difference in the DMN is assumed not to be depression specific. Therefore, the DMN CBF values were submitted to an inter-group correction with the mean GM CBF of the healthy controls as reference value. The comparison of the corrected CBF values within the DMN finally did not produce any group difference. Analysis of the subregions revealed neither a significant group effect, nor any effect of region. The interaction between group and subregions did not reach significance either. However, there was a significant effect of age (covariate) on CBF ($F(1, 41)=7.335$, $p<.01$), which is in line with reports from current literature. The present results indicate that major depression is associated with decreased perfusion in the whole brain GM compared to healthy subjects. However, this decrease is not reflected in the DMN and its subregions. Our findings demonstrate an extended value ASL (compared to BOLD) for network analysis since it provides information about the activity level of a network in addition to the spatial pattern. Although there was no depression-specific modulation in DMN after adjustment for global CBF differences, this approach might help to further understand the pathophysiological mechanisms underlying specific symptoms and cognitive deficits in patients.

methodology, neuroradiology, psychiatry
Independent Component Analysis, arterial spin labeling, default mode network, depression

Poster

MT-11

Assessing slow-diffusion properties using a STEAM sequence

Jennifer Andreotti[1], Claus Kiefer[2], Thomas Dierks[1], Andrea Federspiel[1]

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Objectives: The main aim of the project is to establish the feasibility of extracting a measure of white matter fibers tracts axon's diameter distribution using a clinical scanner (Siemens, VERIO). In particular, measurements are acquired using a STEAM sequence and hence give an opportunity to detect differences and benefits of using this sequence to assess properties of slow diffusion.
Methods: One subject underwent the imaging protocol using a STEAM sequence of a Siemens VERIO 3T. The

sequence was repeated for 12 gradient directions and 10 different b-values increasing linearly from 500 to 5000 s/mm2. The mixing time also increases linearly from 50ms up to 500ms and the gradient duration is 8.9 ms. Data of 10 slices in the corpus callosum were obtained. All images have been co-registered to a common anatomical image. The white matter model assume two separate compartments providing distinguished signals as in [1,2]. The first compartment represent the intra-axonal population of water molecules. Van Gelderen formula [3] for the signal from particles trapped in a cylinder of radius R is used to estimate its signal. The signal for the extra-axonal compartment is modeled by a DT model, with principal direction as in the intra-axonal compartment. The parallel and perpendicular diffusivity are linked by a tortuosity model [1,2] and the parallel diffusivity is equal to the diffusivity of the intra-axonal compartment. An MCMC algorithm assuming a Rician noise is used to estimate the compartment's proportion, the axon radius and the fiber direction, while the diffusion coefficients and the noise level are fixed.
Results: Estimated radii show coherence in the trend of variation found in [2] and in histology although the estimates are in an higher range (8µm-11µm) than those from histology (0.5µm-1µm) and [2] (3µm-5µm). Higher noise level is seen for high b-values, therefore a model with reduced SNR with higher b-values was tested. Results show a more realistic estimation of the compartment's volume with this model.
Discussion: This work shows the possibility of assessing properties of the fiber structure related to slow diffusion using the method of [2], but with lower gradient strength. Long diffusion times, necessary to explore properties of slow diffusion, are obtained using a STEAM sequence. Further analysis on the stability of the measures extracted between subjects as well as in different measurements on a same subject are necessary. The estimate of axon's radius correlate with the mean axon's radius [2] and together with the compartment's volume give an insight into the fiber structure and density which could be useful to establish variations due to fiber degeneration or development.
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methodology
slow-diffusion, white matter, axon radius

Poster

MT-12

Assessing tract-specific scalar measures from voxel-wise MR measures

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Objectives: The objective of the project is to extract white matter (WM) tract-specific scalar measures from voxel-wise scalar MR measures disentangling contributions from fiber crossings. The model assumes two important hypothesis: first that the scalar measure considered adds up linearly for contributions from different tracts and second that there exists a unique tract-specific scalar measure for each fiber tract, i.e. the measure is constant along the tract.
Methods: Data for a single subject were acquired on a Trio Siemens with 32-channel head coil with a q4half DSI sequence (bmax=8000 s/mm2 and a total of 257 gradient directions, TE=144ms, TR=6100ms). Tractography was computed with a deterministic streamline algorithm adapted to account for multiple directions in a voxel [1] with 32 seed points for each diffusion direction in each white matter voxel.
Fiber tracts considered for the analysis are defined using the tractography algorithm results. A fiber tract is given by all the streamlines joining two specific ROI of grey matter. In addition, a minimal streamlines' density is required to define a tract. The model assumes that the scalar measure in a specific voxel is given by the weighted sum of the tract-specific measures of the fiber tracts crossing in that voxel. The weight of a tract is proportional to their volume in the voxel and is estimated using the tractography map as the proportion of streamlines of each tract, corrected by its length. Measures of all WM voxel are considered in a unique linear system in order to use the whole information of the network to extract the fiber tract-specific scalar measures.
Results: First tests of the method were done using simulated data in order to assess robustness to noise as well as effects of a non-constant measure along the tract. Results show a good stability to noise, as all voxel are used to

estimate fiber tract specific measures.
In addition, the model has been applied to both the exponential of -ADC and the ADC itself. Results show very small differences. In addition the structure of differences is non random showing larger differences near WM limits. This is probably do to partial volume effects and may be corrected by estimating the partial volume of CSF or GM in the voxel and including this information in the analysis.
Discussion: Tract-specific scalar measures may be relevant in order to understand the link between it and functionality ([2],[3]). The model is based on two strong assumptions under which it is possible to improve the quality of tract-specific scalar measures. Further tests on simulated data are planned in order to understand if it this model could be useful to determine if a scalar measure is constant along the tract. Also, it would be interesting to assess how diseases with local or global white matter tract degeneration will affect the model results.
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methodology
tract-specific measure

Poster

MT-13

Auditory evoked potentials predict awakening from post-anoxic coma and therapeutic hypothermia

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Background: Awakening from post-anoxic coma is increasingly observed. Adequate prediction of neurological recovery after cardiac arrest (CA) and therapeutic hypothermia (TH) is thus an essential component of post-resuscitation care. Hypothermia alters prognostic accuracy. In this setting, we recently showed that electroencephalographic (EEG) activity might improve outcome prediction.
Aim of the study: Here, we examined whether single-trial EEG analyses of auditory evoked potentials (AEPs) improve outcome prediction of post-anoxic coma. We primarily investigated the early predictive value of auditory processing to standard vs. deviant sounds (i.e. the mismatch negativity, MMN).
Methods: AEPs were recorded twice: during TH and immediately after re-warming in normothermic conditions (NT). We characterized responses to standard vs. deviant sounds using voltage measurements at 19 electrodes over the scalp (voltage topographies), positioned according to the 10-20 international system. We first analyzed the difference in neural responses to standard sounds vs. 3 deviant sounds ("deviant"=sound change in duration, location or pitch). For each subject, MMN was assessed by discriminating single-trial brain responses to standard vs. deviant sounds. Discrimination was evaluated for each of the three types of deviants by computing the Area under the Receiver operating curve (AUC). Outcome prediction was obtained by comparing AUC values obtained during TH and NT. MMN analysis was automatic and blinded to patient outcome.
Results: 21 patients with comatose CA treated with TH (33°C, 24 hours) were studied. Change in the AUC value of MMN during TH vs. NT was the most accurate predictor of awakening from coma. An improvement in AUC values from TH to NT was always observed in survivors (100% positive predictive value for successful awakening). All non-survivors had a decrease in the AUC value between the two recordings (100% specificity for poor outcome).
Conclusions: Early quantitative and automatic assessment of MMN is a strong predictor of outcome after CA and TH. An improvement in the discrimination of single EEG trials from standard vs. deviant sounds was 100% predictive of successful awakening from post-anoxic coma.

methodology

Poster

MT-14

Comparing frontotemporal dementia and schizophrenia using a frontal lobe dysfunction-related EEG microstate

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Objectives: Recently many studies appeared the correlation EEG and fMRI. Britz and his colleges suggested that the duration of the EEG Microstate Map C is associated with the attention and control network (saliency network), where the anterior insula plays an important role, and EEG Microstate Map D is correlated with dorsolateral prefrontal and ventrolateral prefrontal cortex. To determine the specificity of EEG microstate features in frontal lobe, microstate analysis was performed in mild frontotemporal dementia (FTD) patients whose pathological changes are limited paralimbic, frontal neocortical, limbic and subcortical areas in frontal lobe, and compared with schizophrenia (SZ) patients whose microstate abnormalities are well established.
Methods: We performed EEG Microstate analysis in mild FTD (n=15; mean age = 68.27±7.67; mean MMSE= 23.33±2.99), and in SZ (n=14; mean age = 26.07±9.55). Moreover, we collected a sample of age-matched normal controls (NC) for each of the two study groups (n=15 and 19). Firstly, we compared the duration of each Microstate Map (A, B, C, and D) of the FTD and the SZ group separately to the NC using a t-test. Next, we were interested in the comparison of the standardized values (z-scores) of the durations between FTD and SZ.
Results: In FTD patients, the duration of the Microstate Map C was significantly decreased compared to HC (p=0.030). However, in SZ patients, the duration of the maps A, B and D were significantly decreased in comparison to HC (A: p=0.024, B: p=0.019, and C: p=0.009). No group difference in the Map C was detected between FTD and SZ, while the duration of the Map D showed a tendency towards a shorter duration in SZ than in FTD patients (p=0.087).
Conclusions: Our results support the view that the duration of various microstates (Map A, B, D) in schizophrenia are affected, on the contrary, early-stage FTD demonstrates more limited pathological changes (only Map C). We speculate that the decreasing duration in the map C is specific for the FTD, while the difference in the duration of Map A, B and D in schizophrenia may represent the wide range dysfunction in total brain.
Significance: It is possible assume that EEG Microstate maps may show disease specific abnormalities.

methodology
EEG, Microstates, Frontotemporal dementia, schizophrenia, salience

Talk

Neurobiology (NB)

NB-01

Pharmacological neuroprotection in mouse models with retinal degeneration

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Purpose: Programmed cell death is a hallmark of several retinal diseases such as aged-related macular degeneration and retinitis pigmentosa. We have used different mouse models of retinal degeneration that display features of the diseases in order to investigate neuroprotective properties of erythropoietin (Epo).
Methods: C57/BL6 mice received single i.v. injections of sterile 1% NaIO3 (25 mg/kg) to induce retinal degeneration. Control animals were treated with 0.9% NaCl. Furthermore, rds mice (O20/A-Prph2Rd2/J), an animal model of retinitis pigmentosa, were introduced. The animals were treated i.p. with Epo (Recormon 2000). NaIO3/NaCl-injected animals received four times 100 IU, whereas rds mice were treated with 100 IU every other day between postnatal day 6 and 20. Retinal Epo contents were quantified with 125I-Epo-based RIA. Visual acuity was measured using the OptoMotry System and scotopic and photopic electroretinograms (ERG) were recorded. Thickness of the outer nuclear layer (ONL) was measured and the number of rows of photoreceptor nuclei was counted on H&E stained paraffin slides.
Results: RIA–analysis revealed retinal Epo overexpression of 10.7 mIU / mg protein after injections of 100 IU and 101.3 mIU / mg after injection of 650 IU Epo. NaIO3 injected C57/BL6 displayed decreased visual acuity beginning at day 3 post injection and time-dependent decrease in a-, b- and c-waves (ERG). Epo injections did not lead to significantly increased visual function compared to NaIO3. However, in the rds mice treatment with Epo resulted in significant increases of scotopic a-, b-, and c-waves as well as photopic b-wave compared to rds controls. NaIO3 induced patchy and permanent RPE loss with subsequent PR damage and displayed a reduced ONL. Epo treatment did not increase the ONL thickness, as revealed by morphometric measurements. On the other hand, Epo treated rds mice showed a significant increase in ONL thickness compared to NaCl injected animals.
Conclusions: Epo has a neuroprotective effect in the rds mouse but not in the NaIO3-induced retinal degeneration. This indicates pathway-specific effects of Epo treatment. Because of its high safety profile and good bioavailability Epo could possibly be used for new treatment strategies in retinal degenerative diseases.

neurobiology

Poster

NB-02

Molecular structure of nicotinic acetylcholine receptor-rapsyn clusters in native postsynaptic membranes

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Clustering of acetylcholine receptors (AChR) at the neuromuscular junction is essential to muscle function. Decreased levels of clustering are linked with myasthenic syndrome. The scaffolding protein rapsyn directly binds AChR and is required for the onset and the stability of AChR clusters. One model states that rapsyn maintains a locally elevated AChR concentration by creating a large rapsyn-AChR network, thereby reducing molecular diffusion. The mode of rapsyn-AChR binding is debated. We addressed these questions with cryo-electron tomography and subtomogram averaging and classification. We report the molecular structure of AChR-rapsyn clusters in native postsynaptic membranes. From that we conclude on the number of rapsyn molecules binding each AChR. The structure of rapsyn-connected AChR clusters supports the model whereby rapsyn maintain an elevated AChR

concentration by limiting its Brownian diffusion, without the absolute requirement for other cytoskeletal elements.

methodology, neurobiology

Poster

NB-03

Stem Cell Therapies in Neuroinfection: Neuronal Stem Cells Migrate to and Differentiate at the Site of Hippocampal Brain Injury in Experimental Pneumococcal Meningitis

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Background: In pediatric bacterial meningitis (BM), survivors frequently suffer from long-term sequelae which include difficulties in learning and memory. The neurofunctional deficits are associated with the occurrence of apoptotic brain injury to the stem cell niche in the subgranular zone of the hippocampal dentate gyrus in experimental BM. Here the therapeutic potential of grafting of neural stem and precursor cells (NPCs) was evaluated by assessing the migration and differentiation of transplanted fetal NPCs into injured hippocampus *in vitro*, and *in vivo* in an infant rat model of pneumococcal meningitis.
Methods: Green fluorescence protein-expressing (GFP) NPCs from fetal rat hippocampus were grafted into the dentate gyrus hilus of organotypic hippocampal slice cultures injured by challenge with live *Streptococcus pneumoniae* (serogroup 3, n = 9). The migration and differentiation of grafted cells were assessed by immunohistochemistry. *In vivo*, NPCs were stereotaxically transplanted into the hilus of the hippocampus of rats 1 week after cured BM. At 1, 2 and 4 weeks following transplantation, survival, migration and differentiation of transplanted NPCs were evaluated by immunohistomorphometry.
Results: When grafted in hippocampal slices injured by pneumococcal challenge, NPCs migrated to, and differentiated at the site of injury in the granular layer of the dentate gyrus. In rats after cured BM (n = 14), GFP-expressing NPCs migrated from the injection site in the hilus to the injured granular layer of the hippocampal dentate gyrus and expressed markers of neuronal differentiation at 1 (n = 5) and 2 (n = 3) and 4 weeks after transplantation (n = 6).
Conclusions: Fetal NPCs grafted into the hippocampus after BM migrated to the area of hippocampal brain damage and differentiated into neurons in vitro and in vivo. The transplantation of NPCs may hold promise for regenerative therapies aimed at repair of brain damage after BM.

neurobiology
Bacterial meningitis, hippocampus, apoptosis, stem/progenitor cells, differentiation

Poster

NB-04

Grafting of neuronal precursor cells in auditory spiral ganglion loss after experimental bacterial meningitis

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Grafting of neuronal precursor cells in auditory spiral ganglion loss after experimental bacterial meningitis

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BACKGROUND: Bacterial meningitis is the most common cause of acquired profound bilateral sensorineural hearing loss in childhood. Conversely, hearing loss is observed in up to 30% of meningitis-survivors and is characterized by loss of auditory afferent spiral ganglion neurons (SGN) and the loss of hair cells. The ability to regenerate lost sensory hair cells and auditory neurons in the mammalian inner ear is limited. The aim of this study was to establish a proof of concept that surgical grafting of spiral-ganglion-derived stem cells into the cochlear modiolus would allow survival and repopulation of spiral ganglion with neurons, a prerequisite for the functional effectiveness of cochlear implants.
METHODS: 11 day old male Wistar rats were infected intracisternally by injection of 5x10EE5 CFU/ml live Streptococcus pneumonia. Experimental BM was treated with ceftriaxone 100mg/kg, bid, sc for 3d. Two weeks after the infection, spiral ganglion stem cells, isolated from infant (P2-P4) rats constitutively expressing green fluorescent protein (GFP) were injected into the modiolus via a retroauricular, transbullar approach. Presence of grafted cells was documented by 1 week after transplantation by immunohistochemistry using markers for β-III-tubulin and MyoVIIa.
RESULTS: The surgical access and the transplantation of proliferative GFP expressing spiral ganglion cells was performed in three animals with minimal trauma to the middle and inner ear structures. The grafted spiral ganglion-derived stem cells survived and morphologically integrated into the cochlear modiolus rats after experimental bacterial meningitis with the formation of axonal structures.
CONCLUSIONS: The present data demonstrates proof of concept for effective surgical transplantation and survival of spiral-ganglion-derived stem cells into the cochlear modiolus in rats after experimental bacterial meningitis - a prerequisite for the development of regenerative therapies aimed at improving sensorineural hearing loss after bacterial meningitis.

neurobiology
Bacterial Meningitis, Inner ear, Stem cells, Transplantation, Neuroregeneration

Poster

NB-05

Umbilical cord Wharton's jelly-derived mesenchymal stem cells have neural differentiation potential

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OBJECTIVE:
Perinatal brain damage accounts for the major part of the neurological problems in surviving premature infants. A considerable therapeutic potential has been ascribed to multipotent mesenchymal stem cells (MSC). The umbilical cord connective tissue (Wharton's jelly) represents a promising source of MSC. Thus, the aim of this study is to characterize the phenotype of human Wharton's jelly-derived cells and to assess their neural differentiation potential.

STUDY DESIGN:
Wharton's jelly cells from umbilical cord tissues of term and pre-term (gestational age < 37 weeks) pregnancies were evaluated. The expression of the cell surface markers for MSC was measured by flow cytometry. Accordingly, MSC have to be positive for CD105, CD90 and CD73, but negative for CD45, CD34, CD19, CD14 and HLA-DR (Dominici et al., Cytotherapy, 2006, 8:315). Adaptations of previously published multistep protocols (Portmann-Lanz et al, AJOG 2010; 202: 294 e1-11; Fu et al, Acta Neurobiol Exp 2007; 67: 367; Zhang et al, Differentiation 2010; 79: 15) were used to produce neural progenitors, the so-called neurospheres. Analysis of neural differentiation markers was performed by real-time PCR, flow cytometry and immunocytochemistry.
RESULTS:
Isolated umbilical cord Wharton's jelly cells were plastic adherent and highly positive for CD105, CD73, CD90, but negative for CD45, CD34, CD14, CD19 and HLA-DR, independent of gestational age. A subset of Wharton's jelly cells displayed the neural progenitor cell markers Nestin and Musashi-1, and the mature neural markers MAP-2, GFAP and MBP at protein and mRNA levels before any differentiation. Pre-induction into neural precursors resulted in the formation of cell clusters growing in suspension (neurospheres) and in the increased protein and gene expression of Nestin and Musashi-1.
CONCLUSIONS:
Wharton's jelly cells meet the criteria for the phenotypic characterization of MSC, independent of gestational age. The expression of markers specific for immature and mature neural cells in undifferentiated Wharton's jelly-derived MSC, as well as their successful induction into neural progenitor cells, indicates the potential of these cells for neural differentiation and their possible future use in the treatment of neurological diseases.

