Multimodal Insights into Neural Oscillations

Organizers: Christopher Edgar and Karim Jerbi

Room:# 104

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Multimodal Studies of Neural Oscillations: from Basic Systems to Pathology

Accepting the hypothesis that functional brain measures are more proximal to neurobiological mechanisms and/or pathways associated with neurologic and psychiatric disorders than overt behavioral measures, it is hoped that neuroimaging-based endophenotypes will identify biological mechanisms in these populations at the level of neural circuits. This symposium provides an overview of work in this area, with presentations first reviewing basic aspects of neural oscillatory systems, to presentations discussing how these systems can be modulated via pharmacological or cognitive treatment, to presentations reviewing studies of neural oscillations (and the ability to modulate abnormal oscillatory neural rhythms) in schizophrenia and autism. Each speaker is an expert in this area, with multiple publications over the last decade and thus with the ability to provide a broad overview of key topics in this rapidly growing area of research. A strength of the symposium is that each speaker will focus on the use of multimodal imaging to better understand normal and abnormal neural oscillatory activity. Thus, the proposed symposium showcases the increasingly sophisticated research in this area and the continued maturation of MEG psychiatry and neurology research.

Speakers:

- **Karim Jerbi** (Univ. of Montreal, Canada)
  "The curse of modality and why gamma oscillations might be a peacemaker: Bridging MEG, fMRI, intracranial EEG and GABA neurotransmission"

  Progress in monitoring und understanding brain network dynamics in health and disease draws on a wide range of neuroimaging and electrophysiological brain recording techniques. This has also resulted in parallel research fields with difficulties connecting their respective findings. Luckily, the surge in multi-modal investigations of brain function has shed light onto the links between observations made with different techniques, but addressing the same cognitive process or the same patient population. In this context, neuronal oscillations, and in particular gamma-band activity, may provide a useful framework. This talk will illustrate this using recent findings and ongoing research that connects MEG Gamma activity to GABA-A receptor density in working memory and visual processing tasks (Kujala et al. 2015). Ongoing work linking intracranially recorded gamma activity with 3T and 7T BOLD signals during visual search will also be reported. Finally, the complementary information provided by other frequency ranges of the MEG and EEG spectum will be discussed, and current/future challenges will be highlighted.

- **Krish Singh** (CUBRIC, Cardiff Univ., UK)
  "Oscillatory biomarkers in health and disease: Their use, pharmacological manipulation, and neurophysiologically informed modelling"

  It is becoming increasing clear that sensory/motor oscillatory responses, such as visual and motor gamma, may provide a new direct window onto synaptic function, providing translational biomarkers of healthy individual variability, disease state, behavioural performance and pharmacological manipulation that provide extra information that goes beyond that offered by techniques such as fMRI. Using examples from healthy control data, pharmacological studies of GABA and Glutamate modulating drugs and a recent acquired Schizophrenia cohort, this talk will illustrate the use of these measures and how modelling frameworks such as Dynamic Causal Modelling (DCM) can be used to provide

neurophysiologically relevant information that goes beyond, and is more sensitive than, the simple data features.

- **Ole Jensen** (Radboud Univ., The Netherlands)
"Posterior alpha oscillations under top-down control are aberrant in ADHD patients"

Alpha band oscillations in sensory regions have been implicated in the routing of visual input during the allocation of attention. To identify the mechanisms of the top-down control we have conducted a set of MEG (Popov et al., submitted), TMS/MEG (Marshall et al., 2015, J Neurosci) and fMRI/EEG (Zumer et al., 2014 PLOS Biol) investigations. They point to the frontal eye-field playing an important role. A study relating the MEG to DTI (Marshall et al. 2015, PLOS Biol) implicates the superior longitudinal fasciculus in the control. We are currently investigating the contribution of the striatum (Horschig et al., 2015, PLOS One). Problems in the allocation of attention might be associated with an inability to appropriately modulate the alpha band activity. Indeed we have demonstrated that ADHD patients have a reduced ability to sustain the modulations in alpha band during the allocation of attention (terHuurne et al., 2013, Biol Psychiatry; Vollebregt et al., in press, ClinNeurophys). In future work we hope to uncover the frontal structures associated with this aberrant modulation. Furthermore we will investigate if neurofeedback training targeting alpha oscillations (Okazaki et al., 2015, Neuroimage) can be used to reduce the symptoms in ADHD.

