UNIVERSITÄRE PSYCHIATRISCHE DIENSTE BERN

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# Program and Abstracts

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

**http://www.kas.unibe.ch/neuro2015**

Dear participants

It is my pleasure to welcome you to the 10th annual meeting of the Clinical Neuroscience network Bern, which will take place next January 22nd 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 sleep and memory (Prof. P. Peigneux, Bruxelles) and optogenetic modulation of sleep-wake circuits (Prof. A. Adamantidis, Bern), two symposia on the topics of stroke and perception, 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 University Hospital of Psychiatry (infrastructure and catering). A special thank goes to Mr. Grieder for his important assistance in the organization of this meeting.

I hope that the program catches 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

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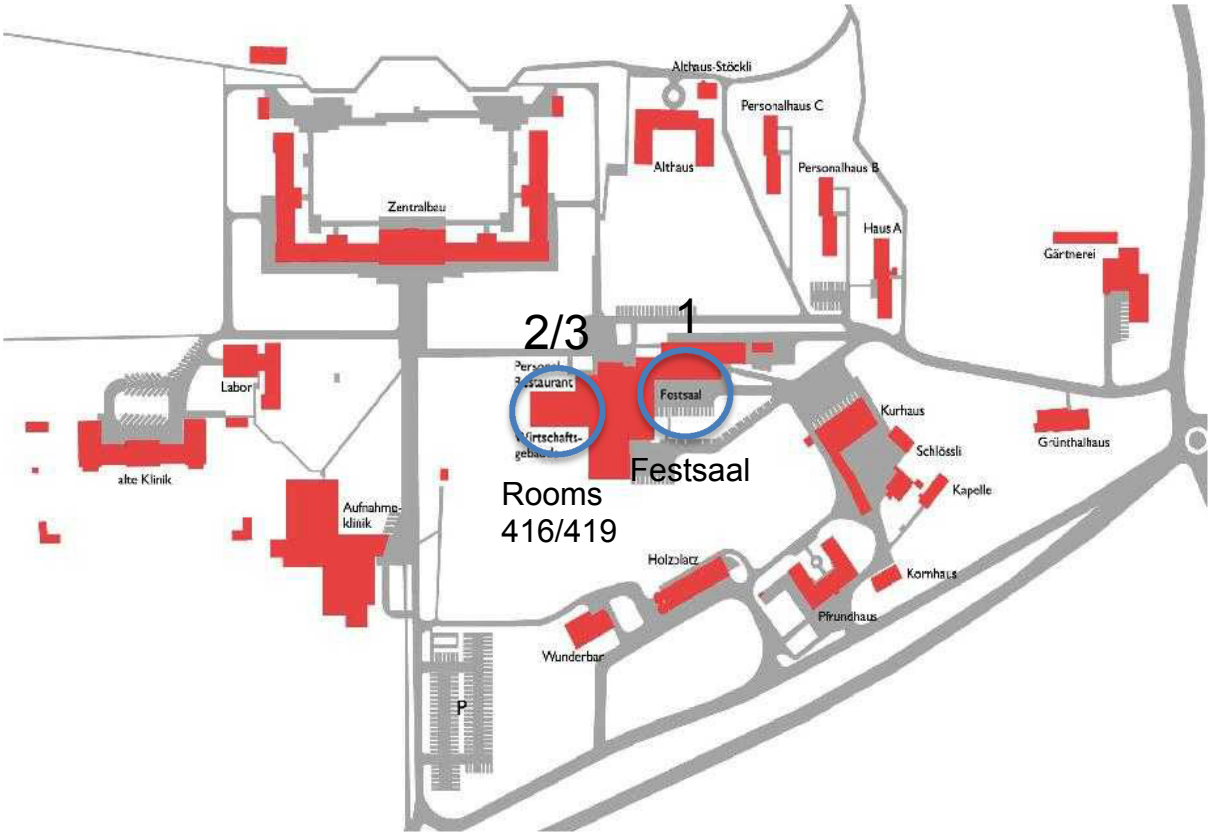
|---|---|---|
| 8:00 – 9:00 | **REGISTRATION AND POSTER SETUP** | |
| 9:00 – 9:15 | **WELCOME ADDRESSES**<br>Martin Täuber, Rector University of Bern<br>Claudio Bassetti, CNB President<br>Werner Strik, Host | |
| 9:15 – 10:00 | **KEY NOTE 1**<br>**«Sleep and memory in the Making. A journey between brain and behavior»**<br>Philippe Peigneux, Bruxelles<br><br>Chair: Claudio Bassetti | |
| 10:00 – 10:30 | **COFFEE BREAK** | |
| 10.30 – 12.00 | **SHORT PRESENTATIONS, 6 selected abstracts à 15 minutes**<br>- Fabian Liechti: **«Lithium attenuates brain injury and improves neurofunctional outcome in experimental meningitis»**<br>- Sebastian Walther: **«Nonverbal social communication and gesture control in schizophrenia»**<br>- Noëmi Eggenberger: **«Perception of co-speech gestures in aphasic patients: an eye movement study»**<br>- Dario Cazzoli: **«Theta burst stimulation improves visual search in spatial neglect independently of attentional load»**<br>- Maria Stein: **«The microstates of emotional change: an ERP investigation»**<br>- Ulf Kallweit: **«Post-H1N1 flu vaccination narcolepsy in Switzerland»**<br>Chairs: René Müri / Andreas Raabe | |
| 12:00 – 14:00 | **POSTER SESSION AND LUNCH** | |
| 14:00 – 15:30 | **SYMPOSIUM I: STROKE**<br>**«Biomarkers in stroke – Interests and Needs of the Clinicians»**<br>Marcel Arnold, Bern<br><br>**«Discovery of Biomarkers in Stroke: from single marker to proteomic approaches»**<br>Joan Montaner, Barcelona<br><br>**«MRI biomarkers of ischemic stroke»**<br>Marwan El Koussy, Bern<br><br>Chairs: Marcel Arnold / Jan Gralla | **SYMPOSIUM II: FROM SENSING TO PERCEIVING**<br>**«Perceptual Rivalry of Homeostatic and Sensory-Evoked Emotions»**<br>Lea Meier, Bern<br><br>**«Hormonal effects on perception»**<br>Janek Lobmaier, Bern<br><br>**«Long-term effects of subliminal perception»**<br>Marc Züst, Bern<br><br>**«Pain perception»**<br>Thomas Nevian, Bern<br><br>Chairs: Katharina Henke / Thomas Dierks |
| 15.30 – 16.00 | **COFFEE BREAK** | **CNB GROUP LEADERS' MEETING** |
| 16:00 – 16:45 | **KEY NOTE 2**<br>**«Optogenetic modulation of sleep-wake circuits in the brain»**<br>Antoine Adamantidis, Bern<br><br>Chair: Thomas Nevian | |
| 16.45 – 17.15 | **POSTER AWARDS**<br>**Committee:** A. Adamantidis, M. Arnold, T. Dierks, J. Gralla, W. Perrig, R. Müri, T. Nevian, C. Pollo, B. Schimmelmann, W. Senn, K. Schindler, H-R. Widmer<br>**Categories:** Clinical research / Basic research animal / Basic research human | |
| 17.15 | **END OF MEETING** | |

Local organizers: M. Grieder, L. Badertscher

Scientific committee: C. Bassetti, T. Dierks, K. Henke, R. Müri, T. Nevian, W. Strik

# Site Map




**1 Wirtschaftsgebäude (Festsaal):**
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Opening addresses
Key note lecture 1
Short presentations
Symposium I
Key note lecture 2
Poster Awards

**2 Wirtschaftsgebäude (basement: room 419):**
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Postersession
Lunch

**3 Wirtschaftsgebäude (basement: room 416):**
Symposium II
CNB group leaders' meeting (for group leaders only)

# Key Note Lecture 1

## Sleep and memory in the Making. A journey between brain and behavior

**Prof. Dr. Philippe Peigneux**

**Neuropsychology and Functional Neuroimaging Research Unit**
**Université Libre de Bruxelles, Belgium**

# Key Note Lecture 2

## Optogenetic modulation of sleep-wake circuits in the brain


### Prof. Dr. Antoine Adamantidis

**Department of Neurology**
**Inselspital, University of Bern**


The neural underpinnings of the sleep-wake cycle involve interactions between sleep-promoting areas such as the anterior hypothalamus, and arousal systems (most are wake-promoting) located in the posterior hypothalamus, the basal forebrain and the brainstem.we and others have implemented *in vivo* optogenetics to probe arousal circuits in the brain with temporal and spatial resolutions relevant to sleep physiology. Optogenetics stands for "*opto*" for optical stimulation and "*genetics*" for genetically targeted cell types – note that optogenetics also include technologies for optical imaging of cellular activities. This emergent technique utilizes light to remotely control genetically targeted neural circuits with millisecond timescale temporal resolution. This technology employs the light-sensitive proteins to either silence or activate targeted cells of interest. As we and others have previously shown, their fast temporal kinetics makes it possible to drive reliable trains of high-frequency action potentials *in vitro* and *in vivo* (using the light-sensitive cation channel Channelrhodopsin-2) or suppress single action potentials (using the light sensitive pumps, halorhodopsin or archeorhodopin. To the functional dissect the neural circuit controlling arousal and sleep (see below) and developed a fiber optic-based system suitable for delivering light *in vivo* to both superficial and deep brain structures in freely-moving mice. This lecture will summarise our recent efforts to better understand the brain mechanisms controlling sleep-wake states, using optogenetic to control hypothalamic circuits *in vitro* and *in vivo.*

# Poster abstracts by discipline

## Clinical research

**ID: 113**

### Structural imaging correlates of impaired nonverbal social perception in schizophrenia

**Sebastian Walther[1], Katharina Stegmayer[1], Petra Viher[1], Andrea Federspiel[1], Roland Wiest[2], Stephan Bohlhalter[3,4], Werner Strik[1]**

*[1]University Hospital of Psychiatry, Bern, Switzerland; [2]Institute of Diagnostic and Interventional Neuroradiology, Inselspital Bern, Switzerland; [3]Neurology and Neurorehabilitation Center, Kantonsspital Luzern, Switzerland; [4]Department of Clinical Research, Inselspital, Bern, Switzerland*

Nonverbal social perception is impaired in schizophrenia. Poor nonverbal social perception has been linked to poor functional outcome. However, the neural correlates of this deficit are unknown. In this study, we aim to investigate whether performance in a nonverbal social perception test was correlated with parameters of structural brain imaging. In 43 patients with schizophrenia spectrum disorders, we applied the Mini-Profile of Nonverbal Sensitivity (Mini-PONS). On the same day, we acquired structural brain imaging at 3T including T1 weighted images and diffusion tensor imaging (DTI). Patients' mean age was 43 years. Average PANSS total scores were 72. Grey matter density was correlated with PONS scores using voxel based morphometry and the intracranial volume as covariate. White matter integrity was correlated with PONS using tract based spatial statistics using age as covariate. VBM results were corrected using family-wise error correction (FWE), DTI results were corrected using Monte-Carlo-Simulations with 5000 iterations
The PONS total score correlated with grey matter density in three clusters at $p < 0.05$ FWE-corrected: left insula, right superior parietal lobe and right precuneus. The subscore for combined face and voice stimuli correlated with grey matter in the left insula (FWE-corrected).
White matter integrity was not correlated with the PONS total score at $p < 0.05$ (corrected). However, white matter integrity was correlated with PONS subscore face and voice stimuli in clusters of the left external capsule close to insula, left superior longitudinal fasciculus close to the superior parietal lobe and in bilateral posterior corona radiata extending in the occipital cortex.
Poor nonverbal social perception in schizophrenia is linked to aberrant brain structure. Particularly the left insula and its adjoining white matter were correlated to PONS performance. The left insula area is critical for correct decoding of gestures, prosody and emotions in healthy subjects. Furthermore, grey matter density of the parietal cortex and white matter integrity of the adjoining superior longitudinal fasciculus were correlated to nonverbal sensitivity. These parietal areas are part of a gesture network. Structural alterations in critical brain areas in schizophrenia contribute to poor understanding of nonverbal communication.

*Keywords:* structural imaging, schizophrenia, social brain

**ID: 114**

### Postural knowledge of gestures in schizophrenia is linked to structural alterations in key regions of gesture processing and connecting long association fibers

**Katharina Stegmayer[1], Petra Viher[1], Tim Vanbellingen[2,3], Andrea Federspiel[1], Stephan Bohlhalter[2,3], Werner Strik[1], Roland Wiest[4], Sebastian Walther[1]**

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Higher order processes such as recognition of gestures rely on a network of distinct and distant brain areas. Particularly the role of key regions such as the left inferior frontal gyrus (IFG) and the inferior parietal lobe is subject to ongoing debate. Schizophrenia patients suffer from impaired gesture performance and recognition. However, neural correlates of impaired gesture recognition have not yet been investigated. We therefore aim to test associations between structural brain imaging and postural knowledge in schizophrenia using voxel based morphometry (VBM) and tract based spatial statistics (TBSS).
In total, 44 patients with schizophrenia (DSM-5 criteria; 59% men, mean age 38) underwent structural MR imaging

and performed the comprehensive postural knowledge task (PKT) for hand gestures. All patients except four were treated with antipsychotics. T1-weighted images were processed using SPM8 and DTI-data using FSL TBSS routines. We explored correlations of PKT scores and gray matter (GM) volume in VBM data and correlations of PKT scores and white matter (WM) integrity in TBSS data. Results were corrected for multiple comparisons using family wise error correction.
Impaired postural knowledge was related to reduced GM volume and WM integrity. Whole brain analyses revealed effects of postural knowledge on gray matter volume within right IFG extending to the insula, the superior parietal lobe and left hippocampus. Furthermore, significant correlations within fiber tracts connecting these regions - particularly alterations within the bilateral cingulum bundle and cingulum, the right superior longitudinal fasciculus, the right anterior limb of internal capsule, and the left fasciculus uncinatus - were associated with PKT performance
Postural knowledge performance in schizophrenia patients was associated with GM volume of meaningful brain regions. Our results are in line with the literature as particularly lesions in the left IFG were found to predict poor gesture recognition in brain damaged patients. In addition an effect of postural knowledge on WM integrity was shown within fiber tracts connecting key regions of gesture processing. Furthermore, hippocampus is part of a brain system responsible for spatial memory and navigation and volume reduction is a consistent structural finding in schizophrenia. The results suggest that structural brain alterations in the common gesture network contribute to impaired postural knowledge in schizophrenia.

*Keywords:* structural imaging, schizophrenia, gesture knowledge

## ID: 116

## Prevalence of dysnatremias and their implication on outcome during acute ischemic stroke and transient ischemic attack: a cross-sectional analysis

**Gregor Lindner[1], Mirjam R. Heldner[2], Georg-Christian Funk[3], Marcel Arnold[2], Christoph Schwarz[4], Alexander B. Leichtle[5], Georg M. Fiedler[5], Jan Gralla[6], Heinrich P. Mattle[2], Aristomenis K. Exadaktylos[1], Urs Fischer[2]**

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Aim: Hypo- and hypernatremia are the most common electrolyte disorders in hospitalized patients. Their impact on outcome has been described in patients with cerebral hemorrhage. However, data in patients with ischemic stroke and transient ischemic attacks (TIA) are scarce. We aimed to assess the prevalence of dysnatremias in stroke and TIA patients and to investigate the impact of dysnatremias on outcome.
Methods: In this cross-sectional analysis we included all patients with acute ischemic stroke (1807) and TIA (157) admitted to the department of Neurology between 01 January 2004 and 31 March 2012 with a measurement of serum sodium at baseline. Clinical data on admission (NIHSS score, Charlson comorbidity index, etiology, cardiovascular risk factors), data on therapy (conservative versus thrombolysis) and outcome at 3 months were assessed prospectively.
Results: 161 of 1964 patients (8%) included in the study had hyponatremia and 56 (3%) hypernatremia. Median serum sodium concentration on admission was 140 mmol/L (138 to 141). 219 patients (11%) died during the observation period. Patients with dysnatremias had higher mortality rates. Patients with serum sodium <140 mmol/L had a significantly lower survival probability (85% vs. 90%, p=0.0022). Moreover, in the multivariate regression analysis serum sodium <140 mmol/L, higher age and higher NIHSS on admission were independent predictors of an increased mortality.
Conclusions: Hypo- and hypernatremia are common in patients with an acute ischemic stroke or TIA, with associated higher mortality rates in these patients. Serum sodium <140 mmol/L was an independent predictor of mortality 3 months after acute ischemic stroke or TIA.

*Keywords:* dysnatremias, acute ischemic stroke, TIA, cross-sectional analysis, outcome

**ID: 119**

## Enhancing treatment effects by combining continuous theta burst stimulation with smooth pursuit training

**Simone Hopfner[1], Dario Cazzoli[1,2,5], René Martin Müri[1,3,4], Tobias Nef[4,5], Urs Peter Mosimann[4,5,7], Stephan Bohlhalter[1,6], Tim Vanbellingen[1,6], Thomas Nyffeler[1,4,6]**

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Continuous theta burst stimulation (cTBS) represents a promising approach in the treatment of neglect syndrom. However, it is not known whether cTBS in conjunction with another technique may enhance the therapeutic effects. In the present sham-controlled study, we aimed to combine cTBS with smooth pursuit training (SPT), another method known to effectively improve neglect symptoms, and to evaluate whether this combination would result in a stronger effect than SPT alone. Eighteen patients with left spatial neglect after right-hemispheric stroke were included in the study and performed a cancellation task on a large 54.6'' touchscreen monitor. A sequential application of cTBS and SPT induced a significantly greater improvement of neglect than SPT alone. After the combined application of these two methods, patients detected significantly more targets and their cancellation behaviour presented a significantly greater shift towards the contralesional hemispace. We suggest that a combined, sequential application of cTBS and SPT have additional therapeutic effects compared to either method alone.

