Program and Abstracts

8th annual meeting of the

Clinical Neuroscience Bern

December 4th 2012

Conference location:
University Hospital of Psychiatry,
Bolligenstrasse 111, Bern

http://www.kas.unibe.ch/neuro12

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BERN UNIVERSITY HOSPITAL

Dear participants

It is my pleasure to invite you to the 8th annual meeting of the clinical neuroscience network Bern which will take place next December 4th at the University Hospital of Psychiatry.

The joint effort of the faculties of medicine and psychology in Bern created a network of over 150 researchers involved in clinical and translational neuroscience in a variety of disciplines such as neurology, psychiatry, psychology, neurosurgery, neuroradiology, neurophysiology, neurobiology and neurogenetics. The main aim of this initiative is to promote knowledge, communication and collaboration between related fields of neuroscience.

The overall structure of this year's meeting is similar to that of the successful past editions. We are very pleased and honored that our event will start with an opening address given by Professor Täuber, the Rector of the University of Bern. The program will include two key-lectures on the genetics of neuropsychiatry (Prof. A. Papassotiropoulos, Basel) and the pre-surgical work-up of epilepsy (PD K. Schindler, Bern), two symposia on the topics of memory and movement disorders, 6 short presentations (selected from the abstracts submitted) and a poster session.

The meeting enjoys the financial support of the neurology department (poster prizes), and the graduate school for health sciences of the University of Bern. A special thank goes to Mr. Grieder for his important assistance in the organization of this meeting.

I hope that the program will catch your interest and am very much looking forward to welcoming you to the 2012 Clinical Neuroscience Meeting.

Prof. Claudio L. Bassetti
for the organizing committee

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

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Program 04.12.2012

08:00 – 09.00 **Registration / Poster attaching**

09:00 – 09:15 **Opening Addresses**

- Prof. Dr. Martin Täuber, Rector of the University of Bern
- Prof. Dr. Claudio Bassetti, 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 1**

- *Prof. Dr. Andreas Papassotiropoulos*, Division of Molecular Psychology, University of Basel
  Human genome-driven drug discovery in neuropsychiatry
  Chair: Claudio Bassetti

10:00 – 10:30 **Coffee Break**

10:30 – 12:00 **Short presentations** (6 selected abstracts à 15 minutes)
Chair: Thomas Nevian / Roland Wiest

- *Mirko Santello* (Dept. of Physiology, University of Bern), Sigrid Marie Blom, Thomas Nevian:
  Plasticity of dendritic properties in pyramidal neurons of the anterior cingulate cortex in a chronic pain model
- *Simone Duss* (Dept. of Psychology, University of Bern), Thomas P. Reber, Simon Schwab, Martinus Hauf, René M. Müri, Peter Brugger, Klemens Gutbrod, Jürgen Hänggi, Katharina Henke:
  Impaired unconscious episodic encoding and retrieval following amnesia
- *Maria Stein* (Dept. of Psychiatric Neurophysiology, University of Bern), Werner Fey, Kay Jann, Andrea Federspiel, Thomas Dierks, Franz Moggi:
  Context-specificity of inhibitory control in alcohol addiction
- *Ursula Wolf* (Institute of Complementary Medicine, University of Bern), Felix Scholkmann, Martin Wolf:
  Effects of inner speech on arterial CO2 tension, cerebral hemodynamics and oxygenation – A functional near-infrared spectroscopy study
- *Theda Heinks* (Dept. of Pediatric Neurology, University of Bern), Kevin Wingeier, Martina Studer, Christina Schäfer, Vanda Lory, Maja Steinlin, Kurt Leibundgut:
  Cognitive functioning in Children with Cancer before and after Medical Intervention
- *Karin Laimboeck* (Dept. of Psychiatric Neurophysiology, University of Bern), Claudio Schneider, Kay Jann, Andrea Federspiel, Sebastian Walther, Roland Wiest, Werner Strik, Helge Horn:
  Altered Functional Connectivity in Formal Thought Disorder in Schizophrenia

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

14:00 – 16:15 **Symposia**

- Symposium 1: **From Cell to Memory: The Plastic Brain**
  Organization: *Prof. Dr. Katrin Henke / Prof. Dr. Walter Senn*
- Symposium 2: **Behind the motor manifestations of human diseases**
  Organization: *Prof. Dr. Dr. med. Alain Kaelin / PD Dr. med. Claudio Pollo / Dr. med. Sebastian Walther*

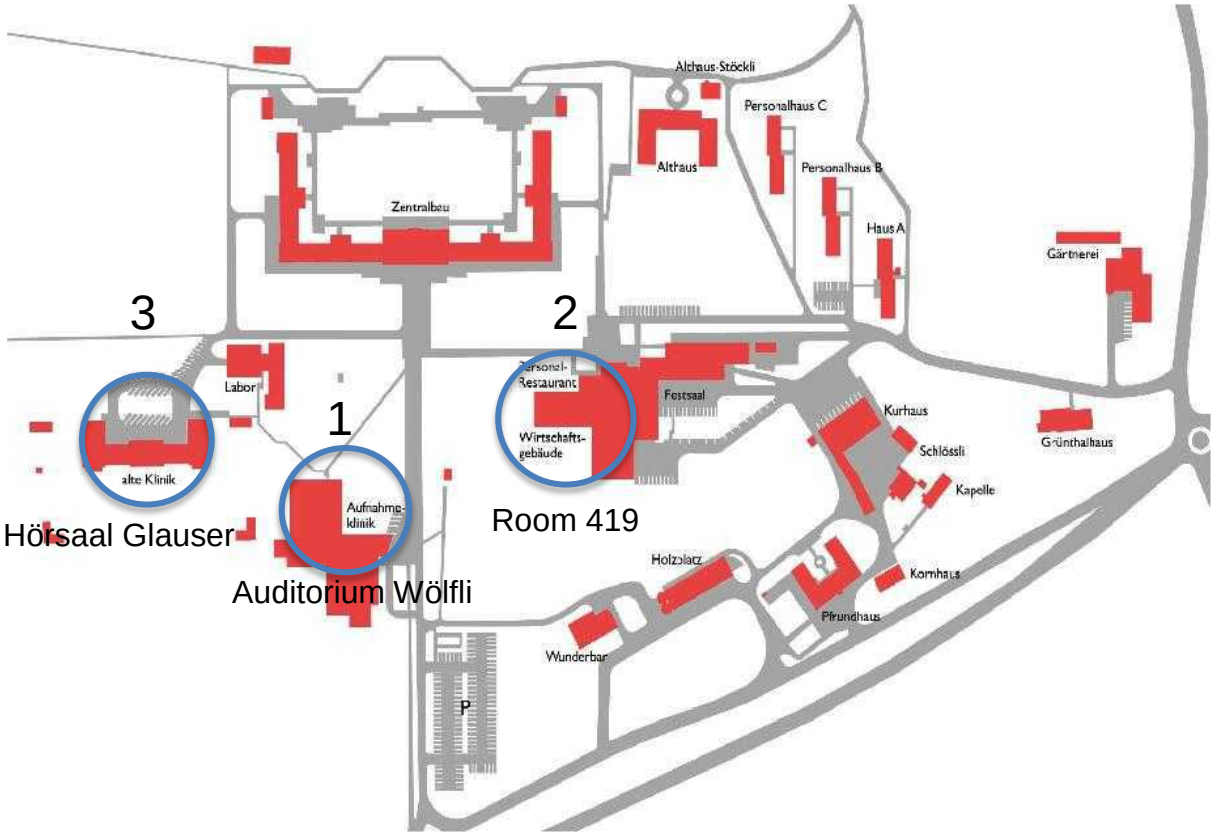
16:30 – 17:00 **Key Note Lecture 2**

- *PD Dr. Kaspar A. Schindler*, Department of Neurology, Inselspital, University of Bern
  Intracranial EEG: a window into the epileptic brain
  Chair: Claudio Bassetti

17:00 – 17:45 **Poster Awards**

17:45 **Poster detaching / End of the meeting**

Site Map



1 Aufnahmeklinik (Auditorium Wölfli):
Registration
Opening addresses, key note lecture 1
Coffee break
Short presentations
Symposium 2, key note lecture 2, poster awards

2 Wirtschaftsgebäude (basement: room 419):
Postersession
Lunch

3 Alte Klinik (Hörsaal Glauser):
Symposium 1

Key Note Lecture 1

Human genome-driven drug discovery in neuropsychiatry

Professor Andreas Papassotiropoulos, M.D.

Director, Division of Molecular Neurosciences
Faculty of Psychology, University Psychiatric Clinics and Department Biozentrum
University of Basel, Switzerland

Genomic research aided by unprecedented technological breakthroughs in DNA sequencing technology revolutionizes our understanding of the genetic basis of complex, multigenic traits and diseases. Indeed, an increasing number of genes, which are related to physiological memory function, to impaired function, and to brain activity, are being identified. In my talk I will demonstrate how the high-throughput use of genomic information provides new insights into the genetic basis of human memory and how it promotes the targeted treatment of memory disorders by identifying relevant genetic pathways in humans. I will also briefly discuss the justified reasons for excitement from a neuroscientist's perspective but also the justified reasons for caution due to misconceptions and some unsatisfiable hypes related to human genetics.

Key Note Lecture 2

Intracranial EEG: a window into the epileptic brain

PD Dr. Dr. Kaspar A. Schindler

Department of Neurology, Inselspital, University of Bern

Epilepsies are one of the most prevalent neurological disorders. They affect approximately 80’000 patients in Switzerland and are highly dangerous. Recurrent epileptic seizures increase significantly mortality and morbidity and they are a tremendous psycho-social burden to the patients and those who are close to them. In particular the unpredictability of seizure occurrence often leads to retreat, isolation and depression. Therefore the goal of therapy is to render the patients completely seizure free. However, with pharmacological treatment alone, complete seizure freedom is only achieved in two thirds of all patients. Many of the remaining patients are candidates for epilepsy surgery, if two conditions are met:

1. The brain areas that are essential for seizure generation can be precisely localized.
2. These brain areas can be surgically removed without neurological sequelae that are unacceptable for the individual patient.

In this talk, basic principles of pre-surgical evaluation for epilepsy surgery and some relevant aspects of cortical neurophysiology will be briefly discussed. Then special emphasis will be laid on intracranial EEG (iEEG), which is the most powerful diagnostic tool to assess electrical brain signals during human epileptic seizures. Using two clinical case studies, it will be demonstrated how the high spatiotemporal resolution of iEEG allows to detect epileptogenic brain areas and how iEEG signals may even help to shed new light on the pathophysiology of epileptic seizures.

Abstracts by discipline

Methodology (MT)

MT-01

Repeatability and variability of graph metrics in a test-retest of whole-brain structural networks

Jennifer Andreotti[1], Kay Jann[1], Lester Melie-Garcia[2], Thomas Dierks[1], Andrea Federspiel[1]

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

Purpose: Whole-brain network analysis of diffusion imaging tractography data is an important new tool for quantification of structural connectivity patterns across individuals and between groups. The concept of communicability was defined in 2007 to quantify the connectivity between two regions by all possible walks (AC) and not only the direct connections (SC). In our analysis we compared network properties as well as their variability for AC and SC graphs of 19 healthy subjects.
Methods: Diffusion Tensor Imaging (DTI) was performed on a Siemens Trio 3T scanner using a spin echo sequence (TR/TE=6800/93ms, 50 slices, slice thickness=2 mm, max b-value 1300 s/mm2,42 non-collinear directions). Each subject underwent two consecutives DTI sessions. In addition, T1-weighted anatomical images were acquired with a 12-channel head coil. Movement and eddy currents corrections were performed in FSL. After coregistration of diffusion weighted images with T1-weighted images an automated cortical parcellation was performed in FreeSurfer. The structures defined then served as seed regions for probabilistic fiber tracking in FSL.
In the SC graph, an undirected arc a_{ij} between ROIs i and j was established if a nonzero connectivity index was found to exist between the voxels of regions i and j. The arc weight was defined as the proportion of streamlines connecting the two ROIs corrected by ROIs' volume. Weighted communicability connectivity matrices (AC) were computed as the exponential $\exp(D^{-1/2} AD^{-1/2})$, where A denotes the adjacency matrix of SC, $D^{-1/2}$ is the diagonal matrix with elements $1/\sqrt{deg\_i}$ and deg_i is the generalized degree of node i in SC [2]. A common threshold on density was applied to all matrices in order to obtain comparable graph metrics. Global and local properties were analysed for every graph. In addition, the similarity of raw connection matrices as well as the intra class correlation (ICC) and the coefficient of variation (CV) of each metric were considered in order to verify repeatability of the network and its metrics [5].
Results: The analysis showed increased similarity R^2 for AC weighted graphs (Mann-Whitney test: within $p=0.0006$, between $p<0.0001$) as well as reduced variability in between subjects similarity (Levene's test: $p<0.0001$). Variability measures (ICC and CV) are slightly better in AC, although results are good in all graphs showing mean ICC over 0.65 for all measures. In general, all nodes' graph measures show a larger variability for SC.
Discussion: Results show that repeatability of graph metrics is overall good for all properties in SC and AC, although AC measures are slightly more robust. Variability is smaller within subjects than between subjects, indicating that the measures extracted can be used to characterize the individual network's structure and for example be compared to behavioural responses. Also AC reduces variability between subjects for all properties, which may be good for group comparison.

References: [1] Estrada E. and Hatano N. Phys. Rev. 2008, E 77 [2] Crofts J. and Higham D. A J. R. Soc. Interface. 2009; 6: 411-414. doi: 10.1098/rsif.2008.0484 [3]Rubinov M. and Sporns O. NeuroImage 2010; 52:1059:1069 [4] Iturria-Medina et al., NeuroImage 2007; 36:645:660 [5] Bassett et al. NeuroImage 2011;54:1262-1279

methodology
structural brain network, graph theory, DTI

Poster

MT-02

A new behavioral analysis in rats to understand motor fluctuations in parkinsonian patients treated with L-DOPA

Stefania Sgroi[1], Christine Capper-Loup[1], Alain Kaelin-Lang[1]

[1]*Dept. of Neurology and Dept. of Clinical Research, Movement Disorders Center, Inselspital and University of Bern, 3010 Bern, Switzerland*

Locomotor disorders like bradykinesia (slowness of movement) or hesitation of gait initiation are a hallmark of Parkinson's disease (PD). In the treatment of PD, Levodopa (L-DOPA) remains the most effective drug. However the majority of parkinsonian patients under L-DOPA therapy develop disabling motor complications like motor fluctuations, characterized by on/off phenomena, and abnormal involuntary movements, called dyskinesia.
The purpose of our study is to establish a behavioral animal model which is close to the locomotor activity performance of parkinsonian patients both during and in the absence of L-DOPA therapy.
Parkinsonian rats with 6-hydroxydopamine (6-OHDA) lesions were treated with chronic intraperitoneal injections of L-DOPA (8 mg/kg) once a day for 21 consecutive days; another group of lesioned rats received chronic injection of NaCl (vehicle) and a third group of naive animals received the standard L-DOPA chronic treatment. The motor activity of all groups was valuated using behavioral analysis software (Ethovision) at 19nd day of L-DOPA and NaCl treatment (ON period) and at 22nd day without L-DOPA and vehicle administration (OFF period), respectively.
Results: Preliminary observations about motor performance in parkinsonian rats demonstrated an higher locomotor activity, expressed as "total distance moved" and "mean velocity", in animals during the L-DOPA ON period than during the L-DOPA OFF period. Furthermore, Levodopa-induced dyskinesia were seen only in the ON-state, similar to what is seen in parkinsonian patients under L-DOPA therapy. On the contrary, no difference in motor activity was found in the parkinsonian rats treated with NaCl during ON/OFF period and naive groups during L-DOPA ON/OFF treatment, respectively.
We conclude that our animal model's behavior is close to motor performances in human suffering from ON/OFF motor fluctuations. This experimental model is better suited for preclinical study in order to test the use of new pharmacological drugs, able to reduce the motor complications induced by L-DOPA treatment.

methodology, neurobiology
Parkinson's disease

Poster

MT-03

ASL based functional connectivity in schizophrenia relates to disease severity

Nadja Razavi[1], Andrea Federspiel[1], Thomas Dierks[1], Martinus Hauf[2], Kay Jann[1]

[1]*Department of Psychiatric Neurophysiology, University Hospital of Psychiatry, University of Bern, Bolligenstrasse 111, CH-3000 Bern 60, Switzerland,* [2]*Institut of Diagnostic and Interventional Neuroradiology, Inselspital, University of Bern, Freiburgstrasse 4, CH-3010 Bern, Switzerland*

Purpose: Functional connectivity (FC) of the human brain has become a widely used method to investigate brain function. Recently, Arterial Spin Labeling (ASL) based cerebral blood flow (CBF) measurements has attained interest to estimate FC. Compared to the conventional BOLD fMRI that is a complex mixture of perfusion, metabolic and oxygenation status of the brain, the CBF measurements represent absolute quantitative brain perfusion, which is a major advantage. Especially in the diseased brain, this additional information might help to better classify pathological alterations and explain inter-individual differences in disease symptoms and their severity.
Methods: pCASL and BOLD fMRI during resting state were measured in 11 patients with schizophrenia (30.5±6.3years; 9M/2F). In addition, a high resolution T1 was acquired and the PANSS scores of all patients were assessed.
BOLD images were slice time and motion corrected to the T1 image, normalized into standard MNI space and smoothed with an 8mm FWHM Gaussian kernel. ASL data was motion corrected and CBF was estimated with a single compartment model. Quantified CBF images were co-registered, normalized and smoothed similar to the BOLD images. T1 images were segmented into grey and white matter (GM/WM) and the thresholded GM map was used as a mask in the subsequent analyses. Normalized BOLD and CBF images were then separately subjected to a group ICA to compute Group Components (GC; 24 and 15 components for BOLD and CBF respectively) and single

subject components (SC). In both datasets the Default Mode Network (DMN) was visually identified. Similarity of GCs and SCs was calculated as the spatial correlation coefficient. In addition, CBF within the global GM and in the ASL-DMN was computed and analysed for possible relation to spatial similarity or disease severity using Pearson and partial correlation analyses with GM-CBF as control variable.
Results: In the BOLD and the ASL dataset a highly similar GC representing the DMN, which was previously related to self-inner processing, could be identified ($r=0.56$, $p<0.001$). Then, the value of the SCs' spatial similarity to the respective GC (ASL/BOLD) was evaluated for each subject. Subject-wise comparison of the two spatial similarity values revealed a high degree of agreement. A further analysis indicated that the spatial similarity of the ASL-SCs to the ASL-GC was negatively correlated to the PANSS positive scores ($r=-0.66$, $p=0.03$). A partial correlation between SC's ASL-DMN and DMN-CBF (using GM-CBF as control variable) yielded a negative trend ($r=0.61$, $p=0.06$).
Discussion: Our results indicate that using ASL data, similar information about spatial pattern of the DMN can be achieved as compared to BOLD based analyses. However, ASL gathers additional information about the absolute perfusion of the brain and network. Moreover, data indicate a relation of the degree of similarity of an individuals' DMN (SC) to the GC to the severity of specific disease symptoms as assessed by PANSS positive. It may thus be argued that spatial altered DMN in schizophrenia reflects the often reported deficits in self-monitoring, which may explain symptoms such as hallucinations. Furthermore, the increased CBF in the altered DMNs suggests a state of hyperactivity that may relate to how processing errors occur due to constant overload.

methodology, psychiatry
schizophrenia, default mode network, functional connectivity, cerebral blood flow, fMRI

Poster

MT-04

Correlation between cerebral blood flow and anisotropy in white matter

Stéphanie Giezendanner[1], Sebastian Walther[1], Jennifer Andreotti[1], Simon Schwab[1], Roland Wiest[2], Thomas Dierks[1], Kay Jann[1], Andrea Federspiel[1]

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

In the human brain changes in cerebral blood flow (CBF) are mostly described for gray matter (GM) but rarely for white matter (WM). Nonetheless, neuroanatomy describes the perfusion of WM by blood vessels. Recently, a study investigated the relationship between CBF and WM properties showing an inverse correlation (rather than a positive) between CBF and fractional anisotropy (FA) values in healthy subjects. It was suggested that CBF in WM may be related to the axonal diameter. Accordingly, in the present study a twofold sample as compared to the study of Aslan et al (2011) was investigated in order to probe the surprising findings. Specifically, if there is a relationship between CBF in WM to the axonal diameter, then this relationship would be most prominent in the genu/splenium of the corpus callosum. We tested specifically for this hypothesis. A total of 24 healthy subjects were included in the study. All MRI scanning were performed on a 3T Siemens TRIO TIM scanner. Multimodal imaging included anatomical scan followed by arterial spin labeling (ASL) scan using pseudocontinuous ASL (pCASL) sequence and a diffusion tensor imaging (DTI) scan. The calculation and diagonalization of the diffusion tensor were based on the multivariate regression approach that finally allowed the estimation of eigenvalues and eigenvectors for each voxel from which fractional anisotropy (FA) values could be calculated. Co-registration of the CBF and FA maps to the 3-D structural images was performed and were then transformed into the normalized Talairach space. Partial Volume Estimation (PVE) was estimated in the segmented anatomical images using a "trimmed minimum covariance determinant (TMCD)" method for the estimation of the parameters of the mixed PVE model. Estimation of signal-to-noise ratio (SNR) was performed for individual CBF and FA maps by first extracting global CBF and FA values for each subject averaged across all WM voxels. For CBF values then individual SNR was defined as the ratio of the temporal mean of the WM and its standard deviation. In the present study a widespread region of statistical significant negative correlations between CBF and FA values in WM was observed. Only one cluster with 161 voxels was present after the application of Bonferroni correction [$r=-0.92$; $p<10\text{-}7$]. Fiber tracking from this ROI showed fiberbundles within the splenium of the corpus callosum. PVE revealed a total fraction of 12.1 % of WM voxels being prone of WM/GM and WM/CSF contamination that were removed from correlation analysis. The effect of the rigorous PVE treatment showed improved SNR estimation on CBF and on FA values. Significant inverse linear regression was observed for each subject. The present study investigates metabolic and microstructural properties within WM in healthy controls and shows a clear significant inverse correlation between CBF and FA values. This finding is in line with previous observations. The most significant negative correlation (Bonferroni corrected) was observed in the splenium of the corpus callosum. This region was described as having small axonal diameter. Overall, the findings in the present study confirm previous findings, but with a larger sample. The relationship of CBF to FA in the present study cannot rule out the proposed mechanism that links CBF to averaged axonal diameter of the tracts within WM.

