Stimulating the brain in the MEG

Organizer: Jim Herring and Markus Butz

Room: # 103

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Entrained Brain Oscillations and the Processing of Complex Auditory or Visual Stimuli
Neurostimulation techniques including transcranial current stimulation (either direct or alternating current (tDCS/tACS)) and deep brain stimulation (DBS) allow us to directly modulate the level and timing of spontaneous neuronal activity while also producing changes outlasting stimulation. Recent methodological advancements provide the unique opportunity to directly study the effects of neuromodulation on neuronal activity and the associated changes in behaviour and disease symptoms on the neurophysiogical level using MEG. However, this is complicated by magnetic artifacts orders of magnitudes larger than the brain signal of interest.

This symposium will present both pioneering research using simultaneous tCS-MEG and DBS-MEG as well as recent advancements in artefact rejection which allow studying the effects of neurostimulation in the MEG 'online'. This symposium aims at giving further insight how neurostimulation modulates oscillatory brain activity and how MEG can be used to further our understanding of its functional relevance.

Speakers:

- **Jim Herring** (Donders Inst., The Netherlands)
  "Modulating stimulus-induced gamma-band activity with tCS in the MEG"

  Cortical alpha oscillations (8-12 Hz) are thought to support 'attentional gating' by suppressing activity from task-irrelevant regions, reflected by 'pulsed-inhibition' of gamma-band activity (40-100 Hz). However, the direct link between excitability and oscillatory activity is currently unclear. We present results from two studies where we attempted to modulate visual cortex excitability by transcranial current stimulation (tCS). In the first study we applied anodal and cathodal direct currents (tDCS) in an Oz-Cz montage while measuring whole-head magnetoencephalography (MEG). Although we were successful in reconstructing visual stimulus-induced alpha and gamma activity in the presence of strong tCS-related artifacts, tDCS did not seem to affect the measured brain activity. In a second study, we applied alternating currents (tACS) at three frequencies centered at subjects' individual alpha frequency (IAF-4 Hz; IAF; IAF+4 Hz). We found a rhythmic modulation of stimulus-induced gamma band activity by occipital tACS at IAF. Importantly, we controlled for potential retinal stimulation using a control montage closer to the eyes (Cz-FPz). Both studies show that it is possible to reconstruct source activity at the region of stimulation in the presence of strong tCS-related artifacts. Importantly, only tACS seemed to modulate gamma-band activity in phasic manner.

- **Surjo R. Soekadar** (Eberhard Karls Universität Tübingen, Germany)
  "Investigating the mechanisms underlying behavioral effects of transcranial electric stimulation (tES): current state and future perspectives"

  Transcranial electrical stimulation (tES) can affect perception, memory, motor, and cognitive function. The mechanisms underlying tES-related behavioral effects are not well understood, but recent advances in multimodal approaches allowing for simultaneous tES during assessment of brain oscillatory activity may substantially contribute to uncovering the complex interactions between externally applied currents, neurophysiology and brain function. Besides providing an introduction to various strategies for assessing neuromagnetic activity during transcranial direct or alternating current stimulation (tDCS/tACS) and their

limitations, most recent results of combined tES and MEG studies performed at the University of Tübingen will be presented. These include tES effects on slow cortical fields and reaction time, mapping of entrained brain oscillations, and purposeful phase-modulation of frontal midline theta oscillations to manipulate working memory performance. Based on insights from these studies, future perspectives, particularly implications for clinical applications, will be outlined.

- **David McGonigle** (Cardiff Univ., UK)
"Exploring Issues of Optimisation in tES-MEG Experiments"

  Transcranial Electrical Stimulation (tES) is a neuromodulation technique capable of producing prolonged, polarity-specific alterations in neuronal excitability. However, the neurobiology underlying the behavioural effects of stimulation remains uncertain, and outside of studies of motor behaviour, data often has high inter-participant variability. At present, combining stimulation and neuroimaging in neurotypical human populations represents one of the most promising routes to better understand the 'online' effects of tES, but significant challenges remain. In this presentation we will discuss recent results demonstrating how optimisation of experimental paradigms at a number of levels can assist in improving data quality when running tES-MEG experiments.

- **Toralf Neuling** (Univ. of Salzburg & Carl von Ossietzky Univ., Austria/Germany)
"Beamforming can recover brain activity in MEG-tACS settings"

  Brain oscillations are putatively crucial for normal cognitive functioning and alterations are associated with cognitive dysfunctions. This made brain oscillations a target to non-invasive brain stimulation, e.g. transcranial alternating current stimulation (tACS). The aim is to apply external rhythms to the brain to modulate internal rhythms and to test if a subsequent modulation of cognition is possible. This way, different parameters of brain oscillations (e.g., amplitude, phase, frequency) become the independent variable and behavioral measures the dependent variable, which in turn allows for causal interpretations. The combination of tACS and MEG opened up the possibility to overcome the obstacles caused by the enormous stimulation artifacts, which previously made it virtually impossible to investigate patterns of brain activity recorded *during* tACS. We present a means to overcome this limitation, showing that we are able to recover meaningful modulations of brain oscillations even at the stimulation frequency. By applying tACS in a phantom study, we can estimate the potential and the limitations of the proposed method. This work effectively opens up the black box of brain activity during tACS, enabling a more detailed understanding of this brain stimulation method with broad implications for its application in cognitive and clinical neuroscience.