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neurobiology
Mesenchymal stem cells, Placenta

Poster

NB-06

Pneumococcal meningitis increases neurogenesis in the rat hippocampus

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BACKGROUND: Bacterial meningitis (BM) leads to long-term neurological sequelae with memory and learning deficits in up to 50% of survivors. Difficulties in learning and memory have been associated with damage to the hippocampus in experimental BM. Hippocampal injury is characterized by apoptosis in the neurogenic niche of the dentate gyrus. We therefore hypothesize that the lifelong persistence of memory and learning disability in patients surviving BM is due to an impediment of neurogenic brain repair function.
The present study investigated the effect of pneumococcal meningitis on stem- and progenitor cells and their proliferating rate over time i.e. at 1, 3, 6 and 12 weeks after infection in the dentate gyrus of the hippocampus by immunohistochemical detection of 5-bromo-2'-deoxyuridine (BrdU) incorporation and by a neuronal colony forming cell (neurosphere) assay. The relative and absolute numbers of proliferating doublecortin (DCX) -positive, glial fibrillary acidic protein (GFAP)-positive and CD68-positive cells were enumerated to characterize the cellular composition of repair function after BM.
METHODS: 11 day old male Wistar rats were infected intracisternally by injection of 5x10E3 live Streptococcus pneumonia or sham-infected with 10 µL sterile saline. 18 h after infection, antibiotic treatment was started (ceftriaxone 100mg/kg, bid, s.c for 3 d). Rats were sacrificed 1, 3, 6 and 12 weeks after infection. In the BrdU study, rats received a single dose of BrdU (50mg/kg) daily for 3 consecutive days prior to sacrifice. Brains were harvested, paraffin-embedded, and 10µm sections were stained by immunohistochemistry. BrdU, DCX, GFAP and CD68 positive cell densities in the dentate gyrus were assessed. For the neurosphere assay hippocampi were dissected after sacrifice and a single cell suspension was prepared to cultivate cells in a collagen matrix under conditions enabling stem or progenitor cells to form neurospheres. For evaluation, cresyl violet stained neurospheres in collagen were quantified in triplicate for each animal.
RESULTS: Pneumococcal meningitis significantly increased cell proliferation in the dentate gyrus of the hippocampus up to 6 weeks post infection ($p < 0.001$ for 1 and 3 weeks after infection and $p=0.037$ for 6 weeks after infection), returning to levels similar to those of sham-infected rats at 12 weeks after infection. Proliferating cells were

60-80% DCX-positive, 10-20% were GFAP-positive and only a minor fraction (about 0-5%) were CD68 positive., Results from the neurosphere assay, performed in parallel, showed a trend for increase in stem-/progenitor cells until 3 weeks after infection .
CONCLUSIONS: Pneumococcal meningitis increases the rate of cell proliferation up to 6 weeks after infection. Thereafter proliferation rates return to physiologic level at 12 weeks after infection. The higher amount of neurospheres in infected animals compared to control animals after 6 weeks is in agreement with the observation that 60 to 80% of proliferating cells in the BrdU study were progenitor cells. Thus, the majority of proliferating cells consecutive to BM are neuronal progenitor cells which are however incapable at restoring neurofunctional integrity since neurological deficits persist in survivors of BM.

neurobiology
meningitis, neurogenesis, stem cell

Poster

NB-07

Studying Functional Regeneration of Propriospinal Connections in the Spinal Cord in a Newly Developed *in vitro* Model

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Over the past two decades, different strategies for improving functional recovery after spinal cord injury (SCI) have been investigated. In most of these studies, lesions of the corticospinal tract have been the model system of choice. However, there is growing evidence that propriospinal connections may also play a pivotal role in recovery after SCI. To study functional recovery of propriospinal circuits *in vitro*, we have developed an organotypic slice culture model that consists of two transversal slices of embryonic (E14) rat spinal cord plated adjacently on a planar multi-electrode array (MEA). The cytoarchitecture of the tissue in this model is well preserved and cultures can survive for several weeks. Within a few days in vitro (DIV), axonal connections form between the two slices. These connections can be shown on the structural level by using immunohistochemistry and on the functional level by measuring the spontaneous network activities of the slices with extracellular multisite recordings. Synchronized network activities suggest axonal coupling between slices, whereas non-synchronous bursting in both slices indicates a lack of connection.
To measure the intrinsic capability to regenerate, we cut these newly-formed connections between the slices with a scalpel blade at different time points in vitro. Two weeks later, we recorded the network activity of the slices and stained the axons. Slices cut up to 11 DIV reconnected to a good extent. Cultures older than 11 DIV at the time point of lesion showed a decreased intrinsic regeneration potential with a minimum reached at 17 DIV. From this time point on, the regeneration capacity is low and therefore comparable to the poorly-regenerating adult CNS.
To evaluate our model, we performed lesions at 21 DIV and supplemented the medium with the phosphodiesterase inhibitor Rolipram, which has been shown to improve axonal growth in vivo. Under standard conditions, more cultures of the Rolipram treated group were coupled compared to the control group (control: 10.3%, Rolipram: 29%, n=29). When we blocked GABAergic and glycinergic transmission using gabazine and strychnine, respectively to disinhibit the network, 75.5% of the Rolipram treated cultures where connected compared to 14.3% connected slices in the control group (n=28). Given these results, we claim our model suitable to pre-evaluate new strategies to promote functional recovery after spinal cord lesions in a quick and easy way.

methodology, neurobiology, physiology

Poster

NB-08

Localized dendritic activity in layer 2/3 pyramidal neurons in vivo

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The dendrites of cortical pyramidal neurons can generate dendritic spikes which are mediated by either NMDA or calcium channels. Although they are initiated at large distances from the axon, dendritic spikes can have a strong influence on the firing of a neuron. Despite being a robust mode of cellular processing in vitro, the relationship between dendritic spikes and somatic spiking has never been shown in vivo. We investigated the occurrence of dendritic spikes in L2/3 pyramidal neurons in the hindlimb somatosensory cortex of urethane anesthetized rats using single-cell calcium imaging and patch-clamp electrophysiology. Spontaneous calcium transients were measured in basal dendrites (0.65±0.02 dF/F; n=148), apical dendrites (0.49±0.02 dF/F; n=235) and tuft dendrites (0.54±0.04 dF/F; n=98). In all dendrites, the amplitude of the calcium transients corresponding to a single somatic action potential increased significantly when multiple (≥ 2) action potentials were recorded at the soma ($p<0.05$). Although most calcium transients were associated with somatic action potentials, 17% of calcium transients in the tuft dendrites were not correlated with somatic activity whereas isolated calcium transients only occurred in 3% and 1% of calcium transients in the apical and basal dendrite (respectively). Furthermore, in the tuft, calcium transients typically spread throughout the entire distal dendritic tree however in approximately 20% of cases, transients were restricted to a single branch.

neurobiology
Dendrite

Poster

NB-09

Callosal activation of interneurons in the sensorimotor cortex in rats in vitro and in vivo

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Numerous studies suggest that activation of one cortical hemisphere can inhibit activity in the corresponding area of the opposite hemisphere. Here, we investigated the activation of local inhibitory neurons by excitatory axons traversing the corpus callosum. ChannelRhodopsin2 (ChR2) conjugation with the AAV-virus was injected in to layer 5 (L5) of the somatosensory cortex of one hemisphere. Following ChR2 expression, callosally projecting axons in the opposite hemisphere were stimulated by 10 whole-field blue (460nm) light flashes at 10 Hz while the electrical activity of interneurons in different layers were monitored via whole-cell patch-clamp recordings in brain slices. To reveal the direct mono-synaptic component, experiments were performed in presence of TTX (1 µM) and 4-AP (100 µM). Putative interneurons in all layers received direct inputs from the opposite hemisphere. However, the integral of the response was significantly larger in L2/3 neurons (11.1 ±2.2 mV*s, n=22) than in L5 neurons ($P<0.001$; 2.2 ±0.8 mV*s, n=25). In vivo, we investigated the activation of interneurons by a sensory hindlimb stimulation in urethane-anaesthetized rats. Electrophysiologically-identified L2/3 and L5 interneurons were monitored via whole-cell recordings and L1 interneurons were monitored via calcium imaging (L1 was bolus-loaded with OGB1-AM). Hindlimb stimulation, known to strongly activate pyramidal neurons in the contralateral hemisphere, also activated 39% of ipsilateral L1 neurons. Furthermore, one out of four L2/3 interneurons, but no L5 interneurons (n=7) were activated by ipsilateral hindlimb stimulation. These results demonstrate that supragranular (L1 and L2/3) interneurons are directly activated by callosal inputs and therefore are likely candidates to mediate interhemispheric inhibition.

neurobiology
inhibition

Poster

NB-10

Long-term Plasticity of Inhibitory Synapses in thalamic nuclei of the rat whisker system.

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Many types of synapses in various regions of the central nervous system are able to change their transmission strength depending on previous activity history – a process known as synaptic plasticity. This property enables the brain to adapt to a changing environment. Many forms of synaptic plasticity require simultaneous activation of both the pre- and the postsynaptic neuron.

Sensory plasticity can be studied in the rat somatosensory (whisker) system. Information flow from the rat's whiskers is gated through the thalamus to the primary sensory cortex. The thalamocortical (TC) neurons are therefore in a pivotal position for signal integration, filtering and processing. TC cells receive strong inhibitory inputs from neurons of the thalamic reticular nucleus and the internal capsule as well as from local interneurons. Although plasticity of excitatory inputs has been well studied, not much is known about plasticity of the inhibitory input to thalamic neurons. One characteristic feature of TC neurons is that they are able to fire in two distinct firing modes:
During wakefulness TC neurons do not typically fire single action potentials (APs) or short high-frequency bursts of APs but instead produce sustained "tonic" AP firing, whereas in sleep states of slow-wave oscillations they fire more, but not exclusively, low threshold bursts. What the impact of these different firing modes is on synaptic plasticity is unknown.

To study long-term plasticity of inhibitory inputs to TC cells in two thalamic nuclei (VPM and Pom), we made patch clamp recordings of TC neurons in acute brain slices from young rats. Inhibitory synapses were stimulated using visually guided extracellular stimulation. After recording baseline synaptic strength, IPSPs were paired with burst activity in TC cells at different time windows. To our surprise, we induced long term potentiation of IPSPs, independent of the timing between pre- and postsynaptic stimulation.
Chelating Ca^{2+} signalling by infusing BAPTA into the postsynaptic TC neuron blocked long-term potentiation (LTP) of the IPSPs.
Therefore, we investigated the Ca^{2+} signalling in TC dendrites by two-photon fluorescence microscopy. We found that burst discharges that were mediated by low threshold spikes that could only be evoked at hyperpolarized membrane potentials resulted in large and widespread elevations of dendritic Ca^{2+} transients. In contrast, depolarized membrane potentials resulted in single or tonic AP firing that evoked much smaller Ca^{2+} signals restricted to the perisomatic domain. We conclude from these experiments that the availability of T-type voltage activated Ca^{2+}channels influences dendritic Ca^{2+} signalling in the dendrites of TC neurons. This suggests that the LTP of IPSPs might be dependent on the membrane potential, i.e. the state the TC neuron is in. We are currently testing this hypothesis.

Our results suggest that LTP of inhibitory transmission in TC relay cells is Ca^{2+} dependent, but that the plasticity does not depend on the timing between pre- and postsynaptic activity. Instead, we assume that this form of intrinsic plasticity is likely to be dependent on the postsynaptic AP discharge mode (wakefulness with tonic firing or sleep with low threshold burst firing).

neurobiology, physiology
Synaptic plasticity, long-term potentiation (LTP), inhibitory postsynaptic potential (IPSP), thalamus, Ca^{2+} imaging

Talk

NB-11

Inhibition of layer 5 pyramidal neuron dendrites during Transcranial magnetic stimulation (TMS).

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Transcranial magnetic stimulation (TMS) is a noninvasive method used to modify neural processing. Although TMS is a common clinical technique, little is known about the cellular basis of its effects. TMS has both excitatory and inhibitory effects in patients and there is some evidence to suggest that TMS evokes inhibition via $GABA_B$ receptors. Since $GABA_B$ receptors are also known to suppress firing in cortical pyramidal neurons via dendritic $GABA_B$ receptors, we tested the effect of TMS on layer 5 (L5) neocortical pyramidal dendrites. Calcium activity in a population of L5 pyramidal neuron dendrites was measured using a fiber optic system ("periscope") during sensory stimulation of the hindlimb and TMS in urethane-anaesthetized rats. Layer 5 pyramidal neurons were pre-loaded via a bolus of the calcium indicator OGB1-AM to L5. For TMS stimulation, a brief magnetic field (500 µs) was applied to a coil placed in close proximity to the head of the rat. This induced a transitory magnetic field in the superficial cortical layers under the coil which induced a brief (38 ± 6 ms) increase in dendritic calcium activity (26 ± 10 dF/F*s; n=4). However, when TMS was coupled with hindlimb stimulation, the amplitude of the dendritic calcium response to hindlimb stimulation was significantly decreased by 27 ± 5 % ($p<0.05$, n=9). This decrease in evoked dendritic activity during TMS was mediated by $GABA_B$ since application of the $GABA_B$ antagonist CGP52432 to the cortical surface prevented the TMS-evoked decrease in neural activity. Further, directly activating $GABA_B$ receptors on the L5 apical dendrite by the local application of the $GABA_B$ agonist baclofen into the superficial layers of the cortex caused a significant decrease in both the area and maximum amplitude of the dendritic calcium signal by 63 ± 13% and 62 ± 9% respectively ($p<0.05$, n=5). These results not only illustrate that TMS induces local $GABA_B$ mediated inhibition, but they also highlight the effectiveness of $GABA_B$ mediated inhibition on dendritic calcium activity.

neurobiology

Poster

NB-12

Neuronal excitability and synaptic plasticity of cortical neurons in neuropathic pain

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Neurons are not hardwired but can undergo plastic changes to adapt to the changing environment. Important learning- and experience-related plasticity mechanisms are long-term potentiation (LTP) and depression (LTD) of synaptic transmission, changes in intrinsic excitability and structural plasticity. Neuronal plasticity usually serves important physiological functions, but might also be the basis of pathological conditions in the diseased or injured nervous system. E.g. chronic pain can be viewed as resulting from an aberrant learning process associated with maladaptive plasticity. Noxious stimuli result in increased activity in several cortical areas, including the primary and secondary somatosensory cortices, the prefrontal cortex, the insular cortex and the anterior cingulate cortex (ACC). This increased activity may cause neurons in these areas to adjust their properties and undergo plastic changes; these alterations might be the basis for chronic pain. We are investigating the cellular and molecular changes that occur with regard to neuronal plasticity in the primary somatosensory cortex (S1) and the ACC under chronic neuropathic pain conditions. Neuropathic pain is induced in mice by chronic constriction injury (CCI) of the left sciatic nerve and we use patch-clamp electrophysiology to record the electrical activity of up to four cells in S1 or in the ACC simultaneously. Our experiments have shown that pyramidal neurons in both S1 and ACC in CCI operated animals have a significantly lower threshold for action potential generation than neurons in sham operated animals, indicating that cortical neurons in animals with neuropathic pain may have undergone some plasticity changes that render them more excitable. This reduced threshold is accompanied by a significant increase in the input resistance, indicating changes in the density of ion channels. Additionally, experiments show a trend towards a change in the neuronal connectivity pattern that would shift the excitation-inhibition ratio in favour of increased excitation. These changes in the cortex may be the basis for persistent pain sensation long after cessation of the acute painful experience.

neurobiology
Neuropathic pain

Poster

NB-13

mRNA translation during sleep consolidates cortical plasticity in vivo

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Sleep consolidates experience-dependent brain plasticity, but the precise molecular mechanisms mediating this process are unknown. We tested the hypothesis that sleep promotes brain plasticity consolidation through de novo protein synthesis. In support of this hypothesis, sleep is associated with heightened brain protein synthesis and increased transcription of mRNAs involved in protein synthesis regulation. Protein synthesis in turn is critical for long-term memory formation and persistent forms of plasticity in vitro. We examined the role of protein synthesis during sleep in a classic form of in vivo plasticity [i.e. ocular dominance plasticity (ODP) in V1] that is triggered by monocular deprivation (MD) and consolidated by subsequent sleep in cat (Franck et al., 2001).
We show that local V1 inhibition of mTOR-dependent protein synthesis during sleep abolishes ODP consolidation, but has no effect on plasticity induced during wakefulness. We then show that sleep promotes translation initiation (via eukaryotic initiation factor 4E (eIF4E)-binding protein 1 [4E-BP1] phosphorylation) and the translation (but not transcription) of key plasticity-related mRNAs (ARC and BDNF). Collectively, these findings suggest that sleep may be a brain state specialized for cortical mRNA translation. Interruption of this process has functional consequences, as it abolishes the consolidation of experience in the cerebral cortex.

neurobiology
Sleep, synaptic plasticity, protein synthesis, visual cortex

Poster

NB-14

Intracerebroventricular Transplantation of Human Placenta-Derived Mesenchymal Stem Cells for the Neuroregeneration in a Rat Perinatal Brain Injury Model

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OBJECTIVE: Peripartal brain injury in the premature infant leads to a large spectrum of clinical problems. There is no established therapy available. Stem cell transplantation has been proposed as a therapy for neurodegenerative diseases. The aim of this study is to assess the therapeutic potential of human stem cell treatment in an animal model of perinatal brain damage.
METHODS: Perinatal brain injury was induced in newborn (postnatal days 2-7) Wistar rats by the administration of LPS (0.1 mg/kg BW, i.p.), followed by the ligation of the left carotid artery and hypoxia (8% O2, 80 min). Injured and sham-treated animals were transplanted 24-48h or 1 week post injury. Newborn anesthetized rats were fixed in a stereotaxic frame (Kopf) and mesenchymal stem cells (MSC) derived from human placenta (chorion) or umbilical cord Wharton's jelly (250'000 cells in 5 µl) were injected intracranially into the left lateral ventricle. The animals were sacrificed 3-4h, 1, 2, 4 weeks and 2 months after transplantation, As a functional test, footprint pattern analysis was carried out in the two later time points before sacrifice. Brain damage was shown by gross macroscopic changes in coronal brain sections, by the loss of myelination (staining with Luxol fast blue) and astrogliosis

