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Dear CNB members,

With the CNB Newsletter, we intend to inform you about upcoming CNB events, ongoing projects and give insights into the research topics of selected CNB members. In this edition we look back on the 16th Annual Meeting in 2021 and are looking forward to the Brainweek 2022.
We are pleased to introduce the research group of Dr. Leila Tarokh, as well as the new research group of Prof. Dr. med. Adrian Guggisberg.

Also note that we are updating and upgrading the CNB-Website, so please feel free to contact Ms. Noémi Allet (noemi.allet@unibe.ch) if you want to make changes on your research group-site (e.g. add photos, videos, members etc.).

Please also send an updated list with all your Group-Members (name, position, contact-information) so that we can update the website.

We hope you enjoy reading the December 2021 edition.

Prof. Dr. Sebastian Walther
President CNB

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16th CNB Annual Meeting

Friday, 29th of October, 9.00-17.15

This Year's Annual Meeting was held at the Inselspital. The welcome address from the dean of the medical faculty and president of the CNB strategic board Prof. Dr. med. Claudio Bassetti pointed out recent developments in the neurosciences. Afterwards, the first key-note speaker Prof. Dr. Britta Engelhardt provided an excellent overview on the blood brain barrier that controls CNS immunity. Next, four junior scientists presented their work. Their abstracts had been selected for oral presentations. These short presentations covered the interplay between brain functional states and the subjective experiences of behavior. Ida Boccalaro reported on the sleep-stage dependency of auditory evoked potentials in different brain regions and its interplay with fear-conditioning. Similarly, we learned from Raquel Sandoval Ortega how the emotional and sensory components of pain processing are differentially affected by sleep-related brain electric rhythms. State-dependency of brain-responses was also shown by Karin Bütler, who systematically modified the subjects' believes about their own body using VR, and finally, Florian Wüthrich presented evidence that slowing of finger-tapping in schizophrenia patients with motor symptoms was associated with a failure to deactivate task-irrelevant brain activity. Therefore, this session proved that CNB includes an inspiring community of young researchers working at the interface between neurophysiology, experiencing and behavior.

The second key-note number 2 was held by Prof. Helbok from the Department of Neurology and ICU of the University of Innsbruck. In his keynote lecture he focused on immediate and long-term effects of pandemics in the 21st century. Beyond the CoVID 19 pandemic, a special focus of his talk was on neurological manifestations and complications of infectious diseases, both in viral and bacterial infections. He also provided an outlook on recurrent and new infectious agents that may constitute novel threats for rural and urban societies in the future.

The poster-session was very interesting for all the fields, the winners were: **Jakub Králik** et al. (Category: Basic research animal) *Title: "ON-bipolar cell targeted optogenetic gene therapy in light of retinal degeneration: Functional evaluation using multi-electrode arrays",* **Mirjam Studler & Lorena Gianotti** et al. (Category: Basic research human) *Title: "Local slow wave activity in regular sleep reveals individual risk preferences"* & **Nicole Gangl** et al. (Category: Clinical Research) *Title: "Volume reductions in the limbic network in patients with paranoia".*

In the afternoon the parallel symposia took place. Prof. Dominique de Quervain from the University of Basel talked about the effects of the COVID-19 pandemic on mental health. He is one of the lead investigators of the Swiss Covid Stress Study that conducted multiple surveys during the pandemic with up to 11'000 responders. His team found self-reported symptoms of depression to be massively increased in adolescents and young adults, but also in citizens facing pandemic related financial troubles. PD Dr. Hofmann reported on the neuroimaging findings and related pathways of cerebral infections. She put a special focus on Malaria and how imaging based disease signatures differ between children and adults as well as between fatal and nonfatal cases. PD Dr. Tobias Krieger from the University of Bern discussed loneliness and perceived social isolation. He demonstrated that loneliness is a fairly common feeling in the general population and some authors even consider it an epidemic phenomenon these days. He also presented evidence that social isolation and loneliness have detrimental effects on health and significantly increase the risk of premature mortality.