*Keywords:* Spatial neglect; pursuit training; continuous theta burst simulation; cancellation task

**ID: 120**

## Perception of sleepiness in a driving simulator is better than perception in the maintenance of wakefulness test

**David R. Schreier, Corinne Roth, Uli Herrmann, Johannes Mathis**

*Sleep-Wake Centre, Dept. of Neurology, Inselspital, Bern*

Objectives: Healthy sleep deprived controls signalled their sleepiness after onset of the first sleep-fragment (SF) in one third of all trials of a maintenance of wakefulness test (MWT) but never in the driving simulator (DSim). Here we aimed to validate these results in patients with sleep-wake disorders.
Methods: Overall 40 healthy sleep deprived controls were tested in the MWT (22.3 y ± 2.3). Thereof 16 completed four MWT's and 24 completed one single MWT and one DSim trial. They were instructed to signal sleepiness as soon as they realised the first symptoms of sleepiness or tiredness by pressing a button. They were rewarded for optimal performance. So far only 12 patients with sleep-wake disorders were included, while testing them for their fitness-to-drive in 4 MWT's and a DSim. A SF was defined by a miniperiod (≥ 3 s) of theta dominance in the EEG while the eyes were closed.
Results: In 11 of the 48 MWT's (23%) patients signalled sleepiness after the first SF in the MWT almost similar to controls (in 27 of the 88 MWT's, 31%). In the DSim no SF and therefore no late signalling occurred in patients whereas at least one SF occurred in 13 of the 24 controls after sleep deprivation, but all controls signalled their sleepiness beforehand.
Conclusion: Similar to healthy controls, optimally treated sleep-patients can fall asleep without prior subjective perception of sleepiness in the MWT, but not in the driving simulator.

*Keywords:* excessive daytime sleepiness, driving simulator, fitness-to-drive, microsleep, vigilance assessment

**ID: 121**

## Chow-Liu Trees Are Sufficient Predictive Models For Reproducing Key Features of Functional Networks of Periictal EEG Time-Series

**Andreas Steimer, Frederic Zubler, Heidemarie Gast, Kaspar Schindler**

*Inselspital Bern, Switzerland*

Seizure freedom in patients suffering from pharmacoresistant epilepsies is still not achieved in 20-30% of all cases. Hence, current therapies need to be improved, based on a more complete understanding of ictogenesis. In this respect, the analysis of functional networks derived from intracranial electroencephalographic (iEEG) data has recently become a standard tool. Functional networks however are purely descriptive models and thus are conceptually unable to predict fundamental features of iEEG time-series, e.g. in the context of therapeutical brain stimulation. Here we present some first steps towards overcoming the limitations of functional network analysis, by showing that its results are implied by a simple predictive model of time-sliced iEEG time-series. More specifically, we learn distinct Graphical models (so called Chow-Liu(CL) trees) as models for the spatial dependencies between iEEG signals. Bayesian inference is then applied to the CL trees, allowing for an analytic derivation/prediction of functional networks, based on thresholding of the absolute value Pearson correlation coefficient(CC) matrix. Using various measures, the thus obtained networks are then compared to those which were derived in the classical way from the empirical CC-matrix. In the high threshold limit we find (a) an excellent agreement between the two networks and (b) key features of periictal networks as they have previously been reported in the literature. Overall, this work shows the validity of CL-trees as simple, spatially predictive models for periictal iEEG data.

*Keywords:* Epilepsy, periictal EEG, predictive modeling, Bayesian inference, Chow-Liu tree

**ID: 125**

## Gesture use in aphasic patients: Evidence from eye tracking during face to face interaction

**Basil Preisig[1], Noëmi Eggenberger[1], Giuseppe Zito[2], Rahel Schumacher[1], Simone Hopfner[1], Thomas Nyffeler[1,3], Klemens Gutbrod[4], René Müri[1,4,5]**

*[1]Perception and Eye Movement Laboratory, Departments of Neurology and Clinical Research, Inselspital, University Hospital Bern, and University of Bern, Switzerland; [2]ARTORG Center for Biomedical Engineering Research, University of Bern, Switzerland; [3]Neurology and Neurorehabilitation Center, Department of Internal Medicine, Luzerner Kantonsspital, Switzerland; [4]Division of Cognitive and Restorative Neurology, Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland; [5]Gerontechnology and Rehabilitation Group, University of Bern, Bern, Switzerland*

Co-speech gestures are a part of non-verbal communication in natural conversations. A speaker conveys nonverbal information to the listener by spontaneous hand movements. At the same time, gesturing also facilitates the speaker's own verbal production. Aphasic patients are restricted in speech production and comprehension. It is unclear to which extent aphasic patients make compensatory use of gestures to express information that cannot be expressed through speech. Moreover, it is unknown whether aphasic patients also gather information from co-speech gestures. In a previous study, we used eye movement recordings to explore if aphasic patients adapt their visual exploration strategies while watching natural interactions. Similar to healthy controls, aphasic patients attend the speaking dialog partner more if he or she is gesturing. This indicates that aphasic patients might be able to disambiguate speech perception by non-verbal cues. In the present study, we are investigating production and perception of co-speech gestures in aphasic patients while they are engaged in face-to-face interaction. We aim to reveal compensatory strategies on the level of language perception and language production. Preliminary data will be presented.

*Keywords:* Gestures, visual exploration, dialogue, aphasia, apraxia, eye movements

**ID: 126**

## Interhemispheric changes after stroke during childhood: a case study

**Salome Kornfeld[1,2], Juan Antonio Delgado Rodriguez[1,4], Sebastian Grunt[1], Regula Everts[1,2], Roland Wiest[3], Christian Weisstanner[3], Claus Kiefer[3], Maja Steinlin[1,2]**

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Aims: Compared to adults, data on reorganizational patterns in resting-state brain networks of children who suffered an arterial ischemic (AIS) stroke is rare. We therefore examined changes in resting-state activity of a seven-year old boy 1 month and 4 months after an acute right sided periventricular AIS.
Methods: One boy who recently suffered an acute AIS was examined. Magnet resonance (MR) images were acquired using a 3T scanner. High-resolution T1-weighted MR structural images were recorded using a magnetization prepared rapid gradient-echo 3D sequence and functional imaging was performed using a multiband echo planar imaging sequence. Conn toolbox 14 was used to descriptively compare resting-state activity in different regions of interest.
Results: 1 month post-stroke, a clear activity shift to the contra-lesional hemisphere resulting in bilateral activation is visible in a number of different regions, such as the primary motor cortex, the inferior frontal cortex pars triangularis, the somatosensory cortex and the primary visual cortex. In those areas, interhemispheric balance is reattained 4 months post-stroke.
Conclusions: The results suggest that in the child's brain, dynamic reorganization processes in resting-state activity over time might happen. As the hemispheric shift to the contra-lesional side 1 month post-stroke and the rebalance 4 month post-stroke are visible in different brain areas, we assume that functional reorganization patterns might be of global character. The present results are based on one single case only, but may serve as an important indicator for dynamic changes in the pediatric brain connectivity after stroke. Therefore, further analyses including more children are necessary.

*Keywords:* arterial ischemic stroke, resting-state activity, connectivity changes

**ID: 127**

## Perception of co-speech gestures in aphasic patients: an eye movement study

**Noëmi Eggenberger[1], Basil Preisig[1], Simone Hopfner[1], Tim Vanbellingen[1], Rahel Schumacher[1], Thomas Nyffeler[2], Klemens Gutbrod[3], René Müri[1]**

*[1]Departments of Neurology and Clinical Research, Inselspital Bern; [2]Neurology and Neurorehabilitation Center, Kantonsspital Luzern; [3]Division of Cognitive and Restorative Neurology, Inselspital Bern*

Introduction: Gesturing, including co-speech gestures, is a crucial part of human communication. The present study aimed to investigate the perception of speech and gestures, and in particular the influence of congruence between speech and gesture on both verbal comprehension and visual exploration. Healthy subjects spend about 88-95% of the time fixating a speaker's face, while only a minority of fixations is directed at gestures. It is unclear whether aphasic patients display a similar pattern.
Method: Twenty aphasic patients and 30 healthy controls watched videos in which speech was either combined with congruent, incongruent, or meaningless gestures. Comprehension was assessed with a decision task, while remote eye-tracking allowed analysis of visual exploration of predefined areas of interest.
Results: Patients displayed a decreased accuracy in incongruent sequences whereas congruence between speech and gesture led to an increase in accuracy. Furthermore, patients fixated significantly less on the face and slightly more on the hands compared to controls.
Conclusion: Co-speech gestures play an important role for aphasic patients as they modulate verbal comprehension. Incongruent gestures evoke significant interference and deteriorate patients' comprehension. In contrast, congruent gestures enhance comprehension in aphasic patients, which might be valuable for clinical and therapeutical purposes.

*Keywords:* Gestures, aphasia, eye movements, visual exploration, verbal comprehension

**ID: 128**

## Cognitive performance is associated with cortical thickness in children born preterm

**Ines Mürner-Lavanchy[1,3,4], Maja Steinlin[1,4], Christian Rummel[2], Regula Everts[1,2,4]**

*[1]Division of Neuropediatrics, Development and Rehabilitation, Children's University Hospital, Inselspital,; [2]University Institute of Diagnostic and Interventional Neuroradiology, University Hospital, Inselspital; [3]Institute of Psychology, University of Bern; [4]Centre for Cognition, Learning and Memory, University of Bern*

Background: Premature birth is accompanied by an increased risk of perinatal brain injury and has serious consequences on brain development. In addition to differences in grey and white matter volume, alterations in cortical thickness have been detected in very preterm born children by more recent methods. These alterations have been suggested to parallel cognitive functioning, which is often at risk in very preterm children. In school-aged very preterm children, there is a lack of studies on the exact relationship between cognitive performance and cortical thickness. The closer investigation of this association in very preterm and term born children may yield important results on atypical as well as typical developmental trajectories of structure-function relationships.
Methods: Forty very preterm (<32 weeks gestational age and/or <1500 gram birth weight) and 30 term born children were included in the study. All children had normal neonatal cerebral ultrasound, no severe chronic illness or medical problems and IQ > 85. The automated surface reconstruction software FreeSurfer was applied to obtain cortical thickness, measured as the shortest distance between tissue boundaries (gray matter/white matter and gray matter/cerebrospinal fluid). An extensive neuropsychological test battery including tests of language, memory, learning, executive functions and attention was administered prior to the MRI examination. To examine the association between cognitive performance and cortical thickness one-sided partial Spearman correlations with sex as covariate were computed with SPSS.
Results: Controls were better than preterms in the domain of verbal learning (U=387, z=-2.65,p=.008). Mean performance did not differ between preterms and controls regarding all other cognitive domains. In preterms, cortical thickness in the right hemisphere correlated positively with working memory (r=.327, p=.026), visuomotor (r=.288, p=.045), verbal learning (r=.472, p=.002) and shifting performance (r=.284, p=.047). Cortical thickness in the left hemisphere correlated positively with working memory (r=.348, p=.010) and verbal learning performance (r=.531, p<.001). In controls, cortical thickness did not correlate with cognitive performance.
Discussion: The association between higher cortical thickness over both hemispheres and better cognitive performance indicates global structure-function relationships in very preterm children. While term born children do not present any link between cortical thickness and cognitive functioning, it is possible that in very preterm children, this relationship serves as a neural compensation for their subtle cognitive deficits in comparison with term born children.

*Keywords:* preterm birth, cognition, cortical thickness, structure-function relationship

**ID: 130**

## Theta burst stimulation improves visual search in spatial neglect independently of attentional load

**Dario Cazzoli[1,2], Clive R Rosenthal[2], Christopher Kennard[2], Giuseppe A Zito[1], René M Müri[1,3], Thomas Nyffeler[3,4]**

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The severity of spatial neglect, i.e., the failure to orient, attend, and respond towards the contralesional side of space, is considerably exacerbated by increases in visual attentional load. It would thus be highly desirable to identify a therapeutic intervention that ameliorates neglect independently of attentional load. Transcranial magnetic stimulation has been shown to reduce neglect severity, the interaction with attentional load is however unknown.
Here, in ten neglect patients, we examined the effect of a continuous theta burst stimulation protocol on neglect severity as a function of high and low attentional load conditions. Search efficiency was assessed by recording the accuracy of visual target detection, and eye movements.
Our results show that continuous theta burst stimulation significantly ameliorates neglect irrespective of the attentional load, equating target detection between low and high load conditions. The results also demonstrate that the significant amelioration in search efficiency was correlated with a re-distribution of visual fixations towards the contralesional side of space.

The application of continuous theta burst stimulation in neglect thus represents a substantive advance, since it is unprecedented in triggering an amelioration of neglect irrespective of the attentional load.

*Keywords:* hemispatial neglect; stroke; repetitive transcranial magnetic stimulation (rTMS); visual attention; eye movements

**ID: 133**

## Detecting activities of daily living of healthy subjects and dementia patients using wireless sensors

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Background: The demographic shift in the global population leads to an increasing prevalence of age-associated disorders, such as Alzheimer's disease and other types of dementia. With the progression of the disease, the risk for institutional care increases, which contrasts with the desire of most elderly who would like to live in their known home-environment as long as possible. In this regard, the occurrence, performance and duration of different activities of daily living (ADL) are important indicators of functional ability. To provide good and effective care and to support aging in place, caregivers need to know how good patients cope with ADL, in particular when patients are unsupervised or are alone at home.
Objective: In contrast to other commercial products available on the market, our aim was to develop a passive, non-intrusive, wireless sensor system to capture ambient environmental data from subject home's and to develop necessary algorithms to recognize the ADL from the captured data.
Methods: The sensor system consists of ten wireless sensor boxes that are distributed in every room of the subject's home. The system was set up in the homes of healthy subjects (N=10) and dementia patients (N=10) to acquire environmental data for 20 days. The collected data was analyzed and classified into ADL using classifiers developed in-house. Activity maps of the ADL were calculated to compare the behavior patterns of both groups (healthy subjects vs. dementia patients). The ADL performance was assessed using Poincare plots.
Results: Ten healthy participants (6 women, 4 men; mean age = 76.7 years; SD = 8.2 years; age range 64-94 years) and ten dementia patients (6 women, 4 men; mean age = 73.9 years; SD = 6.7 years; age range 63-87 years) were included in the study. From the collected data, specific behavior pattern could be determined and allotted to eight ADL. The behavior patterns of the two groups show significant differences. The healthy controls show more regular patterns and a more structured daily routine than the dementia patients.
Conclusions: The wireless sensor system can identify data patterns and assign these to specific ADL. Owing to its non-intrusive approach, the system has a high potential to improve care and provides detailed information about the patient's cognitive status. Moreover, current and future clinical trials of new drug interventions, in dementia patients will need to prove their effects on ADL where accurate and reliable measurements will be of great importance.

*Keywords:* activity of daily living, dementia, sensor, monitoring, recognition

**ID: 135**

## Structural imaging correlates of impaired gesture performance in schizophrenia

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Background: Schizophrenia is associated with poor nonverbal communication. Impairments in the performance of hand gestures have been shown in 67 % of patients with schizophrenia. These deficits are similar to those seen in Apraxia, which is often due to lesions in the inferior parietal (IPL) lobe, insula and inferior frontal gyrus (IFG). In Schizophrenia however, the neural correlates are unknown. Therefore, we investigated structural correlates of impaired gesture performance in schizophrenia.

Methods: In 43 patients with schizophrenia spectrum disorders, gesture performance was assessed by the comprehensive Test of Upper Limb Apraxia (TULIA). Performance was video recorded and blindly rated for accuracy. Structural brain imaging was measured in all patients using a 3-T MR Scanner. Grey matter density was correlated with TULIA scores using Whole-Brain Voxel-Based Morphometry (VBM) and intracranial volume as covariate. White matter integrity was correlated with TULIA scores using Tract-Based Spatial Statistics (TBSS) and age as covariate.
Results: The TULIA total score correlated with grey matter density in three clusters at $p < 0 .05$ FWE-corrected: right insula, posterior cingulate cortex and anterior cingulate cortex. Poor gesture performance was associated with reduced grey matter density in these clusters. In addition white matter integrity correlated significant at $p < 0.05$ (corrected) with the TULIA total score in clusters of the frontal white matter in the anterior cingulum and corona radiate bilaterally as well as left uncinate fasciculus. These clusters were located close to the anterior cingulate cortex cluster of the grey matter results.
Conclusions: Aberrant brain structure is associated with poor gesture performance in schizophrenia. Particularly in key regions of the praxis network, i.e. insula, parietal cortex, we detected correlations of gesture performance and grey and white matter markers. In addition, the anterior cingulate cortex grey matter was correlated to gesture performance, a region implicated in action planning and control. Therefore, specific brain structural alterations may contribute to deficits in nonverbal communication in schizophrenia.