- **J. Christopher Edgar** (Children's Hospital of Philadelphia, USA)
"Auditory encoding in schizophrenia and unaffected relatives: low- rather than high-frequency superior temporal gyrus auditory abnormalities are primary to schizophrenia"

Studies examining superior temporal gyrus (STG) auditory encoding in schizophrenia (SZ) have observed low-frequency (alpha-to-beta) as well as 40Hz auditory steady-state abnormalities. The Edgar et al. (2013) multimodal findings suggested that disease-associated loss of left STG gray matter cortical thickness (CT) in SZ accounted for the 40Hz but not low-frequency abnormalities in SZ. Building on this study, additional analyses were performed in an expanded sample of SZ (50% increase; N=63), an expanded sample of HC (100% increase; N=63), and now also including a group of unaffected relatives (UR; N=29). Less left STG CT and lower left 40Hz steady-state inter-trial coherence in SZ and UR indicated these left STG structure and function measures as markers of genetic liability to SZ. An expected association between increased age and decreased left STG steady-state activity only in HC suggested early damage to auditory gamma circuits disrupting 40 Hz activity in SZ and family members. In contrast, higher left low-frequency (theta-to-alpha) total power and inter-trial coherence in HC and UR versus SZ indicated that left STG low-frequency abnormalities were specific to disease. Present findings are discussed within the context of other studies indicating that low-frequency rather than high-frequency STG auditory abnormalities are primary to SZ.

- **Mingxiong Huang** (Univ. of California San Diego, USA)
"Resting-state MEG Studies of Mild Traumatic Brain Injury and Post-traumatic Brain Disorder and Relationships with Diffusion Tensor Imaging and fMRI"

Mild traumatic brain injury (mTBI) is a leading cause of physical, cognitive, and emotional deficits in military members and the general public. mTBI also substantially increases the risk of post-traumatic stress disorder (PTSD). The pathophysiology of mTBI is not completely understood, and the neuronal mechanisms by which mTBI enhances the likelihood of PTSD even less clear. This presentation reviews resting-state magnetoencephalography (rs-MEG) studies of mTBI and PTSD. Relationships between MEG findings and diffusion tensor imaging and rs-fMRI are also examined. Main findings are: 1) MEG slow-wave (delta-band, 1-4Hz) source magnitude imaging provides mTBI diagnosis on a single-subject basis, with slow-wave abnormalities due, in part, to reduced fractional anisotropy in nearby white-matter tracts.

2) Resting-state MEG functional connectivity measures reveal abnormal excitation in mTBI, with these findings consistent with reduced inhibition and over excitation in gray matter, and thus with a gray matter glutamate and GABA Imbalance after mTBI. 3) In individuals with mTBI with PTSD, MEG imaging identifies neural oscillatory dysfunction in emotion processing neurocircuitry (i.e., amygdala, ventro-medial prefrontal cortex(vmPFC), and hippocampus), with rs-MEG results consistent with resting-state fMRI default mode network findings in PTSD. Given the above, the future clinical use of MEG for mTBI and PTSD is discussed

- **Tzvetan Popov** (Univ. of Konstanz, Germany)
"Training-induced modulation of alpha oscillations and their role in pathophysiology of schizophrenia"

Research has established an important role of brain oscillatory activity as a potential mechanism in cognitive deficits and pathophysiology in schizophrenia. We used a paired-click paradigm to study effects of cognitive training in a neuroplasticity-oriented learning protocol on induced oscillatory activity associated with a sensory gating phenomenon. Three predominant observations emerged from a series of experiments. First, stimulus processing prompts a decrease in alpha amplitude (8-14Hz) in primary sensory (auditory) and higher-order (parietal) cortices. This modulation is less pronounced in patients and is correlated with the gating deficit. Second, 4 weeks of targeted neuroplasticity-based cognitive training influence both the gating deficit and amplitude modulation of alpha oscillations. Third, gating of sensory information is not confined to sensory cortices. Spectrally resolved Granger analysis revealed that, prior to stimulus onset, primary auditory cortices are under top-down control by prefrontal cortex, realized at ~10Hz. Findings are discussed in light of theories of the role of alpha oscillations in organizing functional brain architecture and of schizophrenia conceived as a cerebrally implemented network deficiency manifesting in cognitive deficits.