(immunohistochemistry (IHC) using a anti-rat GFAP antibody). In adjacent brain sections, donor-derived cells were detected by IHC using a mouse anti-human HLA Class 1 ABC antibody.
RESULTS: The neonatal brain injury rat model results in the reduction of brain volume in the hemisphere ipsilateral to the injury site, to the loss of myelination and to reactive glial response. Donor-derived cells were detected in the brains of rats at all time points as single cells as well as cell aggregates. The footprint analysis showed a significant difference in the left vs the right hindlimb stride in the group of injured not treated animals only.
CONCLUSION: Human stem cells were successfully delivered into the lateral ventricle of neonatal rat brains. Donor cells were detected in the hosts' brains. Longer term studies will be done to analyze the proliferation, the long-term survival and engraftment of the donor cells. The co-expression of lineage-specific proteins and human-specific markers will give information about the fate of the transplanted human cells in the brains of both injured and control rats. Preliminary results of the footprint analysis suggest that there might be a functional improvement in treated vs untreated rat. However, the behavioral tests to assess the improvement of motor and memory deficits will be expanded in future experiments.

neurobiology
perinatal brain injury, hypoxic-ischemic encephalopathy, stem cell therapy, animal model

Talk

NB-15

Hydrogen peroxide mediates cortical ERK activation after preconditioning hypoxia

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BACKGROUND. We have previously shown that overexpression of human glutathione peroxidase 1 (GPx1) protects the developing murine brain from hypoxic-ischemic (HI) injury, indicating that hydrogen peroxide contributes to neonatal HI injury. Preconditioning with a short non-injurious period of hypoxia 24 h before the insult (HPC) has also been shown to reduce hypoxic-ischemic (HI) injury. Paradoxically, GPx1 overexpression prevents protection mediated by HPC. ERK has previously been shown to be involved in HPC protection and to be activated by hydrogen peroxide.
OBJECTIVE. To see whether GPx1 overexpression inhibits preconditioning hypoxia-induced activation of ERK in the areas of the brain protected by HPC.
METHODS. Postnatal day 6 wildtype (wt) or human GPx1 overexpressing mice were exposed to global hypoxia (8% oxygen) for 45 min and brain tissue analyzed for ERK1/2 phosphorylation by Western blotting and immunohistochemistry at different time points after reoxygenation.
RESULTS. While the non-injurious hypoxia stimulus caused transient activation of ERK1/2 in cortex of wt animals, no ERK activation was observed in GPx overexpressing animals. In fact, ERK phosphorylation levels dropped 50% below baseline at 24 h after hypoxia in GPx overexpressing animals, while they returned to pre-hypoxia levels at this point in wt animals. Induction of hypoxia-inducible factor 1α (HIF-1α) was not different in wt and GPx overexpressing animals, indicating that the lack of ERK activation in GPx overexpressing animals was not due to a lack of hypoxia response. Hypoxia-induced ERK phosphorylation in wt animals was observed in neuronal and non-neuronal cells of areas known to be salvaged by HPC and associated with nuclear translocation.
CONCLUSIONS. Inhibition of preconditioning hypoxia-induced ERK activation can explain the paradoxical reversal of HPC-mediated protection by GPx1 overexpression. Hydrogen peroxide is thus not only harmful, but also induces neuroprotective pathways.

neurobiology
preconditioning, hypoxia, extracellular signal-regulated kinase

Talk

NB-16

Relationship between hippocampal BDNF levels and neurogenic response after acute pneumococcal meningitis in infant rats and their effect on learning and memory process

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BACKGROUND. Despite the availability of effective antibiotic therapies, pneumococcal meningitis still has a case fatality rate of ~30% and causes neurological sequelae such as motor dysfunction and learning/memory impairment in up to 50% of the surviving patients. Evidence from experimental animal studies indicates that the latter is related to selective apoptotic cell death of newly born neurons in the dentate gyrus and correlates with decreased hippocampal levels of brain-derived neurotrophic growth factor (BDNF), a factor not only involved in survival, but also differentiation and maturation of newborn neurons. On the other hand, bacterial meningitis such as caused by *S. pneumoniae* has been shown to be associated with increased proliferation and maturation of neuronal progenitor cells in the dentate gyrus. Whether this increase in hippocampal neurogenesis makes up for the loss of neurons is unknown.
OBJECTIVE. To study the relationship between hippocampal BDNF levels, the post-injury neurogenic response and the learning and memory process in pneumococcal meningitis we infected infant rats with different doses of infecting bacteria and assessed the these parameters at different time points after the acute phase of the disease.
METHODS. Infant rats were intracisternally infected on postnatal day 11 with either a low (1.5×10^4, n=57) or high (5×10^4, n=43) dose of a type 3 *S. pneumoniae* strain, or mock-infected with sterile saline (n=30). Antibiotic therapy with ceftriaxone was started at 18 h after infection. To assess post-injury neurogenesis, BrdU was injected i.p. at 50 mg/kg at 24, 48, and 72 h after infection. Hippocampal BDNF levels were determined by ELISA, learning and memory function were assessed by the Morris Water Maze test 3 weeks after infection and BrdU immunohistochemitry was performed after this last test. Hippocampal volumes were determined by Cavalieri principle in Nissl-stained sections.
RESULTS. Whereas none of the animals died in the mock-infected group, infection with the low dose was associated with 35% mortality, and 50% with the high dose. Preliminary results show that hippocampal BDNF levels were increased in the low, but not the high dose group, in the first 3 days after infection and were still elevated 3 weeks after infection. In contrast, high dose, but not low dose infection was associated with increased number of BrdU-positive cells 3 weeks after infection. This increased of proliferation and survival precursor was not associated with an increased of generation of new mature neurons in the dentate gyrus (no increased of double-staining BrdU and NeuN was found). However, our data demonstrate a decreased of this population of cells with the low dose. A hippocampal volume reduction was observed only in the low dose. The Morris Water Maze test has showed a poor performance with the both doses of infectious agent.
CONCLUSIONS: Changes in hippocampal BDNF levels after experimental pneumococcal meningitis appear to inversely correlate with post-injury neurogenesis. Despite this discrepancy in neurogenic response, the both doses of bacteria affect the learning and memory process. This fact can be explained by a blocking of the processing of maturation of the new born cells in the dentate gyrus and by a reduction of the hippocampal volume with the low dose.

neurobiology
BDNF, Neurogenesis, Pneumococcal meningitis

Poster

NB-17

Effects of Creatine Supplementation on ATP Reserves, Expansion, Migration and Differentiation of Neural Stem Cells

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The creatine kinase (CK) phosphotransfer system plays a central role in cellular energy buffering and energy transport, particularly in cells with high and fluctuating energy demands like neurons. Given the high expression of CK isoenzymes in the developing central nervous system, creatine (Cr) supplementation might improve the metabolic state of neural stem cells (NSCs). In the present study, we investigated the effects of Cr on metabolic parameters, expansion, differentiation, and migratory capability of NSCs isolated from the subventricular zone of postnatal mice (mNSCs) and NSCs derived from the human fetal cortex (hNSCs).
We found both the brain-specific cytosolic (BB-CK) and the ubiquitous mitochondrial (uMt-CK) isoform of CK expressed in mNSC and hNSC. Accordingly, Cr supplementation at 5 mM for 7 days resulted in higher CK-specific activity as well as PCr and ATP levels in mNSCs and hNSCs, as compared to untreated controls ($p<0.01$).
In both mNSCs and hNSCs, Cr exposure during expansion resulted in a dose-dependent increase in neurosphere size and total cell numbers with a maximal effect at 5 mM after 7 days in vitro ($p<0.05$). Analysis of BrdU incorporation did not reveal a significant increase in proliferation activity, but Cr-treated cultures contained less cells with immunoreactivity for active Caspase-3 ($p<0.05$), pointing towards an antiapoptotic effect of Cr.
Using a modified Boyden chamber assay, we found that both Cr-exposed mNSCs and hNSCs demonstrated an improved migratory potential ($p<0.01$) after 60 min, as compared to untreated controls. In line with this finding, we found that Cr-pretreated, GFP-labeled mNSCs showed improved migration to the ischemic brain area after intrastriatal transplantation in a distal MCA occlusion stroke model in C57/Bl6 mice ($p<0.05$).
Finally, Cr supplementation resulted in higher neuronal cell numbers (TuJ1+, $p<0.05$) at the expense of the glial fate (GFAP+, $p<0.05$) after differentiation in vitro for 5 days. In addition, we found disproportionally higher numbers of GABA-immunoreactive cells in Cr-treated cultures ($p<0.05$), suggesting that Cr acts as a differentiation factor for specific neuronal subpopulations.
In sum, our findings suggest that the CK/PCr system is critically involved in maintaining the energy metabolism of mNSCs and hNSCs. Chronic Cr supplementation resulted in increased CK activity, improved cellular ATP and PCr levels, inhibited apoptosis during in vitro expansion, and promoted NSC migration in vitro and in vivo. Cr exposure also promoted the differentiation of NSCs towards the neuronal lineage, particularly supporting the GABAergic phenotype. Cr pretreatment of NSCs might therefore offer new ways for improving cell replacement approaches for stroke and other diseases of the nervous system.

neurobiology, neurosurgery
Neural Stem Cells

Poster

Neurology (NE)

NE-01

Age-dependent effect on functional visual field

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Background: The functional visual field is the area where targets on a complex background can be recognized and distinguished from distractors. It is hypothesised that the functional visual field is influenced by age and that it is relevant for safe driving. Therefore, a test procedure to measure the functional visual field is of interest. The aim of this study is to develop a functional visual field test for a large field of view of ±50°.
Method: We projected 33 pictures of everyday life into a hemisphere (diameter 60 cm). In addition to the projected pictures, targets and distractors appeared in a randomised order within the ±50° visual field area. 17 subjects (34.6 years ± 16.15 years) volunteered for the study.
Results: Target recognition decreased with increasing eccentricity of the target (10°: 94.36%; 30°: 91.67%; 50°: 79.25%). Whereas subjects younger than 50 years old showed a more or less linear decrease in target detection with increasing eccentricity, subjects over the age of 50 years old showed a sharp drop in target recognition for targets at 50° eccentricity. On the other hand, reaction time increased with increasing eccentricity of the target (10°: 0.95s; 30°: 0.96s; 50°: 1.10s). Again, subjects over the age of 50 years showed a sharp increase in reaction time for targets at 50° eccentricity compared to a linear increase for younger subjects.
Discussion & Conclusion: First preliminary results indicate an age-dependent effect on the functional visual field, especially for targets
appearing at 50° eccentricity. A possible impact of this age-dependent effect could be a delayed detection of peripheral hazards during driving for elderly drivers and thus less time for an adequate reaction. Further research includes testing more subjects and investigating the correlation to driving.

neurology, physiology
functional visual field

Poster

NE-02

Repeated theta burst stimulation in visual neglect: Long-lasting effects on activities of daily living (ADLs) and neuropsychological testing

Dario Cazzoli[1,2], René M. Müri[2,3], Rahel Schumacher[2], Silvia Chaves[2,3], Klemens Gutbrod[3], Tim Vanbellingen[2], Manuel Bertschi[2], Christian W. Hess[2], Daniel Bauer[4], Stephan Bohlhalter[4], Ida Dommen Nyffeler[4], Peter O. Bucher[4], Thomas Nyffeler[2,3]

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Left unilateral neglect – generally defined as the failure to attend to the contralesional side of space – is a frequent neurological disease following right-hemispheric stroke and has a strong adverse influence on rehabilitation outcome. It is assumed that neglect severity is enhanced by an impaired interhemispheric inhibition from the affected towards the unaffected hemisphere, causing a pathological hyperactivity of the latter.

Among rehabilitative approaches, transcranial magnetic stimulation (TMS) gains increasing attention. In a recent study, we applied Theta Burst TMS (TBS) – a TMS protocol which has been shown to exert inhibitory effects on cortical activity – in neglect patients. TBS on the contralesional posterior parietal cortex (PPC) reduced pathological hyperactivity and induced a long-lasting improvement of visual neglect as measured with a visual perception task. The aim of the present double-blind, randomized, sham-controlled study was to evaluate the effects of TBS in neglect patients on a more general level, such as activities of daily living (ADLs) and comprehensive neuropsychological testing.
Patients included in the study underwent two experimental conditions (8 TBS trains or 8 sham stimulation trains over the contralesional PPC, in two daily sessions) in a cross-over design or a control condition without any stimulation. Neglect assessment was performed weekly (at baseline, after the first intervention, after the second intervention, and at follow-up). Assessment included a standardized observation form quantifying neglect in several ADLs (Catherine Bergego Scale) and a comprehensive battery of neuropsychological tests.
The analysis of the data collected in 24 patients shows that TBS over the contralesional PPC induces a specific and long-lasting improvement of left unilateral neglect, not only in neuropsychological tests, but also on the level of the ADLs. These results suggest that TBS may be a new promising and viable add-on therapy in neglect rehabilitation.

neurology, psychology

Poster

NE-03

Using a driving simulator to test intersection crossing behavior

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Context: Crossing an intersection is an activity that requires gathering information over a large area. The challenge in safely crossing the street is to acquire the necessary information for a decision of when to cross within a limited window of time.
Objective: A virtual intersection scenario is developed for testing the visual exploration of healthy and handicapped pedestrians.
Setup: For this study, a fixed-frame driving simulator (Foerst GmbH) is used to implement the virtual intersection scenario. Three projection screens with a surface of 1.80x1.39m are positioned in front of the subject, realizing a 180° field of view.
A head mounted eye-tracking system (SMI) was integrated into the driving simulator to record eye movements. Automated tracking algorithms are used to determine the gaze direction in the canvas coordinate frame.
Procedure: The subject is seated in front of the canvases. An intersection is presented to the subject and he is instructed to press the pushbutton when it is safe to cross the road. The scenes with other cars are characterized by the number and the duration of the gaps between the cars coming from the right and the left. The more gaps there are in a scene and the longer these gaps are, the more possibilities to cross there are, and the easier it is for the test person to cross the street.
Preliminary study: To assess feasibility of the setup, three healthy subjects and three neglect patients were tested. The experimental procedure starts with a test-run where the patient crosses the street three times to get used to the simulation. After a 2min break, 3 static and 3 dynamic scenarios are presented to the person in a randomized order. Outputs of the test setup are collisions with other cars, the number and duration of missed opportunities to cross the street and positions of visual fixations.

neurology

Poster

NE-04

One train of right inferior frontal theta burst stimulation induces improvement of naming in aphasic patients

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Aphasia is a common syndrome after left-lateralized stroke and is characterized by partial or total loss of language functions. Functional imaging studies examining language recovery after stroke often find an overactivation of the non-damaged right hemisphere. One hypothesis is, that the overactivation is dysfunctional which is explained within the framework of interhemispheric inhibition. Non-invasive brain stimulation techniques such as transcranial magnetic stimulation (TMS) allow to modulate cortical activity and may thereby offer novel therapeutic opportunities. Previous studies reported positive effects of the application of inhibitory TMS protocols over right frontal areas in aphasic patients. This indicates that an intervention on the interhemispheric balance positively influences language recovery. A repetitive TMS protocol named theta burst stimulation (TBS) was recently introduced into clinical research. It has the advantage of short application times combined with prolonged effects. Previous studies used different stimulation protocols and examined mainly non-fluent, chronic aphasic patients. For a wider use of this promising method, larger samples and more information about the parameters influencing a patient's responsiveness to TMS are needed.
The first aim of the present study was to extend previous findings of improved naming after rTMS with a different stimulation protocol in a larger sample. The second aim was to evaluate whether the best responders can be distinguished from the other patients of the sample based on patient-specific parameters (e.g. time post stroke, lesion volume).
A randomized, sham controlled, cross-over design was used. Patients performed a naming task before and after the application of one train of TBS. Patients scored significantly higher and were significantly faster after TBS than after the sham intervention. Patients who responded best were in the subacute stage of the recovery process. This effect could be obtained with a simple stimulation localisation procedure (10-20 EEG system) and a short application time of 44 seconds, which makes this procedure very suitable for clinical settings.

neurology, psychology
Aphasia, TBS

Poster

NE-05

Visual exploration behaviour to gestures in aphasic patients: evidence from eye-tracking

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Gestures are crucial in human non-verbal communication. If verbal communication is reduced, such as in stroke patients with aphasia, the reliance on gestures to compensate for this deficit may increase. The presence of limb apraxia in aphasic patients may affect the use of these gestural strategies. It is not known how aphasic patients pay attention to gestures during human interaction. The aim of the present study is to investigate gaze behavior of aphasic patients when exploring communicative and meaningless gestures and how apraxia influences this behavior. Nine patients with aphasia, of which 4 apraxic, and fifteen healthy subjects participated in this study. Their gaze behaviour was measured during the presentation of forty gestures (20 communicative and 20 meaningless), by means of an infrared eye tracking system. Videos of gestures were presented and participants were instructed to

explore them. Mean and cumulative fixation durations were measured in different regions of interest (ROI), such as face and the hand performing the gesture The analyses revealed significantly longer mean fixation durations in aphasic apraxic patients compared to aphasic non apraxic patients when they looked at the left hand performing meaningless gestures. Although, compared to healthy subjects this difference was not found. The overall explorative behaviour did not differ between all groups towards the different ROI's and this for both types of gestures. These findings suggest that communicative and meaningless gestures are overtly attended to. In apraxic aphasic patients visual processing might be slowed towards meaningless gestures due to their rather abstract, complex properties.

neurology
Gestures, visual attention, aphasia, apraxia, eye movements

Poster

NE-06

Inflammatory parameters in patients with acute spontaneous cervicocerebral artery dissection

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Background: Spontaneous cervicocerebral artery dissection (sCAD) is a major cause of stroke in young adults. Its pathogenesis is largely unknown. Recent evidence suggest an increased activity of matrix metalloproteinases (MMPs) and/or quantitative imbalance between MMPs and their endogenous inhibitors i.e. tissue inhibitors of matrix metalloproteinases (TIMPs) as a predisposition factor for sCAD. Moreover, previous studies strongly suggest that inflammation may be involved in the pathogenesis of sCAD. Among environmental factors, recent infection was reported to be associated with sCAD. This study aims at identifying inflammatory parameters associated with acute sCAD.
Subjects and Methods: Sixty four patients with sCAD and 41 matched control patients with brain ischemia unrelated to artery dissection were recruited and their serum levels of defined inflammatory biomarkers were determined in the acute phase of the vascular incidence. Serum samples from 37 healthy controls were concomitantly tested for the same parameters.
Analyses were carried out by using the Luminex xMAP (Multi-Analyte Profiling) technology.
Results: Patients with sCAD had significantly higher levels of MMP-9 ($p<0.05$) as well as an increased MMP-9/TIMP-2 ratio compared to both, matched patients with brain ischemia ($p<0.05$) and healthy controls ($p<0.001$). Moreover sCAD patients showed significantly higher CRP- ($p<0.001$), G-CSF- ($p<0.01$) as well as TIMP-4 ($p<0.001$) concentrations in comparison to healthy controls. In contrast, MMP-2 levels were significantly decreased in sCAD when compared to healthy controls ($p<0.001$). TIMP-2 showed significantly lower concentrations in both patient groups when compared to healthy controls ($p<0.001$ and $p<0.05$ respectively).
Conclusion: Acute spontaneous cervicocerebral artery dissection is associated with an imbalance in the ratio between MMP-9 and their endogenous inhibitor TIMP-2 in serum. This finding combined with higher CRP and G-CSF concentrations suggest a proinflammatory condition that may lead to enhanced ECM degradation in the vessel walls, predisposing patients for sCAD.
other