*Keywords:* schizophrenia, gesture production, white matter

## ID: 136

## Deficits of gesture performance in first episode patients with schizophrenia disorder

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Objective: Gesturing plays an import role in social behaviour and social learning. Deficits of gesture performance have been shown in schizophrenia. They may contribute to impaired social functioning and functional outcome. Information about deficits during the course of the disease and presence of severity and pattern of impairment in first episode patients is missing. Hence we aimed to investigate gesture performance in first episode patients compared to multiple episode patients with schizophrenia and healthy controls.
Method: In 14 first episode, 14 multiple episode patients and 16 healthy controls matched for age, gender and education gesture performance was assessed by the comprehensive Test of Upper Limb Apraxia (TULIA). Performance of two domains of gesturing - imitation and pantomime - was investigated. We assessed videotapes of performance of meaningless, transitive (tool related) and intransitive (symbolic non-tool related) gestures. Ratings of gesture performance were blinded.
Results: Patients with multiple episodes had severe gestural deficits. For almost all gesture categories performance was significantly worse in multiple episode patients compared to first episode patients. First episode patients demonstrated subtle deficits with a comparable pattern.
Conclusion: Severe deficits of gesture performance were found after multiple psychotic episodes while only mild impairments were found in first episode patients, independent of age, gender, education, negative symptoms and extrapyramidal motor function. The results indicate that gesture performance is impairment at onset of the disease and is likely to further deteriorate during the course of the disease.

*Keywords:* neurodevelopment, nonverbal communication, imitation, pantomime, hand gesture

**ID: 137**

## Therapeutic response and neurobiological prediction markers in auditory verbal hallucinations

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Introduction: With a prevalence of 1.1% of the population, schizophrenia is a serious and severe mental disorder. One of the most common symptoms are auditory verbal hallucinations (AVH) occurring in up to 80% of patients. However, pharmacotherapy does not ameliorate AVH in 20-30 % of patients. Recent neurobiological research examined transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) as treatment alternatives for AVH. Treatment is thought to reduce hyper activation in the superior temporal lobe (STL) and involved language networks. Therefore, we aim to investigate network functional connectivity in patients with AVH. We especially focus on resting state networks (RSN) which were found to be altered in schizophrenia patients, however, the exact localization and form is still discussed. We further aim to find possible changes in connectivity induced by the different treatments.
Methods: A total of 100 patients will be recruited between the age of 16 and 65 with a diagnosis of either Schizophrenia (F20) or Schizoaffective disorder (F25), prone to AVH in the acute phases of the disorder. Patients declining medicinal treatment are assigned to either TMS, placebo TMS, tDCS or placebo tDCS. Patients receiving treatment as usual (TAU) will serve as control group. For the assessment of the neurobiology related to the therapy of AVH, pre- and post-MRI and EEG will be conducted.
Hypothesis: 1. Higher responder rates for brain stimulation than for TAU. 2. Brain stimulation will decrease hyperactivity in affected language networks. 3. Patients with more focussed increase of RSN connectivity/activity in language circuits, will show higher responder rates to brain stimulation. 4. Patients with more diffuse connectivity and/or activity will respond better to TAU.
Relevance: Studies with TMS and tDCS have until now only been performed on patients who are non-responders to TAU and this might have influenced the probability of successful intervention. Therefore, we aims to fill this gap by testing TMS and tDCS as primary treatment option in patients declining conventional medication. Further, the investigation of RSN will contribute to a better understanding of disturbances and changes in brain networks caused by schizophrenia and AVH. Thus, it will deepen our understanding of the intrinsic neurophysiological architecture and show if TMS and/or tDCS have an impact on affected networks. In summary, this study will contribute to the evaluation of TMS and/or tDCS as alternative treatment options to TAU.

*Keywords:* TMS, tDCS, AVH, Schizophrenia, RSN

**ID: 138**

## Difficulties of gesture performance: a potential endophenotype of schizophrenia?

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Introduction: Disturbed social functioning including nonverbal communication is a core characteristic of schizophrenia. One crucial factor of nonverbal communication is gesturing. Gesturing is impaired in patients with schizophrenia. We aimed to test whether impairments in gesture performance would be present in unaffected first degree relatives of schizophrenia patients and could therefore be a potential marker of the disorder.
Method: We investigated 29 unaffected first degree relatives of schizophrenia patients and 29 control subjects matched for age, gender, education level and income. Participants performed a comprehensive test for gesture performance. In addition motor behavior, working memory and frontal lobe function was assessed. Furthermore psychic experience was assessed in first degree relatives.
Results: First degree relatives of schizophrenia patients showed relatively severe difficulties during gesture performance. In fact, 24% of the relatives scored below the cut-off scores. In addition motor behavior was impaired in relatives. Relatives showed abnormal involuntary movements (AIMS), neurological soft signs (NSS) and abnormalities in movement (Modified Rogers Scale, MRS) as more prevalent. Moreover gesturing was predicted by impaired motor behavior in relatives.
Discussion: Impairments in gesture performance may be a potential marker of vulnerability for schizophrenia.

*Keywords:* endophenoty, nonverbal communication, imitation, pantomime, hand gesture

**ID: 139**

## Schizophrenia symptom dimensions are associated with cerebral blood flow reduction of the amygdala, the heschl's gyrus and the anterior cingulate cortex

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Background: In order to match behavioural dimensions to specific brain circuitries, we developed the Bern Psychopathology scale (BPS) grouping psychotic symptoms into three biologically relevant dimensions, related to language, motor and emotional dysregulation. The aim of the present study was to investigate whether these dimensions could be linked to abnormalities in resting state cerebral blood flow (CBF) in the respective brain systems.
Methods: 44 patients with schizophrenia (DSM-5 criteria; 59% men, mean age 38) underwent structural 3T-MR imaging. All patients but four were treated with typical or atypical antipsychotics. Psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS) and the BPS. Based on the severity of BPS ratings, patients were grouped into three groups in each dimension (severe, mild, no dysregulation). CBF was measured by arterial spin labeling and was analyzed with own MATLAB programs. The primary focus of the analyses was the effect of the symptom dimensions on CBF. CBF differences were explored among subgroups using whole brain ANOVAs to CBF data.
Results: Subgroups did not differ in duration of illness, number of episodes, Chlorpromazine equivalent dosage, PANSS scores, duration of education, age, gender or global cerebral blood flow. Whole brain analysis revealed different CBF patterns for each dimension. Language dysregulation was associated with increased CBF in Heschl's gyrus (p(FEW-corr) = 0.039), while motor dysregulation was associated with increased CBF in the ACC (p(FEW-corr) = 0.024). Emotional dysregulation showed no effect applying family wise error correction for multiple comparision. However, exploratory analysis revealed a main effect of emotional dysregulation in the amygdala (p<0.001-uncorr).
Discussion: Using the BPS dimensions, we identified subgroups of patients based on the severity of psychotic symptoms referring to language, motor and emotional dysregulation. The associations of these symptom dimensions with regional CBF patterns were meaningful and specific for the respective brain circuitries: Heschl's gyrus as part of the language system, amygdala as crucial for emotional regulation, and the ACC for higher order motor control. The results indicate a central role of different specialized brain systems in generating the different symptom patterns of schizophrenia, and provide further evidence that biological and clinical heterogeneity of schizophrenia can be disentangled.

**ID: 141**

## 4-choice reaction time task reveals abnormalities in schizophrenia

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Hemispheric specialization is an important mechanism to enhance information processing. A reduction of normal hemispheric asymmetry was observed in schizophrenia. The right hemisphere is dominant in visuospatial perception. Faster left hand responses in choice reaction time tasks (CRT) also confirm this. In schizophrenia, however, deficits of the left hemisphere can also contribute to impaired visuospatial perception.
This study aimed to further elucidate the link between hemispheric specialization and schizophrenia by relating differences in the activity of the left and right hemispheres during a lateralized CRT task.
28 healthy controls, 18 schizophrenic patients with hallucinations, and 11 non-hallucinating schizophrenic patients performed a simple 4-CRT task. Four stimuli were presented on a computer monitor to stimulate the left lateral (LL), left medial (ML), right medial (MR), or right lateral (RR) visual field, while EEG was recorded from 76 channels. Participants were asked to respond to a target by pressing the corresponding key.
For the analysis, spatially defined transiently stable states of the ERP (microstates – MS) were identified and quantified for latency and amplitude in each subject as function of visual field and eccentricity.
Response accuracy did not differ between groups and between conditions in patients. In healthy group, differences in accuracy were found only between RR (accuracy=0.985) and MR (accuracy=0.97) conditions (p<0.019). Right hand responses were faster in all three groups. RT differences were not significant, except between RR (RT=435.305

ms) and ML (RT=470.366 ms) conditions ($p<0.018$) in healthy group. RTs were shorter in healthy group ($p<0.05$) compared to patients groups. RTs were slower in non-hallucinating patients group, but RTs did not differ significantly between patients groups.
Across all subjects, the N1 was contralateral to the stimulation side. The two classes of N1-MSs (~100-250 ms) were identified as corresponding to either right (MS 1), or left (MS 2) hemisphere activation. N1-MSs showed stronger activity over the left hemisphere, and medial conditions evoked stronger activation than lateral conditions in both hemispheres ($p<0.05$). P3-MS showed stronger activity over the right hemisphere, and medial stimulation evoked stronger activation than lateral stimulation in both hemispheres ($p<0.05$). The MSs timing had a clear structure in healthy group. However, this structure was less clear in patients groups. Moreover, P3 was associated with different topography MS in non-hallucinating patients group.
The study highlights the importance of understanding the hemispheric specialization and visuospatial information processing in schizophrenia. Results showed that non-hallucinating schizophrenic patients have more abnormalities than hallucinating patients.

*Keywords:* schizophrenia, choice reaction time task, microstates, visuospatial processing, ERP

**ID: 142**

## Deficits in fine motor function are associated with reductions of grey matter volume and resting state perfusion in the motor system in schizophrenia

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Introduction: Motor symptoms are an integral part of the clinical presentation of schizophrenia. Disturbances of fine motor function are frequent. However, only limited knowledge exists about underlying neural correlates. We therefore aimed to investigate associations of fine motor function with whole brain gray matter (GM) volume as well as resting state cerebral blood flow (rCBF) in schizophrenia patients. Our hypothesis was to find alterations in the motor loop associated with fine motor function.
Method: In total 44 schizophrenia patients (DSM-V) underwent 3T MRI-neuroimaging. We implemented two fine motor tasks differing in complexity level: the finger tapping (FT; tapping the index finger against the thumb) and the coin rotation task (CR; rotating a coin using three fingers). The participants were instructed to perform the task as accurate and quickly as possible. In addition, parkinsonism was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS). The main interest was to investigate the effect of task performance on GM volume and rCBF. Therefore task performance was correlated with GM volume (covariates total intracranial volume and UPDRS motor part) and rCBF (covariate UPDRS) using multiple regression analyses. A uniform statistical threshold of p-uncorr < 0.001 (min. cluster size = 17: equivalent to a map-wise false positive rate of alpha < 0.0001 using a Monte Carlo procedure) was applied.
Results: Poor task performance was associated with reduced GM volume and reduced CBF in the motor system. In particular, FT was associated with gray matter volume of the left thalamus, the left pre-SMA, bilateral in the cerebellum, the SMA and the primary motor cortex. In addition, poor FT was associated with reduced CBF in the left cerebellum and the left inferior frontal lobe. Furthermore, poor CR performance was associated with reduced gray matter volume of the dorsal premotor cortex, the pre-SMA, the SMA, the primary cortex and the cerebellum. In addition, poor CR was associated with reduced CBF in the left ventral premotor cortex and the posterior cingulate cortex.
Conclusion: In summary, we found correlations of GM volume as well as resting state perfusion associated with task performance in various regions of the motor system. Difficulties in complex fine motor performance were associated with alterations in higher cortical motor control areas. These findings were corrected for parkinsonism to adjust for treatment side effects. In sum, the results argue for specific alterations of the motor system in schizophrenia as relevant for impaired fine motor function beyond parkinsonism.

*Keywords:* fine motor function, schizophrenia, ASL, VBM, coin rotation task

**ID: 144**

## EEG- Neurofeedback as a Treatment Method for Auditory Verbal Hallucinations - Mixed Effect Modelling in EEG-Neurofeedback

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In about 20-30% of schizophrenia patients, auditory verbal hallucinations are resistant to the conventional pharmacological treatment, and alternative treatment strategies are needed.
In schizophrenia patients, a global reduction of the event-related potential component N100 has been found, which is even more pronounced during the presence of auditory verbal hallucinations. It has been hypothesized that the reduction of the N100 results from a dysfunctional activation of the primary auditory cortex by inner speech, which reduces its responsiveness to external stimuli.
In this study, we intend to use neurofeedback to modify the N100 amplitude in patients with hallucinations. Neurofeedback is an operant learning mechanism allowing to achieve self-control over brain activity and thereby reach an improvement of certain processes or mental states in clinical or non-clinical implications. However, control is typically only gained thru repeated training sessions, and not all subjects learn equally well. Thus, the quantification of learning needs appropriate models.
Our study provides an intuitive visual EEG-neurofeedback training to train the upregulation of the N100. We currently train 30 schizophrenia patients with a training schedule that forsees 20 sessions per patient.
Neurofeedback studies produce multilevel data: Each subject yields measurements that may vary within and between sessions, and within and between conditions. Furthermore, different subjects may show different learning curves. An exhaustive analysis of such data should thus account for this complexity.
Despite many published neurofeedback studies, there is no gold standard of how to analyze these large datasets. We suggest to use mixed effect models, where several fixed and random effects can be included, and different models can be compared for their capacity to explain the data. We will present initial mixed effect analyses of those patients that have already completed their training as a reason to discuss the possibilities to deal with such data.

*Keywords:* EEG-Neurofeedback, schizophrenia, N100, mixed effect modelling

**ID: 146**

## Different forms of skill learning in Parkinson's disease

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The striatal dopaminergic dysfunction in Parkinson's disease (PD) has been associated with deficits in skill learning in a number of studies, but the results are inconclusive so far. Motor sequence learning (especially sequence-specific learning) is found to be deficient in the majority of studies using the Serial Reaction-Time task (Ferraro, Balota, & Connor, 1993; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Muslimovic, Post, Speelman, & Schmand, 2007; Siegert, Taylor, Weatherall, & Abernethy, 2006), although results are mixed when verbal response is required instead of button presses (Westwater, McDowall, Siegert, Mossman, & Abernethy, 1998; versus Smith, Siegert, & McDowall, 2001). While problems with motor sequences seem to be prevalent, PD patients show intact performance on Artificial Grammar Learning tasks, suggesting that the sequencing problem may be response type- or task type-dependent (Smith et al., 2001; Witt, Nühsman, & Deuschl, 2002). Acquisition of non-sequential probabilistic associations also seems to be vulnerable as evidenced by impaired PD performance on a probabilistic category learning task (Knowlton, Mangels, & Squire, 1996; Shohamy, Myers, Onlaor, & Gluck, 2004).
Our aim was to explore the nature of the skill learning deficit by testing different types of skill learning (sequential versus non-sequential, motor versus non-motor) in the same group of Parkinson's patients. 18 patients with PD (mean age: 60.25 range: 43-78) were compared to age-matched typical adults using 1) a Serial Reaction Time Task (SRT) testing the learning of motor sequences, 2) an Artificial Grammar Learning (AGL) task testing the extraction of regularities from auditory sequences and 3) a Weather prediction task (PCL-WP), testing probabilistic category learning in a non-sequential task.
In motor sequence learning on the SRT task, PD patients showed generally higher reaction times. Sequence learning, however, was only marginally different between the groups: with the PD group showing lower learning scores. Results also showed a general deficit in probabilistic categorization, with the clinical group showing a significant decrease in learning. However, results show that learning performance of the PD patients was significantly above chance. Considering the AGL task, we found no group differences.
Results are in line with previous assumptions that mechanisms underlying artificial grammar learning and probabilistic categorization do not depend on the striatum (Reber & Squire, 1999; Skosnik et al., 2002).

*Keywords:* Skill Learning, Parkinson's Disease, Serial Reaction-Time Task, Weather Prediction, Artificial Grammar Learning

**ID: 148**

## Sleep deficiency and sleep disorders and their impact on the short- and long-term outcome of stroke

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Objectives: Project 1 investigates whether Adaptive Servo-Ventilation (ASV) used to treat sleep disordered breathing (SDB; apnoea-hypopnoea-index (AHI) ≥ 30) immediately after stroke is beneficial for stroke outcome. Project 2 assesses the impact of sleep-wake-disorders on new cardio-cerebrovascular incidences and on clinical stroke outcome.
Methods: For project 1, 120 patients with acute ischemic stroke will be recruited over 3 years. Following respiratory polygraphy, SDB-patients will be randomized to treatment with ASV or no treatment. The evolution of the ischemic penumbra within the first week and of the lesion volume from days 1 to 4-7 and to day 90 (primary outcome variable) following stroke will be compared between the two treatment groups. Further, the resting brain's functional connectivity, blood pressure variability and integrity of endothelial functions will be assessed. Comparisons will be carried out between the two treatment groups, as well as with patients without SDB.
For project 2, ~520 patients with ischemic stroke from the Department of Neurology, Inselspital Bern and the

Neurocenter of Southern Switzerland, Lugano, will be recruited over 2 years. During the acute phase, after 3, 12 and 24 months, assessments will include stroke outcome, focusing on new cardio-cerebrovascular events, and sleep-wake/psychiatric questionnaires. Objective activity measurements over two weeks (actigraphy) as well as assessments of blood pressure variability and endothelial function will be obtained in 20% of patients during the acute phase as well as at 3 and 12 months following stroke. The sample will be stratified according to the presence of sleep-wake-disorders (including SDB, insomnia and restless legs syndrome) to assess their short- and long-term impact on new cardio-cerebrovascular events and clinical stroke outcome.
Conclusion: Evidence for a beneficial effect of ASV treatment on stroke outcome in ischemic stroke patients with sleep disordered breathing and a deeper understanding of the impact of sleep-wake-disorders on clinical stroke outcome would influence clinical practice and improve patients' well-being.
Acknowledgements: Supported by the Swiss National Science Foundation grant 320030_149752, the Swiss Heart Foundation and the TROPOS Foundation.