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In the group leaders' meeting outreach and interaction in complicated times were discussed. Members are asked to update their content on the CNB website. The inclusion of video material is strongly encouraged. In addition, scientific communication can be bolstered using social media channels such as Twitter or LinkedIn. CNB has an own Twitter account and will retweet any links to publications or open positions of CNB members (please send a message to or tag Clinical Neuroscience Bern or @clin_neurobern), we can also publish papers (e.g.) on LinkedIn, please send a message to or tag Clinical Neuroscience Bern. Finally, we accepted two new research groups: Neurorehabilitation & Neuromodulation with the Group Leader Prof. Dr. med. Adrian Guggisberg and Neurophysiology & Adaptive Neuromodulation with the Group Leader Dr. med. Gerd Tinkhauser.

Thank you all again for a great annual meeting, with lots of talks, interactions and posters. For some more impressions and the list with all the abstracts, please visit our homepage: https://www.neuroscience.unibe.ch/activities/16th_cnb_annual_meeting/

We're looking forward to hosting next year's annual meeting!

The next Annual Meeting will take place on the 9th of September 2022. The program and further information will be published on our website (www.neuroscience.unibe.ch) and sent out via mail. If you like to participate as a speaker, help organize or have some ideas for the next Annual Meeting please reach out to any member of the Executive Committee. We are looking forward to your inputs, ideas and help.

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Selected Research Group

Dr. Leila Tarokh

Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland
University Hospital of Child and Adolescent Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland

Every night consciousness is temporarily suspended while we sleep. During this time our brain generates an orchestra of oscillatory activity only seen during sleep. One of the guiding principles of our work is that by studying brain activity during sleep, referred to as sleep neurophysiology and measured with the electroencephalogram (EEG), we can gain unique insight into brain function in health and disease. In particular, we are interested in the reciprocal relationship between sleep and psychiatric illness. Disrupted sleep is ubiquitous among individuals with psychiatric disorders and emerging evidence suggests that poor sleep increases the risk of psychiatric disorders.
In order to understand the role of sleep in psychiatric disorders we take a longitudinal approach to test (1) whether sleep neurophysiology is a biomarker that can predict clinical course over a year; (2) whether sleep problems are predictive of future psychopathology and; (3) the stability of the association between sleep neurophysiology and psychopathology at two time points one year apart.

Our group takes a multimodal approach to tackle these questions. Once enrolled in our studies, we set to work characterizing our participants in depth. For one, participants are interviewed to assess clinical symptomology and fill out a series of questionnaires reporting on a wide array of behaviors and traits including psychopathology, personality and sleep. We are currently studying adolescents because this is the period during which most psychiatric illnesses have their onset. For this reason, we also ask parents/guardians to report on their observations of the participant in order to gain an in-depth view. We then perform sleep EEG measurement in the participant's home, effectively transforming their room into a mini sleep lab for the night. While our main focus is on the brain oscillations generated during sleep, we also measure other biological systems known to impact psychopathology, such as cortisol and heart rate.
Once we have carefully characterized our participants, we are poised to assess whether we can predict future psychopathology based on sleep neurophysiology. If our hunch that sleep neurophysiology is a biomarker able to predict future outcomes turns out to be true, then we can help by identifying youth at risk and intervening early, thereby improving outcomes. In order to achieve this aim, we map the trajectory of mental health over a year by administering monthly online questionnaires.

Another key question is whether sleep problems precede the onset of psychopathology, as some studies have suggested, or are a result of it. Sleep is a modifiable behavior and effective behavioral interventions to improve sleep exist, making sleep an important therapeutic target. In order to answer this question, across the year of administering monthly self-report questions, participants also wear a watch-like device called an actigraph on a daily basis. Actigraphs can delineate sleep from waking based on motion and provide an objective measure of sleep timing and behavior over longer periods of time. Preliminary results from our studies suggest that some sleep problems may precede or exacerbate psychopathology.