References: Aslan, S., et al., Neuroimage, 2011. 56(3): p. 1145-53.

methodology, other
Cerebral Blood flow; White matter; Inverse Correlation; Corpus Callosum;

Poster

MT-05

Thalamic relay of frequency-specific EEG scalp field maps

Simon Schwab[1], Kay Jann[1], Andrea Federspiel[1], Thomas Dierks[1], Thomas Koenig[1]

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

Introduction: The thalamus is a fundamental relay structure of the brain that transfers sensory and motor signals to distinct zones of the cerebral cortex. The thalamus has also been argued as the pacemaker of cortical rhythms observed by EEG. Recently, EEG microstates that represent states of synchronized brain activity and EEG spectral fluctuations have been associated to fMRI resting state networks (RSNs). However, the emergence of specific scalp field oscillations and associated thalamic BOLD signal fluctuations has not yet been studied. In the present work, we aimed to define the frequency specific thalamic areas generating distinct synchronized cortical networks, as indexed by EEG scalp fields oscillating with a common phase.
Methods: Fourteen healthy subjects (6f/8m, mean age 26±2.7 years) underwent simultaneous EEG/fMRI in a no-task condition. The EEG was subjected to a topographic time-frequency algorithm that decomposed the EEG into 6 classes of transient states of synchronized oscillations. First, in single-subject GLMs, the BOLD response was fitted by using the 48 timecourses (6 classes of states x 8 frequency bands) as predictors, which were previously convolved with the canonical haemodynamic response function. In the group analysis, we used voxel-wise one-way ANOVA with the 8 frequency bands as within factor to fit the beta values of the GLM. For each of the six state-classes, a statistical map with F values of the main effect of frequency was created (Bonferroni, $p < 0.05$).
Results: Frequency specific areas were identified for the different state-classes (maps) in distinct medial and lateral thalamic subregions, such as dorsomedial nucleus, ventral-posterolateral n., ventral lateral n., pulvinar, and lateral posterior n.
Discussion: In the past, cortical BOLD fluctuations have successfully been correlated with thalamic BOLD to determine the functional thalamo-cortical connectivity. In this study, we have identified a consistent topological mapping of thalamic regions to a set of spatially defined patterns of cortical common phase oscillations at specific frequencies. Since thalamic activity itself is not visible in the EEG, the observed EEG-BOLD relations must be functional, attributing the thalamus a role of mediator, modulator and coordinator of cortical oscillatory activity that is visible in EEG. Synchronization of cortical oscillations is an important candidate mechanism for network formation and feature binding. Therefore, our study provides a novel way to elucidate the systematics of subcortical effects on the formation of large scale cortical networks.

methodology
Thalamus, EEG, Microstates, fMRI

Poster

MT-06

Evaluation of new language stimuli - which linguistic properties best predict reaction times?

Claudio Schneider[1], Karin Laimboeck[1], Thomas Müller[1], Werner Strik[1], Helge Horn[1]

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

We tested the predictive value of linguistic properties of german word pairs on reaction times. Linguistic properties of the target words had more pronounced effects than those of the primes. As expected, the effects of target length and word frequency were highly significant ($p<0.01$). Other important factors included the frequency of the first letter and the cumulated bigramm-frequency. Contrary to our expectations the frequency of the initial bigramm - a frequently used familiarity measurement - did not influence reaction times.

other

Poster

MT-07

EEG and Music: An Overture

Christian Mikutta[1], Gieri Maissen[1], Andreas Altorfer[1], Werner Strik[1], Thomas König[1]

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

Music is able to induce and modulate emotions. Recent studies have shown that limbic, paralimbic and prefrontal networks- all associated with emotions- are activated due to music. But little is known on the mechanisms of music induced emotions. For note to note evaluation of a music stimulus a considerably high time resolution is a necessary prerequisite. Therefor we suggest the EEG as the most suitable solution for investigating music induced emotions. The presentation will cover our own investigations (Emotions, Arousal, and Frontal Alpha Rhythm Asymmetry During Beethoven's 5th Symphony, Brain Topo) and Professionals listen differently to music, in prep.) as well as most recent developments in research concerning music and EEG. Finally we will discuss the advantages of the ECoG method for investigating music.

methodology, physiology
EEG, Music

Talk

Neurobiology (NB)

NB-01

Recruitment and Differentiation of Endogenous Bone Marrow-Derived Mesenchymal Stem Cells After Cerebral Ischemia

Robert Andres[1,2], Alex Filatenkov[3], Jeanette Baker[4], Raphael Guzman[2], Hans Rudolf Widmer[1], Andreas Raabe[1], Robert Negrin[4], Samuel Strober[3], Gary Steinberg[2]

[1]Department of Neurosurgery, University of Berne, Switzerland, [2]Department of Neurosurgery and Stanford Stroke Center, Stanford University School of Medicine, Palo Alto, CA, USA, [3]Department of Medicine, Division of Immunology and Rheumatology, Stanford University School of Medicine, Palo Alto, CA, USA, [4]Department of Medicine, Division of Blood and Marrow Transplantation, Stanford University School of Medicine, Palo Alto, CA, USA

Recent studies have highlighted the possibility that endogenous bone marrow derived stem cells (BM-MSCs) have the potential to give rise to cells of the neural lineage in the mammalian brain. However, it is not known whether this type of endogenous repair might contribute to production of new neurons after ischemic stroke.
In the present study, we therefore investigated the neurogenic potential of BM-MSCs in chimeric mice that underwent whole body irradiation followed by BM reconstitution with green fluorescent protein (GFP) expressing transgenic BM-MSCs. Recruitment and differentiation of GFP-expressing cells was addressed in uninjured controls and in two different murine stroke models, the permanent distal middle cerebral artery occlusion (dMCAO) model and the hypoxia-ischemia (HI) model, which allows reperfusion of the ischemic parenchyma after induction of the insult.
Mice were sacrified at 4 weeks or 3 months after stroke, respectively, and the brains were processed for immunohistochemistry. Co-localization studies were carried out with GFP and the neuronal markers DCX, NeuN and Tuj1, the astrocyte marker GFAP, the oligodendrocyte progenitor marker NG2, the macrophage/microglia marker Iba1 and the endothelial cell marker vWF.
In both the dMCAO and the HI model, we found engraftment of GFP-expressing BM-MSCs, particularly in the stroke borderzone, at 4 weeks and 3 months after the insult. GFP-positive BM-MSCs-derived cells did not co-localize with DCX, NeuN, Tuj1, or NG2. However, abundant co-localization was present with Iba1- and vWF-immunoreactive cells, and sparsely, GFAP-positive astrocytes also co-expressed GFP. The number of GFP-positive cells in the brain as well as the co-localization with Iba1 and vWF were significantly higher in mice after dMCAO or HI when compared to non-stroked controls.
Therefore, our data suggest that endogenous BM-MSCs in the systemic circulation are recruited to the post-ischemic murine brain, but do not contribute to the generation of new neurons. On the other hand, our findings further support the importance of microglia and endothelial progenitors derived from BM-MSCs for the inflammatory response and angiogenesis after ischemic stroke.

neurobiology, neurosurgery
Stem Cells

Talk

NB-02

Cell death pathways in $NaIO_3$-induced retinal degeneration

Jasmin Balmer[1,2], Rahel Zulliger[3], Sebastian Wolf[1], Volker Enzmann[1]

[1]Dept. of Ophthalmology, Inselspital, University of Bern, Switzerland, [2]Graduate School for Cellular and Biomedical Sciences, University of Berne, Switzerland, [3]Department of Cell Biology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, United States of America

Purpose: Programmed cell death (PCD) is a hallmark of several retinal diseases including aged-related macular degeneration. We have used the mouse model of $NaIO_3$-induced retinal degeneration that displays features of the disease in order to investigate involved cell death pathways.
Methods: Adult C57/BL6 mice received a single i.v. injection of sterile 25 mg/kg $NaIO_3$ to induce retinal degeneration. Outer nuclear (ONL) thickness was assessed and TUNEL staining was performed on paraffin sections. Visual function was measured using electroretinogram (ERG). Quantitative RT-PCR was applied to compare gene expression of PCD specific genes in RPE samples from $NaIO_3$-treated and -untreated animals. To further reveal

ongoing apoptotic events in the retina, immunohistological staining using caspase antibodies as well as caspase / calpain activity assays were performed.
Results: $NaIO_3$ induced patchy RPE loss with subsequent reduced ONL thickness and decreased ERG amplitudes beginning at day 3 post injection (PI). TUNEL positive apoptotic photoreceptor cells were detected after administration of $NaIO_3$ in the ONL starting at day 3 PI. Caspase-1 was significantly upregulated in the RPE cells at day 7 PI and cathepsin S expression was increased at day 10, indicating that RPE cells are undergoing necrosis. As a secondary effect of the RPE degeneration, photoreceptor cells are dying by apoptosis, as caspase 3 positive cells were found throughout the ONL. Photoreceptors were also positively stained for caspase 1 (inflammation), caspase 2 (activator of several caspases), caspase 9 (DNS damage/oxidative stress) and caspase 12 (ER stress). Caspase activity assays performed on retinal tissue lysates confirmed the caspases activation at day 10 PI. Calpain positive cells co-localize with TUNEL staining at 7 days PI.
Conclusions:
Caspase-independent as well as caspase-dependent cell death is occurring in the $NaIO_3$-induced RPE necrosis and subsequent photoreceptor cell death. Therefore, combination therapy may be necessary to prevent photoreceptor cells from undergoing apoptosis in the $NaIO_3$ mouse model

neurobiology

Poster

NB-03

Neural differentiation of human bone marrow-derived stem cells in vitro

Isai Mathivanan[1], Jasmin Balmer[1], Toma Luca[1], Volker Enzmann[1]

[1]*Dept.of Ophthalmology, Bern University Hospital, University of Bern, 3010 Bern, Switzerland*

Aim: The aim of the present study was to evaluate the *in vitro* differentiation capacity of human bone marrow-derived stem cells (BMSC) towards neural tissue, preferably retinal pigment epithelium (RPE).
Material and methods: Samples of mobilized peripheral blood (mPB) collected from cancer patients after granulocyte colony-stimulating factor (G-CSF) mobilization were used. Mononuclear cells (MNC) were isolated using Ficoll-Paque density gradient centrifugation, and were sorted by magnetic activated cell sorting (MACS) for the BMSC populations. These cells were than labeled with CFSE and cocultured on human RPE or bone marrow stromal cells (M2-10B4) for 7 days. Cell morphology and expression of RPE-specific markers and markers for other stem cell and neural cell types were examined by immunostaining and reverse transcription quantitative polymerase chain reaction (qRT-PCR), respectively.
Results: Populations of $CD34^+CD38^+$ and $CD34^+CD38^-$ BMSC were isolated with 6.04% and 1.13% of MNC, respectively. After 7 days of coculture, the cells changed from round to flattened, polygonal cells. The proliferation rate was significantly higher on M2-10B4 compared to RPE. $CD34^+CD38^+$ BMSC have higher proliferation than $CD34^+CD38^-$ BMSC. Furthermore, they expressed CD34, RPE65, and BEST1 when cocultured in direct cell–cell contact with RPE. RPE-specific markers and stem cell markers were expressed in both BMSC types.
Conclusion: These results suggest that human BMSC may differentiate towards RPE-like cell type *in vitro* and become a new type of donor cells for regenerative therapy in retinal degenerations.

other

Poster

NB-04

Effects of GHB and baclofen on sleep and motor function in healthy rats and rats with focal cerebral ischemia

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Objectives: Ischemic stroke remains one of the leading causes of death worldwide. However, there is still no available effective treatment for stroke patients. Promoting neuroplasticity during recovery may represent an

alternative strategy in development of new stroke therapy. There is strong evidence that sleep is important in facilitation of neuroplasticity. Sleep promoting drugs, gamma-hydroxybutyrate (GHB) and baclofen (Bac), showed neuroprotective effects when given within 24 hours after ischemia. Our goals were: 1) to check the effects of GHB and Bac on sleep in healthy rats and to determine the optimal drug dose, 2) to evaluate sensorimotor function recovery after delayed repeated treatment with Bac in a rat model of focal cerebral ischemia.
Methods: 1) Adult male rats (n=26) were implanted with EEG/EMG electrodes and assigned to the GHB (150 or 300 mg/kg), Bac (10 or 20 mg/kg) or saline treatment group. Injections were performed 1h after light onset and offset to evaluate time of day effect of the drugs. Every rat received two injections. 2) 24h after initiation of focal cerebral ischemia (permanent occlusion of the distal branches of middle cerebral artery, MCAo) rats were treated with Bac (10 mg/kg) or saline. Then injections were given twice daily during 10 consecutive days. Ischemia/Bac (n=14), ischemia/saline (n=14) and sham/Bac (n=8) groups were designed. Sensorimotor function was evaluated by single pellet reaching test (SPR) every week in the course of 1.5 month after MCAo.
Results: 1) GHB and Bac induced atypical animal behavior and altered EEG pattern. The drugs effect lasted up to 413 min. Amount of vigilance states was evaluated after the end of the drug effect. Bac treatment resulted in the increase in NREM sleep by 16 min in the light phase ($p<0.05$, paired t-test) and by 91 min in the dark phase ($p<0.001$). REM sleep was enhanced by 12 min in the dark ($p<0.05$). Duration and frequency of NREM sleep episodes depended on the timing of Bac administration. Thus, during the light phase Bac increased the duration of NREM sleep episodes ($p<0.01$), but reduced their frequency ($p<0.05$), while during the dark phase it increased the episode frequency ($p<0.0001$). In addition, Bac administered during the dark phase reduced sleep fragmentation ($p<0.001$, paired t-test). GHB had no major effect on the amount of vigilance states.
2) SPR performance dropped to 0 immediately after MCAo in both saline and Bac treated rats. Thereafter, both groups showed a slow recovery of function. No significant difference was observed between ischemia/Bac and sham/Bac groups 33 days after surgery. In contrast, ischemia/saline rats never reached the performance level of sham operated animals. Moreover, ischemic rats treated with Bac performed significantly better than saline treated rats ($p=0.01$, Tukey-Kramer).
Conclusion: Our results demonstrate that: 1) GHB and Bac induced sub-anesthetic state distinct from physiological sleep, confirming previously published mouse data. In contrast to GHB, Bac treatment increased the amount of sleep after the end of drug effect. 2) Delayed repeated Bac treatment might benefit motor function recovery after ischemic stroke.

neurobiology
ischemic stroke, sleep, motor function, GHB, baclofen

Poster

NB-05

Evaluation of Matrix Metalloproteinase Inhibitors in Experimental Pneumococcal Meningitis

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Background
Pneumococcal meningitis (PM) causes high mortality and morbidity and impedes the development of affected children (Brouwer 2010; Edmond 2010). Neuropathological changes in patients and experimental studies are characterized by cortical necrosis and hippocampal apoptosis (Grandgirard 2007). Matrix metalloproteinases (MMP) are proteolytic enzymes; levels of MMP-9 correlate with the severity of neurological sequelae in PM. MMP and TNF-α converting enzyme (TACE) play a critical role in the pathophysiology of PM e.g. in inflammation or blood-brain barrier disruption. Experimental compounds inhibiting MMP and TACE have been shown to be protective in experimental PM (Paul 1998; Leib 2000).
Aim
To evaluate MMP inhibitors with a clinical perspective and different inhibitory profiles for their effect on brain damage and inflammation in an experimental model of PM.
Methods
PM in rats was induced by intracisternal injection of live S. pneumonia. Treatment with MMP inhibitors was started at the time of infection (pre-treatment) or when animals developed symptomatic disease and antibiotic treatment (ceftriaxone) was initiated (adjuvant treatment). The following compounds were used: Ro 113-0830, Trocade, and Ro 32-7315. Therapeutic effects were assessed between 24h and 42h after infection. Primary endpoints included histomorphometric analysis (cortical injury and hippocampal apoptosis) and inflammatory parameters

(myeloperoxidase activity, cyto-/chemokine level). Vehicle-treated animals served as controls.

Results

In pre-treatment studies Trocade and Ro 32-7315 with Physiogel as vehicle showed a protective effect on brain injury. Ro 32-7315 reduced cortical injury ($p<0.05$) and apoptosis ($p<0.01$). Trocade with Physiogel as vehicle reduced cortical injury ($p<0.05$). A non-significant trend for increased survival was observed by pre-treatment with Trocade. Adjuvant treatment with Ro 113-0830 showed no effect on brain injury. Levels of MMP-9/-2 and inflammatory parameters were not significantly altered by any of the compounds.

Conclusion

Identification of clinically well tolerated and neuroprotective MMP inhibitors is a new therapeutic strategy to reduce neurological sequelae in PM. In this study we show that two compounds, Trocade and Ro 32-7315, have a protective effect on brain injury in a pre-treatment scheme. In succession they will be evaluated in an adjuvant therapy model, including assessment of neurofunctional outcome.

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neurobiology
Streptococcus pneumoniae, bacterial meningitis, brain injury, MMP inhibitors

Talk

NB-06

Plasticity in the anterior cingulate cortex of mice with neuropathic pain

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Neurons undergo plastic changes to adapt to a changing environment. Among the many forms of plasticity mechanisms are plasticity of intrinsic excitability, structural plasticity and long-term potentiation (LTP) and depression (LTD) of synaptic transmission. Neuronal plasticity mechanisms are thought to be the cellular correlate of learning and memory and serve several important physiological functions, but may also be the basis for pathological conditions such as chronic pain. It is known that noxious stimuli result in increased activity in several cortical brain areas, including the anterior cingulate cortex (ACC), an area particularly important for interpreting the unpleasantness of pain. This increased activity may cause cortical neurons to undergo long-term plastic changes that are involved in the chronification of pain.

We induce neuropathic pain 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 the ACC simultaneously.

Our experiments show that excitatory pyramidal neurons in the ACC of mice with neuropathic pain have a significantly lower action potential threshold than neurons in control mice, indicating that neuropathic pain induces plasticity of intrinsic excitability. Also, we observe a reduced number of connections between excitatory pyramidal neurons and inhibitory interneurons under neuropathic pain conditions. Such structural plasticity could result in disinhibition of the local microcircuit. Furthermore, we find that excitatory synapses on pyramidal neurons do not undergo LTD in mice with neuropathic pain.

Our data indicate that chronic neuropathic pain induces long-term neuronal changes in the ACC that will keep the neuronal activity at an elevated level. These changes may be involved in the formation of a nociceptive memory and in turning pain from an occasional nuisance to an ongoing agony.

neurobiology, physiology

Talk

NB-07

Plasticity of dendritic properties in pyramidal neurons of the anterior cingulate cortex in a chronic pain model

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Dendrites are the neuronal structures receiving most of the synaptic contacts and they participate in the integration and transformation of synaptic inputs for the generation of action potentials. In this respect, dendritic passive and active properties play a major role. This study aimed to uncover the properties of the main apical dendrite of layer 5 pyramidal neurons of the anterior cingulate cortex (ACC) of adult mice, a region that is involved in pain perception. Because strong activation of the nociceptive sensory system can potentially result in increased neuronal excitability in cortical areas, we studied the plasticity of dendritic properties in the ACC of a mouse model of chronic pain. Dual whole-cell patch clamp recordings were performed to assess changes in dendritic and somatic properties in a brain slice preparation from a mouse subjected to chronic constriction injury of the sciatic nerve (CCI) and are compared with control condition (Sham).
We studied Na^+ and Ca^{2+} electrogenesis, HCN channels activation as well passive cable properties of layer 5 pyramidal neuron apical dendrites in the ACC. We find that these dendrites, compared to those of the somatosensory cortex, display a prominent Na^+ spike upon dendritic depolarization and marked use-dependent attenuation of back-propagating action potentials. Moreover, we found that in CCI animals HCN channels are functionally down-regulated specifically in the dendrites, leading to exacerbated synaptic integration and ectopic neuronal firing. Thus, the excitability and integrative properties of ACC dendrites are modified in neuropathic pain, which might be relevant for the development of the pathological state.

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neurobiology
chronic pain, dendrites, anterior cingulate cortex, synaptic integration, HCN channels

Talk

NB-08

Backpropagating action potentials lower the threshold for the initiation of NMDA-spikes in the basal dendrites of layer 2/3 pyramidal neurons in a narrow time window

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N-methyl-D-aspartate (NMDA)-spikes are large amplitude regenerative potential changes specific for the basal, oblique and tuft dendrites of cortical pyramidal neurons (PC), mediated by the activation of NMDA receptors. Since the generation of an NMDA-spike means a supralinear amplification of the input signal, these events can effectively enhance the influence of the inputs arriving to distal dendritic compartments on the output of the neuron. However, it is not known, whether the output of the neuron also has an effect on the generation of NMDA-spikes in the distal dendrites.
The aim of this study was to reveal whether back-propagating action potentials (bAP) are able to influence the threshold for the initiation of a dendritic NMDA-spike, and if so, how broad is the time window for such an interaction. To answer this we did somatic whole-cell patch-clamp recordings from layer 2/3 PCs of the rat somatosensory cortex in parallel with local extracellular stimulation directly at the basal dendrites of the recorded neurons (50-150 µm from the soma). Excitatory postsynaptic potentials were induced by gradually increasing stimulation strength and paired with somatic action potential with variable onset times (between -50 and 50 ms). The threshold for initiating an NMDA-spike was determined both with and without a somatic action potential. We found that the bAP was able to lower the threshold for initiating an NMDA-spike in the basal dendrites, but only if it occurred within a very narrow time window (0-20ms) before the NMDA-spike.
These results indicate that the generation of NMDA-spikes can serve as a mechanism to detect coincidence of inputs arriving temporally close but at spatially distinct locations to pyramidal neurons.

neurobiology
dendrites

Poster

NB-09

Contralateral compensatory increase in dynorphin gene expression in the striatum of parkinsonian rats

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Parkinson's disease (PD) is typically characterized by a unilateral onset of symptoms. This asymmetry remains during the course of the disease; the side first affected being more affected than the other one. Very little is known about possible adaptive changes in the less affected side. In unilateral PD animal models a few changes have been reported in the basal ganglia contralateral to the lesion; a decrease of glutamic acid decarboxylase (GAD) mRNA was observed in the contralateral internal pallidum. The goal of our study was to analyze contralateral striatal changes of both direct and indirect pathways in a unilateral PD rat model.
We used the unilateral 6-hydroxydopamine (6-OHDA) rat model of PD and control animals. Four weeks after the lesion, animals were killed and their brain extracted. We performed in situ hybridization histochemistry with DNA oligoprobes for dynorphin (DYN), as a marker of the striatal direct pathway, and enkephalin (ENK), a striatal indirect pathway marker, in the striatum as well as for dopamine transporter (DAT) and tyrosine hydroxylase (TH) mRNA in the Substantia Nigra (SN). We also carried out an immunohistochemistry for the striatal TH protein expression. Results were analyzed on film autoradiograms for in situ hybridization and by the use of infrared fluorescence scanning with the LI-COR® system for immunohistochemistry.
In 6-OHDA animals we observed an increase of DYN mRNA expression in the striatum contralateral to the lesion compared to other experimental groups. This increase was larger in the lateral part of the striatum than in the medial part. We also found a significant positive correlation between the expression of D1-class dopamine receptors mRNA, in the lateral part of the contralateral striatum, and the mean velocity at four weeks after surgery in parkinsonian rats but not in controls. There was no difference between 6-OHDA and control animals in the contralateral striatal expression of ENK mRNA and TH protein, as well as in the contralateral nigral expression of both TH and DAT mRNA.
Our results suggest a role for the contralateral striatal direct pathway in compensatory mechanisms, restricted to the lateral striatum which is considered as "motor striatum", which cannot simply be explained by a contralateral increase in nigrostriatal dopaminergic tone. Our finding may be important to understand the course of PD in humans: compensatory mechanisms of the less affected side may improve motor symptoms.

neurobiology
Parkinson's disease

Poster

NB-10

Increased yield of dopaminergic neurons by antagonizing Nogo-receptor 1

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Introduction: The myelin associated protein Nogo-A is a potent growth inhibitor of the central nervous system. It is known that its inhibition leads to functional recovery after spinal cord injuries. Moreover, it has been shown that the inhibition of Nogo-A co-receptors, e.g. LINGO-1, improved the survival of mesencephalic dopaminergic neurons. Therefore, in the present study we investigated the effects of the peptide NEP1-40, which is a Nogo-receptor 1 antagonist, on cell density and morphology of ventral mesencephalic dopaminergic neurons.
Methods: The ventral mesencephalon was dissected from 14 days old rat embryos (E14). The dissociated cultures

were grown for seven days in absence (controls) or presence of NEP1-40 (0.5µg/ml and 2.5µg/ml). The medium was changed every other day. At the end of the experimental period, cultures were fixed with 4%-PFA and immunohistochemically stained for the dopaminergic marker tyrosine hydroxylase (TH). The numbers of dopaminergic neurons in the cultures were assessed by a researcher blinded to the treatment. Morphological measurements of TH positive (TH-ir) neurons included the axon length, the number of primary neurites and the soma size per single cell and were analyzed by means of a bright light microscope equipped with a digital camera and the cell^F software.
Results: Our analysis revealed that 0.5µg/ml and 2.5µg/ml NEP1-40 supplementation significantly increased TH-ir cell densities as compared to controls (by about 35%, $p < 0.05$). In addition, our preliminary experiments revealed that axon length of TH-ir neurons were significantly longer in NEP1-40 treated cultures as compared to controls (by about 35%, $p < 0.05$). The soma size of TH-ir neurons showed a tendency to increase in a dose dependent manner when treated with NEP1-40. Notably, the number of primary neurites was not altered.
Conclusion: In sum, the present study demonstrates that the inhibition of Nogo-A signaling by the Nogo-receptor 1 antagonist NEP1-40 increased the cell densities of mesencephalic dopaminergic neurons and affected their morphology. These findings suggest that Nogo interactions play a critical role in the development of midbrain neurons.

neurobiology
Nogo-A; Development; Dopaminergic neurons; Parkinson's disease

Poster

NB-11

Angiogenin is expressed in cholinergic and dopaminergic neurons

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Background: Angiogenin (ANG) is a secreted protein member of the ribonuclease family. Beside the potent angiogenic functions it has been reported to be neuroprotective and to play a role in neurite pathfinding. Moreover, there is evidence that ANG is involved in the pathogenesis of neurodegenerative disorders such as amyotrophic lateral sclerosis and Parkinson's disease. Notably, little is known about the expression pattern of ANG in the CNS. Given the importance of ANG in the nervous system, the present study aimed at investigating the localization of ANG expressing cells in the rat brain and spinal cord.
Methods: Adult Wistar rats were perfusion-fixed with paraformaldehyde. Brains and spinal cords were cryosectioned and processed for immunohistochemical stainings. Distribution of ANG positive cells were analyzed by means of a bright light microscope equipped with a digital camera and the cell^F software. For co-localization experiments sections were incubated with anti ANG antibodies in combination with either anti-tyrosine hydroxylase, anti-ChAT or anti-vWf and analyzed using an epifluorescence microscope.
Results: ANG expression in the spinal cord was found most prominently in motoneurons. Importantly to note, a strong staining pattern was observed in both the cytoplasm and the nucleus of these neurons. A scattered expression was found in the forebrain and cerebral cortex. Furthermore, ANG was expressed in the substantia nigra with a rather weak but specific staining in neuron-like cells. Co-localization experiments revealed that a subpopulation of ANG positive cells also expressed the dopaminergic marker tyrosine hydroxylase. Finally, brain endothelial cells stained positive for ANG.
Conclusions: The present study confirms recent findings demonstrated an important role for ANG in the nervous system. Further studies are needed to investigate the significance of ANG expression and its possible involvement in the pathogenesis of Parkinson's disease and other disorders of the brain.

neurobiology
Angiogenin; histochemistry; Parkinson's disease; midbrain; spinal cord

Poster

NB-12

Effect of hepatocyte growth factor (HGF) on neural stem cells derived from human chorion mesenchymal stem cells.