*Keywords:* sleep, stroke, sleep disordered breathing, Adaptive Servo-Ventilation (ASV), cardio-cerebrovascular events

**ID: 149**

## Cingulate and insular cortex can predict phobic stimulus material in patients with spider phobia

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Introduction: Spider phobia is one of the most common specific phobias. Phobic related brain regions have been identified in fMRI studies: phobics exhibited larger activity to spider images in the insula, the anterior cingulate gyrus (ACC), and the left dorsomedial prefrontal cortex. However, studies that implemented advanced analysis techniques such as multivoxel pattern analysis (MVPA) to study decoding accuracies in brain areas related of phobic content are sparse. Therefore, the present study implemented MVPA to find sensitive brain areas predicting phobic content.
Methods: Data of nine patients with spider phobia in an event-related fMRI experiment were analyzed (seven female, one male; mean age 23.6 years). During the event-related experiment, participants looked at 80 randomized pictures of four categories: spiders (phobic), animals (non-phobic, positive), averse, and neutral pictures (objects). Functional data were acquired with a 3T Siemens Magnetom Trio, using an interleaved EPI sequence. MVPA was implemented by using the searchlight approach, and a Gaussian Naive Bayes classifier with leave-one-sample-out cross-validation. The classifier was trained to classify phobic spider pictures vs. all the other picture categories.
Results: We found significant positive classification accuracy across subjects in five regions. Three regions passed above chance (>63%, binomial test) categorization accuracies. A region in the middle cingulate gyrus demonstrated the highest mean classification accuarcy of 69% across subjects ($p = .001$, binomial test), followed by the postcentral gyrus (64%, $p = .018$), and the insula (63%, $p = .033$). Individual subject accuracy maps consistently demonstrated increased accuracies in the cingulate gyrus for all of the subjects.
Discussion: The present study showed that the cingulate gyrus can decode phobic vs. non-phobic content with an accuracy of 69%, the insula with 63%, respectively. The results are consistent with previous studies showing that the cingulate gyrus and the insula are key areas in the processing of phobic content. However, the significance of the postcentral gyrus is to some degree unexpected. In conclusion, the present study demonstrates that MVPA is a sensitive approach to find brain areas that can predict phobic content, and may therefore represent relevant key areas in the processing of phobic images in patients with spider phobia.

*Keywords:* spider phobia, anxiety, cingulate, insula, multi-voxel pattern analysis

**ID: 152**

## Effects of high resistance muscle training on cortico-spinal output during motor fatigue. A study using transcranial magnetic stimulation

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Objective: To compare responses to transcranial magnetic brain stimulation during a fatiguing exercise before and after a 3 weeks lasting resistance training, in healthy subjects.
Methods: The triple stimulation technique (TST, Magistris et al., 1998) was used to quantify a central conduction index (CCI = amplitude ratio of central conduction response and peripheral nerve response, obtained simultaneously by the TST). The CCI removes effects of peripheral fatigue from the quantification of the responses to brain stimulation. It allows a quantification of the percentage of the entire target muscle motor unit pool driven to discharge by a transcranial magnetic stimulus.
Subjects (n = 15) performed a 3 weeks training regimen (2 minutes twice per day) of repetitive isometric maximal voluntary contractions (MVC) of abductor digiti minimi (ADM; duration 1s, frequency 0.5Hz). Before and after this training, TST recordings were obtained every 15 seconds during an 2 minutes exercise, where subjects performed repetitive contractions of the ADM, and repeatedly during a recovery period of 7 minutes, using stimulation intensities and facilitatory maneuvers sufficient to excite all cortical motor neurons.
Results: There was a consistent decrease of force to approximately 40% of MVC in all experiments and in all subjects, before and after training. In all subjects, CCI decreased during exercise. While before training, the CCI decreased to 49% (SD 23.7%) after 2 minutes of exercise, it decreased after training only to 79% (SD 26.4%) ($p < 0.01$). Thus, training resulted in a smaller decrease of the CCI during exercise.
Discussion: The training regimen increased the proportion of target motor units that could be activated by transcranial magnetic stimulation during a fatiguing exercise. Possible underlying mechanisms at spinal and supraspinal sites are discussed.

*Keywords:* transcranial magnetic stimulation, motor fatigue, muscle training

**ID: 155**

## Signal improvement in multichannel NIRS by channel redundance over the optode/tissue interfaces

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Introduction: Mapping of the brain with near-infrared spectroscopy (NIRS) allows for non-invasive assessment of brain oxygenation, taking advantage of the differential absorption characteristics of oxygenated and de-oxygenated hemoglobin at different wavelengths. As instance of diffuse optical imaging, infrared light irradiated onto the surface of the head by a transmitting optode is scattered and partially absorbed by the underlying tissue and picked up by a receiving optode. With standard techniques implemented in commercial continuous-wave NIRS devices, only measurements of relative changes with respect to a baseline value are possible, and the reference value can unexpetedly shift and drift, for example due to small or larger dislocations of the optodes due to movement. The aim of this work is to improve this.
Methods: The relative absorptions are usually assessed using the modified Beer-Lambert law. For this work, the law was further extended by additional G factors to model the coupling between device and tissue (mainly at the optodes), i.e. the source of artifacts. Channels were configured from each transmitter optode to more than one receiver optode and vice versa. With other reasonable assumptions (such as, crossing channels essentially measure the same region, and all wavelenghts are similarily affected by changes in optode coupling), the resulting equations can be solved also for the additional unknown coupling factors [1]. The results were tested with data from another study [2].
Results: NIRS artifacts which were prominent in the manufacturers original signal were segregated into the additional factors representing optode to tissue coupling, sucessfully freeing the Hb signal from multiple types of artifact. Observed improvement in signal-to-noise is probably due to the "averaging" effect of the additional assumptions, combining information from several channels.
Conclusions: Using multiple redundant NIRS channels in suitable spatial configurations, it is possible to model, amongst other factors, the effect of optode to tissue coupling and thereby reduce undesired contributions including motion artifacts. This can be done without processing of time course data, but by only processing each time point independently.
References:

[1] A.C. Nirkko, patent pending
[2] C. Rummel et al., Monitoring cerebral oxygenation during balloon occlusion with multichannel NIRS. JCBFM 2014.

*Keywords:* multichannel NIRS, near infrared spectroscopy, diffuse optical imaging, artifact elimination, optode tissue coupling

**ID: 156**

## The Swiss Young Stroke Study (SYSS)

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Background and purpose: Ischaemic stroke (IS) in young adults has been increasingly recognized as a serious health condition. Stroke aetiology is different in young adults than in the older population. This study aimed to investigate aetiology and risk factors, and to search for predictors of outcome and recurrence in young IS patients.
Methods: Prospective multicenter study of consecutive IS patients aged 16-55 years. Baseline demographic data, risk factors, stroke aetiology including systematic genetic screening for Fabry disease and severity were assessed and related to functional neurological outcome (modified Rankin Scale, mRS), case fatality, employment status, place of residence, and recurrent cerebrovascular events at 3 months.
Results: In 624 IS patients (60% men), median age was 46 (IQR 39-51) years and median NIHSS on admission 3 (IQR 1-8). Modifiable vascular risk factors were found in 73%. Stroke aetiology was mostly cardioembolism (32%) and of other defined origin (24%), including cervicocerebral artery dissection (17%). Fabry disease was diagnosed in 2 patients (0.3%). Aetiology remained unknown in 20%. Outcome at 3 months was favourable (mRS 0-1) in 61% and fatal in 2.9%. Stroke severity ($p<0.001$) and diabetes mellitus ($p=0.023$) predicted unfavourable outcome. Stroke recurrence rate at 3 months was 2.7%. Previous stroke or TIA predicted recurrent cerebrovascular events ($p=0.012$).
Conclusions: Most young adults with IS had modifiable vascular risk factors, emphasizing the importance of prevention strategies. Outcome was unfavourable in more than a third of patients and was associated with initial stroke severity and diabetes mellitus. Previous cerebrovascular events predicted recurrent ones.

*Keywords:* stroke young ischemic

**ID: 163**

## Relation of pre-stimulus DMN activity to theta amplitude during working memory in schizophrenia

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Introduction: Deficits in working memory (WM) are a core feature of schizophrenia. WM tasks have typical fMRI and EEG signatures: The fMRI-BOLD signal usually decreases in regions of to the so called default mode network (DMN), while frontal and parietal regions outside of the DMN are activated. Patients with schizophrenia tended to fail to deactivate these task-negative regions and showed less task induced increases in regions typically active during WM tasks. Furthermore, WM tasks induced a load dependent EEG increase in frontal theta power (5 - 8 Hz) in healthy subjects during the retention period. This theta-increase was reduced in patients with schizophrenia.
We aim to study the association of pre-stimulus DMN activity with EEG theta amplitude from the retention periods of a WM task in patients with schizophrenia compared to healthy controls.
Methods: Subjects performed a verbal Sternberg WM task during simultaneous EEG-fMRI acquisition. The task contains two difficulty levels (L2 and L5) where either 2 or 5 consonants are presented. To analyze EEG and fMRI data combined, the so called covariance mapping was used. Thereby, the fluctuations of fMRI functional networks over trials can be temporally correlated with the dynamics of EEG spectral amplitudes. Hence, the spatial distributions of frequency domain EEG fluctuations significantly associated with the dynamics of the functional networks are obtained. In the fMRI data, the DMN was extracted using an ICA and its temporal dynamics were normalized to percent signal change values. Indices of each DMN pre-stimulus trial over the whole task duration were used as

regressors for the theta fluctuation obtained by the momentary EEG theta power (5-7 Hz) from each retention trial over the whole task, extracted using temporal filters. The obtained covariance maps were averaged within groups separately for each load and compared between patients and controls.
Results and Outlook: An initial analysis of 6 healthy controls and 6 patients with schizophrenia showed a consistent inverse relation of pre-stimulus DMN activity and theta amplitude of the retention period whereas in patients, this relation was not visible as clear and strongly. We will present results of a bigger sample.
These results support the notion that patients with schizophrenia may express aberrant patterns of up- or down-regulation of the task-negative network in relation to theta amplitude. These differences might indicate a dysregulation of arousal in regions that are beneficial or detrimental for performance when active during task execution.

*Keywords:* Schizophrenia, working memory, simultaneous EEG-fMRI

**ID: 164**

## Alzheimer's Disease and Semantic Dementia show diverging course of reduced structural connectivity strength with grey and white matter atrophy

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Progressing cognitive deficits in Alzheimer's Disease (AD) and Semantic Dementia (SD) are accompanied by grey matter atrophy and white matter deterioration. While patients with SD show focal atrophy mainly in the anterior temporal lobe, neuronal loss in AD is more distributed over the cortex. The co-occurrence of grey and white matter degeneration has been proven, yet the impact of atrophy on the network connectivity in distinct dementia subtypes is still not well understood.
In order to gain a more refined knowledge of the topological organization of white matter alterations in dementia, a network-based approach was used to analyze the brain structural connectivity network. Diffusion-weighted images and anatomical T1-weighted images of patient groups with AD and SD as well as a healthy control group were recorded and used to reconstruct the individual connectivity networks. In order to compare the network organization, global and local network metrics were computed. Additionally, two voxel-based morphometries using grey and white matter volume served to relate structural atrophy to altered structural connectivity.
Two main findings are discussed here. First, the results showed that in AD, decreased connectivity strength was found in various cortical regions such as superior temporal gyrus, inferior frontal gyrus, inferior parietal gyrus, precuneus, posterior cingulate gyrus, and occipital areas. An overlap with grey matter loss was found only in the inferior frontal and superior temporal regions. In SD, reduced network strength was found mainly in the temporal lobes covering superior, middle, and temporopolar regions. This converged primarily with the grey matter atrophy found in the SD group, which affected the entire anterior temporal lobes. Second, there was no white matter volume reduction observed in the AD group. Contrarily, the SD group showed decreased white matter volumes in both temporal lobes.
Taken together, this study revealed that the disconnection-syndrome in AD goes beyond mere grey matter atrophy and that it is not related to white matter volume loss. A different pathophysiology was observed in patients with SD, who showed grey and white matter volume loss as well as decreased connectivity strength more focally in the anterior temporal lobes.

*Keywords:* Alzheimer's Disease, Semantic Dementia, Diffusion-weighted Imaging, Structural Connectivity, Voxel-based Morphometry

**ID: 166**

## Sleep-disordered breathing in patients with acute ischemic stroke and transient ischemic attack: Short-term evolution and effects on vascular/clinical outcome-

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Background/Objectives: Sleep disordered breathing (SDB) represents an independent risk factor for cardiovascular morbidity and mortality. The aim of this observational multicenter prospective study (SAS-CARE 1) was to assess the frequency and effects of SDB on clinical evolution and cardiovascular parameters within the first three months after stroke and transient ischemic attack (TIA)
Patients/Methods: Patients from five centers were studied within 7 days from stroke onset and 3 months later. Assessment included conventional polysomnography, analyses of stroke characteristics and severity (NIH stroke scale/NIHSS), 24-hour-blood pressure, heart rate variability, endothelial function (measured by ENDOPAT), humoral markers of oxidate stress, vascular and clinical outcome (modified Rankin scale, mRS).
Results: The enrollment in this study was completed in December 2013 with a total of 209 patients (68% males, mean age 61 years, 88% strokes, 42% partial anterior infarcts). Mean NIHSS on admission/after 3 months was 4/1. SDB (AHI>=10) was found in 57% in the acute phase and in 47% of patients 3 months later. Mean oxygen desaturation index was 12/14 per hour in the acute phase/after 3 months.
Age and history of hypertension were independent predictors of moderate to severe SDB (AHI>=20) in the acute and subacute, BMI only in the acute phase. Systolic blood pressure values (mean, maximum, variability) correlated with AHI at 3 months (mean: r=0.344/p=0.001; max: r=0.313/p=0.001, var=0.240/p=0.01). The augmentation index measured by ENDOPAT was significantly different between patients with apnea-hypopnea index <20 and apnea-hypopnea index >= 20 (22.4 ± 15.6% versus 34.6 ± 21.6%; P=0.042), whereas reactive hyperemia index level was not (2.02 ± 0.65 versus 2.31 ± 0.61; P=0.127) at 3 months. No correlation was found between SDB and both NIHSS and mRS. Currently, heart rate variability and humoral data are analyzed.
Conclusions: Our data suggest that SDB 1) is common in stroke/TIA patients, also after 3 months, 2) is associated with high systolic blood pressure values and increased arterial stiffness, but 3) not with stroke severity and short-term outcome.
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*Keywords:* Sleep and stroke

**ID: 167**

## REM sleep reduction identifies patients with poor recovery of neurological function after stroke

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Objectives: To explore whether sleep during the acute phase after ischemic stroke is associated with short or long term recovery of neurological function.
Methods: Sixty five patients with ischemic stroke participating in the prospective, multicentre cohort study SAS-CARE1 (NCT01097967) had polysomnography within 9 days after stroke onset as well as valid NIHSS scores at admission, at discharge, and after 3 months. Patients were classified as having good or poor, short term (discharge) or long term (3 months) recovery of neurological function based on the expected improvement given their NIHSS scores at admission.
Results: Patients with poor short-term and with poor long-term recovery of neurological function had significantly reduced REM sleep (reduced proportion of REM sleep and prolonged REM latency) during the acute phase after stroke independent of stroke severity.
Conclusions: Acute REM reduction after stroke predicts poorer neurological function prognosis independent of stroke severity and sleep disordered breathing. Future studies are needed to confirm this as an early marker that can aid in identifying patients who might profit most from additional and early interventions.

Acknowledgements: Supported by the Swiss National Science Foundation grant 320030_125069 and the Swiss Heart Foundation.

*Keywords:* Sleep, Stroke, Recovery, SAS-CARE, neurological functions

## ID: 168

### Transcranial direct current stimulation effects on semantic cognition

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Semantic cognition encompasses the goal-directed activation of semantic knowledge, e.g. in naming, semantic decision or fluency tasks. Two processes are of importance, the activation of semantic representations and semantic control. It has been shown that the inferior frontal gyrus plays an important role in semantic control processes. The representation of semantic information, in particular category-specific differences (e.g. living vs. non-living; biological vs. manipulable) are still a matter of debate. It has been shown that the left inferior frontal gyrus (among other (prefrontal) regions) is activated during the processing of manipulable objects such as tools. The activation is considered to reflect the retrieval of action knowledge and is in line with theories of embodied cognition where word meaning is constituted in part by activity in brain areas involved in perception and action.
Transcranial direct current stimulation (tDCS) is a noninvasive technique that influences the excitability of neural networks and allows investigating the involvement of specific neural networks in certain tasks. Improvements in naming and fluency tasks after left inferior frontal stimulation have been reported.
We sought to extend the findings concerning the category specificity by administering tDCS to the left inferior frontal lobe. In a within-subjects cross-over design, 20 minutes of anodal tDCS (1.5.mA) or sham stimulation were applied. This was followed by a naming and a word-picture-verification task. On one half of the pictures biological items (plants, animals) and on the other half manipulable items (tools, household devices) were displayed. Accuracy and reaction time data was collected.
Manipulable items elicited slower reactions times in both tasks. Transcranial direct current stimulation differentially affected the processing of biological and manipulable items in the picture-verification task. Following the stimulation, reaction times to manipulable items decreased. This supports previous research proposing an important role for prefrontal regions in the processing of manipulable objects.