Poster

Neurogenetics (NG)

NG-01

Catecholamine Depletion Reduces Appetite for Risk Taking

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There is increasing evidence for an important role played by central catecholaminergic systems in risk taking behavior. In addition, some studies concluded that the catechol-*O*-methyltransferase (*COMT*) val^{158}met polymorphism, encoding the enzyme catechol-*O*-methyltransferase (*COMT*) that degrades catecholamines, is also associated with risk taking behavior. There is evidence that subjects with bulimia nervosa show both dysregulations of central catecholaminergic systems and abnormal risk taking behavior. One instructive paradigm for investigating the relationship between catecholaminergic function and risk taking behavior has involved the induction of catecholamine depletion (CD) achieved by oral administration of alpha-methyl-paratyrosine (AMPT). By using this pharmacological challenge we investigated the role of catecholamines in a sequential risk taking task in remitted bulimic and healthy subjects. In addition we were interested in how different variations in *COMT* val^{158}met polymorphism predicted risk taking behavior.
In a crossover design 23 female subjects remitted from bulimia nervosa (rBN) and age-matched 30 female healthy controls (HC) received AMPT (40mg/ kg body weight, maximum 4g) over 24 hours or sham depletion using diphenhydramine (100mg). After medication intake subjects played a sequential risk taking task. In every trial of this task each action taken (opening boxes) increased dynamically the risk of losing money. The task consisted of two different trial types that had both a different point of risk neutrality (100%), at which the expected value is highest and risk is fully compensated. Data were analyzed using a linear mixed model analysis.
Across groups, subjects opened on average more boxes in the sham condition then in the CD condition (mean ± SE: 104.9% ± 3.8% versus 95.9% ± 3.7%, $F_{1,453.1}$=16.60; p<0.01). There was no main effect of group ($F_{1,85.3}$=1.27; p=0.26). The *COMT* val^{158}met polymorphism did not predict the behavioral effect of CD in HC, however, in rBN, CD had a significantly more pronounced effect on risk taking behavior in carriers of the val/val genotype (sham: 83.9% ± 8.7% opened boxes; CD: 65.1% ± 8.6%) than in carriers of a met^{158} allele (sham: 110.7% ± 5.4%; CD: 108.4% ± 5.3%; significant group-by-genotype interaction: $F_{1,85.3}$=5.04; p<0.05; in rBN: significant condition-by-genotype interaction: $F_{1,188.1}$=4.41; p<0.05).
This study revealed that CD reduced risk taking appetite in a sequential risk taking task. Preliminary results suggested that the *COMT* val^{158}met polymorphism was associated with risk taking behavior following reduced catecholaminergic neurotransmission in subjects at high risk for bulimia nervosa. These results may reflect different disease subtypes and may have implication for the treatment of bulimia nervosa.

neurogenetics, psychiatry
risk taking, catecholamine depletion, bulimia nervosa, COMT, catechol-*O*-methyltransferase

Poster

NG-02

Preconditioning of chorion derived mesenchymal stem cells by different culture conditions for subsequent neural differentiation

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Objective: 1% of newborns are affected by neurological injuries. Treating such complex diseases is difficult. Multipotent mesenchymal stem cells (MSC) have the ability to differentiate towards neuronal lineages with appropriate stimulation. Moreover, MSC are easily accessible in placenta and could be a valuable source as cell graft for pre- and perinatal neuroregeneration. Elucidating the mechanisms behind homing, proliferation and differentiation of transplanted cells as well as support and alteration of the microenvironment will be an essential step towards a successful therapy.
Study Design: MSC were isolated from the chorionic membrane of normal term placentas (chMSC). Two different culture conditions were tested: either in 0.1 % gelatin-coated culture flasks and medium without any serum (G+S-), or in non-gelatin-coated culture flasks and medium containing 10% fetal calf serum (G-S+). The cells were cultured for 5 passages and, thus, analysed for the expression of the minimal cell surface marker set for MSC by flow cytometry. In addition, chMSC were tested for the expression of neural stem/progenitor markers, such as Nanog, Nestin, Oct4, FRZ9, SOX-2 and PAX6 by flow cytometry and real-time RT-PCR. Cell proliferation was assessed by MTS assay. Differentiation of chMSCs was carried out according to Zhang et al. Differentiation 2010, 79:15 and Fu et al. Acta Neurobiol Exp 2007, 67:367.
Results: chMSC expressed the minimal cell-surface marker set for MSC, independent of the culture conditions. chMSC at G+S- conditions had a higher proliferation rate and showed relatively higher expression of Nanog, Nestin, Oct3/4, Sox-2, FRZ-9 and Pax-6, than the cells at G-S+ conditions. Neurogenic pre-induction resulted in the up-regulation of nestin expression and the formation of neurospheres.
Conclusion: By altering the microenvironment, the cells behave differently in terms of proliferation and the expression of neural progenitor markers. More experiments, assays and functional tests have to be carried out to confirm the differentiation capability of the chorion derived MSC.

other
Stem cells

Poster

Neuroradiology (NR)

NR-01

Cerebral vasculitis: optimizing vessel wall MRI imaging at 3-Tesla

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Purpose:
Conventional MRI findings suggestive of cerebral vasculitis are rather non-specific. These range from vessel irregularities to cerebral parenchymal changes. A more optimized approach would include systematic imaging of the arterial vessel wall, which would allow for standardized follow-up studies to monitor disease progress and response to treatment.
Methods:
The MRI sequences are optimized for higher magnetic field scanners, e.g. 3-Tesla MRI, however they can be performed at 1.5-Tesla. In addition to the standard MRI and the MR-angiographic series, the following sequences were performed; isotropic ultrathin heavy-T2-weighted sequence, time-of-flight MR-angiography before and after intravenous gadolinium administration as well as double inversion, dark blood, fat suppressed T2 and gadolinium enhanced T1-weighted images. Co-registration of the sequences provided even more accurate understanding of the pathological process.
Results:
Two cases were followed-up by the aforementioned technique. In a documented case of cerebral vasculitis the follow-up revealed progressive stenosis, with obvious wall thickening and enhancement involving the distal segment of the left internal carotid artery as well as the A1- and M1- segments of the ipsilateral anterior and middle cerebral arteries respectively. The images were of good quality and could be reproduced over several follow-up studies.
Conclusion:
An optimized MRI technique for vessel wall imaging can allow for standardized follow-up examinations for cerebral vasculitis, thus guiding further diagnostic work-ups and therapeutic decisions.

neuroradiology
vasculitis - MRI - 3 Tesla

Poster

NR-02

Fractional anisotropy decrease in the substantia nigra in Parkinson‘s disease - a diagnostic biomarker?

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Introduction
Fractional anisotropy (FA) decrease in the substantia nigra (SN) has been reported to be an early non-invasive biomarker for the presence of Parkinson’s disease (PD). Vaillancourt and colleagues [1] demonstrated that the FA values were reduced in the SN with a rostra-caudal gradient in early stage PD. In a small cohort of patient with drug naive parkinsonian symptoms, they found a sensitivity and specificity of 100% using the FA value in the caudal region of the SN to separate patients from healthy controls. Prior work [2] showed FA differences in a group analysis in a

large cohort but not on the individual level. The aim of the present study was to evaluate the diagnostic value of FA in the SN.
Methods
Four groups of subjects were included: Group1: early stage untreated PD (Hoehn and Yahr (HY) = 1-2) n=6, Group 2: early stage PD on antiparkinson medication (HY = 1-2) n=11, Group 3: advanced PD (HY = 4) n=7 and healthy age matched controls n=10. Diffusion tensor imaging (DTI) measurement were performed with 42 encoding direction on a Siemens TRIO 3Tesla MR. Regions of interest in the rostral, middle, and caudal SN were manually marked according to [1] by two independent raters (DTI studio). Mean FA values for each region of interest (rostral, middle and caudal) were compared with a one-way ANOVA between the four groups (SPSS 19.0).
Results
In PD patients (group 1-3) mean FA of the SN was 0.44 ± 0.08 and in healthy controls (group 4) 0.43 ± 0.05. Statistical analysis showed no difference between the four groups for each region within the SN (Rostral region: $F(3,33) = 1.272$, $p = .30$; middle region: $F(3,33) = .171$, $p = .92$; caudal region: $F(3,33) = .775$, $p = .52$). No rostra-caudal gradient and no significant correlating to disease gravity was observed.
Conclusion
Preliminary data question the clinical utility of FA measurements in the SN for early diagnosis of PD. Given the small sample size of the current study, our data are comparable to [2]. The differences to [1] are confined to different FA values in the healthy control group (0.43 vs 0.58). Possible explanation is the use of different DTI protocols even at an identical field strength (3 Tesla). The midbrain region is prone to susceptibility and partial volume artifacts due 1) to the neighboring sphenoid sinus and 2) to hemosiderin/calcifications of the SN. Here, future work needs to include a careful monitoring of artifacts.

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neuroradiology
Fractional anisotropy, Substantia nigra, Parkinson's disease

Poster

NR-03

Issues for CBF Quantification in Carotid Artery Disease

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Arterial spin labeling (ASL), a non-invasive MR method to quantify cerebral perfusion (cerebral blood flow; CBF), is of increasing interest not only in basic research but also in diagnostic applications. In carotid artery disease (CAD) the application of ASL provides similar information about altered perfusion in vascular territories like PET (Bokkers et al. 2010). Furthermore, the assessment of ASL during the administration of a vasodilatory agent allows the calculation of the cerebro-vascular reserve (CVR). However, during investigating perfusion and CVR in patients with CAD we encountered several critical issues for quantification as well as interpretation of results. Conventionally, in CAD CBF is calculated for flow territories of main feeding arteries but often the watershed areas are ignored although they frequently show the first effects related to diminished CBF and CVR. Furthermore, calculation of CBF is rarely corrected for white matter voxels although white matter is known to have higher transit times and the validity of ASL signal in white matter is debatable (van Gelderen et al. 2008; van Osch et al. 2009).
To account for these issues we adapted our analysis routine to provide CBF and CVR values in GM only. To this end we segmented the T1 weighted images into gray and white matter using the segmentation batch implemented in SPM8 that then served as masks for CBF quantification in the flow territories. This step also excluded non brain tissue voxels form analysis. Analysis was performed in the main vascular territories according to Tatu et al. (1998) and additionally in watershed territories of the middle cerebral arteries (MCA).
WM and non-brain voxel correction significantly increased the CBF values in all analysed flow territories of both hemispheres. This is plausible since WM voxels usually have lower CBF values, which leads to an underestimation of perfusion (partial volume effect). Furthermore, CVR seems to be reduced especially in anterior MCA and posterior

MCA.
Correction for CBF and CVR values originating only from GM voxels removes artificial signals and thus increases validity of the quantification. With respect to flow territories, the watershed areas seem to be a more promising indicator of pathological alterations and cognitive impairments than conventional vascular territories.

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neuroradiology
ASL, Carotid Artery Disease, Cerebral Blood Flow

Poster

NR-04

Restoring Cerebro-Vascular Reserve in Carotid Artery Disease

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In carotid artery disease (CAD) information about cerebral blood flow yields areas with reduced perfusion due to the occlusion of a feeding vessel. Arterial Spin Labeling (ASL) has proven to provide similar information about altered perfusion in vascular territories like PET with the advantage of its non-invasiveness. Furthermore, the assessment of ASL during the administration of a vasodilatory agent allows the calculation of the cerebro-vascular reserve (CVR). CVR indicates the capacity of the vasculature to increase CBF in a specific region, which is a necessity for proper brain function. In CAD this CVR is often reduced which is suggested as the physiological basis for observed cognitive deficits.
In the ongoing project we investigate whether revascularisation therapy is able to restore CVR in afore affected flow territories. In accompanying work we found that CVR is particularly reduced in the water-shed areas between the middle cerebral artery and the anterior and posterior cerebral artery, respectively. Thus, here we focussed especially on these water-shed areas.
Eight patients with CAD (stenosis >70%) were investigated using pseudocontinuous ASL (pCASL) during normal air and 7% CO2 enriched air as the vasodilatory agent. CBF was quantified for both conditions and by subtraction of the CBF values at each voxel the patient's CVR was estimated. The same was repeated one year after revascularisation therapy. In a region of interest analysis within the CVR of the vascular flow territories for anterior watershed (AW), posterior watershed (PW) and posterior carotid artery (PCA) as a control region was performed.
Results: CVR on the stenotic hemisphere markedly increased after revascularisation therapy in the AW (+11.2 ml/100g/min) while the PW (+4.6 ml/100g/min) showed a CVR restoration in the range of the CVR observed in the healthy hemisphere (AW = +5.9 ml/100g/min; PW = +0.7 ml/100g/min). The PCA control areas showed a CVR increase of +6.3 ml/100g/min (stenotic) and +5.0 ml/100g/min (healthy).
Our results indicate the ability of revascularisation therapy to restore CVR in patients with CAD. Specifically, the CVR of the anterior watershed areas was markedly increased after intervention. The next step of our project will be to investigate whether this restoration of CVR also improves neuropsychological functioning, and whether CVR might provide a possible marker for positive outcome.

neuroradiology
ASL, Cerebro Vascular Reserve, Revascularisation Therapy, Carotid Artery Disease

Poster

NR-05

Localizing value of EEG/fMRI in presurgical epilepsy: the influence of alternative tresholding strategies

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Background and Purpose:
Simultaneous EEG/fMRI is a non-invasive tool to identify the seizure onset zone (SOZ) in patients with focal epilepsy. In this study, we evaluated different thresholding strategies for EEG/fMRI in the assessment of hemodynamic responses (HR) to interictal epileptiform discharges (IEDs) in the SOZ of drug resistant epilepsy.
Materials and Methods:
Sixteen patients with focal epilepsy were examined using simultaneous 92-channel EEG and BOLD fMRI. The temporal fluctuation of epileptiform signals on the EEG was extracted by independent component analysis to predict the HR to the IEDs. We applied three different threshold criteria to detect HR within the SOZ: a) peak activity (PA); b) a fixed threshold at $p < 0.05$ corrected for multiple comparison ("family wise error" FWE); and c) fixed activated voxels (FAV;4000 ± 200 activated voxels within the brain).
Results:
PA identified the SOZ in 9/16 patients, FWE resulted in concordant BOLD correlates in 11/16 and FAV in 13/16 patients. HR responses were detected within the resected areas in 5 (PA), 6 (FWE) and 8 (FAV) of 10 patients that remained seizure free.
Conclusion:
EEG/fMRI is a complementary non-invasive tool for the presurgical workup of epilepsy patients that can be performed during seizure free periods. Its localizing value of EEG/fMRI to delineate the SOZ may be further improved by a standardized analysis compared to individual threshold criteria.

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methodology, neurology, neuroradiology
EEG/fMRI; Epilepsy, functional imaging

Talk

NR-06

Influence of foreknowledge on saccadic eye movements – neuronal correlates

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Background and Purpose: Foreknowledge can help humans optimizing their behavior to ongoing events in the environment. Behavioral data on saccadic eye movements confirm findings from other sensorimotor systems and recent work has elucidated the differential influence of particular aspects of foreknowledge on task efficacy (1, 2). Similar efficiency scores to full prior knowledge has been observed if the side of the following motor response was predictable, an intermediate benefit on saccadic performance resulted from predictable task-set (prosaccade vs. antisaccade), while foreknowledge about the stimulus location had no effect on saccadic efficiency (2). Here we investigate neuronal correlates of full and different types of partial foreknowledge.
Methods: 14 healthy subjects underwent 2 runs of functional MRI (TR/TE 2000, 370 volumes, Philps 3 Tesla MR). One run consisted of five blocks of task and one fixation block. In the blocks of task either stimulus location, type of

task, response direction, or then all or no of these three parameters were made predictable. Each block contained a balanced number of prosaccades and antisaccades and left- or rightward stimuli. To construct null events, 20s of fixation events per block were randomly interspersed between the motor trials in pieces of 2, 4, 6 or 8s. In the ANCOVA analysis, each foreknowledge block was then represented by the sum of it's fixation events, as this is the best period with isolated effects of foreknowledge.
Results: A large bilateral network including anterior medial prefrontal cortex, anterior cingulate gyrus, caudate, occipital and parietal regions as well as the parahippocampal cortex is activated with complete foreknowledge. For the different types of partial foreknowledge activated areas were most prominent in parioto-occipital regions and the parahippocampal cortex and only minor positive BOLD correlate in the frontal lobe were present.
Task-foreknowledge was associated to the activation of the superior temporal cortex, which is consistent with a previous study (3).
Conclusion: Foreknowledge about upcoming eye movements results in an activation of a large neuronal network encompassing brain regions subjected to attention, visual working memory and motor response preparation. Complete foreknowledge shows a larger neuronal activation pattern than partial foreknowledge. Different types of partial foreknowledge show a different distribution of neuronal activity. Correlation with the concomitant behavioral data is underway.

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neuroradiology
saccadic eye movements, foreknowledge, partial foreknowledge

Poster

NR-07

Cognitive functions in carotid artery disease before and after treatment

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Background:
Treatment of carotid stenosis may decrease the risk of stroke and increase hemispheric blood flow and may therefore lead to an improvement of cognitive performance. However, the treatment can also lead to microembolisms, new microinfarcts, a decrease of the blood pressure and a transient flow arrest which are all linked to a worsening of cognitive functions. This study examines cognitive functioning in patients with carotid stenosis at baseline and after treatment (stenting, endarterectomy or best medical treatment).
Methods:
Seventy-one patients (59 men, 12 women) with carotid artery stenosis (>70%) were included in the study (mean age 69y, range 51-85y). Forty patients were asymptomatic, 31 patients showed neurological symptoms in the past. Carotid stenosis occurred on the right in 39 patients, on the left in 26 patients and bilaterally in 6 patients. All patients underwent a basline neuropsychological battery no earlier than 3 months after their most recent stroke (if present), measuring language, visual and verbal memory, processing speed, executive functions, motor skills, anxiety and depression. Thirty-eight patients who had treatment (stenting, endarterectomy or best medical treatment) at any time after the baseline testing underwent an parallel version of the neuropsychological test battery 12 months after the initial exam. Pathological performance was defined as $z < -1.0$. Statistical analysis was performed using SPSS 17.0. Changes in cognitive performance were measured by means of a paired t-test.
Results:
Before treatment of the carotid stenosis, short-term memory problems were the most salient cognitive deficit and occurred in 26 of 71 patients (digit span, 36%), followed by verbal learning deficits in 21 patients (Rey words learning, 29%) and problems with verbal processing speed in 20 patients (Stroop Naming, Time, 28%). Motor skills were deficient in 27 of 71 patients (Purdue Pegboard, 38%) and 19 patients reported increased anxiety (HAD, 27%) before treatment of the carotid stenosis.