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Objective: Mesenchymal stem cells (MSC) derived from the chorion membrane of the placenta have the potential to differentiate into neural lineages and could be a valuable cell graft for the neuroregeneration after pre- and perinatal brain injury. Hepatocyte growth factor (HGF), a neurotrophic factor, is widely expressed in the CNS and plays a crucial role in attraction, migration, proliferation and differentiation of cells. Our aim is to provide an optimized MSC graft for neuroregeneration.
Study design: MSC isolated from chorion of term placentas were subjected to 0.1 % gelatin-coated culture flasks/serum replacement (G+S-), or uncoated culture flasks/fetal calf serum (G-S+). Minimal cell surface marker expression was analyzed by flow cytometry.
Expression of neural stem/progenitor cell markers (Nanog, Nestin, POU5F1, SOX2, PAX6, FZD9, Musashi1) and differentiated neural cell markers (GFAP, MBP, MAP2) were measured by flow cytometry and real-time RT-PCR. MSC were differentiated into NSC and the medium supplemented with HGF to enhance the NSC property.
Results: Chorion-derived cells expressed MSC markers independent of culture conditions. G+S- conditions resulted in a higher proliferation rate and higher expression of Nanog, Nestin, POU5F1, SOX2, PAX6 and FRZ9 as compared to G-S+ conditions. Neurogenic pre-induction by epidermal growth factor and N2 supplement resulted in the up-regulation of nestin expression and the formation of neurospheres. Finally, Pre-supplementation of the neurospheres by HGF resulted in the upregulation of cMET (HGF receptor) and CXCR4 (a key chemokine receptor implicated in cell migration).
Conclusion: The combination of gelatin-coating, serum replacement and HGF supplementation could possibly result in a cell population optimized for neural differentiation and could improve the efficacy in cell therapies for pre- and perinatal brain injury.

neurobiology
Stem cells, neural stem cells, prenatal brain injury

Poster

NB-13

Emotional Rivalry: Is There a Neurophysiological Interference of Competing Body Sensations?

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Do different body sensations interfere with each other on a neurophysiological level if they are present simultaneously? This basic research study investigates the interaction of two different kinds of human body sensations: one related to homeostatic imbalance (thirst) and one related to sensory stimulation (disgust). The aim of the study is to investigate whether disgust sensation is modulated under the influence of thirst compared to a satiated condition. Five healthy subjects underwent functional MR imaging after 18 hours of water deprivation. BOLD fMRI was measured during an intense thirst phase and after drinking to satiation. Both during thirst and satiation two odour stimuli (1 disgusting, 1 pleasant) were presented to the subject inside the scanner in an event related paradigm. Subjects rated both odours for pleasantness and intensity. Contrasts of cortical activation between the conditions ‘pleasant odour’ and ‘disgusting odour’ were calculated based on a GLM fixed effect model in order to find specific correlates of disgust sensation in both the thirsty and satiated condition. Analysis of behavioural data shows that the odour ratings during satiation tend to be more negative for the disgusting smell and more positive for the pleasant smell compared to the thirsty state. The results of the disgusting vs. pleasant odours contrast for the thirsty condition revealed brain activations in the insula, ACC and frontal and parietal areas. In the satiated condition the activation pattern is similar. However, cortical activation in response to the disgusting odour in the insula seems to be

diminished in the satiated condition, while frontal areas are more strongly activated. These results may reflect different disgust processing mechanisms for the thirsty and satiated condition.

neurobiology
Body Sensations, fMRI, Homeostasis, Disgust, Olfactory Stimulation

Poster

NB-14

Neurobiology of Hysteria, Migraine and Bipolar Disorder: from Freud & Fliess to the nasal ganglion, cerebral mast cells, and "lymphatic" fibromyalgia

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Introduction: The local anaesthetic nasal work (with Wilhelm Fließ) and the derived basic scheme of Sigmund Freud incorporating sexuality and conflict (FJ Sulloway 1979) have remained enigmatic. They can be traced back plausibly to the rarely investigated, but since long treated (M Piagkou 2012) pterygopalatine ganglion (PPG) and its strong output to the large cerebral arteries (O Taktakishvili 2010), which putatively calms blood-brain-barrier inflammations centred on brain mast cells through muscarinic-2 receptors, which commonly restore cognition. Repeated defeat (ES Wohleb 2012) and infections incite mast cells to cause localized blood-brain-barrier changes or arterial damage. From this hyperactivity, shrinkage or artery-contiguous hypertrophy of basal ganglia (J Hwang 2006) in bipolar disorders could result. The neurobiology of shame is explained via signals from biting nhibition transmitted to the PPG and then to the gyrus rectus. Hysteric sexual dysfunction stems from arterial insular irritation, as do epileptoïd symptoms, PPG-exerted inhibition of pseudopregnancy, and "lymphatic fibromyalgia" in Alcock's channel – completing Freud's scheme.
The possible role of mast cells and the lymphatics in "systemic bipolar disorder" could well be associated with chronic increase of sphingomyosin-1-phosphate (S1P) (Olivera 2011). S1P is a necessary co-factor of the most classic inflammatory pathway induced by TNF-a (Alvarez 2010). S1P is also excreted by mast cells themselves via ABCC1/MRP1, which is inhibited by efavirenz e.g., or also regulated by notch1. S1P is involved in pro-survival actions of TNF-a; some Flaviviridae virus can inhibit its producing enzyme Sphk1 (JM Carr 2012). S1P is essential for the lymphatic endothel barrier function. S1P is competitively targeted by fingolimod which is successful in treating MS. Finally S1P fosters β-cells (Holland 2008), which are often compromised in Bipolar disorder (BPAD).
BPAD is an enigmatic, severe systemic inflammatory condition (M Leboyer 2012), maybe centred on mast cells, which are sensitive to all mood stabilizers. Its high comorbidity with fibromyalgia (LM Arnold 2006) and migraine (OB Fasmer 2001) correlates with cellular pro-inflammatory proteonomics (FM Benes 2006).
Methods / Results / Conclusion: A multi-level enquiry into knowledge from psychology and biomedical fields leads to a meaningful assembly of data allowing to shed light on the neurobiology of psychoanalysis, bipolar disorder, and comorbid conditions.

neurobiology
psychoneuroimmunology, bipolar disorder, pterygopalatine ganglion, brain mast cells, lymphatics, sphingomyosin-1-phosphate

Poster

NB-15

Can the lymphatic system (and a parallel neurogenic inflammation system) provide the adequate anatomic explanations for "unexplained" pain and associated neuropsychiatric symptoms as in fibromyalgia? A new hypothesis

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Introduction: The lymphatic system until recently has been neglected as an inflammatory cauldron outside the

lymphedema, lymphocyte homing and metastasis research, and possibly provides the sought adequate anatomic explanations for many “unexplained symptoms” along its also retro-pelvic ascent to the right armpit from the right arm, and to the left armpit from the three other limbs through interaction with centres of spinal cord.
At several sites with a crossing of lymphatics and nerves, insufficiently isolated lymphatic inflammation could cause a retrograde inflammation of superficial venulae. Such an inflammation at the brachial nerves would have to ascend multi-segmentally to the upper cervical cord in order to influence known cervico-trigeminal reflexes (Arvidsson 1990) and disturb the brainstem, and thereby further brain function.
Methods: Using present biomedical sources (e.g. Baluk 2007) the inflammation-related “conductive” pathways along the lymphatic system and the neurogenic pathways parallel to it are explored as to their capacity to irritate the intra-cranial CNS. Anatomical, physio-logical, and molecular elements in health and various disease states of the lymphatics are contrasted with requirements of the hypothesis and epidemiological insights.
Intrinsic or pathogen-induced deficiencies of components of the immune response like mast cells and of the “lymphatic isolation”; putative diffusible mediators of contiguous axonal inflammation; examples of retrograde inflammatory response of the intra-cranial cns to peripheral nerve injury (e.g. TNF-a; Ren 2011) are adduced as well as arguments from migraine research.
The rapid decay of neurochemical mediators is not an obstacle to long-range distribution anymore, since mast cells have been discovered to release self-fabricated “retard form” (pellet-laden granules) of e.g. TNF-α. (Kunder 2011).
Conclusion: More research on mast cells and the lymphatic inflammatory processes in relation to possible peripheral causes of psychosomatic and neuropsychiatric disorders seems warranted.

neurobiology
psychoneuroimmunology ,fibromyalgia, mast cells, lymphatics, CXCR6, TNF-a

Poster

NB-16

Can bipolar disorder mean proneness to systemic bartonellosis, a suspect for genetic intrusion via VirB/VirD4 causing “Morgellons”? Do periungueal pathogens go dermo-neuro-psychiatric via the “lymphatic cauldron”?

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Introduction: The Peripheral causes project at BipoSuisse (www biposuisse.ch) posits extra-cerebral, “logistic” etiologies as probable.
Bartonella henselae is just one out of 10 pathogenic species infecting up to 1:3 humans, and 1:2 cats. Most mammals harbor Bartionella species, transmitted via arthropods like ticks.
Methods:
A. Case vignettes of 3 bipolar spectrum patients with serology highly suspicious for Bartonella henselae (BH) and diagnoses of resp.
Case 1: Depression, probable 22q11.2DS, and “Morgellons” - an emergent, but long known skin disorder where possibly (according to present beginning evidence) keratinocytes are induced by Bartonella or Agrobacter, which uniquely “inject” human nuclei with Beps through T-4 SS VirB/VirD4. Thus they hijack the host’s DNA-repair machinery to cause e.g. keratin filaments, similar to the common bovine digital dermatitis. Bad hygiene (poverty, war, migration) favours vector contact and pathogen entry at nail-folds, whereupon the “cauldron” of the lymphatics conduces danger signals to the brain. “Morgellons” skin eruptions alternating with manic behaviour likely due to BH were described since 1550 in pest-ridden southern France.
Case 2: Probable BH-caused systemic multimorbidity with brainstem BCT (Brain Capillary Teleangiectasia), moderate mixed episode with indecision despair and apraxia;
Case 3: Tourette/OCD/PTSD/Social phobia with discrete BH exanthema.
Conclusions: Bartonelloses are important emergent zoonoses with neuro-psychiatric pathologies in susceptible (e.g. 22q11.2 DS) or maybe unfortunately co-infected hosts. BH and the extensively used plant genoma modifier Agrobacter are capable of introducing genes into the human genome, and therefore may hide very important (somatic and mental) health hazards especially when the host’s vulnerability is high.

neurobiology
Bartonella henselae, delusional parasitosis Morgellons, bipolar disorder, DNA transfer, ungueal infection, lymphatics

Poster

NB-17

Molecular structure of nicotinic acetylcholine receptor-rapsyn clusters in native membrane by cryo-electron tomography

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Clustering of the nicotinic acetylcholine receptors (AChR) at the neuromuscular junction is essential to muscle function. Decreased levels of clustering are linked with myasthenic syndrome (i.e. muscle weakness) [1]. The scaffolding cytoplasmic protein rapsyn directly binds AChR, which is a heteropentamer formed of two α-subunits, one β-subunit, one δ-subunit and, in the embryo one γ-subunit, or in the adult one ε-subunit [2]. Rapsyn is required for the onset and the stability of AChR clusters [3]. A model states that rapsyn maintains a locally elevated AChR concentration by creating a large rapsyn-AChR network, thereby reducing molecular diffusion. However the mode of AChR clustering is debated. According to different experimental data, rapsyn binds AChR (i) only on its β-subunit [4], or (ii) on α-, β-, and ε-subunits [5], or (iii) on all its subunits [6]. In the first case, another cytoskeletal element is absolutely required to build large AChR clusters, whereas in the two other cases it is not necessary. Indeed, rapsyn can form bridges between AChR nodes. The results mentioned above were obtained by cross-linking of native tissue (case i) or by expressing individual subunits or chimeric proteins in heterologous cell lines (cases ii and iii).
We addressed the mode of AChR clustering by direct visualisation with cryo-electron tomography of AChR clusters in postsynaptic membranes isolated from Torpedo marmorata electric organ synapses, a model system of the neuromuscular junction. Individual AChR and associated cytoplasmic densities were resolved. In order to increase the signal to noise ratio, subtomogram averaging and classification were performed. Thereby we obtained the structure of AChR and its interacting partner in complex. We demonstrated that the partner was rapsyn. From that we concluded on the number of rapsyn molecules binding each AChR. The class averages were positioned in the context of the original tomograms in order to describe the architecture of the AChR clusters and their scaffold.
Our results provide a structural basis to explain the stability and low diffusion of AChR within clusters.

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neurobiology

Talk

NB-18

Embryonic progenitor cell grafts improve functional recovery in the spinal cord in vitro

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Functional recovery after spinal cord injury is limited, mainly due to a hostile environment provided by central nervous system myelin and reactive astrocytes. Recent results indicate that intraspinal connections are a promising target for intervention to improve functional regeneration. To study these fibers, we developed an in vitro model consisting of the following experimental design: Two organotypic spinal cord slices of embryonic rats (E14) are placed adjacently on a multi-electrode array. The electrodes allow us to record the spontaneously occurring neuronal activity, which is often organized in network bursts. Within a few days in vitro (DIV), these bursts become synchronized between the two slices due to the formation of axonal fibers, representing intraspinal connections. Next, we cut these formed connections with a scalpel at different time points in vitro and record the neuronal activity three weeks later. The functional recovery potential is assessed by calculating the percentage of synchronized bursts between the two slices. We found that cultures lesioned at a young age (8-12 DIV) retained the high regeneration ability of embryonic tissue (mean % of synchronized bursts ± SEM; e.g. lesion at 8 DIV: 97.5% ± 1.7%). However, cultures lesioned at older ages (>19 DIV) showed a distinct reduction of synchronized activity (e.g. lesion at 21 DIV: 10.5% ± 3.2%).
To study the effect of embryonic spinal cord progenitor cell grafts on functional recovery, we inserted these cells into the lesion site of old cultures (lesion at 21 DIV). We found a remarkably increased percentage of synchronized bursts in cultures with grafts (75.9% ± 5.3%) compared to control groups. With patch clamp experiments we identified mature neurons in the grafted cell population. These results suggest that embryonic spinal cord progenitors can differentiate in the damaged spinal cord environment, bridge lesions and thereby improve functional recovery.

methodology, neurobiology

Talk

Neurology (NE)

NE-01

Subjective perception of sleepiness in a driving simulator is different from perception in the maintenance of wakefulness test

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Objectives: We have recently described sleep deprived healthy subjects, who did not signal their subjective sleepiness before the first microsleep during the maintenance of wakefulness test (MWT) [1]. Here we tested whether subjects spontaneously signalled sleepiness before their first microsleep in four conditions, the MWT and while steering a driving simulator both, before and after sleep deprivation.
Methods: Twenty-four healthy subjects (20-26y) were tested before and after one night of sleep deprivation in a MWT and in a "divided attention steering simulator" (DASS) during 40 and 60 minutes respectively. Participants were instructed to signal sleepiness as soon as they realized the first symptoms of sleepiness or tiredness in addition to stay awake as long as possible. They were rewarded for optimal performance. Data acquisition consisted of a standard electroencephalography (EEG), electrooculography (EOG), submental electromyography (EMG) and face videography. Microsleep was defined by a sleep fragment in EEG lasting > 3s and overt sleep > 15 sec (AASM criteria) respectively while the eyes were closed. For statistical comparisons between conditions and missed sleep perception Chi-squared test was used.
Results: Seven subjects (29%) missed to signal sleepiness before the first microsleep in the MWT after sleep deprivation and one subject did so in the MWT before sleep deprivation ($p<0.02$). No subject missed to signal sleepiness before the first microsleep in both DASS. After sleep deprivation significantly less subjects missed to signal their sleepiness in the DASS compared to the MWT ($p<0.004$) whereas no relevant difference between the tests was observed before sleep deprivation.
Conclusion: These results confirm our earlier study in MWT [1], but in addition show, that purely internally driven subjective perception of sleepiness is more accurate during tasks which include a permanent feedback of performance such as driving compared to the passive situation of the MWT. Subjective perception of sleepiness is less accurate after sleep deprivation compared to the rested state suggesting that sleepiness impairs perception of sleepiness itself. However this effect is overweighed by the performance feedback while driving.

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neurology

Poster

NE-02

The age-dependent effect on functional visual field and on driving performance

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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.
During driving, it has been shown that older drivers allocate a larger percentage of their visual scan time to a small subset of areas in the image than younger drivers. Therefore, it is hypothesised that older drivers focus on central areas with neglecting peripheral areas for daylight and night driving compared with younger drivers.
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. Furthermore, subjects had to take a drive on a motorway route under day and night condition. 20 young (20-40 years) and 20 old (60-80 years) subjects volunteered for the study.

Results: Target recognition decreased with increasing eccentricity of the target. Whereas young subjects showed a more or less linear decrease in target detection with increasing eccentricity, older subjects 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. Older subjects showed increase in reaction time compared to younger subjects independent of target position.
During driving, older subjects allocated their gaze more to the central area than younger subjects during daylight condition. At night, both age groups focus more to central areas compared to daylight condition.
Discussion & Conclusion: First preliminary results indicate an age-dependent effect on the functional visual field as well as on simulated driving. For the functional visual field, the difference appears mainly 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. This conclusion is further supported by the age-dependent difference in gaze pattern during daylight driving. Further research includes testing more subjects.

neurology

Poster

NE-03

Tempo of penumbral tissue loss in acute stroke: the collaterals set the pace

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OBJECTIVE: To identify factors that determine the evolution of the penumbra in patients who received endovascular therapy because of middle cerebral artery (MCA) occlusion.
METHODS: 51 patients with M1 or M2 occlusions in whom at least minimal reperfusion was achieved were included in this analysis. Their penumbra was assessed with perfusion (PWI) and diffusion weighted imaging (DWI). Loss of penumbral volume was defined as difference of post- minus pre-treatment DWI-volumes and calculated in percent of pre-treatment penumbral volume. Correlations between baseline characteristics, reperfusion, collaterals, time to reperfusion and penumbral volume loss were assessed using analysis of covariance.
RESULTS: Collaterals (p=0.003), reperfusion (p=0.003) and their interaction (p=0.007) independently influenced penumbral tissue loss, but not time from MR (p=0.052) or from symptom onset to reperfusion (p=0.728). When collaterals were poor 22% of penumbral volume was lost, when moderate 8% and when good 7%. Patients achieving good reperfusion and having good collaterals experienced a linear penumbral loss of 5% each hour (p=0.012) corresponding to a mean loss of 0.47 mL penumbra per hour, while in patients with poor or moderate collaterals loss was nonlinear, approximately 1.17 mL per hour.
INTERPRETATION: Collaterals and reperfusion are the main factors determining loss of penumbral volume in patients with MCA occlusions. In patients with good collaterals, time to successful reperfusion accounts only for a minor fraction of penumbral volume loss and collaterals may slow down penumbra loss. These results support the hypothesis that good collaterals extend the time window for acute stroke treatment.

neurology
Stroke

Poster

NE-04

Sleep deprivation prior to stroke increases sleep and attenuates brain lesion in the rat

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OBJECTIVES Sleep-wake disturbances are frequent in stroke patients and linked with a poorer functional outcome. We have provided direct evidence in a rat model of focal cerebral ischemia that sleep disruption shortly after stroke onset aggravates brain damage and impairs long-term stroke recovery. However, sleep deprivation (SD) prior to stroke in rodents is recently reported to be neuroprotective and beneficial for functional recovery. The aim of this study was to test the hypotheses that; SD prior to stroke may be neuroprotective and this effect may be related to an increase in sleep after SD/during the acute phase of stroke.
METHODS Adult Sprague Dawly rats were subjected to continuous polygraphic recordings for baseline, during SD, and 24 hrs after ischemia. SD for 6h was performed by gentle handling before ischemia. Focal cerebral ischemia was induced by permanent occlusion of distal branches of the middle cerebral artery, which induces an injury in the somatosensory cortex. Brains were collected 3 or 7 days after surgery. Control experiments included ischemia without SD (nSD), sham surgery with SD or nSD (n=6/group). Cresyl violet staining was used for assessing the infarct volume.
RESULTS During the first 12 hrs after stroke onset (dark phase), the amount of slow wave sleep(SWS) and paradoxical sleep (PS) increased significantly ($p<0.05$) in both SD groups (ischemia and sham control), resulting in an increase in the total sleep time by 30% compared to baseline (paired t-test), or by 20% compared with the nSD/ischemia group (One way ANOVA: $F_{2,15} =10.4$, $p=0.001$, followed by post hoc comparison). However, the delta power (1-4 Hz) in SWS did not change significantly from baseline in the SD/ischemia group, whereas increased at early hours in the SD/sham control group as expected. The infarct volume reduced significantly by 50% in the SD/ischemia compared to nSD/ischemia group [(SD 28.8+10.4(median 26.5) vs. nSD 57.4+16.2(median 51.3) mm3; $U=1.0$, $p=0.006$] on poststroke day 7. Removal of sleep rebound by allowing SD-rats sleep for 24 hrs before ischemia eliminated the reduction in the infarct volume [48.5+1.8 (48.2) mm3) vs. nSD 57.4+16.2 (51.3) mm3, $p=0.211$].
CONCLUSION These results confirm that prestroke SD is neuroprotective and suggest that sleep rebound during the acute phase of stroke may be responsible for this effect. The molecular mechanisms involved are currently investigated.