*Keywords:* semantic cognition, transcranial direct current stimulation

## ID: 169

### Catecholamine Depletion Influences Neural Processing of Monetary Incentives

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There is increasing evidence that catecholamines are involved in the pathophysiology of bulimia nervosa. Catecholamines, especially the dopamine system, were reported to be crucial related to reward processing and norepinephrine was found to be related to emotional processing. Correspondingly, bulimic subjects revealed dysfunctions in reward and emotional processing.
An instructive paradigm for directly investigating the relationship between catecholaminergic function and psychiatric disorders involves measuring the behavioral and neural response to experimental catecholamine depletion. The purpose of this study was to investigate the impact of catecholamine depletion on reward and emotional processing in remitted bulimic and healthy individuals.
In a double-blind, placebo-controlled, crossover study, 16 unmedicated women remitted from bulimia nervosa (age: 28.3 ± 7.5 yrs) and 20 female healthy volunteers (age: 27.8 ± 9.4 yrs) received alpha-methyl-paratyrosine (AMPT) or sham depletion in a randomized order. The participants performed the monetary incentive delay task (MID) while undergoing functional magnetic resonance imaging (fMRI).
Over all conditions, remitted bulimic participants showed a higher activation in the anterior cingulate cortex and in

the anterior insula than healthy controls ($p < 0.05$, FWE-corrected). All participants revealed a higher activation in the nucleus accumbens during the anticipation of monetary gain or loss than during the anticipation of no incentives ($p < 0.05$, FWE-corrected). The remitted bulimic and healthy participants revealed no differences and, furthermore, catecholamine and sham depletion had no effect on the activation in this region. However, the activation of the right amygdala was increased during catecholamine depletion compared to sham depletion in the female healthy volunteers ($p < 0.001$, uncorrected). The remitted bulimic participants showed under sham depletion increased amygdala activity compared to controls but revealed no effect of AMPT in this region, suggesting a ceiling effect.
The results of this study suggest that catecholamine depletion may have no or only a minor effect on the activation of nucleus accumbens during the anticipation of monetary gain or loss. However, catecholamine depletion appeared to influence the network associated with the reward system that is responsible for the expression of reward- und punishment-related emotions such as fear and disgust. This influence was partly specific for bulimia nervosa underlying the importance of catecholamines in the pathogenesis of this psychiatric condition.

*Keywords:* catecholamine depletion, bulimia nervosa, amygdala, reward, monetary incentive delay task

# Basic research animal

**ID: 106**

## Identification of the aberrant interactome of mutant SOD1 in familial amyotrophic lateral sclerosis model of disease

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Although familial amyotrophic lateral sclerosis (FALS) has been extensively studied since the creation of a transgenic mice overexpressing human mutant SOD1 (SODG93A), the mechanisms underlying the disease are still poorly understood.
We used a conformation specific antibody against misfolded SOD1 (misfSOD1) in order to longitudinally identify its interactome during early stages of disease in mouse spinal cord. Mass spectrometry analysis of the immunoprecipitates allowed us to identify several proteins that uniquely interacted with misfSOD1 but not with wild-type SOD1. Among them, Na+/K+ATPase exhibited a selective association with misfSOD1 from P15 onward. This association was increasing with age and was parallel to the increase in misfSOD1 accumulation.
We investigated further the implication of Na+/K+ATPase in FALS and identified the domain of Na+/K+ATPase necessary for this aberrant interaction. We are at present trying to decipher the mechanisms associated with this aberrant interaction and how this might be associated with the pathology of ALS. For this we are using both viral and genetic mediated approaches. These findings might further provide insights into the mechanism of selective vulnerability of MNs in FALS.

**ID: 143**

## Does Melanin Concentrating Hormone play a role in Neuroprotection? A study on the effect of sleep deprivation on stroke in rats

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Background: The literature states that sleep deprivation (SD) before stroke induces ischemic tolerance and may represent a new form of preconditioning. The microarray analysis performed in our study suggested that the increase of Melanin concentrating hormone (MCH), which was observed in pre-ischemic SD rats, may play a role in mediating this effect. MCH is involved in the regulation of the sleep/wake cycle and other functions such as feeding behaviour and energy balance. The main goal of this new study is to clarify the role of MCH in the neuroprotective effect of pre-ischemic SD.
Methods: The time course of MCH gene expression was performed at: 4h; 12h: 24h and 3 days after treatments in adult Sprague-Dawley rats. Animals were assigned to three experimental groups of four animals each: 1) TSD.IS: total SD performed before stroke; 2) IS: stroke without previous SD; 3) Sham: sham surgery without SD. Quantitative Real-time PCR was performed in order to evaluate the gene expression of MCH in ipsilateral hemisphere. The infarct size was assessed by cresyl violet staining. The electroencephalogram was recorded for all animals to evaluate changes in sleep.
Results: The real-time transcriptional profiling of MCH gene showed a significant increase of MCH during the acute phase of stroke (4h;12h;24h) in IS group compared to TSD.IS and Sham groups. Conversely, an increase in MCH gene expression was observed at 3 days in TSD.IS group compared to IS group. Rats treated with SD before stroke showed a reduction of infarct size at 12h ($p \leq 0.02$) and not at 24h and 3 days. Moreover, changes in the amount of total sleep and wakefulness were observed during the dark phase, but not at the light phase that occurred 12h later.
Conclusion: Sleep deprivation before stroke induced a substantial modification of MCH gene expression. A significant reduction of infarct volume was observed at 12h, suggesting that changes in sleep during the dark phase may play a role in neuro-protection.

*Keywords:* Stroke, Focal Cerebral Ischemia, Sleep deprivation, Preconditioning, Neuroprotection, Animal Models, Rats

**ID: 151**

## Injection of Endothelial Progenitor Cells secretome promotes neural precursor cells in the adult rat brain

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Endothelial progenitor (EPC) cells are promising tools for tissue repair including the Central Nervous System. Notably, the tissue restorative effects mediated by EPC are mainly due to their secretion of soluble factors. In the present study we have ad-dressed the hypothesis that conditioned medium from EPC (EPC-CM) might promote endogenous neurogenesis in the subventricular zone of the lateral ventricle wall and in the dentate gyrus of the hippocampus. EPC-CM harvested under hypoxic conditions was infused in the lateral ventricles of adult rats. One week later rats were sacrificed and the brains processed for histological analyzes. Brain sections were stained for doublecortin (DCX) a marker for neuronal precursor cells. Treatment with EPC-CM resulted in a significant increase in the number of DCX positive cells in the subventricular zone particularly in the dorsolateral part of the lateral ventricle as compared to the control group. Similarly, the number of DCX positive cells in the dentate gyrus was significantly higher in the EPC-CM treated group as compared to controls. Taken together, our findings demonstrate that intracerebroventricular administration of EPC-CM increases the number of neuronal progenitors in both neurogenic niches of the adult rat brain. These observations may offer new therapeutic approaches for neuropathological conditions of the brain.

**ID: 153**

## Improved yield of cultured dopaminergic neurons by a combination of NT4/5 administration and Nogo-receptor 1 antagonization

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Interfering with the neurite growth inhibitor Nogo-A is proposed as a promising tool to promote neuronal repair. We have previously demonstrated that antagonization of Nogo-A receptor (NgR1) using NEP1-40 increases dopaminergic (DAergic) cell densities in ventral mesencephalic (VM) cultures. Additionally, it is known that exposure to neurotrophin-4/5 (NT4/5) which binds to the TrkB and p75 receptors augments DAergic cell densities. In the present study, we investigated the effects of NEP1-40 in combination with NT4/5 on DAergic cell densities in organotypic VM cultures.
Organotypic VM cultures prepared from E14 old rat embryos were grown for 7 days in absence or presence of NEP1-40 and/or NT4/5. Sectioned cultures were immunocytochemically stained for the DAergic marker tyrosine hydroxylase (TH). Cell densities and volumes were assessed blinded using a bright field microscope connected to a digital camera.
We observed that single treatment with NEP1-40 or NT4/5 significantly increased TH positive cell densities, while NEP1-40 also increased the sphere volume. Interestingly, the combination of NEP1-40 and NT4/5 led to significantly higher TH positive cell densities, compared to single factor treatment, and increased sphere volume. In sum, our findings demonstrate that a combination of NT4/5 with NEP1-40 is superior to single factor treatment in promoting DAergic cell survival and/or differentiation. The increase in sphere volume might be due to an increased morphological complexity, as this was observed for NEP1-40 treated primary cultures. These observations may reveal a novel way to improve the yield of DAergic neurons of donor tissue prior to cell transplantation approaches for Parkinson's disease.
Acknowledgements: Supported by the Swiss Parkinson Foundation, the HANELA Foundation and the Swiss National Science Foundation

*Keywords:* Neuroscience, cell culture, Parkinson's disease

**ID: 154**

## Somatic Gene Therapy for Spinal Muscular Atrophy (SMA)

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The hereditary disease Spinal Muscular Atrophy (SMA), is characterized by denervation of α-motor neurons of the spinal cord, causing muscle weakness and paralysis. In its most severe form, patients die in infant age. SMA is due to insufficient levels of an essential protein, survival motor neuron (SMN), caused by either deletions or loss-of-function mutations of the SMN1 gene. A second nearly identical gene, SMN2, produces only low amounts of SMN protein due to a silent single nucleotide difference that leads to the skipping of exon 7 in the majority of its transcripts. Since complete loss of SMN is embryonically lethal, all patients have at least one SMN2 copy producing low levels of SMN. Hence correcting the mis-splicing of SMN2 is an attractive strategy for a somatic gene therapy.
We developed a U7 snRNA (small nuclear RNA) derivative, called U7-ESE-B, with an antisense sequence targeting the 3' end of exon 7 and tailed with a sequence that recruits splicing enhancing factors. Previously, it was shown in our group that the introduction of the U7-ESE-B gene into a severe SMA mouse model by germline transgenesis resulted in an improvement of SMA symptoms and a normal life span of treated mice.
To deliver the U7-ESE-B post-natally to motor neurons as a somatic gene therapy, we have developed our own production/purification system for AAV vectors. Several self-complementary (sc) vectors containing the therapeutic U7 gene were produced with AAV6 capsids and it was confirmed that they correct SMN2 splicing in HeLa cells very efficiently. Then, high viral titers were produced with AAV9 capsids that are less effective in cell culture but have a high potential for moto-neuron transduction in vivo. These viruses were injected into the left cerebral ventricle of newborn SMA mice. With a virus containing five copies of a short version of our most efficient U7 gene (sU7-ESE-B), we obtained a slight extension of survival by about six days (median survival untreated 12.5d; treated 18.5d).
This is less than what we observed with a virus containing an expression cassette for human SMN cDNA (obtained from the Kaspar group, Columbus, OH) that shows a nearly full rescue in the same mouse model. These results suggest that the U7 approach is relatively inefficient in mice. This may have to do with an observation that the U7 gene is poorly expressed in mouse cells as compared to human cells.

*Keywords:* Gene therapy, U7-ESE-B, SMA, SMN, AAV

**ID: 159**

## Lithium attenuates brain injury and improves neurofunctional outcome in experimental meningitis

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Pneumococcal meningitis is associated with high morbidity and mortality rates. Brain damage caused by this disease is characterized by apoptosis in the hippocampal dentate gyrus, a morphological correlate of learning deficits in experimental paradigms. The mood stabilizer lithium has previously been found to attenuate brain damage in ischemic and inflammatory diseases of the brain. An infant rat model of pneumococcal meningitis was used to investigate the neuroprotective and neuroregenerative potential of lithium. To assess an effect on the acute disease, LiCl was administered starting five days prior to intracisternal infection with live Streptococcus pneumoniae. Clinical parameters were recorded, cerebrospinal fluid (CSF) was sampled, and the animals were sacrificed 42 hours after infection to harvest the brain and serum. Cryosections of the brains were stained for Nissl substance to quantify brain injury. Hippocampal gene expression of Bcl-2, Bax, p53, and BDNF was analyzed. Lithium concentrations were measured in serum and CSF. The effect of chronic lithium treatment on spatial memory function and cell survival in the dentate gyrus was evaluated after LiCl treatment during 3 weeks following infection by Morris water maze and BrdU incorporation. In the hippocampus, LiCl significantly reduced apoptosis and gene expression of Bax and p53 while it increased expression of Bcl-2. IL-10, MCP-1, and TNF were significantly increased in animals treated with LiCl compared to NaCl. Chronic LiCl treatment led to improved spatial memory in infected animals. The mood stabilizer lithium may thus be a therapeutic strategy to attenuate neurofunctional deficits as a result of pneumococcal meningitis.

*Keywords:* neuroinfection, bacterial meningitis, lithium, dentate gyrus, Morris mater maze

**ID: 161**

## Successful transnasal delivery of stem cells in a rat model of perinatal hypoxic-ischemic brain injury

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New strategies for cell transplantation route into the brain need to be explored as intacerebral or intrathecal applications have a high risk to cause damage to the central nervous system. It has been hypothesized that transnasally administrated cells may bypass the blood-brain barrier and migrate along the olfactory neural route into the brain and cerebrospinal fluid (CSF). Our goal is to confirm this hypothesis by transnasally administrating Wharton's Jelly mesenchymal stem cells (WJ-MSC) and neural progenitor cells (NPC) to perinatal rats in a model of hypoxic-ischemic brain injury.
Four-day-old Wistar rat pups, previously brain-damaged by combined hypoxic-ischemic and inflammatory insult, were divided into two groups; the first group received WJ-MSC and the second group green fluorescent protein- (GFP-)expressing NPC, both at passage 6. The heads of the rat pups were immobilized by hand and 3 µl drops containing the cells (50'000 cells/µl) were placed on one nostril allowing it to be snorted. This procedure was repeated twice, alternating right to left nostril with an interval of one minute between administrations. The rat pups received a total of 600'000 cells. Animals were sacrificed 24h, 48h or 7 days after the application of the cells. Fixed brains were collected, embedded in paraffin and sectioned.
Transplanted cells were found in the layers of the olfactory bulb (OB), the cerebral cortex, thalamus and the hippocampus. The amount of cells was higher in the OB than in the rest of the brain. Animals treated with transnasally delivered stem cells showed significantly decreased gliosis compared to untreated animals.
Our data show for the first time that transnasal delivery of WJ-MSC and NPC to the newborn brain after perinatal brain damage is successful. The cells not only migrate the brain, but also decrease scar formation and improve neurogenesis. Therefore, the non-invasive intranasal delivery of stem cells to the brain may be the preferred method for stem cell treatment of perinatal brain damage and should be preferred in future clinical trials.
Financial support by Cryosave Switzerland and The Eagle Foundation.

*Keywords:* perinatal brain injury, animal model, stem cell treatment, intranasal application, Wharton's jelly MSC

**ID: 165**

## Towards a stem cell-based therapy for sensorineural hearing loss after experimental pneumococcal meningitis in infant rats

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BACKGROUND: Bacterial meningitis (BM) is the most common cause of acquired profound bilateral sensorineural hearing loss (SNHL) in childhood, which occurs in up to 45% of BM patients with Streptococcus pneumoniae infection. Hearing loss is irreversible because SGNs and hair cells have a very limited regenerative potential. Surviving SGNs are a prerequisite for the correct functioning of cochlear implants, which represents the only treatment option for all forms of SNHL. The aim of the project is to characterize the pathogenesis of sensorineural cell loss in an existing animal model of pneumococcal meningitis and to develop a cell-based therapy to replenish lost SGNs and thereby improve the efficacy of cochlear implants.
METHODS: 11 day old male Wistar rats were inoculated intracisternally with increasing doses of live Streptococcus pneumonia serotype 3 (104, 105, 106 cfu/ml). Antibiotic therapy was initiated 18 hours postinfection with Rocephine® 100 mg kg-1 and continued for 3 days. Samples of cerebrospinal fluid (CSF) were collected to determine the bacterial titers, white blood cell counts (WBC) and measure inflammatory cytokines (Luminex®). Three weeks after the infection, hearing sensitivity was determined with the auditory brainstem response (click-ABR). Inner ear sensorineural cell loss was assessed in histopathological studies, in a spatial relationship from base to apex. Stem

cell transplantations were performed two weeks after the infection (106 cfu/ml) in a different batch of rats with bacteriologically cleared meningitis. Thereby, green fluorescence protein (GFP) expressing spiral ganglion-derived stem cells were transplanted directly into the modiolus via a retroauricular, transbullar approach.
RESULTS: Increasing inoculum concentrations elevated the hearing thresholds in a dose-dependent way. 18 hours after the infection, bacterial titers (Spearman r=0.87, P<0.0005) and WBCs (Spearman 0.82, P<0.0005) were positively correlated with the hearing thresholds. Cytokine measurements and quantification of sensorineural cell loss are currently under examination.
The surgical access and the transplantations have been successfully performed (n=3) and the grafted cells survived and formed axonal structures.
CONCLUSION: The present data demonstrates that the infant rat model of pneumococcal meningitis allows controlling the extent of disease-associated hearing loss. The initial inoculum size, the resulting CSF bacterial load and the following infiltration of white blood cells play a crucial role in the development of SNHL. Furthermore, the initial data demonstrates proof of concept for effective surgical transplantation of stem cells into the cochlear modiolus of rats. We have evidence that the transplanted stem cells can survive and differentiate in cochleas of postmeningitic deafened rats.