Treatment of the carotid stenosis resulted in a significant improvement of the short-term memory (digit span, p=.02) and verbal fluency (animal naming, p=.021) was found. A tendency towards improved motor skills of the dominant hand (Perdue Pegboard p=.065) and improved verbal processing speed (Stroop Naming, Time, p=.079) was also detected.
Conclusion:
Patients with carotid artery stenosis show most deficits in short-term memory, verbal learning and verbal processing speed. Motor deficits often occur and anxiety is clearly increased in patients with carotid stenosis. Treatment of the carotid stenosis can result in an improvement of classical frontal lobe functions such as short-term memory and verbal fluency. These results highlight the potential positive consequences of treatment of carotid stenosis on cognitive performance.

neuroradiology
cognition, treatment of carotid stenosis

Poster

Neurosurgery (NS)

NS-01

Dopaminergic Nogo-A expressing neurons are preferentially lost in a rat model of Parkinsons's disease

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The myelin associated protein Nogo-A is known to be expressed on the surface of oligodendrocytes and has been described to limit neuronal regeneration and plasticity after injury. More recently, Nogo-A expression was also found in a number of neuronal subpopulations of the adult and developing CNS suggesting that Nogo-A serves additional functions in the brain. At present, only little is known about the expression of Nogo-A in the midbrain, a brain structure severely affected in Parkinson's disease (PD). For that purpose the present study aimed at characterizing the expression pattern of Nogo-A- immunoreactive (-ir) cells in the adult midbrain of control rats and in a 6-hydroxydopamine (6-OHDA) rat model of PD. One week and one month after unilateral striatal injections of 6-OHDA, rats were perfusion-fixed and the brains processed for histological analyzes. We found that Nogo-A-ir cells were predominantly distributed in the substantia nigra pars compacta (SNc) and in the ventral tegmental area. Interestingly, a substantial number (about 50%) of tyrosine hydroxylase (TH)-ir neurons in the SN also expressed Nogo-A. Moreover, about 70% of the Nogo-A positive cells coexpressed TH hinting to the idea of a predominant neuronal expression of Nogo-A. In line with this notion, no colocalization was observed for Nogo-A and the astrocytic marker GFAP. Our preliminary data revealed that one week after 6-OHDA injection animals displayed a significant loss of dopaminergic neurons as well as Nogo-A-ir cells in the SNc of the lesioned as compared to the unlesioned side (by 40% and 50%, respectively). The number of both TH-ir neurons and Nogo-A-ir cells was observed to be further decreased after one month (by 90% and 70%, respectively). Interestingly, by means of double-immunofluorescence stainings we detected that this cells loss was predominantly seen in the subpopulation of SNc neurons expressing Nogo-A and TH. Specifically, we found that the percentage of Nogo-A-ir cells also expressing TH was significantly lower both at one week (with 40% colocalization) and one month after the lesion (with 30% colocalization) as compared to control sides (with 70% colocalizations). Based on these results we hypothesize that the subpopulation of dopaminergic neurons expressing Nogo-A is particularly vulnerable to the 6-OHDA lesion, which strongly suggests for a function of Nogo-A in the nigrostriatal system and that Nogo-A may play a substantial role in PD.

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neurosurgery
Parkinson's disease, Nogo-A, dopaminergic neurons

Poster

NS-02

Endothelial Progenitor Cells promote neuronal cell viability through paracrine factors

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Background: There is compelling evidence that stem and exert regenerative actions by means of paracrine factors. In the present study we tested the hypothesis that soluble factors secreted by cultured endothelial progenitor cells (EPC) may support neuronal cell functions and survival.
Methodology: EPC were isolated from peripheral blood of healthy human donors by gradient centrifugation. Cells

were cultured in hypoxic conditions (1.5% O2) to stimulate the secretion of growth factors. Primary cultures from human fetal rat embryonic (E14) cortex, striatum and ventral mesencephalon were treated with EPC derived conditioned medium (CM). The effect of EPC-CM was monitored by immunocytochemical analyzes for neuronal markers including β-III-tubulin, Neuronal Nuclei (NeuN), GABA, tyrosine hydroxylase (TH) and for a marker of microglial cells (Iba1). Cell viability was measured by means of MTT assay.
Results: Incubation of primary cultures with EPC-CM resulted in an overall augmented viability compared to controls. This effect was associated with a significant increase in TH-ir cell densities in mesencephalic as well as NeuN-ir and GABA-ir cell densities in the striatal cultures, respectively. In contrast, the number of β-III-tubulin-ir cells was not increased in cortical cultures exposed to EPC-CM. Most strikingly, treatment of cultures with EPC-CM resulted in a substantial increase of number of microglial cells.
Conclusions: These data suggest that EPC play a role for brain tissue through remarkable paracrine actions. Whether the effect on neuronal cells is directly governed by EPC-CM or is secondary to the microglial activation remains to be elucidated.
Supported by SNF-NRP63

neurosurgery
Endothelial Progenitor Cells, primary neuronal cultures, paracrine factors, microglial cells

Poster

NS-03

Striatal Trefoil Factor 1 positive cells are upregulated in a rat model of Parkinson's disease

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Background: Trefoil factor 1 (TFF1) belongs to a family of soluble peptides with a characteristic tree-looped trefoil structure. TFF's are predominantly expressed in the gastrointestinal tract, where they play critical roles in the function and structural composition of the mucosal barrier. More recently, TFF1 has been suggested to function also as a neuropeptide, but only limited information is available on its expression and function in the CNS. Our previous studies revealed that TFF1 is expressed in the ventral mesencephalon of developing and adult rats. This finding is of particular interest for Parkinson's disease, which is mainly characterized by a progressive loss of dopaminergic neurons in the substantia nigra.
Objective: In the present study we aimed at investigating on the detailed characterization of TFF1 positive cells in the adult rat nigrostriatal system and in a rat model of Parkinson's disease.
Methods: Perfusion fixed brains of control animals and rats that received an unilateral 6-OHDA lesion were sectioned on a cryostat and the sections analyzed for the expression of TFF1 and neuronal and astroglial markers by means of immunohistochemistry.
Results: In the adult ventral mesencephalon, TFF1-ir cells were predominantly observed in substantia nigra pars compacta (SNc) and the ventral tegmental area (VTA) as well as in periaqueductal areas. While we found that around 90% of the TFF1-ir cells in the SNc co-expressed tyrosine hydroxylase (TH), only a subpopulation of TH-ir neurons also expressed TFF1. We observed that some TFF1-ir cells in the SNc co-expressed the calcium-binding proteins calbindin or calretinin and nearly all NeuN indicating a neuronal phenotype, which was supported by lack of co-localization with the astroglial marker glial fibrillary acidic protein. Injection of the tracer Fluorogold into the striatum of adult rats resulted in retrograde labeling of a number of TFF1 expressing cells in the SNc showing that a significant fraction of the TFF1-ir cells were projection neurons. This was also reflected by unilateral loss of TFF1-ir cells in the SNc of 6-OHDA-lesioned hemiparkinsonian rats. Importantly to note, number of striatal TFF1-ir cells were significantly increased after the 6-OHDA lesion. Whether this increase was due to upregulation of TFF1 in already existing cells or reflects TFF1 expression in newly born cells is currently being addressed.
Conclusion: In sum, our study demonstrates that distinct subpopulations of dopaminergic neurons express TFF1 in the ventral mesencephalon and that this expression pattern is altered in a rat model of Parkinson's disease.

neurosurgery
Parkinson's disease, Trefoil Factor 1, dopaminergic neurons

Poster

NS-04

Enhanced viability of dopaminergic cells by HIF-1 stabilization and minocycline treatment

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Background. The lack of effective therapies for Parkinson's Disease has lead to the necessity to explore novel treatment options. In this regard, activation of Hypoxia inducible Factor-1 (HIF-1) is involved in neural progenitor cell propagation and dopaminergic cell differentiation. Moreover, there is increasing evidence the tetracycline derivate minocycline has a neuroprotective effect.
Purpose. Aim of the present study was to investigate the effect of HIF-1 activation by chemical stabilization and minocycline treatment on survival of cultured dopaminergic neurons.
Methods. Ventral mesencephali (VM) were isolated from Wistar rat fetuses (at embryonic day 14) and grown as organotypic free-floating roller tube (FFRT) cultures for one week. HIF activation was induced by dimethyloxallyl glycine (DMOG, [1mM]) incubation starting at day in vitro 2 until the end of the culture period. Minocycline treatment followed the same schedule; untreated cultures served as controls. The cultures were then fixed, sectioned on a cryostat and the sections immunohistochemically stained for the dopaminergic cell marker tyrosine hydroxylase (TH) and for the cell proliferation-associated protein Ki-67.
Results. Chronic DMOG and minocycline treatment resulted in a significant increase of TH cells (by 50% and 75%, respectively) as compared to controls. Despite a parallel augmentation of Ki-67 positive cells by DMOG (by 70%) no colocalization between Ki-67 and TH-positive cells was observed.
Conclusion. Our findings suggest that stabilization of HIF-1 and minocycline provide a means to promote differentiation and / or survival of dopaminergic neurons. Moreover, the increased proliferation rate implies that a pool of precursor cells was stimulated by HIF-1 stabilization. These data support previous reports assessing the possible therapeutic utility of HIF-1 induction for Parkinson disease.

neurosurgery
Parkinson's disease, HIF-1, minocycline, organotypic cell culture

Poster

Psychiatry (PA)

PA-01

Spared semantic priming in Alzheimer's patients and its electrophysiological correlate

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Patients suffering from Alzheimer's disease (AD) exhibit a predominant deterioration of episodic memory functioning. Furthermore, recent studies have demonstrated that AD patients perform weaker than healthy controls in semantic tasks such as verbal fluency or object naming. However, the underlying mechanisms of the semantic memory deficits remain unclear. Therefore, the current study investigated the semantic word processing in early AD patients and a healthy control group by means of a semantic priming task during the recording of event-related potentials (ERP). In particular, the participants performed a lexical decision (LD) task embedded in a semantic priming (SP) paradigm. This methodological approach allowed the investigation of both automatic and controlled semantic memory processes. Concretely, word/non-word (prime and target) word pairs were presented visually with a stimulus onset asynchrony of 700 ms. The outcome measures were target onset reaction times (RT) and a microstate cluster analysis on the ERPs. Additionally, verbal fluency and Boston naming tasks were conducted separately in order to test for the expected semantic deficits in AD.
The AD group showed general slowed RTs for all task conditions (related and unrelated word pairs). However, the size of the SP effect was comparable in both participant groups. The microstate analysis revealed that except for perceptual ERPs, there were topographic differences during the semantic processing between AD and the healthy controls.
Taken together, the results of this study supplement the behavioral findings by electrophysiological evidence of alterations in the semantic memory processes. Although the behavioral SP effect – and thus the automatic spread of activation in the semantic network – appeared to remain stable, the results gave a clear indication of neurophysiological alterations in AD. Together with subsequent studies, these new findings might improve a profound understanding of this disease.

psychiatry, psychology
Alzheimer's disease, semantic memory, reaction time, microstates

Poster

PA-02

Prefrontal white matter integrity predicts treatment response after 4 weeks in major depression

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Major depression has been associated with reduction of white matter integrity in the prefrontal cortex and the left anterior limb of the internal capsule. However, the significance of white matter changes in an episodic form of psychiatric disorders remains unclear. We aimed to investigate whether white matter integrity would predict treatment outcome within one month.
We performed diffusion tensor imaging in 29 patients with a current depressive episode. MR imaging was conducted at a 3 T scanner with 46 diffusion gradients. All patients received antidepressant therapy. After 4 Weeks, clinical rating was repeated. Patients with more than 50% reduction of the baseline Hamilton Depression Rating Scale score were considered as responders. We computed the contrast of whole brain fractional anisotropy (FA) at baseline

between later responders and nonresponders, applying FDR correction ($q < 0.05$) for multiple comparisons.
In total, 13 patients responded, while 16 patients remained nonresponders. The groups did not differ in any of the clinical baseline variables. Responders had increased FA values in the left cingulum bundle close to the posterior cingulate cortex, in the right inferior fronto-occipital fasciculus within the middle temporal gyrus and right caudal cingulum close to the parahippocampal gyrus. Nonresponders had higher FA values in the right superior longitudinal fasciculus in the dorsolateral prefrontal cortex. In these clusters, FA values were neither correlated with the number of the past and the duration of the current depressive episode, nor with the duration of the treatment of the current episode.
We found substantial differences in prefrontal white matter integrity at baseline between patients who responded to treatment and nonresponders. Therefore, the white matter integrity in prefrontal circuits may predict short-term outcome of depressive episodes. The differences between groups were located in prefrontal and limbic areas known to be affected by major depression.

psychiatry
major depression

Talk

PA-03

Longitudinal resting state cerebral blood flow changes in depressed patients

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Major depression has been associated with altered metabolic rates and altered perfusion in prefrontal and limbic brain areas. Most studies applied PET imaging. The literature on perfusion MRI and on longitudinal changes, however, is scarce. We aimed to investigate the longitudinal changes in resting state cerebral blood flow between depressed and non-depressed episodes using perfusion MRI, i.e. arterial spin labeling (ASL). We hypothesized that cerebral blood flow in key regions of the limbic and association cortices would change with clinical presentation.
In total, 16 patients (12 unipolar, 4 bipolar) were scanned twice. Baseline measurements were performed during acute depressive episodes and patients were followed and re-investigated as soon as they achieved complete remission from depression. The mean time between measurements was 181 (SD = 80) days. MRI scans were performed in the mornings of week days. Perfusion was measured using pseudo continuous ASL (pCASL). Paired t-tests were computed for whole brain CBF, applying FDR correction ($q < 0.05$).
In the depressive episodes, the patients had increased CBF in the left amygdala, the right head and tail of the caudate nucleus and the right BA9. In contrast, CBF was increased during remission in the left caudate, the right insula, the right postcentral gyrus and the right inferior parietal lobe.
We found longitudinal changes of the regional CBF in patients with depression. Hyperperfusion during depression was noted in prefrontal and limbic areas. In contrast, hypoperfusion during depression was seen in widespread bilateral brain areas. Therefore, regional cerebral blood flow as measured by ASL could serve as a state marker in affective disorders.

psychiatry
major depression

Poster

PA-04

Impaired pantomime in schizophrenia – association with frontal lobe function

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Gestures are important for nonverbal communication and were shown to be impaired in schizophrenia. Two domains of gestures can be differentiated: pantomime on verbal command and imitation of seen gestures. There is evidence that the neural basis of these domains may be distinct, pantomime being critically dependent on prefrontal cortex function. The aim of the study was to investigate gestural deficits assessed by the comprehensive Test of Upper Limb Apraxia (TULIA) and their association with frontal motor performance in 30 schizophrenia patients. The ratings of videotaped gesture performance were blinded. A battery of rating scales on parkinsonism, dyskinesia, catatonia and instrumental measures of gross and fine motor performance were assessed. Using previously determined cut-off scores of the TULIA, pantomime deficits were found in 40% and imitation deficits in 23% of the patients. Patients with gestural deficits had poorer frontal cortex function, more catatonic symptoms, and more severe psychopathology. Furthermore, trends indicated an association with a more chronic course of the illness. Pantomime was linked to frontal lobe function whereas imitation was associated with catatonic symptoms and basic motor function. In conclusion, pantomime is frequently impaired in chronic schizophrenia and may critically depend on motor planning, reflecting a further example of brain disconnectivity in schizophrenia.

neurology, psychiatry
schizophrenia

Poster

PA-05

Associations of motor behaviour and structural connectivity of the motor system in major depressive disorder

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Objectives:
Psychomotor retardation is a key symptom in major depressive disorder (MDD). However, little is known about the neurobiological background of motor pathways. Our aim was to investigate structural white matter abnormalities of pathways of the motor system in patients with MDD and to relate our findings to objectively measured motor activity. We hypothesize that (i) quantitative motor activity is reduced in MDD, (ii) structural connectivity between key regions of the motor system is altered in MDD and (iii) alterations of structural connectivity in MDD is associated with reduced motor activity.
Methods:
21 patients with MDD and 21 healthy controls matched for age and gender underwent diffusion tensor imaging (DTI) and actigraphy the same day. Probabilistic fibre tracking was started from key regions of the motor system such as the rostral anterior cingulate, the dorsolateral prefrontal cortex, the pre-supplementary motor area (SMA), the SMA-proper, the primary motor cortex, the pallidum, the putamen, the striatum and the thalamus. Resulting probability maps were combined using an extended multiplication of probabilistic maps to identify the most probable anatomical pathways connecting these structures. Independent t-tests were used to compare activity level and probability of connection. We used a general linear model of the probability of connection values with the factors group (healthy controls and MDD) and activity level to explore the relationship between motor behaviour and

structural connectivity for the two groups.
Results and Conclusions:
The data analysis is not yet completed. Results will be presented at the meeting.

psychiatry
depression motor behaviour white matter

Poster

PA-06

Illuminating the resting brain of schizophrenia by using combined EEG/fMRI

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A recent study in healthy controls showed that the topographic spectral power distributions of the standard EEG frequency bands were associated to resting state networks (RSN) measured by fMRI. The present study investigated, if the disconnection theory of the schizophrenia (SZ) disorder can be extended to the coupling between the RSN dynamics seen in fMRI, and the spatial distributions of spectral fluctuations measured by EEG, when SZ patients are compared to healthy controls (HC). Combined resting state EEG/fMRI was therefore collected in a sample of 11 SZ patients and 20 HC. Data was analyzed using Covariance Mapping (CovMap). Ten distinct RSNs were identified for each subject separately. Only the covariance maps for six of them, the Default Mode Network (DMN), the Left Working Memory Network (LWMN), the Somato Motor Network, the Auditory Cortex Network, the Ventral Visual Network, and the Dorsal Visual Network proofed to be consistent in topographic randomization statistics for both groups and most frequency bands and were further analysed. Subsequently, the difference between the CovMaps of SZ and HC, at each consistent frequency, was computed using randomization statistics (TANOVA). The single difference between the SZ- and HC-CovMaps was seen in the LWMN at the Theta2 frequency. In order to look for similarities between SZ and HC-CovMaps across frequencies (frequency shifts), topographic cross-correlations were computed. In two RSNs, the DMN and the LWMN, it could be observed that the coupling of the RSNs with the higher frequency bands in HC shifted to a lower frequency-range in the SZ group. These results suggest that not only the within network connectivity is aberrant in SZ, but also the coupling between the functional networks and their driving frequency. The finding is interesting in the light of state-dependent processing, where pathology, pharmacology, vigilance, task-engagement and age might influence an optimal functional coupling, and as such alter the processing of internal and external stimuli.

psychiatry
schizophrenia simultaneous EEG/fMRI

Poster

PA-07

Amygdala segmentation in spider phobic patients

Melanie Sarah Fisler[1], Andrea Federspiel[1], Helge Horn[1], Thomas Dierks[1], Wolfgang Schmitt[1], Roland Wiest[2], Dominique J.-F. de Quervain[3], Leila Maria Soravia[1]