neurology

Poster

NE-05

Left posterior parietal theta burst stimulation affects gestural imitation regardless of semantic content

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Background and aim: Neuro-imaging studies have suggested that the ability to imitate meaningless and meaningful gestures may differentially depend on superior (SPL) and inferior (IPL) parietal lobule. The aim of the present study was to investigate the role of SPL and IPL in gestural imitation using imaging-guided neuro-navigated continuous theta burst stimulation (cTBS). We hypothesized that SPL stimulation mainly affects meaningless and IPL stimulation predominantly meaningful gestures.
Methods: Twelve healthy subjects participated in this study. High resolution structural MRI was used for imaging guided neuro-navigation cTBS. Participants were targeted with one train of cTBS in three experimental sessions: sham stimulation over vertex and real cTBS over left SPL and IPL, respectively. An imitation task was performed 'offline' including 24 meaningless and 24 meaningful gestures. Performance was scored by two independent blinded

raters based on video recordings using a 6-point scoring method with lower scores representing major gestural errors.
Results: cTBS over left SPL as well as IPL significantly affected gestural imitation, for both meaningless and meaningful gestures similarly. Furthermore, stimulation over IPL significantly increased major gestural errors regardless of the semantic gesture subtype.
Conclusions: The present study suggests, a common left posterior parietal network supporting the imitation of both meaningless and meaningful gestures.

neurology
Neurology

Poster

NE-06

NIHSS score and vessel occlusion in 2152 patients with acute ischemic stroke

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BACKGROUND AND PURPOSE: There is some controversy on the association of the NIH Stroke Scale (NIHSS) score to predict vessel occlusion on arteriography in acute stroke. METHODS: We analyzed NIHSS scores and arteriographic findings in 2152 patients (35.4% women, mean age 66+/-14 years) with acute anterior or posterior circulation strokes.
RESULTS: 1603 patients were examined with magnetic resonance (MRA) and 549 with computed tomography arteriography (CTA). 1043 patients (48.5%) (median NIHSS score 5, median time to clinical assessment 179 minutes) showed an arterial occlusion, 887 in the anterior (median NIHSS score 7/0-31) and 156 in the posterior circulation (median NIHSS score 3/0-32). 860 visualized occlusions (82.5%) were located centrally, i.e. in the basilar, vertebral, internal carotid, or M1/M2 segment of the middle cerebral artery. NIHSS scores turned out to be predictive for any vessel occlusions in the anterior circulation. Best cut-off values within 3 hours were NIHSS scores ≥9 (PPV 86.4%) and NIHSS scores ≥7 within >3-6 hours (PPV 84.4%). Patients with central occlusions presenting within 3 hours had NIHSS scores <4 in only 5%. In the posterior circulation and in patients presenting after 6 hours the predictive value of the NIHSS score for vessel occlusion was poor.
CONCLUSIONS: There is a significant association of NIHSS scores and vessel occlusions in patients with anterior circulation strokes. This association is best within the first hours after symptom onset. Thereafter and in the posterior circulation the association is poor.

neurology
Acute ischemic stroke

Poster

NE-07

Aphasia and Gesture: Gaze behaviour in naturalistic dialogues

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Background: Aphasia is a common disorder typically occurring after left hemisphere brain damage. Patients with aphasia are restricted in their verbal abilities, and may compensate their shortcomings by using gestures. Gesturing is a form of non-verbal communication which can complement, supplement, or even substitute verbal language. It

has been shown that some patients make well use of gestural compensatory strategies (i.e. Herrmann et al., 1988), while others do not (i.e. Cicone et al., 1979). The present project will not only encompass the behavioural analysis of co-speech gestures in naturalistic dialogue situations, it will also extend previous research in aphasic patients investigating visual fixation behaviour by means of eye tracking. Besides, we will carry out lesion syndrome mapping to get further knowledge about the cortical organization of the network controlling co-speech gestures and language.
Methods: In a first experiment, we will compare the visual exploration behaviour of aphasic patients with aged-matched controls during dialogue presentation. Fixation data will be collected by means of an infra-red eye tracking system. In a second experiment, interactive behaviour, with respect to gesture perception and gesture production, will be compared between dyads of an aphasic patient with a healthy control subject and dyads assembled by healthy controls only. Fixation behaviour will be registered by a portable eye tracking device. Speech and gesture production will be qualitatively assessed using an event logging software and correlated with eye tracking data. For lesion mapping of structural MRI data, MRIcron software (Rorden et al., 2007) will be employed for both experiments.
Outlook: In general, we assume that aphasic patients will fixate more on gestures in order to improve language comprehension and will exert more meaningful gestures to express themselves intelligibly.

neurology
aphasia, gesture, speech, dialogue, eye tracking

Poster

NE-08

Neuroprotective effect of Cathodal Transcranial Direct Current Stimulation in a rat model of stroke

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Background and Purpose
In the penumbra, experimental focal ischemia generates recurrent depolarizations (slow potential changes, SPCs) which spread across the injured cortex inducing infarct growth.
Infarct size correlates in the stroke experimental model both with the numbers of SPCs and duration of SPCs aggregates, however SPCs number is the independent, determining variable in this relationship.
This association is thought to be causal as eliciting SPCs by potassium application or electrical stimulation results in larger infarct volumes.
Aim of the study was to verify whether cathodal transcranial direct current stimulation (tDCS) could reduce the infarct size by reducing the number of SPCs in the rat stroke model.
Methods
Ischemia was induced in adult Sprague Dawley rats (165-265 gr) by the 3 vessels occlusion technique.
Cathodal tDCS (0.2 mA) was delivered by an epicranial electrode for 15 minutes alternating with 15 minutes of no stimulation. Rats were assigned to 4 groups: Group 1: n = 12, ischemia + tDCS for 4 hours; Group 2: n = 12, ischemia + tDCS for 6 hours; Group 3: n = 12, ischemia + sham tDCS for 4 hours; Group 4: n = 12, ischemia + sham tDCS for 6 hours.
SPCs were recorded epidurally in group 2 and 4 by a screw inserted in the skull overlying the infarcted hemisphere.
Results
TDCS reduced the infarct volume in rats of group 1 and group 2. The volume reduction between group 1 and group 3 was 20% (independent-sample t-test p=0.002) and between group 2 and group 4 was 30% (independent-sample t-test p=0.003).
SPCc were greatly reduced during the whole period of stimulation. The group-2 rats stimulated with cathodal tDCS for 6 hours displayed a total number of SPCs lower than the group-4 rats receiving sham tDCs (Repeated measures ANOVA Effect: Stimulation Type, p=0.012).
A positive correlation was found between the total number of SPCs and the infarct volume (Spearman rho = 0.521, p= 0.039). No correlation was found between total duration of SPCs and the infarct volume (p>0.200).
Conclusions
TDCS reduces infarct size with a dose dependent effect by reducing spreading depolarizations in the rat experimental model of stroke.
The potential extent of the effect should be explored in a long term stimulation experiment throughout the period of infarct maturation. TDCS is a non-invasive, easy to use, inexpensive, method of modulation of brain excitability already employed in various neurological and psychiatric disorders and it may represent a new avenue in neuroprotection of human stroke.

neurology
Stroke, transcranial direct current stimulation, spreading depression, rats

Poster

NE-09

SAFEMOVE Safe mobility of elderly

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Problem Statement
Numerous elderly people avoid leaving their home because they feel insecure and stressed outdoors [1]. This can lead to a reduced physical and cognitive activity which might have a further negative influence on physical [2] and cognitive performance [3]. Within the framework of EU-project SAFEMOVE, we aim at enhancing outdoor mobility by two means: i) context-aware navigational support while outdoors and ii) physical and cognitive training programs to help elderly people to maintain physical and cognitive fitness.
Methodology
Chronic medical conditions can lead to physical, sensory or cognitive impairment, which then can cause functional impairment in the ability to perform activities of daily living (ADL) and instrumented activities of daily living (iADL) [4]. Outdoor mobility (i.e. walking and using public transportation) is an iADL that requires the integration of high level cognition, vision and motor function [5] and it causes physical load (i.e. use of public transportation) and cognitive load (i.e. complexity of the navigation). We hypothesize that stress occurs when the required physical load is higher than the physical performance of the person; respectively when the cognitive load is higher than the cognitive performance.
The cognitive and physical loads are amplified by sensory, physical and cognitive impairment. Sensory impairment increases the cognitive load, which is required to maneuver through a given environment, because impaired vision needs to be compensated elsewise (i.e. hearing, tactile, etc.). These compensatory actions require additional cognitive/physical work that adds to the total cognitive/physical load.
It is possible to reduce the person's stress by reducing the cognitive/physical load and to enhance the physical and cognitive performance through training that aims at maintaining physical and cognitive fit-ness.
That is why the envisioned SAFEMOVE approach is twofold – a context-aware navigational support that is combined with home-based training.
Expected Results and Outlook
The project has started in July 2012 and current work is to elaborate a comprehensive view of users and stakeholders needs. This includes the context analysis, scenario definition, use-case analysis, requirement engineering, state-of-the art investigation, definition of evaluation and demonstration scenarios. The technical development will be iterative with the first pilot device available for user trails in mid-2013.

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neurology
mobility

Poster

NE-10

Methods to Increase User Comfort in a Driving Simulator

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Background:
Laboratory-based driving simulators are often used to study driving behavior. User comfort during simulated driving is of key importance, since reduced comfort can alter the behavior of the user, confound the experiment and increase dropout rates. A common comfort-affecting factor is the simulator adaptation syndrome, also known as simulator sickness (SS). Symptoms of SS can range from mild discomfort to severe and prolonged nausea, dizziness, and disorientation. SS depends on individual factors of the user (i.e. age, gender, experience), task specific factors (i.e. driving circuit, optical flow) and simulator related factors (i.e. field of view, contrast). The sensory conflict theory explains SS as a result of a mismatch between the sensory information of the visual and the vestibular system. Hence, in simulated driving, the optical flow of the virtual scene indicates motion via the visual system while the vestibular system does not perceive acceleration which indicates no motion. In this study, we propose methods to reduce the optical flow of a virtual driving scene and evaluate whether this reduces SS.
Methods:
For this study, a fixed-frame driving simulator was used to implement the virtual driving scene. The manufacturer provides a virtual scene that is characterized by a high optical flow of 213pixels/s leading to a high sensor conflict. In contrast to the manufacturer-provided High Sensory Conflict Scene (High-SCS), we developed a Low Sensory Conflict Scene (Low-SCS) that is based on three adaptations: (I) Scene optimizations to reduce the optical flow by 68.9%, (II) implementation of an independent visual background and (III) reduction of brightness of lateral projection screens by 48.0%. Note that the driving circuit itself was not changed.
Procedure:
20 young, healthy participants (10 male, mean age = 27.7 ± 2.9 years) drove in both the High-SCS and the Low-SCS scene during 10 min at two different days (same time of day, randomized order). Before and after driving, participants rated SS by completion of the Simulator Sickness Questionnaire (SSQ). A head mounted eye-tracking system was used to measure fixation duration and saccades amplitude. Furthermore, heart rate, respiratory rate, skin conductance as well as skin temperature were recorded during driving in the simulator.
Results:
After 10 min driving in the High-SCS, the SSQ score increased by 122.9% (p=0.002) compared to an increase of 3.4% (p=0.878) after driving in the Low-SCS. Compared to the High-SCS, in the Low-SCS skin conductance was decreased by 13.8% (p=0.041) and amplitudes of saccades were increased by 16.1% (p=0.044). No significant differences were found in heart rate, respiratory rate and skin temperature.
Discussion & Conclusion:
Results show that the investigated adaptations significantly reduce symptoms of SS in the younger population and the Low-SCS is well accepted by the users. We expect that these measures will improve user comfort and reduce dropout rates.

neurology

Poster

NE-11

Aphasia and Gesture: Perception of Co-Speech Gestures in Aphasic Patients

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Healthy subjects communicate in general both verbally (speech) and non-verbally (gestures, facial expressions, body postures). Aphasia is a common consequence of left hemispheric brain damage such as stroke and leads to an impaired speech comprehension and / or production. The impact of aphasia on non-verbal communication, such as the perception of co-speech gestures is indistinct on current research. In addition, the role of oftentimes concomitant apraxia (a higher cognitive deficiency of motor control and conduction of movements) in aphasic patients has not been clearly examined until today. The reciprocal implications and relations of gestures, aphasia and apraxia have therefore been controversially discussed in previous studies.
In the present study, the perception and comprehension of co-speech gestures in aphasic patients is assessed by means of infra-red based eye tracking. Extending previous studies, a gesture comprehension test will be administered to patients to control confounding language problems. Furthermore, concurrent apraxia will systematically be assessed and correlated with results as well as with lesion syndrome mapping.
Both verbal information and simultaneous gesturing is presented in short video sequences. The videos differ in their level of congruity between speech and accompanying gesture and thus in their level of difficulty. Aphasic patients are expected to display a different visual exploration behaviour compared to healthy controls. It will be examined whether they can benefit from additional information (in congruent conditions) or whether they are distracted by multimodal input (especially in incongruent conditions, resulting e.g. in longer fixations compared to healthy controls).
6 aphasic patients have been tested so far in this ongoing study.

neurology
Aphasia, Co-Speech Gestures, Eye Tracking, Apraxia

Poster

NE-12

Effects of repeated theta burst stimulation on aphasia recovery

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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 modulating cortical activity and may thereby offer novel therapeutic opportunities. A repetitive TMS protocol named theta burst stimulation (TBS) is increasingly used in clinical research. It has the advantage of a short application time combined with prolonged aftereffects. In a previous study we found better naming performance in aphasic patients after the application of one train of TBS over the right Broca's homologue. Applying TBS trains repeatedly can furthermore disproportionately prolong the effects, as was for example shown in neglect patients. Thus, repeated trains of TBS are applied in the present study in a randomized, sham controlled, cross-over design. After comprehensive baseline testing, eight TBS trains and eight sham stimulation trains are applied over the right Broca's homologue on two consecutive days separated by one week. On the second days of stimulation, several short language tests are administered. A follow-up with comprehensive language testing takes place one month after the stimulation. Preliminary results of this ongoing study will be presented. The aim of the study

is to evaluate the effects of repeated TBS on several language tasks over a longer time span.

neurology, psychology

Poster

NE-13

Evidence of impaired synaptic homeostasis underlying the appearance of levodopa-induced dyskinesia: an electrophysiological and molecular study in a rat model for PD

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Progression of Parkinson´s disease (PD) is characterized by treatment complications such as levodopa induced dyskinesias (LID). These abnormal movements are linked to impaired striatal synaptic plasticity associated with uncontrolled long-term potentation (LTP). Functionally, there is probably an accumulation of irrelevant information within the cortical-basal ganglia loop that underlies the appearance of LID.
Since physiological control of LTP is guaranteed by homeostatic plasticity that according to the synaptic homeostasis hypothesis (SHY) operates during sleep, we hypothesized that the dyskinetic state is linked to an inadequate synaptic down-scaling.
We employed a 6-OHDA-based parkinsonian rat model chronically treated with levodopa developing abnormal involuntary movements comparable to LID observed in PD patients (Cenci et al., 1998). We analyzed the sleep pattern of four animal groups: (i) sham-lesioned drug-naive rats, (ii) 6-OHDA-lesioned drug-naïve rats, (iii) 6-OHDA-lesioned levodopa-treated rats w/o dyskinesias, (iv) 6-OHDA-lesioned levodopa-treated rats with dyskinesias. ECoG was performed for 24h preceded by 48h of habituation. The off-line analysis aimed to measure the content and specific parameters (amplitude, slope and amount of multipeaks) of slow-wave activity (SWA). We also assessed the gene expression of molecules that reflect the degree of synaptic strength, i.e. Arc protein.
Our data provide evidence that dyskinetic animals present a higher SWA amplitude during late sleep in comparison with the animals without involuntary movements. We also observed a clear increase of Arc protein in dyskinetic animals in comparison with control and parkinsonian animals.
We assume that the progressive reduction of homeostatic synaptic plasticity, in parallel with the disease duration, reaches a critical point beyond which the absence of an adequate downscaling of cortico-cortical and/or cortico-striatal synaptic strength alters the physiological function of basal ganglia (i.e. balanced information storage).

neurology
levodopa-induced dyskinesia, sleep, synaptic down-scaling

Poster

NE-14

Neglect Severity is influenced by motion – Evidence from a Touchscreen Based Cancellation Task

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Neglect is commonly defined as a deficit to orient attention to the contralesional side of brain damage. In a clinical setting, the severity of neglect is usually measured by paper-pencil procedures, such as line bisection and cancellation tasks (i.e. bells test). All these tasks thus represent static procedures. From clinical observations it is known that the severity of neglect might be influenced by motion. However, the performance behavior of neglect patients in dynamic search tasks compared to static ones is still unknown. Therefore, 36 patients with left spatial neglect after right hemisphere damage and 25 healthy control subjects performed simple cancellation tasks on a touchscreen monitor. Several dynamic conditions (dynamic right, dynamic left, dynamic bilateral) were conducted and subsequently compared with a static condition. The results indicate that left sided moving stimuli tend to reduce neglect severity as compared to static stimuli. On the other hand, moving stimuli on the right side of the screen increased neglect severity. Furthermore, moving stimuli on the whole screen deteriorate neglect as well. These results provide implications for new diagnostic and therapeutic settings regarding the consideration and implementation of dynamic components in the training of neglect patients.

neurology

Poster

Neurogenetics (NG)

NG-01

Human Wharton's jelly-derived mesenchymal stem cells as potential cell graft for the treatment of neurodegenerative diseases

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OBJECTIVE:
Perinatal brain damage is a major neurological problem in surviving premature infants. Recent transplantation experiments in various animal models suggest a neuro-regenerative potential of multipotent mesenchymal stem cells (MSC). The curative effect of MSC might be due to their production of neurotrophic factors. The umbilical cord connective tissue (Wharton's jelly) represents a promising source of MSC. Thus, the aim of the study is to assess the expression and release of neurotrophic factors in vitro.
STUDY DESIGN:
MSC from Wharton's jelly of term and pre-term (gestational age < 37 weeks) pregnancies were evaluated. Adaptations of previously published multistep protocols (Portmann-Lanz et al, AJOG 2010; Fu et al, Acta Neurobiol Exp 2007; Zhang et al, Differentiation 2010) were used to produce neural progenitors (neurospheres). The transcription of neurotrophic factors was assessed by real-time PCR. The release of neural growth factors into the cell culture medium was measured by a membrane-based cytokine antibody array.
RESULTS:
At passage five isolated MSC from term and preterm pregnancies were expressing key neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), neurotrophin 3 (NTF3) and glial cell-derived neurotrophic factor (GDNF), and the cytokine interleukin (IL)-6, at the mRNA level. BDNF and IL-6 were detected in the cell culture supernatant after 48 h of cultivation. Pre-induction into neural precursors resulted in the formation of cell clusters growing in suspension, the so-called neurospheres. The transcription of BDNF and NTF3 were significantly reduced in neurospheres relative to MSC, independent of gestational age. However, the gene expression of GDNF was up-regulated in neurospheres compared to the non-induced MSC derived from term pregnancies.
CONCLUSIONS:
MSC derived from Wharton's jelly of term and preterm pregnancies, and the induced neural progenitor cells produce neurotrophic factors in vitro. The role of the released factors in neurogenesis and neuro-regeneration is currently analyzed in co-culture experiments with neural stem cells and in a rat model of perinatal brain damage.
Financial support by Cryosave Switzerland

other
mesenchymal stem cells, neuroregeneration, neurotrophic factors, umbilical cord

Poster

Neuroradiology (NR)

NR-01

Multi-channel and multi-distance NIRS during neuroangiography: Feasibility and technical aspects

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Introduction
Digital Subtraction Angiography (DSA) by its high spatial and temporal resolution is the gold standard in brain vessel imaging. The inherent methodological limitations of DSA are: a) long-time monitoring is impossible because of the limited applicability of X-rays and contrast media, and b) assessment of the hemodynamic state of the brain is restricted to imaging of large vessel collaterals. Non-invasive monitoring of concentration changes of oxygenated and deoxygenated hemoglobin within the outmost millimeters of the brain is possible by NIRS.
Methods
Multi-channel NIRS was measured during DSA examinations and interventions using the FOIRE-3000 system (Shimadzu, Japan). Absorbance of near infrared light was recorded at three wavelengths (780, 805 and 830nm) and relative changes of oxygenated and deoxygenated hemoglobin were calculated. The number of channels varied between 4 and 56. Transmitters and receivers were placed on the scalp at 30 and 42mm distance.
Results
I) Fibre holders and fibre holder caps of the FOIRE-3000 did not significantly interfere with radiography. But the glass fibres of near infrared transmitters and receivers have high radio opacity. Adaption of the positioning of the transmitters and receivers nevertheless allowed simultaneous DSA and multi-channel NIRS measurement.
II) The first pass of the contrast agent bolus could be recorded by NIRS and corresponded to the injection site.
III) Compared with the channels spaced at 30mm, the channels at 42mm yield a lower signal-to-noise ratio (SNR) of the raw NIRS signal. Despite this, their SNR was higher for the NIRS response to bolus injections into brain specific vessels, because these channels cover a higher proportion of brain tissue. Repeated measurements from the same site could be used for further improvement of SNR.
Conclusions
NIRS monitoring during DSA is feasible with the FOIRE-3000 and may provide complementary information specific to vascular territories. Due to their high radio opacity the glass fibres must be placed adequately to avoid restriction of the field of view of the angiographer. Signals measured at optode distance 42mm have larger brain contribution and redundant measurements allow noise reduction.

methodology, neuroradiology
near infrared spectroscopy; digital subtraction angiography; feasibility

Talk

NR-02

NIRS during neuroangiography: First results and potential added value

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Introduction
A prerequisite for planning neuro-vascular interventions such as recanalization therapy in acute stroke is Digital Subtraction Angiography (DSA), which enables imaging of large vessel collaterals. NIRS may monitor non-invasively the hemodynamic changes within the outmost millimeters of the brain and might qualify as tool providing complementary information.
Methods
Relative temporal changes in oxygenated and deoxygenated hemoglobin concentrations during DSA examinations

and interventions were measured using the multi-channel NIRS system FOIRE-3000 (Shimadzu, Japan) with 4 to 56 channels. Recording time varied between 6 and 120 minutes.
Results
I) During unilateral temporary balloon occlusion of the internal carotid artery (ICA) the territory of the ipsilateral middle cerebral artery (MCA) and the watershed areas showed measurable changes in oxygenation.
II) Stenting of stenoses increases tissue oxygenation in the corresponding vascular territories.
III) Brain hyperperfusion due to CO_2 increase during apnea may be detectable by NIRS.
Conclusions
NIRS measurement might offer a non-invasive instrument to monitor the treatment effects of revascularisation threapy and provide additional insights on hemodynamic compromise of the outmost brain layers during DSA. In particular, a compromise of some watershed areas was detectable.