*Keywords:* Pneumococcal Meningitis, Hearing Loss, Auditory neurons, Animal model

# Basic research human

**ID: 105**

## Entrained oscillatory activity modulates long-range neuronal transmission efficacy

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Oscillatory activity is ubiquitous in the brain, and is considered a neural basis of signal transduction. However there is currently no experimental evidence for the causal role of oscillatory activity in modulating signaling efficiency. To address the causal relationship, we employed the simultaneous use of transcranial alternating current stimulation (tACS), transcranial magnetic stimulation (TMS), and EEG. Through tACS we entrain 6Hz oscillatory activity in two regions of the fronto-parietal network (DLPFC and posterior parietal cortex), in a synchronized or desynchronized (180 degrees phase shifted) manner. The concurrent TMS and EEG method was employed for probing online the resultant changes of the functional status of the network, comprising the application of weak single pulse TMS (to the DLPFC) and measuring the spread of evoked potentials with EEG. We furthermore assessed phase-dependency of the evoked potentials by applying the pulses at 4 different phases of tACS (90, 180, 270 and 360 degrees phases). We found that the spread of TMS-evoked potentials through the brain networks depended on the phases of tACS at which we applied TMS, suggesting that signal transmission depends on the phase of oscillatory activity. We also found, in the occipital area, that the phase-dependency of transmission disappeared in the phase-shifted condition. That is, when the oscillatory phase was shifted between the frontal and posterior area, the timing of TMS pulse delivery frontally made less difference for the signal recorded at the occipital electrodes. This implies that the phase-dependent modulation of signal transmission was itself dependent on the tACS-induced state of synchrony in the fronto-parietal network. It importantly agrees with the role of phase synchrony in long-range neuronal transmission. The current results may add new vital parameters constraining models of signal transmission.

*Keywords:* Oscillations, Connectivity, TMS, EEG, tACS

**ID: 107**

## Can transcranial direct current stimulation influence implicit task sequence learning and consolidation?

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With the task sequence learning (TSL) paradigm implicit sequence learning can be measured without the involvement of a motor component. The purpose of this project was to investigate the role of fronto-striatal systems for implicit sequence learning and consolidation. We conducted two experiments with different transcranial direct current stimulation (tDCS) protocols. In both experiments, participants performed the TSL in two sessions. In the first session, they received tDCS on the right and the left dorso-lateral prefrontal cortex (DLPFC). After 24 hours they performed the TSL again without stimulation. Depending on the stimulation type (Anodal vs Cathodal) we expected to enhance or inhibit implicit sequence learning and consolidation. The results showed that, although implicit sequence learning of the specific sequence was present in both sessions, tDCS did not influence participants' performances. Thus, the specific protocols are not suited to manipulate TSL.

*Keywords:* Implicit sequence learning, consolidation, fronto-striatal loops, transcranial direct current stimulation (tDCS)

**ID: 108**

## Improvement of visual motion perception after cathodal HD-tDCS

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Introduction: Visual perception allows for collecting and processing of visible light, in order to create the ability to see. In the brain, there is a particular region responsible for it, the visual cortex, which is divided in the primary visual cortex V1, anatomically equivalent to Brodmann Area (BA) 17, and the extrastriate visual cortical areas V2, V3, V4 and V5, consisting of BA 18 and 19. Among those areas, V5 is known to be mainly responsible for processing of visual motion. People with unilateral brain lesion in V5 may have a distorted perception of moving objects, with impairment in everyday life activities, like walking and obstacles avoidance.
It has been demonstrated that visual perception can be influenced by HD-tDCS (high definition transcranial direct current stimulation), a technology consisting of 5 electrodes placed over the target region on the scalp of the subjects, which apply low constant current directly into the brain. Unfortunately, the interaction mechanisms of HD-tDCS with the brain still need to be fully understood.
The hypothesis of the present study is that tDCS over V5 can modulate the neuronal activity and change the performance at visual tasks involving motion perception.
Methods: 20 healthy volunteers have been tested with a visual test for motion perception in a single blind within-subject, sham controlled randomized cross-over trial. The visual test consists of two patterns of random dots moving with different speed presented in the right and left visual hemifield, respectively. By means of an input device, the test person increases or decreases the speed of the pattern on the right until it moves with the same perceived speed as the pattern on the right.
The visual test has been conducted after the modulation of 20 min of 2 mA cathodal HD-tDCS over the right V5.
Results and discussion: The results showed an improvement in the performance at the proposed balancing task after real HD-tDCS. Such improvement can be explained with the Bienenstock-Cooper-Munro (BCM) rule, which states that a low overall cortical activity is suggested to enhance synaptic strength of active neuronal connections, while a high level of activity should diminish it. If the BCM rule applies, cathodal HD-tDCS would induce an inhibition of the synaptic activity of the neurons in V5. As soon as the stimulation has ceased, the neuronal synaptic strength would be enhanced, with consequent higher performance compared with the previous condition.

*Keywords:* visual perception, transcranial direct current stimulation, visual test

**ID: 109**

## The psychological profile of Alzheimer's disease: an integrative model for a global and process-based intervention

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Alzheimer's disease, the most common form of dementia, refers to a progressive and irreversible neurodegenerative disease characterized by a decline in cognition. Cognition is composed of several aspects, among them memory, executive functions, attention, language and visuospatial abilities. These functions are broad and composed of several subcomponents.
Due to cognitive decline, patients with Alzheimer's disease have difficulties with instrumental activities of daily living (IADL). IADL are crucial for independent living since they consist of, for example, preparing meals, handling finances, taking medication, driving or using public transportation and shopping. These tasks require preserved executive functions, prospective and working memory, attention and many other functions.
In order to predict the functioning in daily living activities and help the patients to preserve their independence, it is important to precisely know which impaired functions are involved in which daily living activities. According to that, we are developing a model based on a decomposition of the cognitive functions linked with a decomposition of the activities of daily living, i.e. the "IADL Cognition Model". We then want to use the Serious Game (i.e. simulations of

real-world events designed for a serious purpose like rehabilitation for example) to simulate four daily living activities (i.e. shopping, navigation, cooking and table preparation) in Alzheimer patients and healthy controls in order to investigate the relationship between the cognitive functions, the neural correlates (through EEG connectivity analysis) and the daily living activities. Therefore we will test and validate the previously developed "IADL Cognition Model", as a first step to design an adapted and targeted rehabilitation for patients with Alzheimer's disease.
So far, some authors have tested cognitive models evaluating multitasking performances using laboratory tasks, questionnaires (e.g. IADL scale) or real life observation. The problems with these methods are respectively, the non-realistic value of the laboratory tasks, the inconvenience of the questionnaire of being subjective for Alzheimer patients who are not always aware of their difficulties and, finally the disadvantage of the real life observation of being expensive and the needs to have the specific infrastructures. Some other authors have shown the ecological validity and the diagnostic value of the serious games. The idea of the present study is to combine and extend these methods, using the Serious Game which is a promising method as it allows testing and quantifying the IADL performances in a fun and motivating way.

*Keywords:* Alzheimer's disease, Serious Games, daily living activities, cognitive functions, dementia

## ID: 110

## Consolidation of habitual prospective memory: An ERP-study

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Prospective memory (ProM) is the ability to form an intention and to remember to perform it as planned at the appropriate occasion in the future. If a prospective memory task is performed repeatedly it changes its nature from episodic to habitual. Our previous research has shown that this transition is characterized by ERP-activation changes in a time-window between 450-650 ms, probably reflecting a change in resource allocation and/or a facilitation of retrieval. Here, we further investigated the time course across a one-week interval. The results for the behavioural data revealed a consolidation effect as indicated by a higher level of performance in the second test session. The results of the ERP-analyses showed a further shift in the same time-window as in the previous study indicating that the transition continues across a one week interval.

*Keywords:* prospective memory, habituation, consolidation, event-related potentials

## ID: 111

## Artistic Creativity Domains Compendium (ACDC): Measuring the beautiful mind

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Creativity is the ability to create new and original ideas. Several instruments exist to measure some aspects of creativity, for example, divergent and convergent thinking. However, only very limited tests exist to measure artistic creativity, that is, the interest in and expression of creative skills. A comprehensive assessment of artistic creativity which is considered a core feature of creativity is still missing. Here we introduce a new self-report measure, the Artistic Creativity Domains Compendium (ACDC), to assess interest, skill and performance in multiple artistic domains such as music, dance and literature. We present first results of a non-clinical norm sample. As the method can be easily used, we suggest further applications, for example, to assess the trajectory of disease-related changes in patients with Parkinson's Disease, in schizophrenia, and in other psychiatric disorders.

*Keywords:* Creative Output, Creative Perception, Creative Performance, divergent thinking, convergent thinking

**ID: 115**

## Parent-Reported sleep problems are associated with lower executive functions in healthy adolescents

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Introduction: Childhood subjective sleep problems have been shown to be associated with neuropsychological functioning. However, less is known about this association in adolescence. Since sleep problems disrupt sleep, they may delay neural and skill development and in turn lead to neuropsychological impairments. Of particular interest are tasks of executive function that require the prefrontal cortex – a region with prolonged maturation into young adulthood, that is particularly sensitive to the effects of sleep disruption. Therefore, we investigated the effects of sleep problems and duration on the development of executive functions in early adolescents. Methods: Cross-sectional data of 24 children (15 females, mean age: 12.49 years, SD: 1.57 years) who underwent neuropsychological testing in verbal learning and memory (German Version of the RAVLT), executive functioning (Regensburger verbal fluency test) and processing speed (Coding, WISC-IV) were examined. Subjective sleep problems were rated by parents; sleep duration and sleep latency was measured using 5 weeknights of actigraphy data. Associations were analysed with two-sided Spearman correlations, controlled for age at testing. Results: Parent-reported sleep problems correlated negatively with processing speed (r=-.64, p=.001) and executive functioning (semantic fluency: r=-.45, p=.03; semantic category change: r=-.49, p=.02), but not with verbal learning or memory. Furthermore, no association was found between actigraphically measured sleep duration or latency and neuropsychological performance. Conclusion: Preliminary results revealed that subjective parent-reported problems are correlated negatively with executive functions in early adolescents, but not with learning and memory. This finding suggests that sleep disruption may have a dissociative impact on these processes. In addition, no relationship was found between objective measures of sleep duration and latency and neuropsychological performance, suggesting that disrupted sleep rather than total sleep time may impart risk. Future analyses will examine longitudinal associations between sleep and neuropsychological performance in a larger sample.

*Keywords:* subjective sleep problems, executive functions, adolescence

**ID: 118**

## Negative emotional stimuli enhance vestibular processing

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Recent studies have shown that vestibular stimulation can influence affective processes. In the present study, we examined whether emotional information can also modulate vestibular perception. Participants performed a vestibular discrimination task on a motion platform while viewing emotional pictures. Six different picture categories were taken from the International Affective Picture System: mutilation, threat, snakes, neutral objects, sports and erotic pictures. Using a Bayesian hierarchical approach we were able to show that vestibular discrimination improved when participants viewed emotionally negative pictures (mutilation, threat, snake) when compared to neutral objects. There was no difference in vestibular discrimination while viewing emotionally positive compared to neutral pictures. We conclude that some of the mechanisms involved in the processing of vestibular information are also sensitive to emotional content. Emotional information signals importance and mobilizes the body for action. In case of danger, a successful motor response requires precise vestibular processing. Therefore, negative emotional information improves processing of vestibular information.

*Keywords:* Bayesian statistics, vestibular cognition

**ID: 122**

## A Comparison of Behavioral Response Latency and P300 Latency in a Modified Hick Reaction Time Paradigm

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Both, reaction time and P300 latency, are measures often used to assess speed of information processing. Although there are studies that report a positive correlation between the two measures, it is also known that they measure different aspects of information processing. While the latency of the P300 component is sensitive to stimulus evaluation and categorization, reaction time is a behavioral measure that includes stimulus- as well as response-related processes. In this study we investigated the functional relationship between P300 latency and reaction time as measures of speed of information processing in 125 participants by using a modified Hick reaction time paradigm with four complexity levels (0-bit, 1-bit, 2-bit, 2.58-bit). Although there was an increase in means over task complexity in both measures, reaction times were more affected by complexity. Furthermore, a principal component analysis (PCA) on both measures of all complexity levels distinguished three factors that explained 70.8% of variance. The first factor included the reaction times of all of the four complexity levels. A second factor including the P300 latencies of the 1-, 2-, and 2.58-bit conditions, was independent of the first factor. The third factor was extracted from the P300 latency of the 0-bit condition only and was also independent of the other two factors. The results reaffirmed that reaction time and P300 latency are not measuring the same aspects of speed of information processing and are relatively independent in a response-related choice reaction time task like the Hick paradigm. Rather surprising was the finding, that unlike reaction time, the P300 latency did not seem to measure the same process over the different complexity levels. The P300 latency of the 0-bit condition was unrelated not only to reaction time but also to P300 latencies of the 1-, 2-, and 2.58-bit condition. Further research is needed to elucidate the different processes involved in P300 latency, and in this way to have a better understanding of information processing in general.

*Keywords:* speed of information processing, P300 latency, reaction time, Hick paradigm, ERP

**ID: 123**

## Microstructure and Cerebral Blood Flow within White Matter of the Human Brain

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White matter (WM) fibers connect different brain regions and are critical for proper brain function. Cerebral blood flow (CBF) is one of the basic quantities that allow measuring the vital functioning of the human brain. Non-invasive methods exist that may assess CBF using magnetic resonance imaging (MRI). The most commonly used method is arterial spin labeling (ASL). However, little is known about the cerebral blood flow in WM and its relation to WM microstructure. Improved ASL methods paved the way to access CBF in WM. For this purpose, CBF and its relation to WM integrity was analyzed across subjects on a voxel-wise basis with tract-based spatial statistics (TBSS) and also across white matter tracts within subjects. Diffusion tensor imaging and ASL were acquired in 43 healthy subjects (mean age = 26.3 years). CBF in WM was observed to correlate positively with fractional anisotropy across subjects in parts of the splenium of corpus callosum, the right posterior thalamic radiation (including the optic radiation), the forceps major, the right inferior fronto-occipital fasciculus, the right inferior longitudinal fasciculus and the right superior longitudinal fasciculus. Furthermore, radial diffusivity correlated negatively with CBF across subjects in similar regions. Moreover, CBF and FA correlated positively across white matter tracts within subjects. These results are partially in line with previous clinical findings showing a positive relationship between the CBF in GM and white matter integrity in adults. Individual variations in the metabolic demand of WM components might affect microstructural properties such as myelination or axon diameter and cerebral blood flow. Although these findings suggest a clear association between white matter perfusion and WM microstructure, the underlying physiological mechanisms of this relationship still needs further evaluation.

*Keywords:* Cerebral Blood Flow, Arterial Spin Labeling, White Matter, Diffusion Weighted Imaging, Tract-Based Spatial Statistics (TBSS)

**ID: 132**

## The functional involvement of the oculomotor system in object memory revealed by TMS over the frontal eye field

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Previous research has found that systematic eye movements occur during memory and imagery, even though there is no visual information to be processed. To date, the role of eye movements during those processes is still debated. Studies providing evidence for an assisting role of eye movements during memory retrieval used tasks that manipulate eye position (e.g. requiring the maintenance of central fixation). However, it remains an open question whether the changes in performance are due to a spatial mismatch between encoding and retrieval (role of spatial information) or whether eye movements per se underlie these effects. The right FEF is a key structure in the cortical representation of the oculomotor system. Thus, in order to manipulate the activity of this key oculomotor area directly, we used a temporary interference approach by means of inhibitory TMS over the right FEF and studied its influence on short- and long-term recall of object and location information in a scene context. Participants encoded a complex scene and performed a retrieval task either immediately after encoding or after 24h. Before recall was tested, half of the sample received TMS over the right FEF, the other half received sham stimulation. The results show that TMS impaired object memory recall, irrespective of delay period between encoding and recall. We conclude that oculomotor mechanisms are functionally involved in short- and long-term object recall.

*Keywords:* transcranial magnetic stimulation, frontal eye field, oculomotor system, object memory, location memory

**ID: 134**

## Serotonin versus catecholamine deficiency: behavioral and neural effects of experimental depletion in remitted depression

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Despite immense efforts into development of new antidepressant drugs, the increases of serotoninergic and catecholaminergic neurotransmission have remained the two major pharmacodynamic principles of current drug treatments for depression. Consequently, psychopathological or biological markers that predict response to drugs that selectively increase serotonin and/or catecholamine neurotransmission hold the potential to optimize the prescriber's selection among currently available treatment options. The aim of this study was to elucidate the differential symptomatology and neurophysiology in response to reductions in serotonergic versus catecholaminergic neurotransmission in subjects at high risk of depression recurrence. Using identical neuroimaging procedures with [18F] fluorodeoxyglucose positron emission tomography after tryptophan depletion (TD) and catecholamine depletion (CD), subjects with remitted depression were compared to healthy controls in a double-blind, randomized, crossover design. While TD induced significantly more depressed mood, sadness and hopelessness than CD, CD induced more inactivity, concentration difficulties, lassitude and somatic anxiety than TD. CD specifically increased glucose metabolism in the bilateral ventral striatum and decreased glucose metabolism in the bilateral orbitofrontal cortex, whereas TD specifically increased metabolism in the right prefrontal cortex and the posterior cingulate cortex. While we found direct associations between changes in brain metabolism and induced depressive symptoms following CD, the relationship between neural activity and symptoms was less clear after TD. In conclusion, this study showed that serotonin and catecholamines play common and differential roles in the pathophysiology of depression.

