

Aberrant Coupling and Oscillations in Parkinson's

Organizer: Elizabeth Heinrichs-Graham

Room: # 104

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Decoding Aberrant Coupling and Oscillatory Dynamics within Motor Circuits in Parkinson's Disease

The advent of deep brain stimulation enabled researchers to directly record local-field potential (LFP) data from basal ganglia structures in humans, and recent work combining magnetoencephalography (MEG) and such LFP recordings has revolutionized our understanding of the pathophysiology that underlies Parkinson's disease (PD). In this symposium, international leaders in this field will discuss their latest findings using LFP, MEG, and LFP+MEG approaches. Specifically, the symposium opens with a discussion of frequency-specific subcortico-cortical connectivity, recorded by simultaneous LFP-MEG recordings, that distinguishes PD from other movement disorders such as dystonia. The second talk will highlight recent data connecting resting tremor to beta oscillatory activity and coherence between the subthalamic nucleus and motor cortices. Next, new data linking the severity of rigidity/bradykinesia in patients with PD to phase-amplitude coupling between ongoing beta and ultra-high frequency oscillations (150-400 Hz) will be presented. Finally, recent MEG findings will be presented that identify the physiological signature of symptom laterality in PD. Together, this series of talks will demonstrate the groundbreaking progress that has recently emerged in our understanding of the pathophysiology of PD, and will introduce critical new avenues in the search for a physiological marker of disease progression and treatment efficacy.

Speakers:

- **Wolf-Julian Neumann** (Univ. Medicine Berlin, Germany)
"What local field potentials have taught us about the pathophysiology of movement disorders"

Deep brain stimulation (DBS) is a highly effective treatment in movement disorders, such as Parkinson's disease (PD) and dystonia. Traditionally regarded as basal ganglia disorders, recent evidence points to more wide spread dysfunctions in these disease entities across the motor network. Therefore, both PD and dystonia are now referred to as circuit disorders. Local field potential recordings from subcortical DBS targets during and after the implantation of electrodes have revealed crucial findings that have contributed substantially to our understanding of the pathophysiology of these movement disorders. In PD subthalamic and pallidal oscillatory activity is synchronized in a beta rhythm (13 - 30 Hz) that is suppressed by dopaminergic medication and DBS in parallel with alleviation of motor symptoms in these patients. In dystonia, low frequency activity (4 - 12 Hz) is most prominent in the same structures and both, beta oscillations for PD and low frequency activity in dystonia, are hypothesized to reflect pathophysiological hallmarks of the respective disorders that may have a causal role in the development of abnormal movement and posture. Parallel magnetoencephalography and local field potential recordings have now opened the window to investigate oscillatory subcortico-cortical network connectivity and studies using this innovative methodological approach further corroborate the pathophysiological role of aberrant oscillatory activity across the motor network in movement disorders. The proposed talk will give an overview on the significance of pathological oscillatory activity in the motor network.

- **Markus Butz** (Heinrich-Heine-Univ. Düsseldorf, Germany)
"Oscillatory basal ganglia - cortex signature of Parkinsonian rest tremor"

Motor symptoms of Parkinson's disease (PD), such as akinesia and rest tremor, seem to be associated with pathological oscillatory activity in basal ganglia and cortex. Therapeutic implantation of deep brain stimulation (DBS) electrodes into the subthalamic nucleus (STN) provides a unique opportunity to directly

measure local field potentials from the human STN. To analyse STN and cortical oscillatory power as well as coherence between STN and cortex associated with PD rest tremor we simultaneously recorded STN-LFPs, whole-head MEG, and tremor-EMG in tremor-dominant PD patients with DBS electrodes externalized after DBS surgery. We took advantage of naturally occurring spontaneous tremor fluctuations and compared oscillatory activity in the presence and absence of rest tremor. We found tremor-related oscillatory changes in distinct frequency bands: STN and cortical beta power (13-30 Hz) decreased as tremor becomes manifest. STN power at double the individual tremor frequency increased following tremor onset. Coherence between STN and cortical areas at tremor and double tremor frequency increased during tremor. The ratio between slow and fast high frequency oscillation (HFO; > 200 Hz) power in STN increased when tremor became manifest. These findings advance our pathophysiological understanding of PD rest tremor and may provide a neurophysiological marker for closed-loop DBS in tremor treatment.

- **Bernadette Van Wijk** (Univ. College London, UK)
"High-frequency oscillations as a new window into Parkinson's disease"

The subthalamic nucleus (STN) is one of the primary targets for deep brain stimulation (DBS) treatment in Parkinson's disease. Local field potentials recorded from the STN have revealed a strong association between beta band oscillations and bradykinesia/rigidity symptoms. Both dopaminergic medication and DBS reduce beta band amplitude along with improvements in clinical motor scores. However, it remains unclear how excessive beta band oscillations mechanistically lead to motor impairment. Here, I propose that more insight into Parkinsonian neurophysiology might be obtained by focusing on another spectral peak that can frequently be observed: high-frequency oscillations (HFO) within the 150-400Hz range. Activity within this frequency range is especially relevant as it typically shows a movement-related increase in amplitude. I will present our findings indicating that HFO may express abnormally strong phase-amplitude coupling with ongoing beta band oscillations that correlates with severity of bradykinesia/rigidity. In addition, our intraoperative recordings identified that HFO and beta band oscillations are likely to arise from spatially close neural populations. Future work will be necessary to determine whether HFO can help fine-tune deep brain stimulation targeting.

- **Elizabeth Heinrichs-Graham** (Univ. of Nebraska Medical Center Omaha, USA)
"The importance of symptom laterality in studying oscillatory patterns in Parkinson's"

Patients with Parkinson's disease (PD) initially present with unilateral motor symptoms. Importantly, the side of symptom onset has been associated with distinct symptom trajectories in PD, yet the aberrant cortical neurophysiology that underlies such symptom asymmetry has been largely overlooked. Here, I demonstrate that the side of symptom onset and degree of symptom laterality results in a distinct pattern of cortical oscillatory aberrations in PD. Using MEG and beamforming methods to examine cortical beta oscillations during a right-hand movement task in right-handed patients who exhibited either right- or left-dominant symptomatology, I show that the pattern of beta activity prior to, during, and after transient movement is significantly different between patients who exhibit right-dominant compared to left-dominant symptomatology, and that the laterality of beta activity during movement uniquely correlates with symptom laterality. This data is the first to directly probe the relationship between symptom laterality and neurophysiological laterality during movement in patients with PD, and highlights the importance of symptom variability in the search for a reliable physiological marker of disease progression on the individual patient level.