methodology, neuroradiology
near infrared spectroscopy; digital subtraction angiography

Talk

NR-03

T_2 relaxation time of brain intra-voxel incoherent motion for diffusion weighted magnetic resonance images

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Diffusion weighted magnetic resonance images of the brain has been demonstrated to have two diffusion components. This work investigates if both these diffusion components have different T_2 relaxation time. Initial result shows only a single T_2 component was found. This could mean that both diffusion components are composed of the same protons. Hence, this could serve to validate the model proposal that the slow diffusion pool is from protons close to the cell membrane and the fast diffusion pool is from protons far from the cell membrane.

neurobiology
Diffusion MRI, T_2 relaxation time

Poster

NR-04

Automatic surface based morphometry: Necessity, effort and success of manual intervention in a homogeneous group of healthy subjects

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Background
Computational neuroanatomy is a growing field of research to verify morphological and structural changes in the brain. In recent years a number of automated and more objective techniques have been described to characterize cerebral changes including measurement of cortical thickness. One of them is the widely used FreeSurfer software package. High resolution imaging with a high cortico-medullary contrast is necessaryto facilitate labeling of the surface of pial and white matter.
Aim of this study was to investigate, whether an optimized T1 weighted MPR is sufficient to provide reliable measurements. Alternative hypothesis was that a highly specialized sequence (MDEFT) with further optimized corticomedullary contrast is mandatory for this purpose.
Methods
We investigated a homogeneous group of 36 healthy subjects, which had served as a control group in a study on

multiple sclerosis (MS). Two structural T1w MR images were acquired in a single session on a 3T scanner (MDEFT and a specialized MPR optimized for cortico-medullary contrast). Both sequences were processed by FreeSurfer's fully automatic recon-all pipeline. Positioning of the pial and white matter surface labeling was visually inspected in all data sets. Where necessary the data sets were manually corrected and reevaluated. Data sets with insufficient quality after the second iteration were excluded from further analysis.
Results
As the data were acquired in an MS study the gender ratio was 27 females to 9 males. Mean age was 34.6 (+/-10.4 years). The distribution of the data sets in the categories “correct”, “correct after first manual intervention”, ,,correct after second manual intervention” and “drop out” was significantly different between the MR sequences ($p<0.001$ for a chi2 test). For MDEFT manual correction was necessary in 9 subjects, of which 3 were drop outs, whereas for the specialized MPR the corresponding numbers were 26 and 6. Time required for manual correction per data set did not significantly depend on the MR sequence. However, the total correction time was 110 minutes for MDEFT and 835 minutes for the specialized MPR. For MDEFT there was no gender dependence. In contrast, manual correction was necessary in a larger fraction of male controls ($p=0.03$) and more time was spent ($p=0.02$) for the specialized MPR. Visual inspection showed that both MR sequences had labeling weaknesses approximately in the same regions, including the pre- and postcentral gyrus, the superior and medial frontal gyrus, and, to a lesser degree, the inferior frontal and medial temporal gyrus. After exclusion of all subjects that could not be corrected in one of the two MR sequences, MDEFT yielded a larger cortical thickness in the bilateral cuneus, the right gyrus frontalis orbitalis lateralis and the left gyrus orbitalis medialis. Smaller thickness was obtained by MDEFT in the bilateral sulcus temporalis superior and the bilateral sulcus precentralis. The larger cortical thickness of MDEFT in the cuneus was significant ($p<0.05$, FDR).
Conclusions
Our results indicate that MDEFT is the MR sequence of choice when aiming at measurement of cortical thickness with FreeSurfer. Less data sets have to be corrected manually and drop out rate is smaller, consequently the post processing time for MDEFT is much less compared to the optimized MPR. Compared to the specialized MPR the MDEFT yields significantly larger thickness in the bilateral cuneus.

methodology, neuroradiology
cortical thickness, freesurfer, MDEFT, MPR, MRI

Poster

NR-05

Performance of fully automatic cortical thickness measurement using FreeSurfer: First results from a large and inhomogeneous clinical data set

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Background
The relevance of cortical thickness analysis is growing for certain diseases. Freesurfer is a software package, which is widely used for automated cortical thickness measurement. For reliable thickness estimates high resolution imaging is necessary. A high cortico-medullary contrast facilitates correct labeling of the surface of pial and white matter. For this purpose usually a conventional T1 weighted MPR sequence is used. The aim of our study was to evaluate an inhomogeneous data set of different T1 weighted images with respect to their surface labeling quality, comparability and handling of post processing.
Methods
We retrospectively investigated a large and inhomogeneous clinical data set of 395 subjects. Different structural T1 weighted MR images were acquired for all subjects (159 standard MPR, 103 specialized MPR that optimizes contrast between grey and white matter and 133 MDEFT). 204 subjects were healthy controls, 123 suffered from multiple sclerosis, 42 were very preterm born children and 26 were dementia patients (AD and MCI). Two 3T scanners and one 1.5T scanner were used. Subjects included healthy controls as well as patients suffering from different pathologies. All images were processed by FreeSurfer's fully automatic recon-all pipeline. Positioning of the pial surface and the boundary between grey and white matter was visually inspected and data was categorized as “correct” and “not correct”.
Results

No significant correlation between age and gender or field strength and gender in our data set was found. There were significant associations of field strength and MR sequence with age and pathology. Only 33% of data sets (129) were categorized as “correct”. The percentage of “correct” data sets was much larger for MDEFT (62%) than for the specialized MPR (23%) and the standard MPR (14%). 41% of healthy data sets were “correct”, whereas the percentage of correct data was only 32% for MS patients and 23% for dementia patients. Not a single data set acquired in very preterm born children was classified as “correct”.
Conclusions
Our first results strongly indicate that MDEFT is the preferential MR sequence when aiming at post-processing with FreeSurfer. The reason is the much better grey-white contrast. A disadvantage is the much longer acquisition time, which might provoke motion artifacts. Best results were achieved by the data set of healthy controls with significant more correct labeled surface. A main reason for that is the higher compliance of this group with consequently less motion artifacts. A high proportion of MDEFT data in this group is another reason. On the other hand the data set of the children showed the worst surface labeling results, mainly due to more motion artifacts compared to adults. Further the data set consisted only of conventional T1 weighted MPR. Due to the association between patient groups, age and MR sequence a more detailed statistical analysis is required.

methodology, neuroradiology
cortical thickness, freesurfer, MRI, MDEFT, MPR

Poster

NR-06

Neuropsychological outcome in patients with symptomatic and asymptomatic carotid stenosis one year after treatment

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Background:
Treatment of carotid artery stenosis enhances the cerebral blood flow and therefore can lead to an improvement of cognitive performance (Grunwald et al. 2010). However, the treatment can also lead to microembolisms, new microinfarcts, a transient decrease of the blood pressure and/or flow arrest which are all potential factors linked to a post-interventional worsening of cognitive functions. This study examines cognitive functioning in patients with carotid stenosis before and one year after treatment with endarterectomy, stenting or best medical treatment.
Methods:
Forty patients (7 women, 33 men; mean age 69y, range 51-84y) with symptomatic (n=13) and asymptomatic (n=27) carotid artery stenosis more than 70% were included. All patients underwent a neuropsychological assessment before and one year after treatment. The assessment included language(verbal fluency and word production), visual and verbal memory, motor speed and executive functions, anxiety and depression. Standardized scores (z-scores) were used. For the assessment of motor skills we defined the dominant hemisphere based on the handedness. Statistical analysis was performed using SPSS 20.0. Neuropsychological performance before and after treatment were compared with Wilcoxon Signed Ranks Test. Since we expected an improvement in performance after treatment, we report the probabilities for the 1-sided test. It is an exploratory study, therefore the test results were not corrected for multiple tests.
Results:
Statistically significant improvement of the verbal learning (Rey word learning p=.028), short-term memory (digit span, p<.001), verbal fluency (p=.047) and executive functions (Stroop interference time, p<.001) was observed for the whole cohort after treatment of the carotid stenosis. In the asymptomatic stenosis subgroup significant improvement was noticed for the verbal learning (Rey word learning p=.006), and recognition (Rey words recognition p=.025), verbal memory (Rey words late recall p=.033), executive functions (Stroop interference time, p<.001) and short-term memory (digit span, p=.001). In the symptomatic stenosis subgroup processing speed (TMT A, p=.023) and short-term memory (digit span, p=.023) were significantly better after one year.
Conclusion:
Treatment of carotid stenosis can result in an improvement of cognitive performance particularly frontal brain functions such as executive functions and short-term memory.
This positive effect is also noticed in the asymptomatic patients, a finding which can influence the indication of best

medical therapy or intervention for such cases.

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neurology, neuroradiology, psychology

Poster

NR-07

Arterial wall imaging on 3-Tesla MRI for detection of active cerebral vasculitis

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Introduction:
The MRI findings of cerebral vasculitis using conventional sequences are rather non-specific ranging from vessel irregularities to cerebral parenchymal changes. The aim of this study is to examine the feasibility of dedicated sequences for arterial wall imaging in this clinical setting.
Methods:
We prospectively examined 13 consecutive patients (10 women, age 16-65 years) with suspected cerebral vasculitis in a 3-Tesla clinical scanner (Magnetom Verio, Siemens, Erlangen, Germany). In addition to the standard MRI and the MR-angiographic series, the following sequences were performed; isotropic ultrathin heavy-T2-weighted sequence (CISS), time-of-flight MR-angiography before and after intravenous gadolinium administration as well as double inversion recovery, dark blood gadolinium enhanced T1-weighted images. Several follow-up MRIs were performed if necessary.
Results:
In six patients a vessel wall thickening and enhancement was detected (group I) involving only the anterior circulation arteries (internal carotid artery in 3, middle cerebral artery in 6 and anterior cerebral artery in 1 case). In all these six cases the vasculitis involved only the CNS. In the remaining seven cases (group II) an isolated CNS vasculitis was present in three patients. Stroke or/and transient ischemic attack occurred in all group I and in three group II patients. Clinical progression occurred in group I patients only.
Conclusion:
Dedicated vessel wall MRI is feasible. It enhances the diagnostic and prognostic value of MRI and can allow for standardized follow-up examinations for cerebral vasculitis, thus guiding therapeutic decisions.

neuroradiology
3-Tesla, MRI, Vasculitis, Brain ischemia

Poster

NR-08

Comparison of quantitative magnetic resonance angiography and Duplex ultrasound of brain supplying arteries

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Introduction:
Quantitative magnetic resonance angiography (qMRA) has emerged as an alternative non-invasive technique for flow assessment. The aim of the study was to validate qMRA velocities in intra- and extracranial arteries using percutaneous Duplex ultrasound (Duplex) as reference.

Methods:
Twenty-nine patients (17 males, mean age 66 ±8 years) were retrospectively examined. Duplex and qMRA mapping (total n= 106 vessel segments) was performed within a mean period of 8 days (max 43 days). Sonographic examinations were performed by >3 different experienced neurologists. QMRA was performed on a 3T MR imager (Siemens MAGNETOM Verio). The MR velocity measurements were calculated from NOVA software (VasSol, Chicago, IL).

Results:
QMRA systematically delivered lower velocity values than Duplex. For peak systolic velocity the mean difference and variance of difference between Duplex and qMRA was 28.6 cm/s and 1201 $(cm/s)^2$ for all vessels. Pearson correlation showed good correlation between qMRA and Duplex for CCA and ICA measurements (r=0.78, 0.55) and no significant correlation for MCA, PCA and ACA (r=0.26, 0.16, 0.48).

Conclusion:
QMRA and Duplex-ultrasound velocity measurements correlate well in the large extracranial arteries, however qMRA values were systematically lower. Missing correlation for measurements of intracranial vessels should be investigated in a prospective study with larger case series to establish qMRA as a complementary technique for the evaluation of intracranial vessels.

neuroradiology
Quantitative magnetic resonance angiography, Duplex ultrasound, Brain supplying arteries

Poster

NR-09

Cerebro-Vascular Reserve in Carotid Artery Disease correlates with deficits in cognitive functions

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Purpose:
In carotid artery disease (CAD) information about cerebral blood flow identifies areas with reduced perfusion due to the flow restriction of a feeding vessel. Arterial Spin Labeling (ASL) has proven to provide similar information about altered perfusion in vascular territories as PET with the advantage of its non-invasiveness. More recently, cerebro-vascular reserve (CVR) in ASL was suggested to be valuable in CAD. In CAD this CVR is often reduced which is suggested to be the physiological basis for observed cognitive deficits. Therefore, in this study we investigated CBF and CVR in the watershed areas of CAD patients and correlated them with neuropsychological performance.

Methods:
Thirty-two patients with CAD (grade of stenosis >70%) were investigated using pseudocontinuous ASL (pCASL). Acquisitions were performed in resting condition with ambient air and during vasodilatation stimulated with either 7% CO2 enriched air or Diamox. CBF was quantified for both conditions within gray matter voxels (estimated after segmentation of a T1 weighted image and coregistration in SPM8). Region of interest analysis was performed in the anterior watershed (AW) areas as defined with the WFU Pickatlas. By subtraction of the CBF values for vasodilatation and baseline the patient's CVR was estimated. In addition to the MR measurements all participants were tested for neuropsychological performance (language skills, executive functions, visual and verbal memory) by expert neuropsychologists.
A repeated-measures ANOVA with within subject factors Hemisphere (left/right) and Condition (baseline/vasodilatation) and between subject factor AffectedSide (left/right) was performed (post hoc tests were calculated with 1-sided t-tests for significance). Partial correlations between CBF / CVR and neuropsychological performance were done, using global baseline perfusion as control variable. In addition, the patients were grouped into terciles (3-quantiles) based on CVR in the AW on the stenotic hemisphere.

Results:
ANOVA revealed significant effects of Condition ($F(1,29)=13.50$; $p=0.001$) and significant interaction effects of Hemisphere*AffectedSide ($F(1,29)=10.69$; $p=0.003$). A t-test showed significant reduction of CVR in the AW on the stenotic side ($t(31)=-1.83$; $p=0.039$). ANOVA of terciles showed a significant interaction effect of Subgroup*Hemisphere ($F(2,29)=7.37$ $p=0.003$). Post Hoc tests revealed that only the group with lowest CVR showed a significant difference between stenotic and healthy hemisphere. However, both, lowest and average CVR group showed reduced CVR on both hemispheres as compared to the highest CVR group. Significant negative correlations between AW-CVR on the stenotic side and the neuropsychological performance were found in the domain of verbal working memory (Digit span;$r=-0.37$, $p=0.035$, one-sided) as well as for executive functions (processing speed i.e. TMT A time; $r=-0.45$, $p=0.015$; inhibition i.e. Stroop interference time; $r=-0.38$, $p=0.033$).

Discussion:
Our results indicate reduced baseline perfusion as well as impaired CVR in the anterior water shed areas of the affected side in CAD patients. Moreover, patients showed deficits in cognitive functions (working memory and executive functions) that could be associated with reduced CVR.

Disclosure: Project was financed by Swiss National Science Foundation: SPUM Consortium (33CM30-124114).

neuroradiology
Cerebro-Vascular Reserve, Carotid Artery Disease, Cognitive Functions

Poster

NR-10

Perfusion Analysis of MS Lesions with Dynamic Texture Parameter Analysis (DTPA) Preliminary Results

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Background:
In several studies demyelinating lesions in Multiple sclerosis (MS), active enhancing lesions (ELs) and inactive chronic non-enhancing lesions (NELs), showed differences in perfusion behavior on dynamic susceptibility contrast enhanced imaging (DSCE). Texture analysis, a new analysis method, enables quantitative intensity analysis of tissues of interest in MR images. In several studies this technique showed the ability to differentiate between ELs and NELSs. However, texture analysis was only performed on static sequences like T2w, T1w or fluid attenuated inversion recovery (FLAIR). Our group recently developed a new software tool, called dynamic texture parameter analysis (DTPA) which combines DSCE perfusion imaging with texture analysis by evaluating the time evolution of texture parameters of dynamic susceptibility contrast enhanced (DSCE) images.

Methods:
This study was performed on 13 MS patients. 12 active (enhancing) MS-lesions (ELs), 13 inactive (non-enhancing) lesions (NELs), and 15 NAWM localizations were examined.
DTPA is an interactive JAVA-application which enables loading of DSCE images time series and computation of histogram based texture parameter maps (TPMs) and reporting. A twofold normalization of the DSCE images relative to normal appearing white matter (NAWM) enables comparison between patients. After normalization, interindividual comparisons of the time averaged texture parameter values were feasible. Four phases, baseline, inflow, outflow and reperfusion phase, were evaluated. From the DSCE image time series, seven additional time dependent TPMs series were computed and statistically analyzed. Statistical analysis was performed by both, -testing and mixed model analysis.

Results:
Tissue- and time-dependent differences were observed in the dynamics of computed texture parameters. Texture parameters highly significantly discriminated all examined tissue types between ELs, NELs and NAWM. Best differentiation between NAWM and NELs was observed in the DSCE time series during reperfusion. Differences in skewness and kurtosis were in general less significant, due to the relatively small number of voxels incorporated in the computation of these maps.

Conclusion:
We developed a novel software tool to investigate time dependency of image texture parameters of user-defined tissue regions in DSCE image time series. The tool was applied to study MS-lesions. We detected dynamic texture features that revealed highly statistically significant differences between ELs, NELs, and NAWM. Based on these dynamic texture parameters, novel grading parameters for MS lesions may be introduced allowing for grading of MS-lesions on a numerical scale instead of an ordinal scale as is the case with pre/postcontrast T1w image analysis. Our data support the hypothesis that depending on the tissue type, subtle differences in microcirculation are present in enhancing and non-enhancing MS lesions.

methodology, neuroradiology
Dynamic Parameter Texture Analysis, Multiple Sclerosis, MRI, Perfusion, Texture Analysis

Talk

Neurosurgery (NS)

NS-01

Increased endogenous neurogenesis in the rat subventricular zone by infusion of soluble factors derived from Endothelial Progenitor Cells

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Background: Endogenous neurogenesis in the adult life is limited to specific regions as the subventricular zone. However, its extent is considered to be insufficient for functional brain repair after insults. In line with this notion, there is increasing evidence for a regenerative potential of soluble factors released from stem and progenitor cells. We have previously shown that Endothelial Progenitor Cells-derived factors (EPC-CM) promoted survival of cultured neuronal cells. In the present study we investigated the effects of EPC-CM on the neuronal stem cell niche in the subventricular zone.
Methods: EPC were isolated from peripheral blood of healthy human donors by gradient centrifugation. Cells were cultured in hypoxic conditions (1.5% O2) for 3 days to enhance the secretion of growth factors. Adult Wistar rats were anesthetized (Ketamin and Xylazin, i.p.). After a cranial midline incision EPC-CM was infused by means of a mini osmotic pumps implanted into the right lateral ventricle. Basal cell culture medium was used as control. The infusion rate was 0.5ul/h and the cannula was left in place for 7 days. Animals were injected daily with the proliferation marker BrdU. At the end of the experimental period the rats were perfusion fixed using 4% PFA and the brains sectioned on a cryostat. Brain slices were immunostained for BrdU and markers of neuronal progenitor cells.
Results: Intraventricular infusion of EPC-CM was observed to significantly increase the number of BrdU positive cells in the subventricular zone as compared to controls. Furthermore, we could demonstrate that the number of double-cortin, KI-67 and Vimentin positive cells were significantly higher in the EPC-CM treated group as compared to controls.
Conclusions: Taken together, our findings demonstrate that EPC-CM administration resulted in enhanced cell proliferation and promoted endogenous neurogenesis. These observations indicate that EPC-CM may be offering a new therapeutic strategy to induce neuroregeneration.

neurosurgery
Neurogenesis, Endothelial Progenitor Cells, growth factors, paracrine secretion

Poster

NS-02

Angiogenesis of brain endothelial cells is promoted by conditioned medium treatment

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Introduction: Increasing evidence demonstrates that the regenerative properties of stem and progenitor cells are exerted primarily on secretion of soluble factors. In the present study we investigated whether paracrine factors derived from cultured endothelial progenitor cells (EPC) may support brain endothelial cell angiogenesis. More-over, we addressed the signaling pathways that may be involved.

Methods: Cultures from rat brain endothelial cells were incubated with EPC-derived conditioned medium (EPC-CM). Angiogenic response of the microvascular endothelial cells was assessed by measuring tubulogenesis on Matrigel™. In vitro cell migration was measured by wound closure in the scratch assay. The specific PI3K/AKT inhibitor LY294002 and the MAPK/ERK inhibitor PD98059 were used to analyze the involvement of these two signaling pathways in the transduction of the effects of EPC-CM.

Results: Incubation of brain microvascular endothelial cells with EPC-CM resulted in a significant increase of tubule and network complexty. The wound closure was likewise augmented after incubation with EPC-CM. Inhibition of the PI3K/AKT signaling pathway resulted in a significant reduction of the length, the complexity of the tubule network

formation as well as the cell migration. Conversely the inhibition of the MAPK/ERK pathway did not affect the angiogenic response of the brain microvascular cells to EPC-CM.

Conclusion: In sum, our findings show that EPC derived paracrine factors substantially promote angiogenesis of brain vessels. The factors present in the EPC-CM most likely activate a variety of signaling cascades, however, the PI3K/AKT pathway seems to play a major role.

neurosurgery
Angiogenesis, Endothelial Progenitor Cells, paracrine factors, Brain Microvascular Endothlial Cells

Poster

NS-03

Vascular endothelial growth factor therapy promotes neuronal plasticity in an ischemic mouse model.

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Background: Axonal plasticity and myelinisation are important elements in the maturation of the infant brain. An ischemic lesion appeared in an adult brain reactivate ontogenetic processes responsible for axonal sprouting and white matter remodeling. Vascular endothelial growth factor (VEGF) is a potent angiogenic factor, which also has neuroprotective activity. In view of these dual actions on vessels and neurons, we aimed at investigating the effects of VEGF on neuronal survival and angiogenesis in the ischemic brain.

Methodology: Male C57Bl6/j mice were submitted to 30 min of left middle cerebral artery occlusion (MCAO). At 72 h post ischemia, mini-osmotic pumps either filled with vehicle or VEGF were implanted into the left lateral ventricle. The pumps were left in place during the subsequent 4 weeks and then removed. Animals were transcardially perfused 14, 30 and 52 dpi (days post ischemia) and the brains sectioned on a cryostat. Immunochemical analyses were performed for the neuronal marker NeuN and the endothelial marker CD31. For the evaluation of DNA fragmentation, adjacent brain sections were stained by terminal transferase dUTP nick end labeling. Surviving NeuN positive neurons, CD31 positive microvessels and DNA-fragmented cells were analyzed in a blinded way by counting numbers of cells or profiles in six defined regions of interest per striatum, both ipsi- and contralateral to the ischemia. RT-PCR analysis were performed to detect RNA expression levels of *Egr1* and *CXCL2*. Obtained data were compared to healthy animals.

Results: We observed a slowly progressive degeneration in the ischemic striatum of vehicle-treated mice, reflected by a loss of surviving neurons. Notably, VEGF is significantly involved in the rise of neuronal survival at 14 dpi. Furthermore, a significant increase in the density of CD31 positive brain capillaries was observable whereby it affected the ipsilesional to a larger extent than the contralesional striatum. Additionally, VEGF treatment significantly upregulated the fold change in expression of the target gene *Egr1*, which corresponding protein is believed to play a major role in neuronal plasticity. Similarly, the expression of the cytokine CXCL2 was upregulated in VEGF treated mice. The expression level of CXCL2, found almost exclusively in the ipsilateral striatum, seemed to be influenced predominantly by the ischemic lesion.