*Keywords:* Major depressive disorder, serotonin, catecholamines, PET

**ID: 145**

## Stable and changeable aspects of face processing influence neural predictors of memory encoding

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Effective encoding relies on the neural activity before and after the onset of an event. Recent studies have shown that pre-stimulus activity can predict retrieval success. In the present experiment we investigate how identity (stable) and emotional (changeable) aspects of face processing modulate this preparatory activity and influence memory formation. Electrical brain activity was recorded from 27 healthy participants while they were presented with unfamiliar faces. Two types of cues shown immediately before the presentation of the face stimuli indicated what task to perform: in one condition the cue induced an age judgment and an emotional judgment in the other condition. A recognition memory task followed after a break.
The results revealed distinct activation for subsequently remembered versus forgotten faces (SME) before stimulus onset, between emotion and age conditions. Brain activity in these two conditions differed in topography from -1300 to -700 ms before faces presentation, suggesting the recruitment of different generators in the two conditions.
In addition, this activity was also correlated with recognition performance at test. This finding indicates that in the pre-stimulus interval there are neural sources that are predictive for performance levels and these sources are distinct in the two tasks. Inverse solutions in this time interval, confirmed the involvement of distinct neural sources in the two conditions. The superior temporal cortex was mostly active during the Emotion condition and the fusiform gyrus in the Age condition, consistently to the model of Haxby et al. (2000).
Our data provide evidence that focusing on stable or changeable aspects of face processing such as age-identity or emotional expressions, differentially influence preparatory processes that enable successful encoding of unfamiliar faces. Moreover, emotional and age judgments recruit distinct neural sources already during task preparation.
These findings further confirm that these preparatory processes are task-specific and allow to predict if a face will be later recognized, analysing the neural correlates that precede its presentation.

*Keywords:* prestimulus neural activity, memory encoding, long term memory, face processing, subsequent memory

**ID: 150**

## Context effects in prospective memory: An ERP study of the after-effects following a bivalent prospective memory target.

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In prospective memory (PM) research a prospective memory target is embedded in an ongoing task that triggers a specific response. In the presented study, a bivalent prospective memory target (i.e., stimulus with relevant features for two tasks), pseudo occasionally appearing in a regular order task-switching ongoing task, was supposed to slow down the reaction times only on subsequent univalent stimuli with overlapping feature. Here reaction time slowing was observed for all univalent stimuli including stimuli with no relevant feature. ERP analysis reveal the component N300 and a bivalency effect (parietal positivity frontal negativity peaked at 650 ms) for ongoing univalent stimuli in the PM block. These components are associated with context. Specifically, N300 is associated with context and monitoring, until now measured only for PM memory targets. The bivalency effect on the other hand is associated with cognitive conflict adaption induced by a bivalent stimulus and episodic context binding processes. These findings lead to the conclusion that context might be relevant for the ongoing task in which the PM target appears.

*Keywords:* prospective memory, context, bivalency effect, task switching, monitoring, context effects

**ID: 158**

## Impacts of a word-picture training on reading in youth with mixed intellectual disabilities: A waiting-list control group comparison

**Katja Margelisch[1,2], Walter Perrig[1,2]**

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Individuals with intellectual disabilities (ID) often struggle with learning how to read. Only one in five children with mild or moderate ID achieves even minimal literacy skills. However, literacy education for children and adolescents with ID has been largely overlooked by researchers and educators. However, many training studies have been conducted with other populations with reading difficulties. The most common approach of acquiring literacy skills consists of sophisticated phonological trainings. Only few studies investigated the influence of implicit learning on reading. Implicit learning processes seem to be largely independent of age and IQ. Children are sensitive to the statistics of their learning environment. By frequent word reading they acquire implicit knowledge about the frequency of letter patterns in written words. Additionally, semantic connections not only improve the word understanding, but also facilitate storage of words in memory. Advances in communication technology have introduced new possibilities for remediating literacy skills. Computers can provide training material in attractive ways, for example through animations and immediate feedback. These opportunities can scaffold and support attention processes central to learning.
Thus, the aim of this intervention study was to develop and implement a computer based word-picture training, which is based on statistical and semantic learning, and to examine the training effects on reading, spelling and attention in children and adolescents (9-16 years) diagnosed with mental retardation (general IQ < 74). Fifty children participated in 4-5 weekly training sessions of 15-20 minutes over 4 weeks, and completed assessments of attention, reading, spelling, short-term memory and fluid intelligence before and after training. After a first assessment (T1), the entire sample was divided into a training group (group A) and a waiting control group (group B). After 4 weeks of training with group A, a second assessment (T2) was administered with both training groups. Afterwards, group B was trained for 4 weeks, before a last assessment (T3) was carried out in both groups.
Overall, the results showed that the word-picture training led to substantial gains on reading and attention for both training groups. These effects were preserved six weeks later (group A). There was also a clear tendency of improvement in spelling after training for both groups, although the effect did not reach significance. These findings highlight the fact that an implicit statistical learning training in a playful way by motivating computer programs can not only promote reading development, but also attention in children with intellectual disabilities.

*Keywords:* word-picture training, statistical learning, intellectual disabilities, reading, attention

**ID: 162**

## Umbilical Cord Mesenchymal Stem Cells Prime Neural Progenitor Cells towards an Oligodendrocyte Fate

**Marianne Jörger-Messerli[1], Byron Oppliger[1,2], Ursula Reinhart[1], Philipp Schneider[1], Andreina Schoeberlein[1], Daniel Surbek[1]**

[1]Department of Obstetrics and Gynecology, and Department of Clinical Research, University of Bern, Switzerland;
[2]Graduate School for Cellular and Biomedical Sciences (GCB), University of Bern, Switzerland

Using Wharton's jelly mesenchymal stem cells (WJ-MSC) from the umbilical cord as a regenerative approach may cure perinatal brain damage and other central nervous system in the future. Their secretome has been shown in vitro and in vivo to stimulate neurogenesis and neuroregeneration. Therefore, the objective of this study is to assess the effect of the neurotrophic factors produced by WJ-MSC on neuroregeneration in vitro.
The secretome of WJ-MSC was analyzed by mass spectroscopy and with a membrane-based antibody array. The effect of these factors on the expression of neuroglial markers in neural progenitor cells (NPC) was assessed in vitro in conditioned medium and co-culture experiments by immunocytochemistry, real-time PCR and western blot. Furthermore, the differences between WJ-MSC derived from term or preterm birth were evaluated.
Over 500 secreted proteins were identified. Several of these proteins are involved in glio- and neurogenesis. Hippocampal NPC at passage 3 showed an increased expression of glial markers such as glial fibrillary acidic protein (Gfap), myelin basic protein (Mbp) or galactocerebroside after exposure to WJ-MSC-conditioned medium (CM) or after direct contact to WJ-MSC. Interestingly, MSC from term pregnancies induced more strongly the expression of glial markers when compared to preterm. The co-culture had a more prominent effect on the expression of glial markers compared to CM.
WJ-MSC derived from term have a different secretome compared to preterm pregnancies. This was demonstrated by mass spectroscopy as well as by in vitro experiments. Moreover, cell contact may be necessary to induce

neuroglial differentiation on resident NPC. In conclusion, transplanting WJ-MSC into damaged brains of neonatal infants may enhance and support endogenous remyelination and neuroregeneration.
Financial support by Cryosave Switzerland and The Eagle Foundation.

# Talk abstracts

**ID: 112**

## Nonverbal social communication and gesture control in schizophrenia

**Sebastian Walther[1], Katharina Stegmayer[1], Jeanne Sulzbacher[1], Tim Vanbellingen[2,3], René Müri[2,4], Werner Strik[1], Stephan Bohlhalter[2,3]**

*[1]University Hospital of Psychiatry, Bern, Switzerland; [2]Department of Clinical Research, Inselspital, Bern, Switzerland; [3]Neurology and Neurorehabilitation Center, Kantonsspital Luzern, Switzerland; [4]Dept. of Neurology, Inselspital, Bern, Switzerland*

Schizophrenia patients are impaired in nonverbal communication, including gesture production and social perception. However, the impact of gestural behavior on nonverbal social perception remains unknown, as is the contribution of negative symptoms, working memory and abnormal motor behavior. Thus, the study tested whether impaired gesture performance was related to poor nonverbal social perception, gestural knowledge or motor abnormalities. Forty six patients with schizophrenia (80%), schizophreniform (15%) or schizoaffective disorder (5%) and forty four healthy controls matched for age, gender and education were included. Participants completed four tasks on nonverbal communication including gesture performance, gesture recognition, nonverbal social perception and tool use. In addition they underwent comprehensive clinical and motor assessments. Patients presented impaired nonverbal communication in all tasks compared to controls. Furthermore, in contrast to controls, performance in patients was highly correlated between tasks, not explained by supramodal cognitive deficits such as working memory. Schizophrenia patients with impaired gesture performance also demonstrated poor nonverbal social perception, gestural knowledge and tool use. Importantly, motor abnormalities negatively mediated the strong association between nonverbal social perception and gesture performance. The factor negative symptoms and antipsychotic dosage were unrelated to the nonverbal tasks. The study confirmed a generalized nonverbal communication deficit in schizophrenia. Specifically, the findings suggested that nonverbal social perception has a relevant impact on gestural impairment in schizophrenia, which is independent of negative symptoms but mediated by motor abnormalities.

*Topic:* Clinical research

**ID: 124**

## Gesture use in aphasic patients: Evidence from eye tracking during face to face interaction

**Basil Preisig[1], Noëmi Eggenberger[1], Giuseppe Zito[2], Rahel Schumacher[1], Simone Hopfner[1], Thomas Nyffeler[1,3], Klemens Gutbrod[4], René Müri[1,4,5]**

*[1]Perception and Eye Movement Laboratory, Departments of Neurology and Clinical Research, Inselspital, University Hospital Bern, and University of Bern, Switzerland; [2]ARTORG Center for Biomedical Engineering Research, University of Bern, Switzerland; [3]Neurology and Neurorehabilitation Center, Department of Internal Medicine, Luzerner Kantonsspital, Switzerland; [4]Division of Cognitive and Restorative Neurology, Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland; [5]Gerontechnology and Rehabilitation Group, University of Bern, Bern, Switzerland*

Co-speech gestures are a part of non-verbal communication in natural conversations. A speaker conveys nonverbal information to the listener by spontaneous hand movements. At the same time, gesturing also facilitates the speaker's own verbal production. Aphasic patients are restricted in speech production and comprehension. It is unclear to which extent aphasic patients make compensatory use of gestures to express information that cannot be expressed through speech. Moreover, it is unknown whether aphasic patients also gather information from co-speech gestures. In a previous study, we used eye movement recordings to explore if aphasic patients adapt their visual exploration strategies while watching natural interactions. Similar to healthy controls, aphasic patients attend the speaking dialog partner more if he or she is gesturing. This indicates that aphasic patients might be able to disambiguate speech perception by non-verbal cues. In the present study, we are investigating production and perception of co-speech gestures in aphasic patients while they are engaged in face-to-face interaction. We aim to reveal compensatory strategies on the level of language perception and language production. Preliminary data will be presented.

*Topic:* Clinical research
*Keywords:* Gestures, visual exploration, dialogue, aphasia, apraxia, eye movements

**ID: 129**

## Perception of co-speech gestures in aphasic patients: an eye movement study

**Noëmi Eggenberger[1], Basil Preisig[1], Simone Hopfner[1], Tim Vanbellingen[1], Rahel Schumacher[1], Thomas Nyffeler[2], Klemens Gutbrod[3], René Müri[1]**

*[1]Departments of Neurology and Clinical Research, Inselspital Bern; [2]Neurology and Neurorehabilitation Center, Kantonsspital Luzern; [3]Division of Cognitive and Restorative Neurology, Inselspital Bern*

Introduction: Gesturing, including co-speech gestures, is a crucial part of human communication. The present study aimed to investigate the perception of speech and gestures, and in particular the influence of congruence between speech and gesture on both verbal comprehension and visual exploration. Healthy subjects spend about 88-95% of the time fixating a speaker's face, while only a minority of fixations is directed at gestures. It is unclear whether aphasic patients display a similar pattern.
Method: Twenty aphasic patients and 30 healthy controls watched videos in which speech was either combined with congruent, incongruent, or meaningless gestures. Comprehension was assessed with a decision task, while remote eye-tracking allowed analysis of visual exploration of predefined areas of interest.
Results: Patients displayed a decreased accuracy in incongruent sequences whereas congruence between speech and gesture led to an increase in accuracy. Furthermore, patients fixated significantly less on the face and slightly more on the hands compared to controls.
Conclusion: Co-speech gestures play an important role for aphasic patients as they modulate verbal comprehension. Incongruent gestures evoke significant interference and deteriorate patients' comprehension. In contrast, congruent gestures enhance comprehension in aphasic patients, which might be valuable for clinical and therapeutical purposes.

*Topic:* Clinical research
*Keywords:* Gestures, aphasia, eye movements, visual exploration, verbal comprehension

**ID: 131**

## Theta burst stimulation improves visual search in spatial neglect independently of attentional load

**Dario Cazzoli[1,2], Clive R Rosenthal[2], Christopher Kennard[2], Giuseppe A Zito[1], René M Müri[1,3], Thomas Nyffeler[3,4]**

*[1]Gerontechnology and Rehabilitation Group, Artorg Center, University of Bern, CH; [2]Nuffield Department of Clinical Neurosciences, University of Oxford, UK; [3]Perception and Eye Movement Laboratory, Department of Clinical Research, Department of Neurology, University of Bern, and Inselspital, Bern University Hospital, CH; [4]Centre of Neurology and Neurorehabilitation, Luzerner Kantonsspital, CH*

The severity of spatial neglect, i.e., the failure to orient, attend, and respond towards the contralesional side of space, is considerably exacerbated by increases in visual attentional load. It would thus be highly desirable to identify a therapeutic intervention that ameliorates neglect independently of attentional load. Transcranial magnetic stimulation has been shown to reduce neglect severity, the interaction with attentional load is however unknown.
Here, in ten neglect patients, we examined the effect of a continuous theta burst stimulation protocol on neglect severity as a function of high and low attentional load conditions. Search efficiency was assessed by recording the accuracy of visual target detection, and eye movements.
Our results show that continuous theta burst stimulation significantly ameliorates neglect irrespective of the attentional load, equating target detection between low and high load conditions. The results also demonstrate that the significant amelioration in search efficiency was correlated with a re-distribution of visual fixations towards the contralesional side of space.
The application of continuous theta burst stimulation in neglect thus represents a substantive advance, since it is unprecedented in triggering an amelioration of neglect irrespective of the attentional load.

*Topic:* Clinical research
*Keywords:* Hemispatial neglect; stroke; repetitive transcranial magnetic stimulation (rTMS); visual attention; eye movements

**ID: 147**

## The microstates of emotional change: an ERP investigation

**Kristina Barbara Rohde[1], Franz Caspar[1], Antonio Pascual-Leone[3], Thomas Koenig[2], Maria Stein[1,2]**

*[1]Department of Clinical Psychology and Psychotherapy, University of Bern, Switzerland; [2]Deparment of Psychiatric Neurophysiology, University of Bern, Switzerland; [3]Department of Clinical Psychology, Windsor University, Canada*

Change in emotional schemes is critical to promote therapeutic change. The empty chair dialogue is an emotion-focused and Gestalt therapy technique to foster emotional change. This technique has proven helpful in alleviating long-standing interpersonal grievances ('unfinished business') and thus facilitating change in emotional schemes. However, little is known about the neural signature of such emotional change.
The present project combined psychotherapeutic process research with a neurophysiologic approach in order to investigate the neural processes linked to emotional change. Individuals experiencing 'unfinished business' participated in a one-session emotion-focused intervention. Event-related brain potentials were recorded before and after the intervention while participants were attentively looking at pictures of the person with whom they had 'unfinished business' and pictures of control persons. Microstate analysis with the factors time (pre, post) and picture type (unifinished business-person, control person) revealed significant interactions in three microstates occurring around 100ms, 500ms and 600ms. These effects will be discussed with respect to sensory processing, memory updating, emotional salience and emotion regulation.

*Topic:* Clinical research
*Keywords:* emotion, psychotherapy, ERP, EEG

**ID: 157**

## Signal improvement in multichannel NIRS by channel redundance over the optode/tissue interfaces

**Arto C. Nirkko[1], Christof Zubler[2], Christian Rummel[2]**

*[1]Neurology, University of Bern, Switzerland; [2]Neuroradiology, University of Bern, Switzerland*

Introduction: Mapping of the brain with near-infrared spectroscopy (NIRS) allows for non-invasive assessment of brain oxygenation, taking advantage of the differential absorption characteristics of oxygenated and de-oxygenated hemoglobin at different wavelengths. As instance of diffuse optical imaging, infrared light irradiated onto the surface of the head by a transmitting optode is scattered and partially absorbed by the underlying tissue and picked up by a receiving optode. With standard techniques implemented in commercial continuous-wave NIRS devices, only measurements of relative changes with respect to a baseline value are possible, and the reference value can unexpetedly shift and drift, for example due to small or larger dislocations of the optodes due to movement. The aim of this work is to improve this.
Methods: The relative absorptions are usually assessed using the modified Beer-Lambert law. For this work, the law was further extended by additional G factors to model the coupling between device and tissue (mainly at the optodes), i.e. the source of artifacts. Channels were configured from each transmitter optode to more than one receiver optode and vice versa. With other reasonable assumptions (such as, crossing channels essentially measure the same region, and all wavelenghts are similarily affected by changes in optode coupling), the resulting equations can be solved also for the additional unknown coupling factors [1]. The results were tested with data from another study [2].
Results: NIRS artifacts which were prominent in the manufacturers original signal were segregated into the additional factors representing optode to tissue coupling, sucessfully freeing the Hb signal from multiple types of artifact. Observed improvement in signal-to-noise is probably due to the "averaging" effect of the additional assumptions, combining information from several channels.
Conclusions: Using multiple redundant NIRS channels in suitable spatial configurations, it is possible to model, amongst other factors, the effect of optode to tissue coupling and thereby reduce undesired contributions including motion artifacts. This can be done without processing of time course data, but by only processing each time point independently.

References:
[1] A.C. Nirkko, patent pending
[2] C. Rummel et al., Monitoring cerebral oxygenation during balloon occlusion with multichannel NIRS. JCBFM 2014.