[1]Introduction: Patients with spider phobia (SP) exhibit exaggerated responses to phobic stimuli, which are characterized by anxiety upon exposure as w, [2]Department of Neuroradiology, Inselspital, University Hospital of Bern, University of Bern, [3]Division of Cognitive Neuroscience, Faculty of Medicine & Faculty of Psychology, University of Basel

Introduction:
Patients with spider phobia (SP) exhibit exaggerated responses to phobic stimuli, which are characterized by anxiety upon exposure as well as anticipatory anxiety and avoidance behaviour. Fear acts as a pivotal signal in terms of threat and danger. The amygdala appears to play a crucial role in the rapid detection of basic emotional properties of incoming stimuli. In this study, we compared amygdala volumes in patients with spider phobia and healthy subjects. The goal was to investigate differences in amygdalar volume and surface properties.
Methods:
Twenty female patients with SP (mean age: 29.9; SD: 11.3) and twenty matched female controls (mean age: 27.1; SD: 5.9) were included in the analysis. MRI was performed on a 3T Siemens Magnetom Trio Scanner (Erlangen, Germany). For structural images, a high-resolution 3-D T1-weighted imaging protocol (Magnetization Prepared Rapid Acquisition Gradient Echo, MPRAGE) was used, resulting in 176 sagittal slices (slice thickness=1.0 mm, FOV 256 mm x 256 mm, matrix size=256 x 256, TR=1950 ms, TE=2.6ms).
Shape analysis was carried out using the software package FSL-FIRST.
Results:
Compared with controls, spider phobic patients had significantly reduced left amygdalar volume. There was no significant difference in the right amygdalar volume between the two groups. Smaller volumes of the left amygdala in spider phobic patients were significantly related to higher degree of spider phobic symptoms. There were also significant differences between these two groups regarding the shape of the left but not right amygdala. Shape analysis revealed atrophy within the basolateral and central nuclei of the left amygdala. The volumetric and shape differences did not correlate with the age of subjects.
Conclusion:
The mechanisms underlying these changes are not well understood. Small amygdala size might increase the risk for developing anxiety. Acute threat initializes behavioral and endocrine responses to enable adaption to the environment. The amygdala plays an essential role in the generation of responses to stressors by activating the hypothalamic-pituitary-adrenal (HPA) axis. Thus, another possibility could be an amygdala degeneration due to exaggerated fear which is followed by increased glucocorticoid release.
Within the amygdala, the basolateral nucleus plays an important role in the regulation of anxiety. Thus, abnormalities in this region could be an important pathology leading to phobic symptoms.

psychiatry

Poster

PA-08

Infant cuteness discrimination in women suffering from post-partal depression: an fMRI Study

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Post-partum depression (PPD) is a serious medical condition that typically develops during the first year after childbirth. Core symptoms of PPD are sleeplessness, sadness, anxiety, hopelessness, irritability, and poor concentration. Because PPD interferes with the mother's ability to bond with the child, it affects both mother and baby

and, as a consequence, negatively influences child development and safety. Endocrine factors have been discussed in the etiology of PPD, especially changes in estradiol and progesterone. Given that gonadal steroids have been suggested to modulate emotional reactions towards infant cuteness, we examine whether there is a link between mothers suffering from PPD and a reduced reaction towards cute infants. Computer-manipulated pictures of infant faces varying in cuteness will be presented to a group of mothers with PPD, to a group of matched healthy controls (also young mothers and fathers), and to patients with major depression, while they lie in a 3 Tesla functional Magnetic Resonance Imaging (fMRI) scanner, adopting an event-related design. All participants will view gray-scale images of infant and adult faces varying in cuteness/attractiveness. The brain activity in response to cute and less cute babies (and attractive/unattractive adults, respectively) will be measured to test the following predictions: a) mothers with PPD show different brain activity patterns than healthy mothers in response to baby faces, but not adult faces, b) activity difference occurs in basal ganglia and in amygdala, insula, and orbito-frontal cortex. Finally, we expect to isolate brain systems involved in rewarding aspects of infant facial configuration and parental care. First pilot data will be presented and discussed.

psychiatry
infant face perception, postpartal depression, fMRI, reward system

Poster

PA-09

Reduced focused attention in paranoid schizophrenia during a visual task

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Attentional problems are a major symptom in schizophrenia. To investigate attention, we created a visual recognition task presented in the periphery of the visual field. In this task, a first target was presented in the center, and a second target in the periphery. Subjects could focus their attention towards the visual targets with an eye saccade and a head shift. In such attentional shifts, first, a saccade is performed, and during the saccade the head shifts in the same direction. Eye saccades and head shifts were measured with video-based pupil oculography and magnetic coils, respectively. We found a reduced accuracy and longer response times during the task in patients (n = 10) compared to healthy controls (n = 11). In the control group, saccade delays (the time between the visual target onset and the saccade onset) were dependent on task difficulty, i.e. more difficult visual targets caused shorter eye delays. However, this pattern was absent in the patient group. We conclude that patients failed to direct more attentional resources to the difficult, and less resources to the easy visual targets. This finding might be a specific trait marker for attentional symptoms in schizophrenia.

psychiatry
Schizophrenia, eye movements

Poster

PA-10

Ventral striatum volume correlates with specific psychotic symptoms associated with disturbance of the limbic system. A voxel-based morphometry (VBM) study.

Katharina Stegmayer[1], Helge Horn[1], Andrea Federspiel[1], Nadja Razavi[1], Werner Strik[1], Thomas Dierks[1], Roland Wiest[2], Thomas Müller[1], Sebastian Walther[1]

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Introduction:
Recently, a psychopathology scale (Bern Psychopathology Scale) for the assessment of System-Specific Psychotic Symptoms has been proposed. The authors defined three symptom domains which were matched on three

candidate brain circuitries, namely the language, the limbic and the motor system. The aim of the present study was to investigate the hypothesis that a patient subgroup showing prevalent symptoms of emotional dysregulation would show structural neuronal differences of the limbic system.
Method:
In total, 32 right-handed patients with schizophrenia (14 male and 18 female, mean age 33.3±10.3 years) were assessed with the Bern Psychopathology Scale (BPS) and underwent structural imaging at a 3T MRI scanner. Patients had been suffering from schizophrenia for 7.4±8.5 years, experienced 4.2±5.4 psychotic episodes and were treated with atypical antipsychotics (chlorpromazine equivalents (CPZ) = 438.3±330.6 mg) except two patients who did not receive antipsychotic medication at the time of the study. A control group of 32 healthy individuals were matched pair-wise for gender and age (14 women and 18 men mean age 33.7±10.6 years).
Items of the BPS-subscale attributed to the limbic system comprise symptoms of emotional dysregulation such as tensions, worry, anxiety, specific disorders of interpersonal behaviour, and body sensations. Moreover, a global score in the BPS assesses the severity of the valence of the limbic symptoms, ranging from -3 to +3, while zero defines patients without limbic symptoms. Whole brain voxel-based morphometry (VBM) was compared between patients with different BPS ratings of the limbic domain. Structural images were processed using SPM8. The images have been normalized and modulated and smoothed with 8mm full-width at half maximum (FWHM) kernel.
Results:
Contrasting patients without limbic symptoms and those with limbic symptoms in the global BPS score revealed decreased grey matter volume in the right ventral striatum ($t=7.14$, $p<0.001$) in patients with limbic symptoms. When comparing patients with prevalent limbic symptoms and healthy controls several clusters of decreased GM density were detected in patients, e.g. bilateral thalamus, ventral prefrontal cortex, the right ventral striatum and the left insular cortex. Comparing the GM density of all schizophrenia patients irrespective of the psychopathology versus controls revealed decreased GM density in bilateral thalamus, ventral prefrontal cortex, temporal cortex, parietal cortex and the left anterior cingulate gyrus, but not in the ventral striatum. No significant correlations were found between grey or white matter volume with number of episodes, duration of illness, and medical treatment.
Discussion:
Decreased grey matter volume in the right ventral striatum was associated with prevalent symptoms in the domain of emotional dysregulation in schizophrenia patients. The right ventral striatum is an important part of the limbic system, and was indicated to be involved in the generation of psychotic symptoms. The present results support the hypothesis that specific clinical symptoms can be matched to brain systems, and allow identifying patient subgroups with structural abnormalities in the limbic network. Comparing all patients with healthy controls revealed several grey matter density differences. These findings are consistent with previous research on grey matter differences in schizophrenia.

neurobiology, psychiatry
schizophrenia, limbic system, ventral striatum, psychosis, VBM

Talk

PA-11

Psychotic symptoms associated with disturbance of the motor system correlate with supplementary motor area (SMA) volume. A voxel-based morphometry (VBM) study.

Katharina Stegmayer[1], Helge Horn[1], Andrea Federspiel[1], Nadja Razavi[1], Werner Strik[1], Thomas Dierks[1], Roland Wiest[2], Thomas Müller[1], Sebastian Walther[1]

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Introduction:
There is still a large heterogeneity across studies investigating changes in grey matter in schizophrenia. Besides differences in methodology, variance in schizophrenia symptom patterns may contribute to the inconsistent findings. Recently, a psychopathology scale (Bern Psychopathology Scale) for the assessment of System-Specific Psychotic Symptoms has been proposed. The authors defined three symptom domains which were matched on three candidate brain circuitries, namely the language, the limbic and the motor system. The aim of the present study was to investigate the hypothesis that a patient subgroup showing prevalent symptoms of motor dysregulation would show structural neuronal differences of the motor system.
Method:
In total, 32 patients (14 women and 18 men; mean age 33.3±10.3 years) of the University Hospital, Bern, Switzerland,

meeting DSM IV criteria for schizophrenia have been included. Patients had been suffering from schizophrenia for 7.4±8.5 years, experienced 4.2±5.4 psychotic episodes and were treated with atypical antipsychotics (chlorpromazine equivalence (CPZ) = 438.3±330.6 mg), except two patients who did not receive antipsychotic medication at the time of the study. Psychopathology was assessed using the Positive and Negative Syndrome Scale (total score: 57.4±16.9; positive syndrome scale: 14.2±5.7; negative syndrome scale: 15.3±6.7) as well as with the Bern Psychopathology Scale (BPS). All participants underwent structural imaging at a 3T MRI scanner. Items of the BPS-subscale attributed to the motor system comprise spontaneous movements, spontaneous rest, velocity, variability of movements, excitability, motion sequence, movement order, functionality of movements, motor drive and motor pleasure. Each item may be rated as normal, abnormally inhibited or abnormally excited. A global score in the BPS assesses the severity of the motor symptoms, ranging from -3 to +3, while zero defines patients without motor symptoms. Whole brain voxel-based morphometry (VBM) was compared between patients with different BPS ratings of the motor domain. Structural images were processed using SPM8. The images have been normalized and modulated and smoothed with 8mm full-width at half maximum (FWHM) kernel.
Results:
Patients without motor symptoms and prevalent positive motor symptoms (related to exitation) and those with prevalent negative motor symptoms (related to inhibition) have been compared. Patients with prevalent negative motor symptoms in the global BPS score revealed decreased grey matter volume in the right SMA (x=16, y=0, z=62, Brodmann area 6) compared to patients without and with positive motor symptoms. No significant correlations were found between grey or white matter volume with number of episodes, duration of illness, and medical treatment.
Discussion:
Decreased grey matter volume in the right SMA was associated with prevalent symptoms in the domain of motor dysregulation in schizophrenia patients. The SMA is an important region of the motor system, and was repeatedly found to be involved in motor sequencing. The present results support the hypothesis that specific clinical symptoms can be matched to brain systems, and allow identifying patient subgroups with structural abnormalities in the motor network.

neurobiology, psychiatry
Schizophrenia, motor system, psychosis, supplementory motor area, SMA, VBM

Talk

PA-12

Relationship of white matter integrity and PANSS scores in schizophrenia

Stéphanie Giezendanner[1], Nadja Razavi[1], Claudia Van Swam[1], Melanie Fisler[1], Leila Soravia[1], Sebastian Walther[1], Kay Jann[1], Roland Wiest[2], Thomas Dierks[1], Andrea Federspiel[1]

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Objective: The clinical assessment of schizophrenic patients often involves the classification into positive and negative symptoms. Regarding the hypothesis that schizophrenia is a disorder of brain connectivity, white matter (WM) has become increasingly important in schizophrenia research (Andreasen, Paradiso, & O'Leary, 1998). Thus, the clinical correlates of WM abnormalities in schizophrenia patients are investigated in this study.
Method: Brain WM integrity was investigated in 34 schizophrenic patients (F20, F23) and 33 age and gender matched healthy subjects with diffusion tensor imaging (DTI). Positive and negative syndrome scale (PANSS) was used to assess the severity and type of patients' symptoms. Ellipsoidal area ratio (EAR) maps were calculated according to Xu and colleagues (Xu, et al., 2009). EAR is an anisotropy index indicating WM integrity in the brain. Voxelwise group comparison and correlation analysis of EAR maps were performed using tract-based spatial statistics (TBSS) (Smith, et al., 2006). Differences in WM integrity between groups and the relationship of WM integrity and positive, negative and total PANSS scores within patients were investigated. All statistical analyses were accounted for confounding variables such as age, illness duration, chlorpromazine equivalents and were corrected for multiple comparisons.
Results: There was no significant difference in WM integrity between patient and control group. Neither was there a significant correlation of WM integrity with the positive nor with the negative PANSS score. On the other hand, the total score of PANSS showed a significant negative correlation with WM integrity in several WM areas; in the entire corpus callosum, in the posterior part of the right inferior fronto-occipital fasciculus, in the left uncinate fasciculus and in the left inferior fronto-occipital fasciculus.
Conclusions: The total PANSS score, indicating overall severity of symptoms, was correlated negatively in various

large WM areas in accordance to recent findings (Szeszko, et al., 2008). The apparent absence of significant group differences in WM integrity, as well as the absence of significant correlations of positive and negative PANSS scores might originate from the large symptom heterogeneity of the investigated group and are at odds with recent studies. Therefore, a more elaborate way of subdivision of the patient group into homogeneous groups will be aimed in a further step.

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neuroradiology, psychiatry
DTI, white matter, schizophrenia, PANSS

Poster

PA-13

A Comparison of the Bern Psychopathology Scale (BPS) with the Positive and Negative Symptom Scale (PANSS)

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Introduction The Bern Psychopathology Scale (BPS) categorizes core psychotic symptoms into three major brain systems (language, motor behavior, affectivity) and assesses their specific exaltation state. Thus, it has the advantage to dissociate core psychotic symptoms based on neurophysiological assumptions. The Positive and Negative Syndrome scale (PANSS) is the most frequently used psychopathology rating scale and was developed to estimate the degree of presence of the positive and negative syndrome. In this study, we conducted a comparison of the BPS with the PANSS on the basis of 174 datasets derived from ratings of psychotic patients with the BPS and the PANSS simultaneously in order to do an external validation of the BPS.
Methods A sample of 174 inpatients (85 males (48, 9%), 89 females (51, 1%)) was recruited at the University Hospital of Psychiatry Bern, Switzerland. Inclusion criterion was an ICD-10 diagnosis of schizophrenia, schizotypal disorder, persistent delusional disorder, acute and transient psychotic disorders, or schizoaffective disorder. The BPS Global Scores were correlated with the 30 PANSS items. Multiple linear regressions with BPS Global Scores as dependent and the formerly assessed correlating PANSS items as independent variables were computed.
Results and Discussion PANSS items with a high conceptual overlap with the BPS global scores do show high correlations and do predict high amounts of variance of the respective BPS Global Scores. While the BPS is not apt to differentiate a positive and negative syndrome as measured by the PANSS, the PANSS fails to depict the positive affective state as measured by the BPS Global Score for affectivity. Moreover, the bipolar dimension of formal thought disorders as measured by the BPS global score for language is not assessed by the use of the PANSS.

methodology, neurobiology, psychiatry

Poster

PA-14

Electrophysiological correlates of auditory verbal self-monitoring in healthy subjects

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Objectives: Auditory verbal hallucinations in schizophrenia have been hypothesized to result from inefficient self-monitoring of inner speech. Neurophysiological experiments in this domain are however still sparse, because the processes of speech generation, speech perception and self-monitoring overlap and are difficult to disentangle. The aim of this project was to develop and test a paradigm and analysis methods to isolate and quantify self-monitoring processes with ERPs.
Methods: The experimental stimuli consisted of visually presented single words that subjects were instructed to read aloud, and auditory feedback delivered through a headphone. This feedback consisted of the subject's normal own voice, either presented in real-time or delayed by 200 msec, a foreign voice of the subject's gender saying the same word, or a mute condition. In an additional condition, self and foreign spoken words were heard without visual stimulation. 13 healthy subjects performed the experiment while 76-channel EEG was recorded. ERPs were computed for all conditions, and contrasts were built to assess the effects of physical mismatch (feedback at inadequate latency), agency mismatch (feedback with foreign voice) and auditory verbal self-monitoring.
Results: Using microstate analysis and spatial filtering, we could identify a strong and reliable reduction of the auditory N1 ERP component during intact audio-verbal self-monitoring in a timewindow around 100msec after voice onset. Agency mismatch did not affect the N1, but increased the amplitude of the later auditory P2.
Discussion: With appropriate experimental designs and analysis methods, agency monitoring processes can be isolated from activity related to language-motor production and auditory sensory processing. This is particularly interesting for the investigation of schizophrenia patients with auditory verbal hallucinations.

psychiatry
Self-monitoring, collateral discharge, language, auditory verbal hallucination

Talk

PA-15

Emotion induction in patients suffering from schizophrenia spectrum disorders: preliminary results of a behavioral study using musical stimuli

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BACKGROUND Patients with schizophrenia show differences in perception and experience of emotions compared to healthy individuals. Musical stimuli are apt to induce specific emotions in healthy subjects. Vieillard et al. (2008) provided a set of musical stimuli exclusively generated to induce four different categories of emotions for research purposes. Their validity was repeatedly shown in behavioral and psychophysiological experiments in healthy controls and patients with brain lesions. The aim of our study was to identify possible behavioral differences in induced emotion between patients and healthy controls and to relate these deviations to psychopathology. METHODS We included 34 healthy subjects and 15 inpatients (male=10; female=5; mean age 37.73; SD±13.21) of the University Hospital of Psychiatry Bern suffering from psychosis. Eight patients suffered from schizophrenia, four from a schizoaffective disorder, and three from an acute polymorphous psychotic disorder according to ICD-10. All patients had treatment as usual. The participants were asked to listen to six musical stimuli of each of the following four categories: threat (high arousal/low valence), sadness (low arousal / low valence), happiness (high arousal / high valence), and peacefulness (low arousal / high valence). The 24 stimuli were presented one-by-one in a randomized order, via headphone. After each stimulus the participants were asked to categorize (forced choice) and rate the felt emotion regarding arousal and valence on a seven point scale. The psychopathology was measured using the Positive and Negative Syndrome Scale (PANSS) and the Bern Psychopathology Scale (BPS). RESULTS In healthy controls, the music pieces reliably distinguished the evoked valence and arousal in the four possible combinations, confirming the results of Vieillard et al (2008). In psychotic patients, there were differences in the ratings related to the

two subjective axes compared to controls. The analysis of these differences in relationship to the symptom domains measured with the BPS is ongoing and will be presented on the poster. DISCUSSION The validity of the applied music paradigm was confirmed in an independent group of healthy subjects. They therefore appear to be apt to study the emotional dimension in psychiatric patients. The specific value for understanding the temporal dynamics and the specifity for investigating emotional dysregulation will be further studied in this and in an extended patient group.