Conclusions: Taken together, our study revealed that VEGF treatment increased neuronal survival and promoted angiogenesis in the striatum of ischemic mice. These findings are relevant to identify the optimal therapeutic window of VEGF administration after stroke.

neurosurgery
VEGF, plasticity, ischemia, stroke

Poster

Psychiatry (PA)

PA-01

Altered N400 correlates with reduced neuronal activity in anterior temporal lobes in dementia

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With the progressing course of Alzheimer's disease (AD), deficits in declarative memory increasingly restrict the patients' daily activities. Besides episodic memory impairments, semantic memory is affected by this dementia subtype. In contrast, patients suffering from semantic dementia (SD) show isolated semantic memory impairments. With the aim to establish biological markers for the early differentiation of symptom dimensions in dementia subtypes, the present study compared 14 early AD and 5 mild SD patients with 19 healthy, age matched controls.
In particular, the participants' electrophysiological brain activity during semantic word processing was correlated with their baseline cerebral blood flow (CBF). In detail, a voxel-wise linear regression between regional CBF of each participant at rest and individual event-related potential (ERP) topographies, obtained while the participants performed lexical decisions in a semantic priming task, was conducted.
The analysis revealed that a deviant topography of the N400, an ERP sensitive to semantic word retrieval, was related to decreased CBF mainly in the anterior temporal lobes. Although the altered N400 topography was not specific for AD and SD, it differentiated dementia patients from healthy controls with a sensitivity of 0.8. Thus, the present study proposed N400-topography alterations as a possible candidate marker for impaired semantic word retrieval occurring in early dementia.

methodology, psychiatry
Alzheimer's Disease, Semantic Dementia, ERP, ASL

Poster

PA-02

Assistive technology to enhance safety and autonomy of patients with Alzheimer's disease at home

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Background
In the first-world countries of Asia and Europe, people continue to age. This trend leads to an increased prevalence of neurodegenerative diseases, and it is expected that the number of dementia patients in Switzerland will increase to 300'000 by 2050. Most of these patients have the strong desire to live autonomously in their known home-environment as long as possible. To fulfill this desire, we aim at developing an assistive technology system that facilitates the formal and informal care of dementia patients that live alone at home.
Method
We hypothesize that knowing the patient's physical and mental state can help formal and informal caregivers to deliver good and effective care. Hence, we aim at developing a system that can estimate the physical and mental state of dementia patients. For this purpose, environmental data are captured by using a passive non-intrusive sensor network. In the actual evaluation phase of the project, we are collecting data from 40 healthy subjects aged between 65 and 95 years. The data are processed by an algorithm that is based on Artificial Intelligence methods, to determine the patient's current activity, acute events, its well-being, and the long-term risks. In case of need the system will notify informal or formal caregivers.
Results
Preliminary tests have proven the technological concept. It is possible to retrieve environmental data from a network of different wireless sensors, within a sufficient range, over a long time term. By analyzing the logged data it becomes

possible to identify different activities of daily living.
Discussion
A common limitation of existing approaches in this field is that they either require the subject to wear body-mounted sensor devices for data acquisition or they make use of intrusive image-based sensors (i.e. cameras). To overcome this limitation, and to guarantee the subjects privacy, the proposed assistive technology system uses only passive, non-intrusive sensors measuring, light, motion, temperature and humidity.

other
Assistive technology, Alzheimer

Poster

PA-03

Relationship between season of birth and white matter integrity in schizophrenia

Stéphanie Giezendanner[1], Sebastian Walther[1], Nadja Razavi[1], Claudia Van Swam[1], Melanie Fisler[1], Leila Soravia[1], Jennifer Andreotti[1], Simon Schwab[1], Kay Jann[1], Roland Wiest[2], Helge Horn[1], Thomas Müller[1], Thomas Dierks[1], Andrea Federspiel[1]

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In patients with schizophrenia, widespread white matter alterations have been observed. According to the neurodevelopmental hypothesis of schizophrenia and the increased occurrence of harmful environmental factors during cold winter months, the aim of this study was to investigate whether white matter integrity was related to the season of birth in patients with schizophrenia. Thirty-four patients with schizophrenia and 33 healthy controls underwent diffusion tensor imaging. Fractional anisotropy maps were calculated, and group analyses were performed with tract-based spatial statistics. Two-sample t-tests were conducted in order to evaluate the differences in the fractional anisotropy maps of schizophrenia patients and healthy controls born in different seasons. Compared to winter-born patients, summer-born patients with schizophrenia had significantly lower fractional anisotropy in in circumscribed WM regions. In contrast, season of birth did not affect the white matter in controls. The current findings indicated that the season of birth was related to white matter alterations in schizophrenia and support the neurodevelopmental hypothesis of early pathological mechanisms in schizophrenia. These findings suggested that summer-born patients experienced accumulating harmful factors that affected white matter development.

methodology, neuroradiology, psychiatry
Schizophrenia

Poster

PA-04

Is excessive EEG beta activity associated with delinquent behavior in adult subjects with ADHD?

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Objective: The attention deficit/hyperactivity disorder (ADHD) shows an increased prevalence in arrested offenders compared to the normal population. ADHD and delinquency seem to share some neurophysiological abnormalities. In recent studies, a subgroup of subjects with ADHD as well as delinquents displayed excessive EEG activity in the beta band compared to controls, which has been associated with antisocial behavior and aggression in ADHD children. The goal of the present study was to investigate whether delinquent behavior in ADHD is related to excessive beta activity.
Methods: We compared the resting state EEGs (eyes closed and eyes open) of 13 non-delinquent and 13 delinquent

subjects with ADHD and 13 controls regarding power spectra and topography of the EEG activity.
Results: Offenders with ADHD showed more beta power mainly at frontal, central and parietal brain regions than non-delinquent subjects with ADHD.
Conclusions: Excessive beta power may represent a risk-factor for delinquent behavior in adults with ADHD.
Significance: The awareness of such risk-factors may be helpful in the assessment of the risk for delinquent behavior in a psychiatric context and may provide a neurobiological background for therapeutic interventions.

psychiatry
EEG, excessive beta activity, ADHD, adults, delinquency

Poster

PA-05

Microstate duration and sequence in frontotemporal dementia

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Frontotemporal dementia (FTD), one of the most common forms of dementia, has pathological changes in orbitofrontal cortex, insula and anterior cingulate cortex. Some of the functional magnetic resonance imaging (fMRI) studies reported that this anterior insula and anterior cingulate network, called salience network (insular-cingulate network), is considered to be important for switching and maintaining the balance between the executive-network and the default-mode network. Interestingly, recent study combining EEG with fMRI revealed the relationship between salience network and microstate class C. We speculated that microstates class C deviates from the norm in patients with frontotemporal dementia (FTD). In this present study, we investigated microstate parameters (duration and sequence) in FTD patients (mild stage, n=18), using resting EEG recorded from 19 scalp electrodes. In FTD patients, the duration of microstate class C was significantly shorter than in age-matched controls (n=19). This result is consistent with previous studies that salience network dysfunctions to early stages of FTD. The syntax analysis showed that the sequence of activation of class C and D is reversed in FTD patients compared to healthy controls, with controls preferring transitions from C to D, and patients preferring D to C. This aberrant syntax may support that network plays a critical role in switching RSNs. These results, thus, suggest that the duration and the sequence of EEG microstates could help explain the characteristics of the alterations in pathological states.

neurobiology
microstate, frontotemporal dementia, salience network

Poster

PA-06

The basic mechanisms of self-monitoring: ERP study in healthy controls

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Introduction The self-monitoring system helps us to distinguish our own actions from those others caused. An excellent example of deficient self-monitoring can be found in psychotic disorders such as schizophrenia. At least two factors contribute to the processes of intact self-monitoring: Ownership and agency. We developed an experimental ERP design to disentangle the different components and their representation in the N1 component.
Methods Right handed healthy controls (n=13; 6 men; age: 19-34) with normal hearing functions performed the experiment while 76-channel EEG (extended 10-20 system) was recorded. The experimental stimuli consisted of visually presented two-syllable, neutral words that subjects were instructed to read aloud, and auditory feedback delivered through a headphone. The chosen conditions followed a two-by-two design with the factors ownership and agency. To realise this, the feedback consisted of the subject's normal own voice or replaced by a foreign voice of the subject's gender saying the same word. In additional conditions, self and foreign spoken words were heard without

visual stimulation, or with a 200ms delay. A mute condition served as control condition. To address the question of the self-monitoring effects, difference maps were computed. ERPs were computed for all conditions, and divided into temporal components based on the grand mean's dissimilarity. Main effects for ownership and agency were computed. Finally, the topography of the self-monitoring effect was analysed.
Results For the N1, a time period between 84 and 174ms was identified. The effects of ownership and agency seem to be independent and quite orthogonal. The self-monitoring effect was significant in the N1 ($p=0.003$), also the delay made an effect at the N1 ($p=0.034$, after normalization). Both topographies resembled the agency effect, but not the ownership effect.
Conclusions It is possible with our experimental design to analyse different processes contributing to the complex self-monitoring mechanism. We found that in the N1 agency is the main determining factor of the self-monitoring as well as for the delay effect. That means, the effect of expecting anything is stronger than the effect of a violation of the expectancy.

psychiatry
self-monitoring, ERP, healthy controls, N100

Poster

PA-07

Context-specificity of inhibitory control in alcohol addiction

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Current neuroscientific models of addiction postulate enhanced cue-reactivity and impaired inhibitory control as central neural correlates of addiction.
The present study investigates these neural correlates in patients with alcohol use disorders (AUD) and healthy controls using a response-inhibition-task during functional magnetic resonance imaging (fMRI). An alcohol-specific Go-NoGo-task using pictures of alcoholic beverages and neutral control pictures was used to enable the investigation of drug-specific inhibitory processes in the addictive brain.
In consistency with prior research, preliminary results (including data from 9 patients and 8 healthy controls) indicate that successful inhibition (i.e. stop trials) activated a predominantly right lateralized fronto-parietal network. To investigate the context-specifity of inhibitory control processes, alcoholic stops were compared to neutral stops. Only in the AUD patient group this comparison yielded a number of clusters with significantly higher activation for inhibition in the alcohol-specific context, including right dorsolateral prefrontal and insular cortices as well as bilateral cingulate cortex. These preliminary results thus indicate that successfull inhibition in a alcohol-related context demands additional resources in AUD patients. Furthermore, the newly developed alcohol-specific Go-NoGo-task may be a sensitive tool to assess context-specific effects on inhibitory function.

psychiatry
inhibition, control, Addiction, alcohol, fMRI

Talk

PA-08

Emotions in Music are modulated due to depression

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There is some evidence that music has a positive influence on depressed patients. Music is shown to be apt for changing heart rate and blood pressure. The present study focuses on the differences in heart rate, heart rate variability, and breathing frequency in depressed patients and healthy controls. 10 depressed patients and 10 healthy controls listened to Chopins „Tristesse". Electrocardiogramm (ECG), breathing frequency, subjective arousal (via Joystick), and sound intensity were measured simultaneously. Depressed patients showed a significant higher arousal during the resting states. Furthermore, the changes in heart rate variability and heart rate were significantly lower. Depressed patients seem to have a lower ability of psychophysiological modulation compared to normal controls. The results direct to music therapeutic interventions, which are able to influence the physiological reagibility of patients. In this respect, it is proposed to focus on listening to different interpretations of musical scores to practice different ways of emotional involvement.

physiology, psychiatry
Music, depression, HRV

Poster

PA-09

Resting states of the brain and state dependent information processing in health and disease Study part: schizophrenia

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This SNSF-Sinergia project aims to investigate the interaction of resting state and pre-stimulus brain activations respectively with working memory processes in a broad range of healthy and clinical populations. The involved institutions will collect data from children with and without ADHD, professional musicians, schizophrenia patients, healthy subjects and healthy individuals after sleep deprivation. The common research protocol involves the simultaneous measurement of EEG and fMRI during resting state as well as during the performance of the well-established Sternberg task to assess working memory capacities.
Our subproject will investigate aberrant patterns of resting state networks in schizophrenia patients compared with healthy controls and elucidate the influence of these resting state characteristics on the networks related to working memory. Confirming the dysconnection hypothesis in schizophrenia, several studies have found de-synchronization within particular networks at rest as well as during task execution in this population. To date, this is the first study investigating the interaction of resting state and task related network activations in schizophrenia using simultaneous EEG-fMRI.
The findings will foster the understanding of the neural mechanisms underlying schizophrenia and may thereby help to improve diagnostic and therapeutic approaches. Furthermore, as this study is part of a larger project including various subject groups and paradigms, cross-references will be allowed to gain a better understanding of how resting and pre-stimulus brain states are affected by development, skills, psychopathology or vigilance and how they in turn affect human cognition and information processing.

psychiatry
EEG-fMRI, resting-state, state dependency, schizophrenia, working memory

Poster

PA-10

Altered Functional Connectivity in Formal Thought Disorder in Schizophrenia

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In our previous work we described four language regions in right-handed schizophrenic patients. Recently we identified four additional brain regions showing symptom-specific connectivity changes in formal thought disorder (FTD). We now tested different models of predicting symptom severity by specific alterations in the connectivity of these eight regions (Broca, TPJ, MTG, temporal pole, precuneus, caudate nucleus, Heschl's gyrus and ACC). Symptom-scores were best predicted by increased connectivity between the TPJ and the precuneus and decreased connectivity between the MTG and the ACC. Adding more predictors and interactions slightly increased accuracy. Further research is needed to understand the involvement of the precuneus and the ACC in FTD.

psychiatry
schizophrenia

Talk

PA-11

Is TMS a treatment option for formal thought disorder in schizophrenia?

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First experiences with the use of TMS in formal thought disorder (FTD) indicate TMS significantly reduces symptom scores in FTD-specific rating scales. However other symptoms of schizophrenia (e.g. persecutory ideas) are not alleviated by this intervention. Contrary to our hypothesis Cerebral Blood Flow (CBF) in the target-region was increased after repetitive intervention with inhibitory 1 Hz transcranial magnetic stimulation (TMS). Functional Connectivity of frontal and posterior language regions was increased after the intervention. Since these changes were associated with symptom reduction, our findings could contribute to a better understanding of the connectivity changes underlying FTD in schizophrenia.

psychiatry
TMS

Talk

Physiology (PH)

PH-01

Non-Hebbian Long-term Potentiation of Inhibitory Synapses in the Thalamus

Andrea R Sieber[1], Rogier Min[1], Thomas Nevian[1]

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The thalamic nuclei function as processing and relaying stations of sensory signals from the outside world to the cortex. They are involved in the regulation of alertness and sleep. During sleep, thalamocortical (TC) cells fire bursts of action potentials, whereas in the awake state, TC cells tonically fire single spikes.
The thalamic nuclei of the rat whisker system, the ventral posterior ncl. (VPM) and posterior medial ncl. (PoM), contain no interneurons. Instead, all inhibitory inputs come from the thalamic reticular nucleus, zona incerta and the anterior pretectal ncl. These inhibitory inputs play an important role in suppressing whisker responses and in controlling the thalamocortical output. Although these synapses play a crucial role in regulating thalamic activity, it is not known whether they can undergo long-term changes in synaptic strength.
Here, we studied long-term plasticity of inhibitory inputs to TC cells in the PoM /VPM by patch clamp recordings in acute brain slices from young rats. Inhibitory inputs were activated by extracellular stimulation.
First, we tested different correlated pre- and postsynaptic activity patterns to induce long-term plasticity and found always a potentiation of the inhibitory postsynaptic potentials (IPSPs), independent of the timing between pre- and postsynaptic stimulation. Moreover, we found that only spiking of the postsynaptic cell is sufficient to potentiate IPSPs. This inhibitory plasticity represents a form of non-Hebbian plasticity, where induction depends only on either pre- or postsynaptic activity. Interestingly, the majority of cortical synapses show Hebbian plasticity rules, meaning that plasticity induction requires correlated pre- and postsynaptic activity.
Second, the infusion of BAPTA (Ca^{2+} chelator) into the postsynaptic TC neuron blocked inhibitory long-term potentiation (iLTP) of IPSPs, indicating a Ca^{2+}-dependent postsynaptic induction mechanism. Next, we investigated Ca^{2+} signalling in TC dendrites by two-photon fluorescence microscopy. We found that iLTP depends on the membrane potential and on the postsynaptic discharge mode: tonic or burst firing.
Third, analysis of the paired-pulse ratio indicates that iLTP is expressed presynaptically.
Finally, iLTP was abolished by the application of a nitric oxide scavenger or an inhibitor of the nitric oxide sensitive guanylyl cyclise. This indicates that this form of iLTP requires retrograde nitric oxide signalling.
Since iLTP depends on the discharge mode, we suggest that iLTP is mainly induced during sleep when TC cell burst fire. iLTP might play a role in processing of thalamic information during sleep and in the regulation of thalamic oscillations.

physiology
Long-term Plasticity, Inhibition, Thalamus, Non-Hebbian, Sleep

Talk

PH-02

Reinforcement learning in dendritic structures: functional requirements and computational advantage.

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In vitro experiments on cortical pyramidal cells suggest that the main impact of dendritic input onto somatic firing is exerted via dendritic spikes. These spikes are triggered locally in dendritic branches receiving strong synaptic inputs and are supported by local NMDA-currents. Somatic firing is caused by the summation of dendritic spikes propagating to the soma, together with shorter postsynaptic currents impinging the somatic region. Such a neuron can be seen as a 2-layer feedforward network with a single output unit represented by the soma and multiple input units represented by the dendritic branches.
Although the 2-layer nonlinearities endow a neuron with a high computational power, it is not clear how synapses on the dendritic branches must adapt to learn complex stimulus-response pairs. In fact, synaptic plasticity experiments typically explain synaptic modifications as a function of the pre- and postsynaptic spike timings and neglect possible nonlinearities within the dendritic branches.

Here we show that a neuron endowed with classical reward-modulated spike-timing dependent synaptic plasticity (R-STDP) cannot exploit its full computational power inherited from dendritic NMDA-spikes. For instance, when trying to learn the XOR-problem, R-STDP fails as it does not distinguish whether the corresponding dendritic branch did or did not elicit a NMDA-spike. As a consequence, synapses are adapted as they would directly project onto a single compartment, for which it is known for instance that the XOR problem is not solvable. In contrast, reward-modulated somato-dendritic STDP (Rsd-STDP) which takes account of NMDA-spikes is able to learn the XOR problem. We suggest a biologically implementable version of Rsd-STDP which follows the stochastic gradient of the expected reward. We show that Rsd-STDP has distinguished advantages when the learning task employs temporal codes.

other

Poster

PH-03

Cellular mechanisms of long-term depression at neocortical L4-L2/3 synapses in juvenile rats

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Spike-timing dependent depression at L4-L2/3 synapses in the developing somatosensory cortex depends on retrograde endocannabinoid signaling via astrocytes. We found that the activation of astrocytic cannabinoid receptors leads to increased calcium activity and astrocytic glutamate release, which activates presynaptic NMDA receptors during the induction of spike timing-dependent depression. Furthermore, direct activation of astrocytes by depolarization paired with presynaptic activity alone also results in LTD. This form of astrocyte mediated LTD shares the same signaling cascades as timing-dependent LTD and also requires activation of presynaptic NMDA receptors. However, the functional role of presynaptic NMDA receptors in LTD induction is still elusive. Here we show preliminary results addressing this question. Using bath application of endocannabinoid receptor agonist together with selective blockade of calcium signaling in astrocytes we show that endocannabinoid-dependent astrocytic calcium signaling and the resulting release of glutamate onto presynaptic NMDA receptors is necessary and sufficient for the induction of LTD. This strengthens our hypothesis that presynaptic cannabinoid receptors are not involved in LTD, but presynaptic NMDA receptors are. We further present our optical imaging approach with which we plan to demonstrate that presynaptic NMDA receptors are specifically activated by astrocytic glutamate release. This would suggest that presynaptic NMDA receptors are shielded from synaptic glutamate release by neighboring astrocytes.

physiology
Neurophysiology, long term depression, cortex, astrocyte, electrophysiology, optical imaging

Poster

PH-04

Emotions, Arousal, and Frontal Alpha Rhythm Asymmetry During Beethoven's 5th Symphony

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Music is capable to evoke emotional arousal. While previous studies used brief musical excerpts to induce one specific emotion, the current study aimed to identify the physiological correlates of continuous changes in subjective emotional states while listening to a complete piece of music. A total of 19 participants listened to the first movement of Ludwig van Beethoven's 5th symphony (duration: *7.4 min), during which a continuous 76-channel EEG was recorded. In a second session, the subjects evaluated their emotional arousal during the listening. A fast Fourier transform was performed and covariance maps of spectral power were computed in association with the subjective arousal ratings. Subjective arousal ratings had good inter-individual correlations. Covariance maps showed a right-frontal suppression of lower alpha-band activity during high arousal. The results indicate that music is a powerful arousal-modulating stimulus. The temporal dynamics of the piece are wellsuited for sequential analysis, and could be necessary in helping unfold the full emotional power of music.

physiology
Music, EEG

Poster

PH-05

Chopin modulates heart rate

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Music is able to evoke emotions in nearly every human being. In a two dimensional model including valence and arousal, arousal can be depicted by peripheral physiological measures like heart rate or heart rate variability. In music arousal may be modulated by using changes in tempo (i.e. tempi rubati). It was the aim of the present study to show the influence of tempi rubati on the heart rate and the heart rate variability. 26 participants listened to 2 different versions of Chopin`s “Tristesse” (both played with tempi rubati, but in a different way, see Hudson, 1994). Electrocardiogramm (ECG), sound intensity and subjective arousal rating (on a joystick scale 1-10) were recorded simultaneously with the music. There was a good correlation between heart rate, subjective arousal, and sound intensity in both versions. In the version with “organic” tempi rubarti following the concept of “stolen time” with a compensation in other parts of the piece there was a far bigger variance of heart rate which was independent of the sound intensity, compared to the version with unbalanced compensation in time after a rhythmic acceleration. In this respect, playing with tempi rubati has differential influence on physiological arousal dependent on the concept used by an interpreter. The difference in autonomic reactions may be seen as base for the emotional valence attributed to a musical interpretation (e.g. emotional involvement vs. emotional indifference).

physiology
Music, HRV

Poster

PH-06

Professionals listen differently to music

Christian Mikutta[1], Gieri Maissen[1], Andreas Altorfer[1], Werner Strik[1], Thomas König[1]

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Professional musicians have more precise abilities to listen to music. However, music is able to evoke emotions in nearly everybody. It was the aim of this study to find central nervous correlations of music induced emotions in the EEG in professional musicians. The data were compared to earlier experiments including non-professional subjects. The musicians listened to Beethoven`s 5th symphony while a 75 channel EEG was recorded. In a second session the subjective arousal was evaluated. A fast Fourier transformation was performed and covariance maps were calculated. The subjective arousal ratings showed an excellent interindividual correlation. The covariance maps showed a suppression of the lower alpha spectrum during arousal and a mid frontal theta during the whole piece. The results indicate that professional musicians process music more intense on a emotional bases than hobby musicians.

physiology
Music, EGG

Poster

PH-07

Sound therapy is apt for changing heart rate.