*Topic:* Clinical research
*Keywords:* multichannel NIRS, near infrared spectroscopy, diffuse optical imaging, artifact elimination, optode tissue coupling

**ID: 160**

## Lithium attenuates brain injury and improves neurofunctional outcome in experimental meningitis

**Fabian D. Liechti[1,2], Nicolas Stüdle[1,2], Regula Theurillat[3], Denis Grandgirard[1,2], Wolfgang Thormann[3], Stephen L. Leib[1,2,4]**

*[1]Neuroinfection Laboratory, Institute for Infectious Diseases, University of Bern, Bern, Switzerland; [2]Cluster for Regenerative Neuroscience, Departepement of Clinical Research, University of Bern, Bern, Switzerland; [3]Clinical Pharmacology Laboratory, Institute for Infectious Diseases, University of Bern, Bern, Switzerland; [4]Biology Division, Spiez Laboratory, Swiss Federal Office for Civil Protection, Spiez, Switzerland*

Pneumococcal meningitis is associated with high morbidity and mortality rates. Brain damage caused by this disease is characterized by apoptosis in the hippocampal dentate gyrus, a morphological correlate of learning deficits in experimental paradigms. The mood stabilizer lithium has previously been found to attenuate brain damage in ischemic and inflammatory diseases of the brain. An infant rat model of pneumococcal meningitis was used to investigate the neuroprotective and neuroregenerative potential of lithium. To assess an effect on the acute disease, LiCl was administered starting five days prior to intracisternal infection with live Streptococcus pneumoniae. Clinical parameters were recorded, cerebrospinal fluid (CSF) was sampled, and the animals were sacrificed 42 hours after infection to harvest the brain and serum. Cryosections of the brains were stained for Nissl substance to quantify brain injury. Hippocampal gene expression of Bcl-2, Bax, p53, and BDNF was analyzed. Lithium concentrations were measured in serum and CSF. The effect of chronic lithium treatment on spatial memory function and cell survival in the dentate gyrus was evaluated after LiCl treatment during 3 weeks following infection by Morris water maze and BrdU incorporation. In the hippocampus, LiCl significantly reduced apoptosis and gene expression of Bax and p53 while it increased expression of Bcl-2. IL-10, MCP-1, and TNF were significantly increased in animals treated with LiCl compared to NaCl. Chronic LiCl treatment led to improved spatial memory in infected animals. The mood stabilizer lithium may thus be a therapeutic strategy to attenuate neurofunctional deficits as a result of pneumococcal meningitis.

*Topic:* Basic research animal
*Keywords:* neuroinfection, bacterial meningitis, lithium, dentate gyrus, Morris water maze

**ID: 170**

## Post-H1N1 flu vaccination narcolepsy in Switzerland

**Ulf Kallweit, Johannes Mathis, Claudio L.A. Bassetti**

Bern University Hospital, Neurology Department, Switzerland

Narcolepsy-cataplexy is a chronic sleep-wake disorder and suggested to be immune-mediated, involving genetic and environmental factors. The autoimmune process probably leads to a loss of hypocretin neurons in the lateral hypothalamus. Epidemiological studies in several countries proved an increased incidence of narcolepsy after influenza (H1N1) vaccination and after infection. This survey in the 30 sleep-centers in Switzerland led to the identification of nine H1N1 vaccinated children and adults as newly diagnosed narcolepsy. Clinical features including the abrupt and severe onset of sleepiness and cataplexy confirmed data from previous studies. Striking new features of our series were sleep fragmentation at disease onset, in particular in children and adolescents and spontaneous improvement of cataplexy in some patients later on.

*Topic:* Clinical research
*Keywords:* Post-H1N1 narcolepsy, narcolepsy-cataplexy, vaccination, certified sleep-centers, hypocretin

# Symposia

## Symposium I: Stroke

**Time:** 14:00-15:30

**Place:** Festsaal

Chairs: Jan Gralla, Marcel Arnold

Marcel Arnold, Bern

### Biomarkers in Stroke – Interests and Needs of the Clinicians

Stroke is a very frequent and dynamic disease. More than 200 blood biomarkers have been evaluated. However none of these markers have yet been implemented in routine clinical practice. Nevertheless, stroke biomarkers have a big potential to reach the clinical setting because stroke medicine struggles with many unsolved questions.
In the acute setting there is need for biomarkers which distinguish between ischemic stroke and intracerebral hemorrhage. In addition it would be helpful to have blood biomarker predicting response to revascularization therapy and complications.
In the acute setting of stroke, the results of biomarker blood tests should be immediately available and easily interpretable and need to have a very high diagnostic accuracy. Moreover an ideal blood biomarker should give additional information to the clinical examinations and neuroimaging findings and be cost-effective.
In the subacute and chronic setting of cerebrovascular diseases, blood biomarkers may be helpful to determine stroke etiology and to guide the timing and need of additional examinations. Moreover, the risk of complications, the individual benefit from secondary preventive therapies and the clinical long term prognosis are very important questions for the clinicians.
In the design of future biomarker studies the potential clinical impact of the results should be emphasized. A prospective multicenter and multifactor approach is mandatory for many clinical questions.

Joan Montaner, Barcelona

### Discovery of Biomarkers in Stroke: from single marker to proteomic approaches

Emerging data suggest that a wide array of measurable biomarkers in blood may provide a novel window into the pathophysiology of stroke. In this talk I will combine state of the art in the field with own recent data on biomarkers discovered at my lab.
I will stress difficulties in stroke biomarkers discovery due to the complexity of this approach at several levels: At the *cellular level* with many different components of the neurovascular unit (neurons, astrocytes…) contributing to the release of potential biomarkers; at the *organ level* since other diseases than stroke produce acute brain damage and finally at the *disease level* with several stroke subtypes that might have different biomarkers profiles.
I will review technical ways of discovering new biomarkers (omics approaches), giving specific examples on proteomics. Interesting candidate biomarkers coming from 3 relevant described human proteomes of the CSF, microdialysate and brain under ischemia conditions will been described.
Main indications for future stroke biomarkers are: (1) To predict stroke risk; (2) To make stroke diagnosis; (3) To differentiate stroke subtypes; (4) To establish outcome and (5) To use biomarkers as treatment end-points.
The use of specific brain biomarkers might aid stroke diagnosis allowing rapid referral of stroke patients to hospitals with acute treatments, such as t-PA being available. Considering prognosis, we will discuss the role of outcome biomarkers to add patient and relatives information, to weight potential risks/benefits of

treatment options and to make rationing decisions to safe resources, i.e. stroke unit patient allocation… A panel of biomarkers covering different worsening causes should be needed (Infarct growth, hemorrhagic transformation, cardiac complications, infections, recurrences…).
In conclusion, many encouraging molecular candidates have been found that appear to match the known cascades of neurovascular injury after stroke. However, whether these putative biomarkers may indeed have direct clinical utility remains verification, validation and replication in well-designed multicentric and international studies.

Marwan El Koussy, Bern

**MRI biomarkers of ischemic stroke**

# Symposium II: From sensing to perceiving

**Time:** 14:00-15:30

**Place:** room 416

Chairs: Katharina Henke, Thomas Dierks

Lea Meier, Bern

## Perceptual Rivalry of Homeostatic and Sensory-Evoked Emotions

The ability to experience a wide variety of emotions is a fundamental characteristic of mankind. Neural correlates have been described for emotions evoked by states of homeostatic imbalance (e.g. thirst, hunger, and breathlessness) and for emotions induced by external sensory stimulation (such as fear and disgust). However, the neurobiological mechanisms of their interaction, when the two kinds of emotions are experienced simultaneously, are still unknown. We investigated the neurobiological and behavioural interaction using subjective ratings, blood parameters, and functional magnetic resonance imaging (fMRI) in a situation of emotional rivalry, when both a homeostatic emotion (thirst) and a sensory-evoked emotion (disgust) were perceived at the same time. Twenty highly dehydrated male subjects rated a disgusting odour as significantly less repulsive when they were thirsty. On the neurobiological level, we found that this reduction in subjective disgust perception during thirst was accompanied by a significantly reduced neural activity in the insular cortex, a brain area known to be considerably involved in processing of disgusting stimuli. Furthermore, during disgust perception in the satiated condition, we observed significant functional connectivity between disgust related brain areas, which was absent during the stimulation in the thirsty condition. These results suggest interference of conflicting emotions: A homeostatic imbalance can attenuate another emotion evoked by the sensory perception of a potentially harmful external agent. This finding offers novel insights with regard to the behavioural relevance of biologically different types of emotions, indicating that some types of emotions are more imperative for behaviour than others. As a general principle, this modulatory effect during emotional conflicts may function to safeguard survival.

Janek Lobmaier, Bern

## Hormonal effects on perception

Hormones are molecules which our body uses for the communication between organs and tissues to regulate physiological and behavioral activities such as such as digestion, metabolism, perception, sleep, lactation, stress, movement, reproduction, and mood. In this talk I will focus on hormonal effects on social perception and cognition. A natural way to investigate hormonal influences on (social) perception is to study naturally cycling females during different menstrual cycle phases. Indeed, the menstrual cycle has been shown to affect socially relevant aspects of perception and behaviour. For example, women have been shown to dress, dance and walk in more attractive ways during days of high compared to low fertility. Conversely, evidence has accumulated that emotion recognition performance is highest during the non-fertile luteal phase. We tested whether the female menstrual cycle affects the amount and willingness to exhibit facial mimicry. Facial mimicry describes the unintentional imitation of another person's non-verbal displays. Facial mimicry assists in recognizing the emotional expression of another person and at the same time it can signal empathy and compassion of an observer towards a counterpart. Given that increased progesterone levels during the luteal phase underlie increased social monitoring, we expect that women show more facial mimicry during the non-fertile luteal phase than during the late follicular phase. To test this, we measured zygomaticus major and corrugators supercilii activity in 50 naturally cycling women while they viewed short video clips of 8 male and 8 female actors each showing happy, angry, and neutral expressions. Each woman was tested twice, once near ovulation and once during the luteal cycle phase. The order of testing sessions was counterbalanced across participants and ovulation was determined using ovulation test strips. We additionally measured salivary estradiol, progesterone and testosterone levels to ascertain whether hormone levels could predict facial mimicry. We found that during the luteal

phase (when progesterone levels are high) women mimicked more than near ovulation. These results may explain why women are better at emotion recognition during the luteal phase. Further implications of these findings are discussed.

Marc Züst, Bern

**Long-term effects of subliminal perception**

Subliminal stimulus presentation, i.e. presenting a stimulus very briefly between pattern masks, is an effective way to prevent information from reaching conscious awareness. Nevertheless, stimuli are physically present, picked up by the retina, and transferred to the visual cortex. But what happens to this unconscious information in the brain, how far is it processed and does it get stored long-term for later retrieval? Single unit recordings in primates show that subliminal stimulus presentation elicits neuronal firing in higher level areas of the ventral visual stream, but the mask that follows the stimulus interrupts the stimulus-related firing reducing processing strength and breadth. As preliminary data from single unit recordings in humans suggest, such reduced subliminal signals can still propagate along the ventral visual stream and activate neurons in hippocampus, amygdala and entorhinal cortex.
We found that subliminally presented face-occupation pairs are processed and stored by the hippocampus yielding behaviorally significant retrieval effects over at least 20 minutes. Because this unconsciously encoded information was rapidly encoded, relational in nature, stored for long-term, and flexibly retrieved, we take it for an unconscious form of episodic memory. This is the first study demonstrating long-term retention of subliminally encoded material. Earlier studies of subliminal perception yielded behavioral effects with study-test intervals of in the millisecond or second range. Those studies were conducted with encoding stimuli consisting of single rather than multiple items. We assume that subliminal stimuli must be complex and new to engage the hippocampus and capitalize on its neuroplasticity that provides for efficient long-term storage.
This study suggests that unconscious episodic memory traces are not short-lived “artifacts” but rather genuine, behaviorally relevant signals worth maintaining over an extended period of time. Taking into account that humans are not able to consciously maintain every association between the facets of their environment, the capability to do so unconsciously can be very helpful.

Thomas Nevian

**Pain perception**

The perception of a painful stimulus is a very important warning signal for the organism. It signals potential or acute tissue damage and results in an immediate response to prevent further damage. Pain induced by injury causes a sensitization of the pain transmission system triggering behaviour that guards and protects the injury site to promote healing. Pain is a complex sensory modality that not only involves the somatosensory perception of a noxious stimulus, but it also causes an emotional evaluation of it. I will discuss nociception and the processing of this information that leads to the perception of pain. This involves the activation of a number of cortical and subcortical brain areas. Insights in the mechanisms of nociception are important for our understanding of the pathological conditions of chronic pain.

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| Arnold | Marcel | Inselspital Bern | Neurology |
| Badertscher | Lilo | University of Bern | Department of Psychiatric Neurophysiology |
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| Manconi | Mauro | Neurocenter of Southern Switzerland | Sleep Center |
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| Mast | Fred Walter | University of Bern | Psychology |
| Meier | Beat | University of Bern | Psychology |
| Meier | Lea | University Hospital of Psychiatry, University of Bern | Department of Psychiatric Neurophysiology |
| Meissner | Erik | Universität Bern | Allgemeine Psychologie und Neuropsychologie |
| Moeseneder | Laura | University of Bern | Psychology |
| Montaner | Joan | University of Barcelona | |
| Morishima | Yosuke | University Hospital of Psychiatry | Department of Psychiatric Neurophysiology |
| Mosimann | Urs | University Hospital of Old Age Psychiatry | |
| Müller | Stefanie | University of Bern | University Hospital of Psychiatry |
| Müri | René | Department of Neurology | |
| Mürner-Lavanchy | Ines | University Hospital Bern | Neuropaediatrics |
| Nauer | Sonia | University of Bern | |
| Nevian | Thomas | University of Bern | Institut für Physiologie |
| Nirkko | Arto C. | Neurology | |
| Oppliger | Byron | University of Bern | Department of Obstetrics and Gynecology, and Department of Clinical Research |
| Orosz | Ariane | University Hospital of Psychiatry | Department of Psychiatric Neurophysiology |
| Pace | Marta | ZEN – Center for Experimental Neurology, | Department of Neurology, University Hospital (Inselspital), Bern, Switzerland |
| Padovani | Tullia | University of Bern | |
| Paladini | Rebecca | ARTORG Center | Gerontechnology and Rehabilitation |
| Peigneux | Philippe | University of Bruxelles | |
| Perny | Michael | University of Bern | |
| Perrig | Walter | University of Bern | Psychology |
| Pollo | Claudio | University of Bern | |
| Preisig | Basil | University of Bern | Neurology and Clinical Research |
| Raabe | Andreas | Insel University Hospital | Department of Neurosurgery |

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|---|---|---|---|
| Rösler | Kai M. | Neurologische Universitätsklinik | Dept. of Neurology |
| Ruch | Simon | Center for Cognition, Learning and Memory | |
| Ruegsegger | Céline | University of Bern | Institute of Cell Biology |
| Rummel | Christian | Support Center for Advanced Neuroimaging (SCAN) | University Institute for Diagnostic and Interventional Neuroradiology, Inselspital |
| Savic | Branislav | University of Bern | General Psychology and Neuropsychology |
| Saxena | Smita | University of Bern | Institute of Cell Biology |
| Saxer | Elsbeth Ursula | none (retired) | |
| Schimmelmann | Benno | University of Bern | |
| Schindler | Kaspar Anton | Inselspital | Neurology |
| Schoeberlein | Andreina | University of Bern | Department of Obstetrics and Gynecology, and Department of Clinical Research |
| Schreier | David | Inselspital | Neurology |
| Schumacher | Rahel | Inselspital | Departments of Neurology and Clinical Research |
| Schwab | Simon | University Hospital of Psychiatry | Dept. of Psychiatric Neurophysiology |
| Seiler | Stefanie | University Hospital Bern | Neurosurgery |
| Senn | Walter | Universität Bern | Institut für Physiologie |
| Stalder | Franziska | University of Bern | Allgemeine Psychologie und Neuropsychologie, CCLM Dienstleistungszentrum |
| Stegmayer | Katharina | University Hospital of Psychiatry | |
| Steimer | Andreas | Inselspital Bern | University Hospital for Neurology |
| Stein | Maria | University of Bern | Department of Clinical Psychology and Psychotherapy |
| Stephan | Marianne Anke | CHUV | Neurosciences Cliniques |
| Strik | Werner | University of Bern | Psychiatry |
| Studer | Martina | University Children's Hospital, Inselspital Bern | Department of Pediatric Neurology, Development & Rehabilitation |
| Täuber | Martin | University of Bern | Rector |
| Urwyler | Prabitha | University of Bern | Gerontechnology and Rehabilitation |
| Urwyler | Stephan | University of Berne | Dept. of Chemistry and Biochemistry |
| Vallejo | Vanessa | ARTORG Center for Biomedical Engineering Research | Gerontechnology and Rehabilitation |
| Viher | Petra Verena | Universitätsklinik für Psychiatrie und Psychotherapie Bern | |
| Walter | Stefan | University of Bern | Psychology |
| Walther | Sebastian | University Hospital of Psychiatry | |
| Wapp | Manuela | Inselspital Bern | Diagnostische und Interventionelle Neuroradiologie / SCAN |
| Widmer | Hans Rudolf | University Hospital | Neurosurgery |
| Winkelbeiner | Stephanie Andrea | University Clinic of Psychiatry | Departement of Psychiatric Neurophysiology |
| Witmer | Joëlle | Universität Bern | Institut für Psychologie |
| Wurtz | Pascal | University Hospital of Old Age Psychiatry | |
| Wüthrich | Sergej | University of Bern | Psychology |
| Zito | Giuseppe Angelo | University of Bern | ARTORG Center for Biomedical Engineering Research |
| Züst | Marc | University of Bern | Psychology |