Finally, humans are dynamic, as are our moods and behaviors. Therefore, we repeat all baseline measures (e.g., sleep EEG) after a year. This allows us to determine how stable the association between sleep neurophysiology and psychopathology is.
In addition to the basic science questions described above, we are currently testing the efficacy of simple behavioral sleep intervention on depression and sleep in depressed adolescents. Thus, though rooted in basic science, our research program takes a translational approach to addressing mental health issues during adolescence – a period in which many mental health disorders have their onset and interventions are more effective.

Our vision is that by melding clinical assessments with measures of brain activity we can understand the etiology of psychiatric disorders and contribute to their management and care. We are grateful to our participants, their families and our many collaborators who are helping us to realize this vision.

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Recent Publications:

- o Fontanellaz-Castiglione, Chiara, Andjela Markovic, and Leila Tarokh. "Sleep and the Adolescent Brain." Current Opinion in Physiology, n.d. https://doi.org/10.1016/j.cophys.2020.01.008.

- o Hamann, Christoph, Thomas Rusterholz, Martina Studer, Michael Kaess, and Leila Tarokh. "Association between Depressive Symptoms and Sleep Neurophysiology in Early Adolescence." Journal of Child Psychology and Psychiatry, and Allied Disciplines 60, no. 12 (December 2019): 1334–42. https://doi.org/10.1111/jcpp.13088.

- o Markovic, Andjela, Michael Kaess, and Leila Tarokh. "Gender Differences in Adolescent Sleep Neurophysiology: A High-Density Sleep EEG Study." Scientific Reports 10, no. 1 (28 2020): 15935. https://doi.org/10.1038/s41598-020-72802-0.

- o Markovic, Andjela, Michael Kaess, and Leila Tarokh. "Environmental Factors Shape Sleep EEG Connectivity During Early Adolescence." Cerebral Cortex (New York, N.Y.: 1991) 30, no. 11 (October 1, 2020): 5780–91. https://doi.org/10.1093/cercor/bhaa151.

- o Markovic, Andjela, Ashura Buckley, David I. Driver, Diane Dillard-Broadnax, Peter A. Gochman, Kerstin Hoedlmoser, Judith L. Rapoport, and Leila Tarokh. "Sleep Spindle Activity in Childhood Onset Schizophrenia: Diminished and Associated with Clinical Symptoms." Schizophrenia Research, September 23, 2020. https://doi.org/10.1016/j.schres.2020.08.022.

- o Markovic, Andjela, Ashura Buckley, David I. Driver, Diane Dillard-Broadnax, Peter A. Gochman, Kerstin Hoedlmoser, Judith L. Rapoport, and Leila Tarokh. "Sleep Neurophysiology in Childhood Onset Schizophrenia." Journal of Sleep Research 30, no. 2 (April 2021): e13039. https://doi.org/10.1111/jsr.13039.

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## New Research Group

Prof. Dr. med. Adrian Guggisberg

Neurorehabilitation and Neuromodulation
Dept. of Neurology, Inselspital Bern

Neurological and cognitive deficits are frequent and highly disabling. Intensive training and rehabilitation can lead to improvement, but the selection of efficient treatment strategies for the individual patient is often difficult because of insufficient knowledge about how the human brain can recover lost functions. We make use of recent advances in neuroimaging techniques to non-invasively assess the network organization of the brain and to optimize treatment of patients with brain lesions.

My group has pioneered the development of electroencephalography (EEG) analysis procedures that enable the localization and assessment of neural interactions between brain networks (i.e., of functional connectivity, FC). They allow a quantitative assessment of the functional organization of the entire cerebral cortex and can be applied to recordings obtained during tasks but also in a resting-state condition. Recordings obtained at the surface of the scalp are processed with source localization algorithm in order to reconstruct the underlying brain activity. FC can then be calculated on the estimated source activity. The analysis procedures are made freely available to other research labs as open source software (NUTMEG).