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[1]*Sound therapy is used more commonly during the last years as training of emotional reactivity for depressive patients. In the therapeutic procedure, p*

Sound therapy is used more commonly during the last years as training of emotional reactivity for depressive patients. In the therapeutic procedure, patients are placed e.g. on a monochord bed (bed with 50 strings on the lower side). First sound tubes are used to establish an acoustic ground, thereafter the strings of the monochord bed are involved to produce fine variations, and finally the gong is played to get back to a ground tonality. The present study shows – for the first time - the influence of the different sound therapy interventions on heart rate and heart rate variability. 24 healthy participants were treated for 24 minutes with the mentioned sound therapy. Heart rate and breathing frequency were recorded simultaneously. For the comparison of the different interventions (sound tubes, monochord bed, gong) heart rate variability was used. In comparison to the initial resting state the heart rate and the sympathetic activation (high frequency/low frequency ratio) rised. After ending the sound therapy in the final resting state a significantly lowered heart rate and a lowered sympathetic influence was found. Therefore, sound therapy is effective to moderate autonomous reactions especially in the direction of tension and relaxation. In this respect, the therapeutic efficacy of sound therapy concerning improvements of the emotional variance may be analysed by using psychophysiological evaluation.

physiology
Sound therapy

Poster

PH-08

The Effect of Cortisol on Cerebral Blood Flow within Functionally Connected Networks as Investigated by Pseudo Continuous Arterial Spin Labeling (pCASL)

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The investigation of functionally connected networks (FCN) exhibiting synchronized low frequency fluctuations is of growing interest for a wide range of basic and clinical research questions. FCNs representing motor, auditory and visual systems and also higher cognitive functions as well as emotional processing have been described. Numerous of such cognitive and emotional brain functions can be modulated by cortisol, the so-called stress hormone, via receptors located in the cortex, limbic system, hippocampus, thalamus, and the hypothalamus. As the cortisol level is fluctuating in a diurnal rhythm, it might alter network connectivity and metabolism in FCNs. In the present study we therefore investigated the effect of different cortisol levels on cerebral blood flow (CBF) within FCNs using arterial spin labeling (ASL). ASL allows the identification of FCNs as well as the quantification of CBF within the same measurement session. 54 subjects were assigned to three groups according to the cortisol level: exogenously high cortisol (H) with ASL measurement at 2 pm 1 hour after oral administration of 20 mg hydrocortisone; medium cortisol (M) with ASL measurement at 8 am when the endogenous cortisol level is high; and low cortisol (L) with placebo administration 1 hour before the ASL session at 2 pm when the endogenous cortisol level is low. Salivary cortisol level analysis confirmed a significant group effect (H: 45.98±SE5.7 [nmol/L]/ M: 20.26±SE1.6 [nmol/L]/ L: 6.24±SE0.6 [nmol/L]; $p<.000001$). The FCNs displaying the spatial pattern of the medial-temporal network (MTN), the default mode network (DMN) as well as the occipital visual network (OVN) were identified by independent component analysis and the network CBF was quantified. We found significant CBF differences between each of the FCNs with the CBF values in the MTN being the lowest and the ones in the DMN being the highest. Group M showed significantly higher CBF in the DMN ($p<.01$) compared to group L, indicating a positive relation between cortisol level and CBF. As this effect was shown only in the DMN (no effect in the MTN or OVN) between the groups M and L, but not between H and M, or H and L, we suggest that not cortisol level might be the influencing variable but rather daytime: as the M group was measured in the morning, the subjects might have been in a more relaxed state and thus their DMN more active. This result would indicate that cortisol level has no particular impact on the different FCNs at a resting state, but daytime, i.e. the time of ASL measurement might influence the metabolic activity within

particular networks.

methodology, neuroradiology, physiology
functionally connected networks, arterial spin labeling, cortisol

Poster

PH-09

Effects of inner speech on arterial CO2 tension, cerebral hemodynamics and oxygenation – A functional near-infrared spectroscopy study

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Introduction:
In previous studies, using functional near-infrared spectroscopy (fNIRS), we showed that that guided rhythmic speech exercises in the context of arts speech therapy (AST) caused changes in cerebral blood circulation and tissue oxygen saturation [1,2]. Parallel to these changes, changes in arterial carbon dioxide pressure (PaCO2) were observed [2], the latter possibly accounting for the former. To further investigate the effect of PaCO2 variations on hemodynamics and oxygenation and in order to avoid a CO2 reaction, the aims of the present study were 1) to possibly reduce the influence of PaCO2 by using inner speech instead of externally voiced speech and 2) to test how inner speech affects cerebral [O2Hb], [HHb], [tHb].
Material and methods:
Seven adult volunteers participated in the study after written informed consent was obtained. The 3 different tasks (inner recitation of hexameter (IRH) or prose (IRP) verses) and a control task (mental arithmetic (MA)) on different days according to a randomized crossover design. During the measurements, the subjects sat opposite a speech therapist who recited the respective text verse by verse or asked the subjects to perform the MA task. The subject repeated the texts with inner speech. Each measurement lasted 38 min (8 min pre-baseline, 5 min task, 5 min recovery, 5 min task, 15 min post-baseline). Absolute concentrations of cerebral oxy-, deoxy- and total hemoglobin concentration ([O2Hb], [HHb], [tHb]) and tissue oxygen saturation (StO2) were measured using an ISS OxiplexTS NIRS instrument. NIRS sensors were placed over the left and right pre-frontal cortex (PFC). A Nellcor N1000 gas analyzer measured end-expiratory CO2 pressure, which represents PaCO2. Statistical analysis was applied to the differences between pre-baseline, 2 task and 4 post-baseline periods. The 2 brain hemispheres and 3 tasks were tested separately.
Results:
During the tasks: 1) PaCO2 decreased significantly ($p<0.05$) during the IRH (~3 mmHg) and MA (~0.5 mmHg) task. 2) [O2Hb] and StO2 decreased significantly during IRH (~1.5 µM; ~1.5 %), IRP (~1 µM; ~1.5 %) and MA (~1 µM; ~1.5 %) tasks. During the post-baseline period: [O2Hb] and [tHb] of the left PFC decreased significantly after the IRP and MA task (~1 µM and ~2 µM, respectively).
Conclusion:
The study showed that even inner speech affects PaCO2, probably due to changes in respiration. Although a decrease in PaCO2 is causing cerebral vasoconstriction and could potentially explain the decreases of [O2Hb] and StO2 during inner speech, the changes in PaCO2 were significantly different between the three tasks (no change in PaCO2 for MA), but led to very similar changes in [O2Hb] and StO2. Thus, the changes in hemodynamics and tissue oxygen saturation in the PFC cannot solely be explained by PaCO2.

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methodology, neurology, physiology
Functional near-infrared spectroscopy

Talk

PH-10

Motion-induced Gain Modulation In V1 Improves Contour Detection

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The recurrent interaction among orientation selective neurons in the primary visual cortex (V1) is well suited to enhance contours in a noisy visual scene. Motion selective neurons in V1 additionally support contour de- tection beyond the cooperative effect of the orientation selective neurons. In fact, slight motion of an object hidden in a still background can cause a strong pop-up effect. We ask how to wire a microcircuitry in V1 of orientation and motion selective neurons to explain the motion-induced pop-up effect exerted on contours. The circuitry has to cope with the observation that motion selective neurons themselves may show only weak orientation selectivity, and that motion may even be equally strong on the background than on the contour itself. This precludes a simple summation of orientation and motion induced evidence on the existence of local contours. We show that best performances of the contour detection network are achieved if the motion selective neurons locally enhance the gain of all orientation selective neurons at the spot of the motion. This local gain modulation makes use of the recurrent connectivity between the orientation selective neurons. Due to the local gain increase, the excitatory feedback loop among co-aligned neurons with the same orientation selectivity locally enhances the response to contours. Both, the locality of the modulation and its multiplica- tive form are crucial for the contour enhancement: a global gain modulation would unspecifically make the network over-excitable, and a local additive modulation would not fully exploit the power of a local self- excitation. The suggested local gain modulation of orientation selective neurons by motion selective neurons may readily be implemented by known elements of a cortical microcircuitry. Motion input to the apical tree of layer 5 pyramidal neurons may increase their gain to recurrently enhance their response to co-aligned oriented input.

visual system, V1, gain-modulation, contour integration, network model, simulation

Poster

PH-11

Heart rate, heart rate variability and music

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Music is able to modulate arousal and valence in nearly every person. Therefore it is an ideal stimulus to evaluate emotions. In the proposed presentation we will cover our own work regarding heart rate (HR) and heart variability (HRV) changes in a complex musical stimulus. We will describe new methods of evaluation especially for wavelet-based correlations (“semblance-analyses”) and suggest updates to actual guidelines for HRV-analysis of 1997 focusing on the specific problems with music as complex stimulus. First results are presented which evaluate the psychophysiological impact of different interpretations of Chopin's piano music. Further we describe possibilities of combining HR and HRV with other Methods such as EEG and ECoG.

methodology, physiology
Music, HRV

Talk

Psychology (PO)

PO-01

Language lateralisation increases with age in very preterm born 7-12 year-olds but not in term born control children

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Background: Neural structural abnormalities as well as cognitive difficulties in language processing have been described in children born very preterm (<32 weeks of gestational age and/or <1500 g birth weight). These findings raise the question how premature birth is related to neural language organisation and lateralisation. The aim of the study was to test the following hypotheses: a) VPT/VLBW and control children show different language organisation b) language organisation in VPT/VLBW children is more bilateral compared to language organisation in control children c) positive correlations between language performance measures and language lateralisation exist in VPT/VLBW children and controls.
Method: Brain activity was measured during a phonologic detection task in 56 very preterm born children and 38 term born control children aged 7 to 12 years using functional Magnetic Resonance Imaging. General IQ, verbal IQ, verbal fluency and reading comprehension were assessed outside the scanner.
Results: Language organisation and lateralisation did not differ in very preterm and control children in overall comparisons. However, in very preterm children lateralisation increased between the age of 7 to 12 years. This correlation was not found in control children. Language organisation in very preterm children was bilateral in young children and left-sided in old children, whereas language organisation in control children was left-sided in the young and old age group. Frontal lateralisation correlated with General IQ in controls, but no other correlations between lateralisation and verbal performance were found.
Discussion: The results of this study suggest different developmental patterns of language processing in very preterm born and term born control children. While very preterm born children showed atypical language organisation and lateralisation in younger years, typical left-sided patterns were found at the age of 12 years.

neuroradiology, psychology

Poster

PO-02

Cognitive functioning in Children with Cancer before and after Medical Intervention

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Extensive research has shown that survivors of childhood cancer often demonstrate neurocognitive deficits especially when the malignancies and/or the treatments (surgery, chemotherapy, radiation therapy) involve the CNS. Even without CNS involvement negative effects of chemotherapy on cognitive functions have been shown mainly in adults. So far mostly children who have been off treatment for one year or longer have been included in studies on cognitive outcome. Few studies have investigated the "baseline" of cognitive abilities before the start of any treatment. In the study presented here all children (ages 4-18; n=61) hospitalized at the University Children's Hospital Berne for treatment of malignancies and benign brain tumors underwent their first extensive neuropsychological assessment in the days following initial diagnosis. The second neuropsychological assessment was performed 8 weeks after the end of chemo- and/or radiation therapy. Results show that immediately after diagnosis children with brain tumors show significantly worse performance on tests of verbal learning and long-term memory as well as attention compared to children with non-CNS malignancies. At this point the two groups do not differ, however, in

other cognitive areas (FSIQ, performance speed, executive functions, short-term memory). After the end of medical treatment the differences between the two groups are still evident and in some measures of attention and memory these differences grow even more significant. This shows that even before medical treatment verbal memory and attention are cognitive areas especially vulnerable to malignancies involving the CNS. At both time points the patient groups do not (yet) differ in IQ, performance speed, working memory and executive functions nor do they show a general decline in these areas. However, this might become evident in the long-term. Future steps of this study will include – besides long-term follow up assessments - implementation and evaluation of cognitive training programs for affected children as well as neuro-imaging. DTI and fMRI might help to link impairment as well as treatment effects to changes in brain activity or white matter volume.

psychology

Talk

PO-03

Measuring Driving-relevant Cognitive Performance

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Introduction. A number of specific cognitive skills are fundamental for the ability to drive safely. Some of them can be affected by age-related cognitive changes. In this study, we develop a computer-based screening tool to investigate the age-dependent performance in different driving-relevant cognitive tasks and compare it with the outcome of cognitive and motor screening tests.
Method. A newly developed screening tool that consists of five subtests (maximum duration 3 min.) was used to assess the following driving-relevant cognitive skills: selective and divided attention, eye-hand coordination, executive functions, and regulation of distance and velocity. The tests were presented on a computer screen and the reactions of the participants were captured with a commercially available steering-wheel and foot pedal. Performance in 88 healthy subjects divided into two groups was measured: 30 young active drivers (mean age = 31 years, SD = 5.5), 44 older drivers without recent accident involvement (mean age = 69 years, SD = 5.1), 14 older drivers with recent accident involvement (mean age = 71, SD = 5.0). Participants also completed the Montreal Cognitive Assessment, Trail Making Test A & B, Clock Drawing Test, and the Timed-up-and-go Test.
Results. In this study, we could show that the five subtests of the screening tool discriminate between younger and older participants, with younger subjects outperforming older subjects. We also found that older subjects with recent accident involvement showed significantly poorer performance in the five subtests compared to older drivers without accidents. No significant differences were found in paper-pencil screening tests between the two groups of older drivers.
Discussion & Outlook. Results show that the newly developed computer-based screening tool but not the paper-pencil screening tests discriminates between younger and older subjects, as well as between older subjects with and without recent accident involvement.

neurology, psychiatry, psychology
Older drivers

Poster

PO-04

Improving children's cognitive performance – Effect of a memory strategy training in children born very preterm

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Aims: To examine the effect of memory strategy training on different aspects of memory in children born very preterm and to determine whether there is a generalization of the training effect to non-trained functions. The influence of individual factors such as age and performance level on the training success will be determined.
Methods: In a randomized, controlled and blinded clinical trial, 46 children born very preterm (aged 7-12 years) were allocated to a memory strategy training (MEMO-Training, n=23) or a control group (n=23). Neuropsychological assessment was performed before, immediately after the training and at a 6-month follow-up. In the MEMO-Training, five different memory strategies were introduced and practiced in a one-to-one setting (4 hour-long training sessions over 4 weeks, 20 homework sessions).
Results: A significant training-related improvement occurred in trained aspects of memory (verbal and visual learning and recall, verbal working memory) and in non-trained functions (inhibition, mental arithmetic). No performance increase was observed in the control group. At six months follow-up, there was a significant training-related improvement of visual working memory. Age and performance level before the training predicted the training success significantly.
Conclusion: Teaching memory strategies is an effective way to improve different aspects of memory but also non-trained functions such as inhibition and mental arithmetic in children born very preterm. Age and performance level influence the success of memory strategy training. These results highlight the importance of teaching children memory strategies to reduce scholastic problems.

psychology

Poster

PO-05

Relationship between postconcussive symptoms and neuropsychological performance after pediatric mild traumatic brain injury

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Introduction: Epidemiological studies indicate that traumatic brain injuries (TBI) are very common in childhood and adolescence. Fortunately, most of these injuries are mild in severity. Although recent reviews and studies have shown repeatedly that mild TBI (mTBI) has little effect on children's neurocognitive functioning in standardized cognitive testing, there is growing evidence, that children with mTBI display more postconcussive symptoms (PCS) in the months after the injury compared to children with orthopedic injuries (OI) not including the head. PCS include somatic, cognitive and emotional complaints. Only few studies have investigated the relationship between PCS and neuropsychological performance with divergent results. Methods and Participants: The aim of this ongoing pilot study is to investigate the short-term development of PCS and its relationship with neuropsychological performance 1 and 4 months after injury. PCS were rated in children (age 6-16 years) after mild TBI (n = 45, mean age at injury: 10.8 years) and children after mild OI (n = 25, mean age at injury: 9.8 years) in a prospective short-term longitudinal design with following time points (T0 = at injury, T1 = 1 week after injury, T2 = 4 weeks after injury, T3 = 16 weeks after injury). PCS were rated on a 4 point Likert scale questionnaire with 29 questions. All children underwent neuropsychological assessment 1 and 4 months after the incidence. We focus here on results from complex span tasks (backward digit recall & listening recall) and verbal memory performance (recalled words after 30 minutes). Results: Parent ratings of PCS were at all five time points higher for mTBI group compared with OI control group. At T0 preinjury and T3, mean parent ratings of PCS sum did not differ significantly between both groups. At all other time

points, mTBI PCS ratings were significantly higher compared with the ratings of the control group. Neuropsychological Performance did not differ significantly at both neuropsychological time points (T2 and T3) between mTBI and OI group. Nonparametric correlations revealed only for the mTBI group significant negative correlations between parent PCS ratings at timepoint T3 with complex span and verbal memory performance at T3. Conclusions: Preliminary results from this pilot study reveal that parents of children after mTBI observe significantly more PCS in the first weeks after the injury, compared with the parent ratings of the OI control group. Similar to previous studies, there is no significant difference in complex span & verbal memory performance in the weeks after the injury (T2 and T3). Although the sample size is very small, the significant negative correlation between the observed amount of PCS and neuropsychological performance in children after mTBI might indicate that shortly after an mTBI some children with a high level of PCS show a reduced neuropsychological performance in working memory and/or verbal memory tasks which could affect their school performance right after the injury. Future steps will involve recruiting more control group children and analyzing possible relationships between PCS, neuropsychological performance and the Neuroprotein S100 b, which was measured at T0.

psychology
Pediatric mTBI, postconcussive symptoms, neuropsychology

Poster

PO-06

Experimental induction of psychotherapeutically relevant emotional states

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Background: Emotion research in neuroscience targets brain structures and processes involved in discrete emotion categories (e.g. anger, fear, sadness) or dimensions (e.g. valence, arousal, approach-avoidance), and usually relies on carefully controlled experimental paradigms with standardized and often simple emotion-eliciting stimuli like e.g. unpleasant pictures. Emotion research in clinical psychology and psychotherapy is often interested in very subtle differences between emotional states, e.g. differences within emotion categories (e.g. assertive, self-protecting vs. rejecting, protesting anger or specific grief vs. global sadness), and/or the biographical, social, situational, or motivational contexts of the emotional experience, which are desired to be minimized in experimental neuroscientific research.
Objective: In order to facilitate the experimental and neurophysiological investigation of psychotherapeutically relevant emotional experiences, the present study aims at developing a priming procedure to induce specific, therapeutically and biographically relevant emotional states under controlled experimental conditions.
Methodology: N = 50 participants who reported negative feelings towards another close person were randomly assigned to 2 different conditions. They fulfilled 2 different sentence completion tasks that were supposed to prime either 'therapeutically productive' or 'therapeutically unproductive' emotional states and completed an expressive writing task and several self-report measures of specific emotion-related constructs. The sentence completion task consisted in max. 22 sentence stems drawn from psychotherapy patients' statements that have been shown to be typical for productive or unproductive therapy sessions. The subjects of the present study completed these sentence stems with regard to their own negative feelings towards the close person.
Results: There were a substantial inter-individual variability concerning the number of completed sentences, and significant correlations between number of completed sentences and problem activation in both conditions. No differences were observed in general mood or problem activation between both groups after priming. Descriptively, there were differences between groups concerning emotion regulation aspects. Significant differences between groups in resolution of negative feelings towards the other person were found.
Discussion: The results point in the expected direction, however the small sample sizes (after exclusion of several subjects) and low power hinder the detection of convincing significant effects. More data is needed in order to evaluate the efficacy of this emotional priming procedure.

methodology, psychology, other
emotion

Poster

PO-07

Caloric Vestibular Stimulation Influences Emotional Processes in Healthy Participants and Patients Suffering from a Manic Episode

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Introduction
Recent evidence suggests that processing of emotional and vestibular information shares some common mechanisms. In addition, research suggests a dominance of the right hemisphere for both, vestibular processes and processing of negative emotions (for overview see Carmona et al., 2009). The goal of the present study was to investigate the effect of caloric vestibular stimulation (CVS) on mood and emotional processes in healthy participants and in patients suffering from a manic episode.
Methods
32 healthy participants and 3 manic patients performed an affective Go/NoGo (AGN) task while they were exposed to cold left or right ear CVS (20°C) and sham stimulation (37°C). Pictures showing positive or negative content were presented. In each trial, either positive or negative pictures were specified as targets. Participants had to respond to targets by means of a response button (Go), but to withhold responses to distractors (NoGo). Patients with an affective disorder usually show a mood congruent response bias in an AGN. In addition, healthy subjects and manic patients answered *The Positive and Negative Affect Scale* (PANAS; Crawford & Hendry, 2004) after each experimental block in order to measure changes in affect.
Results
D' (*hits – false alarms*) was used to measure task performance. In healthy participants, D' increased for positive stimuli during right ear CVS but not for negative stimuli. In contrast, D' decreased for positive stimuli during left ear CVS but not for negative stimuli. A similar pattern was found in the PANAS. Right ear CVS did not modulate positive affect when compared to sham stimulation. However, CVS decreased positive affect after left ear CVS. In general, there was no influence on negative affect. Furthermore, in two of three manic patients, CVS exerted a regulating effect on mood and task performance.
Discussion
The results suggest that CVS, depending on side of stimulation, has a modulating effect on mood and emotional processes and that patients with an affective disorder could profit from the effects of CVS.

psychiatry, psychology
Emotional processing

Poster

PO-08

Implicit sequence learning during self-motion perception

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The ability to implicitly learn about sequential regularities helps to simplify our daily activities. According to the correlated streams account, sensory information regardless of modality is expected to contribute to sequence learning. Typically, a sequence of stimulus locations is correlated with a sequence of response keys. The present study used an adapted version of the serial reaction time task to investigate whether sequence learning can also be found in self-motion perception, which relies predominantly on vestibular information. A total of 16 participants were tested. They were seated, blindfolded and exposed to combinations of the following six motions on a MOOG motion platform: up, down, right, left, forward, backward. The participant's task was to judge the experienced motions as fast and accurately as possible by means of two response buttons according to a previously acquired response mapping. Each motion lasted 500ms and displaced the participants by 2 cm. A fixed response to stimuli interval was deployed. The sequence of motions was manipulated by presenting either a fixed sequence of motions or a randomized order of motions. 8 blocks consisting of 96 motions were presented. After two initial practice blocks involving a random order of motions, a 12-element sequence of motions, which was correlated with the sequence of responses, was used in

blocks 3, 4, 5, 6 and 8. To distinguish sequence learning from a general learning effect, block 7 applied a random order of motions. The cost in reaction time of this random block in comparison to blocks 6 and 8 is taken as indication for sequence learning. Most importantly, the results showed that exposure to a randomized order of motions in block 7 significantly slowed down reaction times. To our knowledge, the present study is the first to demonstrate sequence learning with predominantly vestibular information as sensory input, an effect in line with the correlated streams account.

psychology

Poster

PO-09

Colored Digits and Mathematical Abilities in School Children

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Grapheme-color synesthesia denotes the idiosyncratic, automatic and consistent experience of color whenever perceiving graphemic information. Previous studies with graphem-color synesthetes suggest performance detriments in mathematical tasks when digits are printed in incongruent colors, both in adults as well as in school children. One could argue, however, that such tasks incorporate artifical situations that do not yield for a general relationship between graphem-color synesthesia and mathematical abilities. Thus, the aim of the present study was to investigate, whether consistent digit-color associations are generally related to maths skills in school children. A total of 134 children between second and sixth grade were recruited from two Swiss public schools. To detect possible consistent and unconventional digit representation formats, participants were asked to assign colors to the digits one to nine and to draw their mental number line in two sessions with an interval of two weeks. Further, math grades of the last school report were provided by the teachers. Consistency of digit-color and, to a weaker degree, digit-space associations positively correlated with math grades, indicating a general relationship between consistent, unconventional digit representations and maths skills. It might be concluded that such representations create a richer sensory world, providing additional cognitive tools which might account for a general advantage.

psychology
Synesthesia

Poster

PO-10

Switching between the senses: imagination interferes with perception in stimulus detection tasks

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In an attempt to examine whether stimulus detection in a simple reaction time task is expedited by an imagined stimulus, participants were asked to imagine a familiar stimulus in one sensory modality (e.g., sound) while waiting to signal the onset of a target stimulus in the other modality (e.g. vision). Contrary to what could be expected from research into multi-sensory integration, namely the occurrence of redundancy gains, imagination of an additional stimulus decreased response speed. The result is explicable, however, by a mechanism that requires the dynamic allocation of a limited processing capacity - attentional weight - to sensory modalities, which results in reaction time costs when observers are required to switch from imagination in one modality to perception in another modality.
In a reaction time experiment participants first learned to indicate by a speeded manual response (a button press), the onset of a sensory stimulus that could be either auditory (600 Hz sound), visual (bright green disk), or both auditory and visual. As expected from and in accordance with the literature on multisensory integration, mean behavioural reaction times to bimodal stimuli were markedly accelerated in comparison to responses to unimodal stimuli. This is what is referred to as the “redundant signals effect” or “bimodal advantage”. Further, analysis of the entire reaction time distributions of bimodal and unimodal stimuli indicated co-active integration of the bimodal

sensory stimuli. Participants were than asked to imagine the now familiar stimulus in one modality (e.g., the sound) while they were waiting to manually respond to the onset of a stimulus in the respective other modality. Contrary to the result of the pure sensory presentation condition, and to expectation, imagination of an additional stimulus did not expedite the response to the sensory stimulus. Not only was there no co-active integration of the imagined and the physically presented stimuli; there was no parallel race between signals, either. Rather, responses were actually slower when participants imagined a stimulus in the other modality than when they did not imagine anything while waiting for the sensory stimulus to appear. An almost identical follow-up experiment showed that these response costs were not due to an increase of general cognitive load caused by the imagination task. Participants now had to imagine the auditory or visual stimulus but then indicate the onset of a bimodal sensory stimulus. No response speed costs were found in this imagine-bimodal-sensory condition in a comparison with responses to bimodal stimuli without the imagination component. One possible explanation for these results would be a mechanism in which imagining a stimulus in one modality requires the shift of attentional weight to that modality and, by decreasing the processing weight available in the other modality, affects detection performance. A scenario in which the target signal is presented in both modalities would always include the modality with greater attentional weight. Consequently one would not expect a unimodal imagination task to cause decreased response speed. This way the described "modality switching costs" explanation could account for the absence of impairing effects due to the imagination task in the results of our follow-up experiment.

psychology
multisensory integration, perception, mental imagery, auditory, visual, reaction time

Poster

PO-11

Do cognitive and behavioral assessments of executive functions measure the same concept in children born very preterm?