neurobiology, psychiatry
schizophrenia, emotion, psychosis, behavioral study

Poster

PA-16

Gray matter abnormalities in spider phobic patients

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Introduction:
Spider phobia (SP) is characterized by excessive and unreasonable fear and avoidance-behaviour when exposed to spiders. Despite the accumulating knowledge about fear-related brain regions, links between brain architecture and brain functions in SP are limited and controversial. Morphological alterations in SP are supposed to involve not only a single brain area, but different structures within a globally affected neuronal (fear-) network. Measuring the gray matter (GM) density may contribute to the understanding of aberrant fear mechanisms. The goal of this study was to investigate brain GM abnormalities in spider phobic patients.
Methods:
Twenty female patients with SP (mean age: 29.9; SD: 11.3) and twenty matched controls (mean age: 27.1; SD: 5.9) were included in the analysis. MRI was performed on a 3T Siemens Magnetom Trio Scanner (Erlangen, Germany). For structural images, a high-resolution 3-D T1-weighted imaging protocol (Magnetization Prepared Rapid Acquisition Gradient Echo, MPRAGE) was used, resulting in 176 sagittal slices (slice thickness=1.0 mm, FOV 256 mm×256 mm, matrix size=256×256, TR=1950 ms, TE=2.6ms).
GM density was analyzed with FSL-VBM, a voxel-based morphometry style analysis [Ashburner 2000, Good 2001] carried out with FSL tools [Smith 2004]. Finally, voxel-wise GLM was applied using permutation-based non-parametric testing.
Results:
Compared with controls, spider phobic patients showed significantly reduced GM density in the right superior frontal gyrus and bilateral frontal medial cortex. On the other hand, patients showed increased GM density in the right amygdala, left orbitofrontal gyrus, bilateral frontal gyrus (pars triangularis) and bilateral insula compared to healthy controls.
Conclusion:
Dysfunction within this larger network of regions is consistent with the clinical features of spider phobia, which includes acute sensitivity to phobic stimuli, characterized by an inability to suppress excessive fear responses, covering emotional, autonomic, cognitive and attentional elements.
However, abnormalities in gray matter density probably do not essentially represent major sites of pathology, but substrates of vulnerability factors or secondary changes due to the disease.

psychiatry

Poster

PA-17

Assistive Technology to enhance safety and autonomy of dementia patients at home

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Background
Today, almost all over the globe, people are continuously growing older accompanied by an increased risk to develop dementia. Independent living of these patients is often a trade-off between the desire to live autonomously at home as long as possible and the risks that increase with the progression of dementia. Assistive technology can be used to detect dangerous situations, to reduce their risks, and to inform the caregivers. Examples are falls, wandering, sudden changes in mood, accidents during activities of daily living and others. There are numerous commercial products in the field of assistive- and smart home technology for the elderly available on the market. The aim of this project is to use existing technology and develop a system that meets the specific needs of patients with cognitive impairments.
Method
Based on a set of discreet data, both actual and historical, it could be possible to estimate the patient's physical and mental state. The data are captured with the aid of a sensor network. A set of discreet sensors is placed in the patient's environment to collect the data. The retrieved data will be processed by a sophisticated algorithm to conclude the patient's condition. In case of emergency, an alarm will be set to inform the caregivers about the situation.
Preliminary Results
First tentative tests have proven the technological concept. It is possible to retrieve miscellaneous data from a network of different wireless sensors within a sufficient range over several weeks. By analyzing the logged data it becomes possible to identify basic scenarios of daily living.
Outlook
Preliminary studies indicate great interest in such a technology. The objected solution will allow patients to stay home safely and independently. By reducing the number of unnecessary control visits, using the system might also relieve formal and informal caregivers. The scientific challenge lies in the processing and analysis of the retrieved data. Thereby it could also become possible to recognize specific patterns as a predictor of severity or future progression of the patient's disease.

other
assistive technology, dementia

Poster

Physiology (PH)

PH-01

Changes in the vegetative nervous system during listening to different interpretations of Chopin's "Tristesse"

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Introduction: Music is able to evoke positive and negative emotions in nearly every listener. Defining emotions in two dimensions with arousal and valence, arousal can be measured with the surrogate marker of peripheral reactions. An impact of music on autonomic functions like heart rate and its variance, skin conductance, respiration rate, blood pressure and muscle tension was shown. Due to specific use of "tempi rubati", an artist is capable of heightening the tension in certain music delaying the ongoing progression of the melody. Target of this study was to compare the arousal patterns of two versions of Chopin's etude "Tristesse". An increased arousal was expected after sequences played with "tempo rubato".
Methods: The participants were asked to listen to Chopin's "Tristesse". While listening they were asked to rate their arousal level. Simultaneously skin conductance level was measured. We used Agustin Anievas' interpretation as metronomic and Boris Berezovsky's interpretation as as interpretation with "tempi rubati". The slower version was speeded up thus both versions had a duration of 265.2 seconds. Statistical method: 10 segments were identified with a "tempo rubato". The segments' length was between 4 and 10 seconds. Arousal ratings and peripheral physiology were compared immediately after these segments.
Results: A higher subjective arousal rate and an elevated skin conductance level was found related to sections played with "tempo rubato".
Conclusions: There was a significant difference between the two interpretations. The segments played with "tempo rubato" showed a higher subjective arousal and a heightened skin conductance, indicating an increased emotional load provoked by delays of the expected course of the music piece.

physiology
Music - Neuroscience

Poster

PH-02

Neocortical spike timing-dependent depression requires astrocyte mediated retrograde signaling

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Astrocytes make up a large part of the mammalian brain. However, unlike neurons, astrocytes do not propagate electrical signals. Therefore, they have been thought to play no role in information processing in the brain, but to be solely passive supporters of neuronal function. Contrasting this view, recent studies show that astrocytes can signal to neurons, and vice versa. Because synapses are closely associated with astrocytes, this bidirectional signaling between neurons and astrocytes could play a crucial role in learning and memory formation.

We studied the involvement of astrocytes in spike timing-dependent plasticity in the primary sensory cortex. This form of synaptic plasticity is essential for the proper formation and refinement of sensory circuits. In particular, spike timing-dependent long-term depression (t-LTD) of synapses between L4 spiny stellate neurons and L2/3 pyramidal neurons plays a critical role in sensory development. The signaling cascade governing this process is not completely understood. t-LTD at L4-L2/3 connections depends on activation of presynaptic, but not postsynaptic, NMDA receptors. Furthermore, t-LTD requires endocannabinoid synthesis and subsequent activation of the cannabinoid

CB1 receptor (CB1R). However, it is unclear how presynaptic NMDAR activation and endocannabinoid signaling act in concert to achieve synaptic depression.

Recent studies have shown that astrocytes express CB1Rs, and that activation of these receptors initiates astrocytic calcium signaling. Furthermore, upon activation astrocytes can release gliotransmitters, like glutamate, which can activate presynaptic NMDA receptors. Therefore, we investigated whether astrocytes are involved in t-LTD at synapses between L4 spiny stellate and L2/3 pyramidal neurons in rat barrel cortex. We made whole-cell patch-clamp recordings from L2/3 pyramidal neurons and neighboring astrocytes in acute brain slices. Using 2-photon imaging, we showed that there is an increase in the number of calcium events in astrocyte processes when t-LTD is induced in a neighboring neuron. Furthermore, we showed that t-LTD is abolished when astrocytic calcium signaling or vesicle release from astrocytes is blocked. Our results suggest that vesicular release of gliotransmitter from astrocytes is necessary for t-LTD induction. Taken together, these findings show that astrocytes mediate retrograde signaling in t-LTD, and highlight the importance of astrocytes for sensory development.

neurobiology, physiology
Astrocytes, Synaptic plasticity, Endocannabinoids

Talk

PH-03

Heart rate variability during listening to Beethoven's "Für Elise"

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Introduction: When listening to music, we can often generate expectancies about the future course of a melody and anticipate the occurrence and recurrence of certain themes. Meyer (1956) linked the expression of emotion to the confirmation and violation of expectancies. It is argued that the fulfilling or denial of certain expectations may activate the autonomic nervous system. Therefore, by stressing certain melodic structures via latening them rhythmically, an artist is capable of creating a heightened arousal. There is well-established evidence for heart rate variability (HRV) to serve as marker for arousal. By comparing the HRV during different parts of Ludwig van Beethoven's "Für Elise" with the resting state of the participant we tried to show the impact of different melodic and formal situations on arousal rates.
Material and Procedure: The participants were asked to listen to Beethoven's "Für Elise". While listening they were instructed to rate their arousal level. The arousal rating, skin conductance and heart beat (ECG) was measured and recorded via PowerLab 8/30 and LabChart 7.2. Recording frequency was set up at 4kHz. The music was presented as wave file via Technics RP F-550 headphones. We used Siang Wong's interpretation as an interesting interpretation with "tempi rubarti". The duration of the piece is 180 seconds.
Statistical method: In four distinct parts (due to formal analysis) of "Für Elise " HRV of the participants was calculated and compared with HRV in a resting state (two minutes).
Results: In the time- as well as in the frequency-domain, significant changes of HRV-indices between defined segments as well as between segments and relaxation are detected. These results may reflect the listeners' involvement that is varying through the progression of the piece. Additionally, the second segments - including the most dynamic part - and the third segment - including the most "rubato" section in the presented interpretation of Siang Wong - are connected with reduced HRV compared with the beginning and the end of the piece (formal exposition vs. Reprise).
Conclusions: HRV is seen as good parameter to evaluate the emotional involvement of listeners during the presentation of classical music. Even short-term segments (<60 s) show variations, which are correlated with the musical content in terms of, melodic (and harmonic) as well as time-related ("tempo rubato") elements. HRV with its complex variables may serve as an indicator of emotional involvement in music, which can explain the listeners' emotionality produced by musical elements in a given interpretation.

methodology, physiology, psychology
Heart rate variability, emotion, music, expectation violation

Poster

PH-04

Motion-Orientation interactions in a recurrent V1-network

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Experimental evidence reveals different types of orientation and motion selective neurons in the primary visual cortex (V1). While most motion selective neurons are selective to a specific direction, other motion selective neurons are non-directional and respond to motion whatever its direction is. Almost nothing is known how these neurons interact in V1. Here we ask how directional and non-directional motion selective neurons should modulate orientation selective neurons in order to improve figure-ground separation in a noisy background. This task profits from highlighting co-aligned edges, which represent potential object boundaries. Motion and orientation selective neurons both represent cues for such co-aligned edges. From a theoretical point of view we therefore ask how to optimally combine these cues to reliably detect co-alignments. As directional neurons yield evidence for an orthogonally oriented edge, this information is expected to be additively combined with the information from orientation selective neurons. In contrast, non-directional motion neurons are expected to multiplicatively modulate orientation selective neurons and to sharpen edge extraction via recurrent circuitry

other
V1, gain-modulation, recurrent networks

Poster

PH-05

Spike-based decision learning in socio-economic interactions

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In a natural environment humans and animals face decision tasks where the outcome depends on the environment, as e.g. in social interactions, where reward may depend on the decisions of other players. Game theory attempts to mathematically capture behavior in those situations. Often, the players do not know the action of the opponent, although reward depends on it and is uncertain. The optimal strategies can be deterministic or stochastic and are known as pure or mixed Nash equilibria, respectively. We propose a population coding model of spiking neurons that successfully copes with game theoretical tasks where reward is delivered stochastically. We study a simplified version of blackjack giving rise to a pure strategy and the inspection game known from economics that requires a mixed strategy. In both cases the neuronal populations playing against each other converge to the Nash equilibrium after long enough learning periods. For short learning periods, on the other hand, the populations mimic the behaviour of humans and monkeys playing the inspection game (Dorris et al., 2004).

other

Poster

PH-06

Sequence learning with hidden units in spiking neural networks

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Learning to produce temporal sequences is a general problem that the brain needs to solve. Movements, songs or speech, all require the generation of specific spatio-temporal patterns of neural activity that have to be learned. We consider a statistical framework in which recurrent networks of spiking neurons learn to generate spatio-temporal spike patterns. Given biologically realistic, stochastic neuronal dynamics we derive a learning rule for the synaptic strengths that leads to optimal recall of the training sequences. We show that learning the strength of synapses that connect to hidden neurons significantly improves the storing capacity of the network. Furthermore, we derive an approximate online learning rule and show that our learning rule is consistent with Spike-Timing Dependent Plasticity in that if a presynaptic spike shortly precedes a postynaptic spike, potentiation is induced and otherwise depression is elicited.

other
sequence learning, artificial neural network, generative model

Poster

PH-07

Reinforcement learning with active dendrites

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The discovery of binary dendritic events such as local NMDA spikes in dendritic subbranches led to the suggestion that dendritic trees could be computationally equivalent to a 2-layer network of point neurons, with a single output unit represented by the soma, and input units represented by the dendritic sub-branches with clustered inputs. Although this interpretation endows a neuron with a high computational power, it is functionally not clear why nature would have preferred the dendritic solution with a single but complex neuron, as opposed to the network solution with many but simple units. We show that the dendritic solution has a distinguished advantage over the network solution when considering different learning tasks. Its key property is that the dendritic branches receive an immediate feedback from the somatic output spikes, while in the corresponding network architecture the feedback would require additional backpropagating connections to the input units. Assuming a reinforcement learning scenario we formally derive two learning rules for the synaptic contacts on the individual dendritic trees which depends on three quantities: the presynaptic activity, the local membrane potential/NMDA spikes and a delayed reinforcement signal. In addition the second rule uses the backpropagating action potentials and the somatic membrane potential deflections as an immediate feedback signal.

We test the model for two scenarios: the learning of binary classifications and of modulation of the firing rate. Comparing the learning performances of the two learning rules, we show that the local one turns out less efficient compared to the global rule. We deduce that the immediate feedback signal represented by the backpropagating action potentials and the somatic membrane potential deflections supply the individual dendritic branches with enough information to efficiently adapt their synapses and to speed up the learning process.

other
Reinforcement learning, synaptic plasticity, dendritic computation

Poster

Psychology (PO)

PO-01

When healthy elderly outpace the young folks in semantic processing

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Investigations on semantic memory abilities in the course of healthy aging have shown both declining and stable processes. In particular, controlled semantic mechanisms seem to decay with increasing age. On the other hand, previous studies on automatic semantic processes reported ambiguous findings. In order to dissolve these inconsistencies, the current study aimed at examining age-related alterations in automatic semantic word retrieval. To this end, it was attempted to optimize the control of critical methodological factors such as experimental task, electrophysiological methods and subject selection.
In detail, thoroughly screened healthy young and elderly subjects performed lexical decisions (LD) on visually presented word/non-word pairs (prime and target) with a stimulus onset asynchrony of 150 ms. Reaction times (RT) on target word onset and event-related potentials (ERP) were recorded. Separately, a motor control task was measured in order to control for age related motoric slowing. The ERPs were computed by means of a microstate cluster analysis.
Behaviorally, both subject groups exhibited the well-described semantic priming effect. However, no significant age-related RT differences were found. Interestingly, when correcting the RT of the LD task with the RT of the motoric task, the elderly responded even faster than the young. Focusing on the microstates, both groups showed similar activation during perceptual processing stages. However, in the automatic time window, different microstates were found between the groups. Finally, during the controlled and late processing stage, the elderly showed a comparable but delayed microstates pattern.
The current results imply that the elderly compensate for their motoric slowing with a faster automatic semantic word processing, possibly reflecting their more efficiently interconnected semantic network compared to the young.

psychology
Healthy aging, semantic memory, reaction time, microstates

Poster

PO-02

Unconscious Relational Inference Recruits the Hippocampus

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Relational inference denotes the capacity to encode and flexibly retrieve multiple memories to combine knowledge from several episodes to improve decision-making. Although relational inference is thought to depend on the hippocampus and consciousness, we now show that it also occurs outside consciousness but still recruits hippocampus. In temporally distinct and unique subliminal episodes, we presented word pairs that either overlapped ('winter-red', 'red-computer') or not. Effects of unconscious inference emerged in reaction times recorded during encoding and in the outcome of decisions made one minute later at test, when participants judged the semantic relatedness of two supraliminal words. These words were either episodically related through a common word ('winter-computer') or unrelated. Hippocampal activity increased during unconscious encoding of overlapping versus non-overlapping word pairs and during the retrieval of episodically related versus unrelated words. Hippocampal

activity at encoding predicted the outcome of decisions at test. Together, unconscious inference may influence decision-making in new situations.

psychology, other
episodic memory; associative; awareness; consciousness; flexibility; nondeclarative; implicit.