- **Nima Noury** (Univ. of Tübingen, Germany)
"Physiological processes non-linearly affect electrophysiological recordings during transcranial electric stimulation"

  Transcranial electric stimulation (tES) is a promising tool to non-invasively manipulate neuronal activity in the human brain. Several studies have shown behavioral effects of tES, but stimulation artifacts complicate the simultaneous investigation of neural activity with EEG or MEG.
  In this talk, I first show for EEG and MEG, that irrespective of stimulation frequency (i.e. for both tACS and tDCS) and contrary to previous assumptions, artifacts do not simply reflect stimulation currents, but that heartbeat and respiration non-linearly modulate stimulation artifacts.Second, I show that, although at first sight previously employed artifact rejection methods may seem to remove artifacts, data are still contaminated by non-linear stimulation artifacts. Because of their complex nature and dependence on the subjects' physiological state these artifacts are prone to be mistaken as neural entrainment.

- **Omid Abbasi** (Heinrich Heine Univ. Düsseldorf, Germany)
  "Deeply stimulating the brain at 130 Hz and 340 Hz in the MEG scanner"

  With DBS, subcortical structures are stimulated electrically by implanted macro electrodes. Recording MEG during DBS comes along with technical challenges such as DBS artefact removal as DBS distorts MEG data significantly.
  We developed a method based on the combination of independent component analysis (ICA) and mutual information theory to remove DBS artefact from MEG data. We applied it on MEG data from 5 Parkinsonian patients with implanted stimulator during DBS. Patients performed an established visual attention task known to induce gamma band activity and median nerve stimulation yielding sensory evoked field. With the proposed artefact rejection approach, we could retrieve the signal of interest and reproduce the expected neurophysiological activity.
  In a second study, we recorded MEG during stimulation of the subthalamic nucleus in 17 Parkinsonian patients at 130 Hz and 340 Hz using an external brain stimulator. Here, we could show that DBS at both stimulation frequencies led to widespread suppression of cortical oscillatory activity in the alpha and beta band over bilateral motor cortices. Our two studies demonstrate that (i) it is possible to remove the DBS artefact from MEG data and (ii) MEG can be used as a tool for a better understanding of DBS mechanism.

- **Jyrki Mäkelä** (HUS Medical Imaging Center, Finland)
  "The effects of DBS on MEG spontaneous oscillatory activity in patients with late-phase Parkinson's disease"

  We have studied the effects of bilateral electrical stimulation of subthalamic nucleus on MEG cortical spontaneous activity in patients with Parkinson's disease (PD). Large artifacts produced by deep brain stimulation (DBS) were suppressed by the tSSS algorithm. The methodology enables reliable recording of evoked fields in vast majority of PD patients and reveals slight enhancement of AEFs and SEFs when DBS on. The pericentral source strengths of oscillatory alpha and beta-band signals did not differ between the DBS on and off conditions. When DBS on, rigidity scores correlated significantly with 6-10 Hz and 12-20 Hz source strengths whilst eyes open. Corticomuscular coherence (CMC) was not systematically modified by DBS. Our most recent dataset of spontaneous oscillatory activity revealed a significant, widespread frontotemporal suppression of high alpha and low beta-band activity in the sensor space when DBS was on and eyes open in 14 out of 16 patients. Similarly distributed but less strong suppression was observed when eyes closed or during an active wrist flexion. STN DBS thus modulates cortical brain oscillations both in alpha and beta bands and some of these modulations correlate with the clinical condition of the patient.

- **Vladimir Litvak** (Univ. College London, UK)
  "Simultaneous MEG and intracranial LFP recordings during Deep Brain Stimulation"

  Deep Brain Stimulation (DBS) is an effective treatment for several neurological and psychiatric disorders. In order to gain insights into the therapeutic mechanisms of DBS and to advance future therapies a better understanding of the effects of DBS on large-scale brain networks is required.
  We developed an experimental protocol and analysis pipeline for simultaneously performing DBS and intracranial local field potential (LFP) recordings at a target brain region during concurrent MEG measurement. A phantom setup allowed us to precisely characterise the MEG artefacts that occurred during DBS at clinical settings and show that when properly handled, they do not preclude the analysis of LFP-MEG coherence using the methodology we previously described for recordings without concurrent DBS. A group study in 15 Parkinson's disease patients stimulated at 130Hz showed that DBS selectively suppressed synchronisation of activity in the beta band between the STN and mesial premotor regions, including the supplementary motor areas. These results are in line with the previously suggested antidromic activation of the cortico-subthalamic hyperdirect pathway by DBS.