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Aims: This study investigated whether children aged between 8 - 12 years born very preterm (VPT) and/or at very low birth weight (VLBW) performed lower than same-aged term-born controls in cognitive and behavioral aspects of three executive functions: inhibition, working memory, and shifting. Special attention was given to sex differences.

Methods: Fifty-two VPT/VLBW children (26 girls) born in the cohort of 1998–2003 at the Children's University Hospital in Bern, Switzerland, and 36 same-aged term-born controls (18 girls) were recruited. As cognitive measures, children completed tasks of inhibition (Colour-Word Interference Test, D-KEFS), working memory (digit span backwards, WISC-IV) and shifting (Trail Making Test, number-letter switching, D-KEFS). As behavioral measures, mothers completed the Behavior Rating Inventory of Executive Function (BRIEF), assessing executive functions in everyday life.

Results: Analyses of the cognitive aspects of executive functions revealed that VPT/VLBW children performed significantly lower than controls in the shifting task, but not in the working memory and inhibition tasks. Analyses of behavioral aspects of executive functions revealed that VPT/VLBW children displayed more problems than controls in working memory, but not in inhibition and shifting in everyday life. No sex differences occurred, neither in cognitive nor behavioral aspects of executive functions.

Conclusion: Results of cognitive and behavioral assessments of executive functions were incongruent in VPT/VLBW children. In clinical practice, the combination of cognitive and behavioral assessment instruments is required to properly disclose children's executive functions.

psychology

Poster
PO-12

In search of the implicit self as a possible biomarker of depression

Yvonne Egenolf[1], **Helen Wirz[1]**, Maria Stein[1,2], Thomas Koenig[2], Martin Grosse Holtforth[3], Thomas Dierks[2], Franz Caspar[1]

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Aim: Negative biases in self-evaluation have been linked to various psychological disorders including depression. Today, little is known about brain processes involved in implicit self-evaluation. An understanding of the neural processes associated with implicit self-evaluation in healthy subjects could provide a basis for the investigation of the implicit self in depressed patients, the development of differential psychotherapeutic interventions and the prediction of relapses in remitted patients.
Methods: 25 healthy subjects performed of the self-relevant Implicit Association Test (IAT) while brain activity was measured with 70-channel EEG. Individual ERPs of the implicit (congruent) and explicit (incongruent) condition were used for group-analyses of differences in topography (TANOVA) and amplitude (GFP). The neural generators of the topographical differences were estimated by using the LORETA inverse resolution method.
Results: The ERP analysis showed significant topographical differences in the late ERP, which were driven by higher activation in the anterior cingulated cortex, the subgenual cingulated gyrus and the middle frontal gyrus during the incongruent condition.
Discussion: The processing of incongruent information is associated with additional activation of brain regions that were implicated in conflict monitoring and cognitive control. This might reflect the neural basis of explicit processes, which over-rule the response tendency that is more consistent with the implicit self-evaluation. Thus, EEG activations correlating with implicit self-evaluation might serve as a neural biomarker for depression.

psychology
implicit self, IAT, ERP, depression

Poster

PO-13

Cognitive Interventions with Children with Special Needs - Transfer effects and multidisciplinary perspectives

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Our last study with regularly developed children demonstrated a positive effect of working memory training on cognitive abilities. Building upon these findings, the aim of this multidisciplinary study is to investigate the effects of training of core functions with children who are suffering from different learning disabilities, like AD/HD, developmental dyslexia or specific language impairment. In addition to working memory training (BrainTwister), we apply a perceptual training, which concentrates on auditory-visual matching (Audilex), as well as an implicit concept learning task. We expect differential improvements of mental capacities, specifically of executive functions (working memory, attention, auditory and visual processing), scholastic abilities (language and mathematical skills), as well as of problem solving. With that, we hope to find further directions regarding helpful and individually adapted interventions in educational settings.
Interested parties are invited to discuss and comment the design, the research question, and the possibilities in recruiting the subjects.

psychology
cognitive interventions, learning disabilities, transfer effects, individualized education

Poster

PO-14

Reading Strategies across Languages in early and late Bilinguals: an Eye-Movement Study

D. de León Rodríguez[2], K. Butler[2], N. Eggenberger[1], B. Preisig[1], S. Hopfner[1], R. Schumacher[1], L. Sprierer[2], M. Laganaro[3], T. Nyffeler[1], J -M. Annoni[2], R. Müri[1]

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Reading strategies, as indexed by variations in eye-movement patterns during reading, have been shown to vary across languages. Because respectively involving direct vs. complex grapheme/phoneme conversions, different strategies are indeed engaged when reading transparent vs. opaque languages, respectively. The literature so far, however, investigated this question using between-subject factors designs which where potentially confounded by differences across groups unrelated to reading per se. To circumvent this issue, we examined reading strategies between the two languages of early and late bilingual individuals. Participants were French/German bilinguals divided into three groups according to their language proficiency: Early bilinguals (EB, second language (L2) acquired before 7 years), late bilinguals T (LBT, L2 after 7 years, German as L1) and late bilinguals O (LBO, French as L1). Participants were instructed to read aloud isolated words and pseudowords in a French (opaque) or German (transparent) context. We measured the landing position of the First Fixation Location (FFL). We expected the FFL to be done nearer to the center of the stimulus in the opaque than in a transparent context in early bilinguals but not for participants performing preferentially an opaque or a transparent language. Preliminary results from EB group suggest no difference inter-contexts; however, we collected so far only 30% of the planned sample size.

other
Eye movements, Bilingualism, Lecture

Poster

PO-15

Self-motion perception thresholds do not improve as a function of perceptual training

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Perceptual learning refers to a long-lasting improvement of perceptual skills after repeated exposure to a stimulus. Perceptual learning has been found in visual, auditory, tactile or olfactory perception. For example, participants can learn to better discriminate visual contrast, line orientation, or the taste of different wines. Here, we report results from the first perceptual learning study in the vestibular domain. Particularly, we investigated perceptual learning in self-motion perception. Blind-folded participants were displaced leftward or rightward by means of a motion platform, and asked to indicate the direction of motion. A total of eleven participants underwent 3360 practice trials, distributed over twelve (Experiment 1) or six days (Experiment 2). Several self-motion perception thresholds were measured before and after the training to assess whether participants became more sensitive through training and to assess potential transfer effects. We found no improvement in motion discrimination in both experiments. These results are surprising since perceptual learning has been demonstrated for visual, auditory, and somatosensory modalities. The multisensory nature of vestibular information is discussed as a possible explanation of the absence of perceptual learning. Especially, the interaction with visual information may play a crucial role in improving self-motion perception. In order to assess this hypothesis, a follow-up study in which self-motion perception training is performed in a visually rich environment is in progress.

physiology, psychology
self-motion thresholds, whole-body motion, perceptual learning, vestibular thresholds, vestibular learning

Poster
PO-16

Illusory direction in self-motion perception: influence of preceding body motion

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Most studies on self-motion perception assess regular motion thresholds with the aim to develop new clinical diagnostic tools for vestibular disorders. However, little is known how a preceding motion affects the perception of a subsequent motion. Thus, the aim of this study was to investigate how body motion influences subsequent perception of self-motion. In two experiments blindfolded participants were seated on a MOOG motion platform and asked to indicate the direction of the second of two subsequent movements. In the first experiment, a short left or right translation (200 ms) was followed by a short left or right rotation (200 ms). The first stimulus was 3.6 times above the threshold for single translations and the second stimulus was 2.6 times above the threshold for single rotations. The two movements were presented with inter-stimulus intervals (ISI) of 50 ms, 100 ms, 200 ms and 600 ms. Error rates and reaction times of the direction discrimination task were measured. Results show that prior movements in general have an impeding effect on the perception of subsequent movements. Interestingly, it was also found that congruent directions of the two stimuli (i.e. right-right or left-left) lead to a consistent misperception of the target stimulus for short ISI. In the second experiment, the two stimuli were interchanged. The intensities were adopted to match the relations with respect to the thresholds used in first experiment. Again, error rates were higher for combined movements and participants had an erroneous direction perception for congruent stimuli when ISI was short.
These findings may have important practical implications. Knowledge about such self-motion misperception could be crucial for preventing accidents, for example when airplanes or helicopters have to be controlled under visually poor conditions. Moreover, there is a potential use for two-motion designs in clinical diagnostic testing. Yet, future studies need to explore the occurrence of the effect for other types of motions (e.g. up-down) and the origin of the effect remains to be determined.

psychology
vestibular perception, illusion, self-motion

Poster

PO-17

Visual Awareness at sensory discrimination threshold depends on the pre-stimulus EEG microstate.

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[1]University of Bern, Switzerland, [2]University of Geneva, Switzerland, [3]The City College and Graduate Center of the City University of New York, USA

Changes in perceptual awareness for multi-stable stimuli can arise from different pre-stimulus EEG microstates. Here, we investigated whether the perceptual awareness for stimuli at the discrimination threshold can likewise arise from pre-stimulus microstate differences. We used a metacontrast masking paradigm in which subjects had to discriminate between two stimuli while their EEG was recorded from 256 channels. We used 4 ISIs and obtained measures of accuracy and awareness. For each subject, we chose the ISI with nearly equal numbers of trials in the correct aware (CA) and correct unaware (CU) conditions, which allows contrasting differences in awareness by keeping both behavioral accuracy and physical stimulus constant. We determined the pre-stimulus microstates in the CA and CU conditions, and a cluster analysis identified two template maps that doubly dissociated aware from unaware correct identification. We computed distributed inverse solutions for the templates, and statistical parametric mapping of their differences yielded increased activity in primary visual cortex in the CU condition. These results suggest that if primary visual cortex is already pre-activated, stimuli at the discrimination threshold cannot excite it sufficiently to attain awareness even though they are correctly identified.

methodology, psychology
state-dependency, metacontrast masking, EEG, visual awareness, prestimulus microstate

Poster
PO-18

Allocentric frame of reference in pseudoneglect - evidence from eye movements

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Neglect refers to the phenomenon that attention towards the left space can be impaired after right hemispheric lesions. Patients suffering from neglect show a rightward bias when asked to bisect a horizontal line or explore only the right half of an image. Interestingly, neglect can also be based on an allocentric frame of reference. In this case, the left side of an object is neglected, irrespective of its position and orientation in space. There is also a small attentional bias in the healthy population, labeled pseudoneglect. For example, healthy participants typically show a small leftward bias when asked to bisect a horizontal line, or predominantly explore the left half of an image. The aim of this study was to investigate whether pseudoneglect manifest itself also in an allocentric reference frame. Participants were asked to explore symmetric images of objects (e.g., car, house) for 4 s while their eye movements were recorded. Each image was presented in an upright position and rotated clockwise by 90°, 180°, and 270°. We found that participants looked more often at the left screen half when the image was in the upright when compared to the upside down orientation (52.0% vs. 48.9%). Moreover, participants looked more often at the upper screen half when the image was rotated 90° when compared to 270°. The latter difference was only significant in the first second of free exploration (64.3% vs. 59.0%). These results show that attention is shifted toward the intrinsic left side of an object. Therefore, we provide evidence that pseudoneglect is also defined with respect to an allocentric frame of reference.

psychology
Pseudoneglect, attentional bias, object-centred, eye movements

Poster

PO-19

Impaired unconscious episodic encoding and retrieval following amnesia

Simone B. Duss[1,2], Thomas P. Reber[1,2], Simon Schwab[6,2], Martinus Hauf[4], René M. Müri[3,2], Peter Brugger[5], Klemens Gutbrod[3,2], Jürgen Hänggi[7], Katharina Henke[1,2]

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An unconscious form of episodic memory that is dependent on the hippocampus was suggested by several behavioral and neuroimaging studies in healthy participants. However, these studies left open whether the hippocampus was merely co-activated and perhaps not really necessary for unconscious memory formation. Here, we report on 11 amnesic patients who suffered both a deficit in conscious and unconscious episodic encoding of new word-word associations. Amnesic patients exhibited lesions to the medial temporal lobe or diencephalon. The 11 controls were age-, sex- and education-matched. All participants underwent a comprehensive neuropsychological assessment. Further, all control participants and five amnesic patients underwent functional (fMRI) and structural magnetic resonance imaging. We collected fMRI data while participants performed an unconscious associative encoding and retrieval task. This task had activated the hippocampus in a previous study with young, healthy participants. All encoding word pairs were presented subliminally to avoid conscious encoding of words (e.g., desk – bus). Hence, memories of word pairs were formed unconsciously. For retrieval, participants judged the semantic fit on test word pairs that were either analogs (e.g., table – car) or broken analogs (e.g., counter – pear) to the unconscious encoding word pairs. We also included a classical subliminal priming task, which is thought to be hippocampus-independent. Patients and controls performed equally well on this task. However, unlike controls, patients' performance on the unconscious episodic encoding and retrieval task was not better than chance. Although the patients' performance was numerically lower than the controls' performance, this difference did not reach significance. Hence, some patients must have retained some relational processing capacity. Indeed, the pattern of neural activity during unconscious encoding and retrieval suggests that remaining functional tissue in the medial temporal lobe and adjacent structures underlay the speared performance in four of 11 patients. The dissociation between nearly absent conscious and partly diminished unconscious episodic encoding performance in amnesic patients indicates that a larger hippocampal network might be required for conscious than unconscious episodic encoding. Together, these findings point to a role of the hippocampus in both conscious and unconscious episodic encoding and retrieval.

psychology
Episodic memory, amnesia, hippocampus, unconscious, subliminal, memory systems, fMRI.

Talk

Symposia

Symposium 1: Center for Cognition, Learning and Memory (CCLM)

Time: 14:00-16:15

Place: Lecture Hall Glauser, UPD

From Cell to Memory: The Plastic Brain (chair: K. Henke/W. Senn)

Why does a child have a brain like a sponge, while an older adult tends to have a brain more like a sieve? What changes in our brains as we get older and how do those changes affect our ability to learn, develop new skills, and recover from brain injury? Recent research is beginning to answer these fundamental questions. Contrary to the common assumption that you can't teach an old dog new tricks, there is evidence that the adult human brain is remarkably capable of new feats even in the last decades of life. To learn and discuss about brain plasticity, we invite CCLM experts. The expert's input talks are short (10 min.) and have the primary purpose of spanning a topic broadly by putting a few pillars of knowledge that pave the way into the discussion (15 min.). Speakers and organizers formulate discussion points that ignite the discussion. Participants in the workshop receive abstracts and discussion points beforehand (with the program of the meeting) to prepare for a lively conversation. The seating will be in a circle to face each other.

1. How is information coded in neurons? (T. Nevian)

One of the most fundamental properties of the brain is its ability to adapt rapidly to environmental changes. How can the experiences of a lifetime—the sights and sounds, people and places, successes and failures—be recorded in the soft tissue of the brain? This is mainly achieved by changes in the connectivity between individual nerve cells. Synapses, the connection elements between neurons, can be modulated in their strength by a variety of different mechanisms, a process called "synaptic plasticity". Researchers gained new insights into the basic mechanisms that are involved in synaptic plasticity, dendritic excitability and signal integration of cortical neurons. Synaptic plasticity may be accompanied by structural changes of dendritic spines. But how can those memories persist for decades even as the neurons that encode them undergo constant molecular remodeling?

Discussion point 1: How can memories last if neurons are modified over time?

Discussion point 2: How does memory reactivation during off-line states (sleep) contribute to long-term potentiation?

Discussion point 3: Are early and late phases of long-term potentiation underlying all forms of memory?

Discussion point 4: What is the neural correlate of forgetting? What determines, which memories are preserved and which ones are forgotten?

2. How do adult brains make memories? (S. Ruch)

Most researchers agree that memories are initially encoded and stored by way of the hippocampus. For long-term storage, memories are filed away to other areas, including the neocortex. A memory of any given event is represented by a sparse and scattered network of neurons, such that the sights, sounds, and emotions associated with the experience may each reside in a different location. To recall that memory, the brain must somehow reactivate just the right subset of neurons. Some researchers say it is time to revise some aspects of this standard view—such as the notion that the hippocampus is not involved in retrieving older episodic memories (-> multiple trace theory) and that memories become fixed and unchangeable once transferred to the neocortex (-> reconsolidation). Work suggests that learning new information proceeds rapid once a schema exists (schema theory) and may even succeed without the hippocampus (-> fast mapping). Our repository of memories may be less like a library and more like Wikipedia, where each entry is open to editing anytime it is pulled up. This type of plasticity may be crucial for fitting new memories into the existing network of old memories.

Discussion point 1: Plasticity is good, but can we retrieve information without distorting the memory trace? What are the implications for courtroom testimony?

Discussion point 2: If the hippocampus is necessary for the retrieval of all episodic memories (multiple trace theory), why do amnesic patients remember things back in time?

Discussion point 3: I how far does the new view of consolidation foster constructivism?

3. Can we make our brains more plastic? (R. Müri)

Our brains become less flexible as they mature for good reasons: A developing brain gives up some of its plasticity in favor of efficiency and stability. In certain situations, however, more plasticity could be helpful, making it easier for patients to recover after a stroke or spinal cord injury, for example. So, are there ways to turn on—and control—our brain plasticity? Some evidence suggests that the brain's plasticity can be augmented without the danger posed by completely removing the brakes. E.g., Fluoxetine seems to influence brain plasticity, the growth of new neurons throughout life in certain parts of the brain. Although most neurogenesis stops in childhood, two areas of the brain keep producing new neurons: the subventricular zone, which connects to the olfactory bulb; and the subgranular zone of the dentate gyrus, a part of the hippocampus. There are several ways to boost the production of new neurons in these regions; increased physical exercise and exposure to unfamiliar or complex environments are two clear neurogenesis enhancers. Fluoxetine and other antidepressants that act through the dopamine pathway also increase the neuronal birthrate and may keep the newborn neurons flexible longer. What this ongoing production of neurons means for the brain and its rehabilitation following damage, is under investigation. Determining how those new neurons interact with the circuits already in place might help scientists better understand how the circuits are wired in the first place—and how to safely and efficiently rewire when needed.

Discussion point 1: How much stimulation is just enough for maximal brain plasticity?

Discussion point 2: One loses what the other gains?

Discussion point 3: What is best following stroke - cognitive rehabilitation, social interaction, sports, healthy foods or a lot of rest?

4. Depression and hippocampal neurogenesis: A road to remission? (W. Strik)

The neurogenic hypothesis of depression states that new neurons in the adult brain are needed for proper mood control and for antidepressant efficacy. The generation of new neurons in discrete regions of the adult brain has been repeatedly confirmed by using modern techniques. One of these neurogenic niches, the subgranular zone of the dentate gyrus, lies within the hippocampus. Because the hippocampus is a brain region involved in memory and mood control, the discovery of adult neurogenesis launched two parallel investigations into its functional roles in memory and mood control. Humans with depression had decreased hippocampal volume; decreased neurogenesis could lead to a smaller hippocampus. In laboratory animals, antidepressants enhanced hippocampal neurogenesis and did so with a lag time similar to the delay between antidepressant administration and clinical efficacy in humans, reflecting the time of neuronal maturation in the adult hippocampus. In nonhuman primates, stress (a predisposing factor to depression in humans) decreased neurogenesis, and neurogenesis levels were normalized by antidepressants.

Discussion point 1: Are adult-generated hippocampal neurons needed for proper mood control and for antidepressant efficacy?

Discussion point 2: Does stress decrease neurogenesis/neural plasticity and thereby invoke mental illness?

Discussion point 3: Can we trick or even change our genetic make-up (vulnerability genes) by good living?

5. Promoting cognitive performance (F. Mast)

The main pillars of cognitive training are 1) the ability to improve performance, which can 2) transfer to untrained tasks, and 3) the ability to better maintain and coordinate cognitive functions. Recent research shows an emerging interest in cognitive psychology and cognitive neuroscience. Are the effects of cognitive training long-term? There is evidence that specially designed computer games can improve performance on memory and other cognitive tasks in both children and older adults, even months after the training stops. Under certain circumstances brain training can boost performance in cognitive domains that were not trained. Who profits most from training: individuals with poor or good baseline performance?

Discussion point 1: What are the boundary conditions for transfer effects of training?

Discussion point 2: What are the neuronal underpinnings of training effects?

Discussion point 3: How does cognitive training interact with pharmacological interventions?

Symposium 2: Behind the motor manifestations of human diseases

Organization: *Prof. Dr. Dr. med. Kaelin Alain, PD Dr. med. Pollo Claudio, Dr. med. Walther Sebastian*

Location: Auditorium Wölfli

Program:

14:00 **Introduction:** *Alain Kaelin*
Chair: Sebastian Walther

14:10 *Stephan Bohlhalter*
Apraxia: behavioral and neural correlates of a higher-order motor disorder

14:40 *Alain Kaelin*
Sensorimotor interaction in health and disease

15:10 *Sebastian Walther*
Hypokinesia in psychiatric disorders

15:40 *Claudio Pollo*
Translational research in deep brain stimulation for movement disorders

16:10 **Concluding remarks:** *Claudio Pollo*

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