We have used modern neuroimaging tools to advance our understanding of how acquired brain lesions influence brain function and how the brain is capable of recovering lost functions. We have shown that brain lesions are associated with a disruption of neural interactions between brain areas (i.e., of functional connectivity, expressed as weighted node degree) in the alpha frequency range (~8-13 Hz, see Figure, part a). This disconnection concerns brain areas that are clinically dysfunctional. For instance, a patient with Broca aphasia shows reduced global alpha coherence in left front-temporal areas (part b, blue color; stroke lesion is marked in dark gray), a patient with motor deficits in precentral areas (part c). Local decreases in alpha-band coherence between a given brain area and the
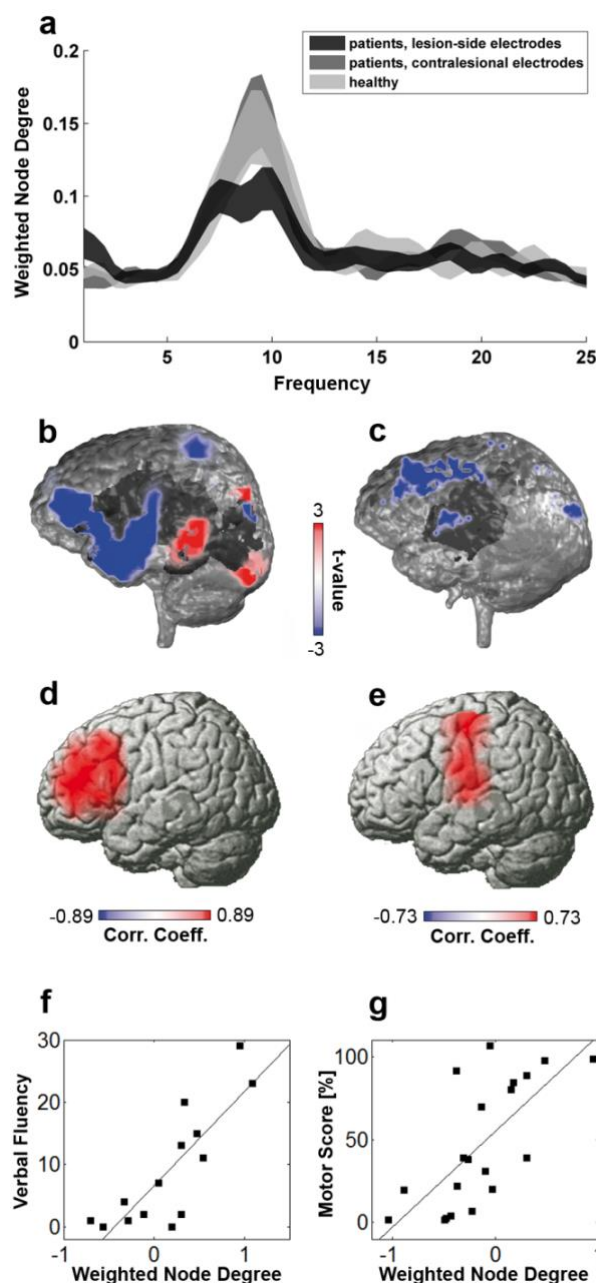
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rest of the brain are linearly correlated with neurological deficits. In other words, the less a brain region remains coherent with the rest of the brain after a lesion, the worse patients perform in corresponding language (parts d, f) and motor (parts e, g) functions. Hence, neurological deficits do not only arise from local tissue damage, but are also associated with a loss of neural interactions of structurally preserved areas.

Patients with stroke also show adaptive increases in neural interactions, which are associated with future clinical improvements. Spontaneous neural beta oscillations (13-30 Hz) at perilesional regions show enhanced coherence with the rest of the brain during the first weeks after stroke. This increase in neural interaction is associated with better clinical recovery in the subsequent months. Hence, preserved ipsilesional brain areas can enhance their interactions with the rest of the brain during a critical time window of opportunity for brain repair, and this might contribute to repair and recovery.