Talk

PO-03

Conscious intentions modulate the way subliminal words are processed

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Prime-stimuli that are presented too briefly to be consciously perceived can nevertheless affect responses to subsequent target stimuli. Such effects are evidence of unconscious cognition. Here, we investigated whether the meaning of subliminal words is processed automatically, or whether the focus of ongoing conscious cognition affects the way we process subliminal words. We manipulated the participants' focus of conscious cognition by using two different task instructions. Half of participants judged the target words' meaning according to pleasantness (yes, no) and the other half according to comprehensibility to a child (yes, no). Prime-target pairs were either semantically related (desk-table) or not (desk-car). Following the main experiment, all participants also judged the prime words (that were invisible) according to this (focused) instruction. Then, participants viewed all words (primes and targets) again to evaluate them according to the instruction given to the other half of participants in the main experiment (non-focused instruction). This procedure allowed to sort trials into congruently and incongruently evaluated prime-target pairs according to the focused and non-focused instruction. An effect of congruency manifested only for the focused but not for the non-focused instruction. This effect emerged if primes and targets were semantically related. This is evidence that subliminal words underwent genuine semantic analyses, and that these analyses were affected by the focus of ongoing conscious cognition. Hence, even unconscious processing of information can be intention-driven, which restricts the possibility of automatic, unintended manipulation by subliminal stimuli.

psychology
Unconscious; Semantic priming; Intention

Poster

PO-04

Habituation and consolidation of prospective memory over a week: An ERP-study

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Prospective memory (ProM) is the ability to remember and perform an intention in the future. If a prospective memory task is to be performed only once, it is episodic. If it is repeated, then it becomes habitual. Thus, with repetition, a task changes from episodic to habitual. The goal of this study was to investigate the transition from episodic to habitual prospective memory with event-related potentials (ERP). The ProM task was to respond to a target word which was embedded in an ongoing lexical decision task. 40 ProM trials were administered in each of two sessions that were separated by a week. The results revealed a behavioural consolidation effect with increased ProM performance after one week. The ERP-analyses showed that when the task became more habitual a difference occurred in a time-window between 450-650 ms post-stimulus in an ERP-component. In addition, a covariance analysis revealed that this transition is continued in the second session. These results demonstrate that the transition from episodic to habitual prospective memory is long-lasting and continuous.

neurology, psychology
prospective memory, habituation, consolidation, event-related potentials

Poster

PO-05

The bivalency effect results from the interference of episodic context binding: Evidence from an ERP-study

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When bivalent stimuli (e.g., Stroop-like stimuli) occur occasionally, performance is slowed on subsequent univalent stimuli. This "bivalency effect" may result from episodic context binding. That is, the occasional occurrence of bivalent stimuli creates a more demanding context, to which subsequent univalent stimuli and tasks are bound. This episodic context binding interferes with performance on univalent stimuli, thus causing the bivalency effect. However, an orienting response caused by the infrequence of bivalent stimuli might also contribute. The purpose of the present study was to provide more evidence for the episodic context binding account using event-related potentials (ERPs). We used a paradigm requiring predictable alternations between three tasks, with bivalent stimuli occasionally occurring on one task. To eliminate the orienting response, we excluded the first three univalent stimuli following bivalent stimuli in the ERPs analyses. The results revealed a lateral frontal negativity and a parietal positivity in a time window about 650 ms after stimulus onset. This neural signature is typically associated with an increase in interference. Thus, these results support the view that the bivalency effect results from an episodic context binding, which interferes with performance on subsequent univalent stimuli.

psychology
cognitive control, conflict, task switching, bivalent stimuli

Poster

PO-06

Does the administration of glucocorticoids affect working memory functions in spider phobic patients?

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Background: The main functions of our working memory are maintaining, updating, and manipulation of input information for further processing. Previous findings suggest that glucocorticoids affect working memory through simultaneous activation of the hypothalamic-pituitary-adrenal axis (HPA axis). Although performance in working memory tasks was shown to be impaired after acute stress, it is outstanding whether or not exogenous glucocorticoids affect working memory function. Further working memory functions are associated with activation in the prefrontal cortex. Method: In a double-blind, placebo-controlled study, 30 spider phobic patients receive either 20 mg hydrocortisone or placebo 1hour before a n-back task in the scanner. Psychological and physiological measures are repeatedly assessed. Results: Preliminary data will be presented. Conclusion: We hypothesize that the administration of glucocorticoids does not influence working memory processes.

psychology

Poster

PO-07

Whole-body motion modulates the perception of temporal intervals

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The aim of this study was to investigate the potential role of vestibular information in the processing of time by means of a time reproduction task. Blindfolded participants were seated on a motion platform and asked to reproduce the interval of a tone while they were passively displaced leftward and rightward. In Experiment 1, the velocity of the motion varied between 0, 0.07, 0.14, or 0.20 m/s. We found that the reproduced intervals were significantly shorter with increasing velocity of self-motion. In Experiment 1, participants were displaced during both the perception and reproduction phase whereas in Experiment 2, the motion was only present either during the perception of the tone or during the reproduction of the interval (or absent in both phases). Shorter intervals were produced only when the motion was present in the perception phase. This result rules out a general response bias caused by body motion. Our findings suggest that vestibular information modulates the perception of temporal intervals. These results could reflect interactions in brain areas that show activity during reproduction of temporal intervals as well as during vestibular stimulation, such as the cerebellum and areas within the parietal and temporal cortex (e.g., Bottini et al., 2001; Jech et al., 2005). Moreover, we found in both experiments that the reproduced time was shorter during rightward as compared to leftward whole-body motion. This result is in contrast with earlier studies showing that a leftward shift in spatial attention leads to underestimation of temporal intervals (e.g., Vicario et al., 2007).

psychology
body motion, time perception, vestibular system, time reproduction task, mental time line

Poster

PO-08

Executive functions of children born very preterm - deficit or delay?

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This study examined performance of children born very preterm or at very low birth weight (VPT/VLBW) and term-born controls aged 7 to 12 years in three frequently postulated executive functions (EFs), inhibition, working memory (WM), and shifting. The aim of the study was to investigate whether a) VPT/VLBW children differ in their developmental pattern of EFs when compared to controls, and b) whether VPT/VLBW children and controls perform differently in EFs across age groups, implying a deficit, or catch up with increasing age. Seventy-two VPT/VLBW children with no or minimal brain lesions and no or minimal history of neurodevelopmental impairments and fifty term-born controls were recruited and divided into three age groups (young: 7-8 years; middle: 9-10 years; old: 11-12 years). Children completed tasks of inhibition (D-KEFS, Color-Word Interference Test), working memory (WISC-IV, digit span backwards), and shifting (D-KEFS, Trail Making Test, Number-Letter-Sequencing). Across the ages of 7 to 12 years, the same developmental pattern was found in both VPT/VLBW children and controls, with large gain in shifting, medium gain in WM, and low gain in inhibition. Comparisons of age groups revealed that younger VPT/VLBW children (7-8 years) performed significantly lower in shifting and tendentially lower in inhibition and WM when compared to controls, whereas older VPT/VLBW children (11-12 years) approached the control's level of performance across all three EFs. Together, VPT/VLBW children showed a catch-up in performance of inhibition, WM, and shifting to the performance level reached by controls by the age of 11 to 12 years. In conclusion, difficulties

in inhibition, WM, and shifting of our VPT/VLBW sample reflect a delay rather than a deficit.

psychology
children; preterm; working memory; inhibition; shifting; catch-up

Poster

PO-09

The Effect of Caloric Vestibular Stimulation on Risky Decision Making

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Objective:
The aim of this study was to investigate the effect of vestibular stimulation on risky decision-making. Vestibular cortical projection areas include several brain areas, including insular cortex (for overview see Lopez & Blanke, 2011). The insula is known for its involvement in risky decision-making (Paulus et al., 2003) and it has been suggested as a basic neural substrate for subjective awareness and the representation of the emotional self (Craig, 2009). The latter is associated with the right hemisphere (Berlucchi & Aglioti, 1997). We used caloric vestibular stimulation (CVS), which is a non-invasive brain stimulation technique (Been, Ngo, Miller, & Fitzgerald, 2007) that is routinely used by ENT doctors to examine the vestibulo-ocular reflex. However, CVS not only activates the oculomotor pathways but also the ascending vestibular projections to the cortex. We hypothesize that right hemispheric activation induced by CVS involves brain areas involved the representation of the emotional self (e.g. insula), which in turn leads to a more risk-averse behavior in a gambling task.
Method:
We tested 20 right-handed healthy participants. They performed a risky decision-making task ('Devil Task') while they were exposed to cold air (20° C) caloric vestibular stimulation to the left ear. This stimulation leads to a right hemispheric activation of the insula and anterior cingulate cortex (for overview see Lopez & Blanke, 2011). For sham stimulation we irrigated the external auditory canal with air at body temperature, which is inefficient. We monitored eye movements to ensure that the stimulation was applied properly.
Results:
We compared risk behavior after loss and after win trials. Interestingly, type of stimulation (CVS, sham) interacted with risk behavior (after loss, after win). CVS led to a temporarily more risk-averse behavior after loss trials when compared to the sham condition. The effect was specific for trials after loss; no difference was found after win trials.
Conclusion:
CVS was shown to evoke a more critical and risk-averse gambling behavior only after loss trials. We conclude that the effect of CVS on risk behavior results from the activation of brain areas involved in the representation of the emotional self and heightened awareness of bodily states.
Acknowledgments:
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psychology
Risk behavior, insula, vestibular stimulation

Poster

PO-10

The efficacy of working memory training in improving higher-level cognitive abilities in typically developing children and the influence of neuroticism

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Working Memory (WM) is deemed a good indicator of children's learning potential, and regarding the influence of personality, neuroticism was found to be negatively associated with neuronal efficiency and therefore with less effective learning. Building upon studies revealing transfer effects of WM trainings on non-trained cognitive abilities, the aim of this study was two folded. First, we aimed to implement a WM training in an inartificial learning setting with regularly developed school children and investigate the effects on non-trained tasks. Secondly, we aimed to investigate the moderating effects of neuroticism on these variables. 99 elementary school children participated in the project. During four weeks, one group of each participating class trained with computer-based adaptive WM tasks, whereas a second group who trained on reading tasks served as an active control group and a third group served as a non-contact control group. In the pre- and posttest we assessed performance in cognitive and academic tests. On a general level, our analyses revealed near transfer on memory span tasks as well as far transfer on an index of intelligence, but only a tendency for increased academic achievement (reading, math), in the AG training group. Results furthermore disclosed that neuroticism not only correlated with lower cognitive ability and academic measures, but also with lower WM training and transfer to non-trained tasks.
Our results hold possible implications regarding the attempt to improve educational achievement. They suggest that a WM training can enhance higher-level cognitive abilities of school children and therefore may serve as an important and precious enrichment in ability-specific lessons. With regard to individual difference in personality, they confirm the validity of neuroticism as a contributing factor to cognitive and academic performance, and extend its validity as a contributing factor to cognitive training success in a school setting.

psychology
working memory training, neuroticism, higher-level cognitive abilities

Talk

PO-11

How glucocorticoid administration affects phobic fear processing: a fMRI investigation

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Background: Previous experiments in patients with phobia have shown that the administration of glucocorticoids reduces fear in phobic situations. Extensive evidence indicates that elevated glucocorticoid levels inhibit memory retrieval processes. In patients with phobia, exposure to a phobic stimulus provokes retrieval of stimulus-associated fear memory that leads to the fear response. It is therefore possible that glucocorticoids reduce phobic fear through an inhibition of fear memory retrieval. This is the first study investigating the acute anxiolytic effect of cortisol administration in spider phobic patients with fMRI when exposed to a phobic stimulus. Method: In a double-blind, placebo-controlled study, 30 spider phobic patients receive either 20 mg hydrocortisone or placebo 1 hour before the confrontation with a phobic stimulus in the scanner. Psychological and physiological measures are repeatedly assessed. Results: The cortisol group shows a greater amygdala activation (amygdala right: $t=2.983$, $p<.003$; amygdala left: $t=2.997$, $p<.003$) in the fast fear reaction but less amygdala activation (amygdala right: $t=-2.762$, $p<.006$; amygdala left: $t=-1.911$, $p<.058$) in the late fear reaction than the placebo group. Furthermore, only the cortisol group shows a reduction of subjective fear over the course of the experiment. Conclusion: The analysis of the preliminary data show that the administration of glucocorticoids enhance the activation of the amygdala during the

fast fear reaction while it reduced the amygdala activation of the late fear processing in the cortisol group compared to the placebo group. The finding supports the view that glucocorticoids reduce phobic fear through an inhibited retrieval of fear memory in patients with phobia.

psychology
Phobia, Glucocorticoids, fMRI

Poster

PO-12

Development of the visuo-spatial working memory network in childhood

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Background:
Working memory (WM) is a core cognitive ability, influencing the development of basic academic skills, planning and problem solving. Neuroimaging studies in adults have mapped visuo-spatial WM in a fronto-parietal network, shown to be related to WM performance. Little is known about changes in the WM network in the developing brain. This study aimed to characterize development of the visuo-spatial WM network and its relation to WM performance in childhood.
Methods:
A total of 44 healthy children aged 7 to 12 years (y) were recruited from the NEMO study. All children underwent a neuropsychological assessment to measure WM and general intellectual abilities and completed fMRI to detect the neural network of visuo-spatial WM (dot location task, Klingberg et al. 2002). Data of 39 children (20 males) were included in the analysis performed with SPM8. Laterality indices (LI) were calculated to assess the asymmetry of visuo-spatial WM activation.
Results:
Three main activation clusters were found in the superior and mid frontal region and the superior parietal region bilaterally. The WM network differed with age, sex and with WM performance. Younger children used more frontal areas in the right hemisphere to perform the WM task than older children. Lateralisation of frontal and parietal areas slightly increased with age towards the right hemisphere (n.s.). Regarding sex differences, girls showed a right hemisphere dominance during the WM task (LI=-0.35), whereas the activation pattern of boys was bilateral (LI=0.08, p=.045). WM activation correlated with WM performance. High-performers showed significantly stronger right-sided parietal activation (LI=-0.45) than low-performers (LI=-0.06, p=.01), even when correcting for age and sex.
Conclusion:
Age, sex and WM performance influence the maturing visuo-spatial WM network. Increasing age leads to a functional specialization of the WM network which comes along with a decrease in activation of frontal areas, and hence a decrease of executive demands. Furthermore, better WM capacity comes along with a shift from a bilateral to a right-sided WM network. Overall, this study highlights the importance to consider the influence of individual factors (such as age, sex and WM performance) on the visuo-spatial WM network when interpreting clinical and research neuroimaging data of children.

psychology
fMRI, visuo-spatial working memory, development, children

Poster

PO-13

Glucocorticoids reduce the recognition of emotionally significant material in patients with spider phobia

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Background: There is extensive evidence that glucocorticoids affect memory processes and cognitive performance. In particular, stress hormones play a crucial role in in the long term memory system where they enhance the consolidation while they inhibit the retrieval of emotional stimuli. Compared to healthy control subjects, phobic patients have a greater degree of activation in the amygdala and enhanced secretion of stress hormones while processing phobia-relevant stimuli. Previous studies have shown that the administration of glucocorticoids can suppress traumatic memories in patients with PTSD and have an anxiety-reducing effect in phobic patients. This effect is explained by an inhibition of the retrieval of emotional memories due to high levels of glucocorticoids. Therefore we hypothesize that spider phobic patients who have received glucocorticoids remember spider pictures worse and show reduced emotion triggering than spider phobic patients who have received a placebo. Method: 14 spider phobic patients and 7 control subjects were randomly exposed to phobic, emotional negative and neutral stimuli in the scanner. Patients received either 20 mg of hydrocortisone or placebo on hour before the experiment. Psychological and physiological parameters were repeatedly measured over the course of the experiment. All subjects completed a recognition task one week after the experiment in the scanner. Results: Preliminary data will be presented. Conclusion: Even though glucocorticoids enhance the consolidation of memories, we expect that the spider phobic patients who have received glucocorticoids during the experiment in the scanner recognize the phobic stimuli worse than the placebo group one week later because of the reduced anxiety during the consolidation of the spider pictures.

psychology
Spider Phobia

Poster

Workshops

Workshop 1: Deep brain stimulation as a treatment for obsessive/compulsive disorder: What animal models tell us about mechanisms (Chair: Anthony A. Grace)

Workshop 2: Sleep (Chair: Johannes Mathis / Katharina Henke)

Sleep research and sleep medicine have gained much interest in the last few years, since it became possible to treat sleep disorders such as insomnia, narcolepsy or sleep apnoea syndrome and much better insight was obtained into the fundamental functions of sleep.
For both fields, sleep medicine and sleep research, polysomnography is the gold standard examination to get insight into physiological sleep mechanisms or sleep disorders.
One important function of sleep is memory consolidation, and exciting research is going on to understand the underlining processes.
Apart from insomnia, the most prevalent sleep disorder, a similar amount of patients suffers primarily from excessive daytime sleepiness, with important consequences on daytime performance. Objective Assessement of this poorly characterized construct of “sleepiness” is particularly important in view of its consequences in the industrialized societies.

Lectures:

Polysomnography a Goldstandard in Sleep Research and Sleep Medicine
Corinne Roth, University of Bern

The contribution of sleep stage II to the consolidation of episodic memories.
Simon Ruch, University of Bern

Maintaining memories by reactivation
Björn Rasch, University of Zurich

Multimodal assessment of daytime sleepiness
Johannes Mathis, University of Bern

Workshop 3: Optogenetics (Chair: Thomas Nevian)

Optogenetics comprises techniques for the genetic manipulation of cells to express light-sensitive proteins. Optogenetics is a rapidly growing field in neurobiology and it holds many promises in basic neuroscience research as well as future clinical applications. Genetically encoded light-activatable proteins allow the electrical or biochemical control of neuronal function with light. Especially channelrhodopsin, a light-activated ion channel can be used to activate a defined population of neurons with light, which has many advantages over conventional electrical stimulation methods. In this workshop, three distinct speakers will present different aspects of optogenetic approaches. Georg Nagel, who is one of the scientists that discovered channelrhodopsin will talk about recent advances in the field of optogenetics. Thomas Oertner will show how optogenetic approaches can be used to study synaptic plasticity, while Botond Roska will give insight into how this technique might be clinically relevant in the visual system.

Lectures:

Introduction
Thomas Nevian, University of Bern

Characterization and application of microbial photoreceptors
Georg Nagel, University of Würzburg

Long-term depression: Adjusting synaptic strength or changing network connectivity?
Thomas Oerter, Friedrich Miescher Institute, Basel

TBA
Botond Roska, Friedrich Miescher Institute, Basel

Workshop 4: Clinical Neurogenetics (Chair: Jean-Marc Burgunder)

Clinical and molecular genetics play an increasing role in the investigation and management of patients with neurological and psychiatric disorders. Already during history taking aspects of family history are inquired and patients often ask about a hereditary risk for the same disorder in their relatives. This stresses the importance of psychological and ethical awareness about issues at hand, this being particularly true during a formal neurogenetic counselling.
In this process involving sharing of information it is important to understand the clinical background of the disorder under consideration, as well as the specific genetic aspects, both in terms of clinical genetics and of molecular genetic testing. Proper use of appropriate techniques to discover genetic mutations offers on one hand the opportunity for precise diagnostics in a particular patient, opening up the way for genetic counselling of his family. On the other hand, the discovery of numerous genes involved in, for example in Parkinson's disease and other movement disorders, has lead to the establishment of more rational therapies based on a better understanding of the molecular features underlying the disorders.
In this workshop, basic principles and ethical considerations in the approach of patients with neuropsychiatric disorders will be discussed, including history taking, understanding levels of neurogenetic diagnosis and principles of genetic counselling.
As an example, the clinical presentation of common movement disorders, like Parkinson's disease and dystonia will be presented and some of the hereditary forms discussed.
In the clinical setting, it is important to understand the work in the laboratory, therefore, the basic molecular techniques, will be presented and methods to detecting mutations in these patients discussed.
Even with the future prospects of next generation sequencing a thorough analysis of correlation between molecular findings and clinical presentation as well as neurobiological mechanisms will be needed in order to give meaning of these findings in the clinical context. Therefore, leveraging on above information we shall finally discuss some examples of the chain of knowledge from genes to molecular pathophysiology and treatment in selected movement disorders.

Lectures:

Clinical neurogenetics: principles and ethical considerations
Jean-Marc Burgunder, Department of Neurology

Clinical genetics in movement disorders
Michael Schüpbach, Department of Neurology

Basics of molecular genetic diagnostics
Franziska Joncourt, Department of Pediatrics

From genes to molecular pathophysiology and treatment
Jean-Marc Burgunder, Department of Neurology

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