When studying white-matter tracts of patients with stroke using diffusion tensor imaging, we observed that patients with particularly poor recovery were characterized by a great initial damage to the cortico-spinal tract (CST). Hence, motor recovery depends on at least partial integrity of the CST while more severe CST affection leads to poor recovery.

Based on the neural patterns associated with brain plasticity summarized above, we have examined how we can modulate correlates of recovery and improve performance with therapy. Intensive rehabilitation programs were found to induce an increase in neural interactions (FC) between brain regions mediating the trained function and the rest of the brain, which was associated with corresponding clinical improvements. We then tested the effect of novel treatment strategies and found that network interactions can be specifically modulated with therapy such as transcranial magnetic stimulation and neurofeedback and that this can lead to clinical gains.

Our work has revealed that spontaneous activity occurring at rest is not mere noise that has to be subtracted from task-induced neural activity or that can be ignored. On the contrary, we have demonstrated that states of intensive neural interactions between brain areas occurring spontaneously are correlated with successful performance in a wide variety of cognitive and motor tasks. We additionally demonstrated that these spontaneous interaction states enable a more efficient neural processing than the classical task-induced activations. Indeed, task-induced activations are present only in subjects with low spontaneous neural interactions and are associated with effortful and less efficient task execution. The same conclusion can be drawn for learning: spontaneous neural interaction seems to enable more training gains.

Since August 2021, I am head of the Division of Neurorehabilitation at the University Hospital of Berne. I look forward to continue the work here in Bern.

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Recent publications

- Nguyen-Danse DA, Singaravelu S, Chauvigné LAS, Mottaz A, Allaman L, Guggisberg AG. Feasibility of Reconstructing Source Functional Connectivity with Low-Density EEG. Brain Topogr 2021; 34:709-719.

- Allaman L, Mottaz A, Guggisberg AG. Disrupted resting-state EEG alpha-band interactions as a novel marker for the severity of visual field deficits after brain lesion. Clin Neurophysiol 2021;132:2101-2109.

- Koch PJ, Park CH, Girard G, Beanato E, Egger P, Evangelista GG, Lee J, Wessel MJ, Morishita T, Koch G, Thiran JP, Guggisberg AG, Rosso C, Kim YH, Hummel FC. The structural connectome and motor recovery after stroke: predicting natural recovery. Brain 2021;144:2107-2119.

- Egger P, Evangelista GG, Koch PJ, Park CH, Levin-Gleba L, Girard G, Beanato E, Lee J, Choirat C, Guggisberg AG, Kim YH, Hummel FC. Disconnectomics of the Rich Club Impacts Motor Recovery After Stroke. Stroke 2021;52:2115-2124.

- Allaman L, Mottaz A, Kleinschmidt A, Guggisberg AG. Spontaneous network coupling enables efficient task performance without local task-induced activations. J Neurosci 2020; 40:9663-9675

- Trofimova O, Mottaz A, Allaman L, Chauvigné LAS, Guggisberg AG. The "implicit" serial reaction time task induces rapid and temporary adaptation rather than implicit motor learning. Neurobiol Learn Mem 2020;175:107297

- Bonkhoff AK, Hope T, Bzdok D, Guggisberg AG, Hawe RL, Dukelow SP, Rehme AK, Fink GR, Grefkes C, Bowman H. Bringing Proportional Recovery into Proportion: Bayesian Hierarchical Modelling of Post-Stroke Motor Performance. Brain, 2020;143:2189-2206

- Guggisberg AG, Koch PJ, Hummel FC, Buetefisch CM. Brain networks and their relevance for stroke rehabilitation. Clin Neurophysiol 2019;130:1098-124

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③ Upcoming events

14th – 17th March 2022	Brainweek Bern
9th September 2022	17th CNB Annual Meeting

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