PAPER OF THE YEAR 2025

TRR 295 ReTune

Gamma entrainment induced by DBS as a biomarker for motor improvement with neuromodulation.

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Finely tuned gamma (FTG) oscillations in the subthalamic nucleus (STN) and cortex have been implicated in the development of dyskinesia in Parkinson's disease (PD) patients. While FTG is frequently observed in these individuals, its precise functional significance has remained elusive. Recent research has shed light on a potential mechanism by which DBS interacts with these oscillations. Specifically, it has been demonstrated that DBS can entrain gamma activity at a subharmonic frequency—1:2 of the stimulation frequency—suggesting a structured neural response to stimulation rather than random activation. Despite this, the role of such entrained gamma rhythms in motor behavior or symptom modulation remains not fully understood.

To investigate this further, local field potentials (LFPs) were recorded from the STN in a cohort of 19 PD patients who had been chronically implanted with DBS electrodes. All recordings were performed while patients were on dopaminergic medication and included periods of rest, on/off DBS, and repetitive voluntary movements. The results showed that high-frequency DBS elicited 1:2 gamma entrainment in 15 out of the 19 patients. Spontaneous FTG, independent of stimulation, was observed in 8 patients. Notably, in 5 of these patients, the presence or enhancement of FTG coincided with the emergence or worsening of dyskinesias during DBS-induced entrainment, suggesting a complex interplay between stimulation, gamma activity, and involuntary motor symptoms.

Moreover, a significant increase in the power of entrained 1:2 gamma oscillations was observed during movement tasks compared to resting conditions. Patients who exhibited this entrainment also demonstrated faster movement speeds than those who did not, indicating a potential prokinetic role of this neural signature. Importantly, while entrained FTG may sometimes co-occur with dyskinesia, its presence does not appear to be inherently pathological. Instead, it may represent a physiologically meaningful pattern that supports improved motor performance.

These findings support the hypothesis that DBS-induced 1:2 gamma entrainment serves a functional role in enhancing motor activity in PD patients, rather than merely being a by-product of pathological processes. This entrainment could, therefore, serve as a valuable neurophysiological marker for optimizing stimulation parameters. In the context of closed-loop DBS systems, monitoring entrained gamma power could help in real-time adjustment of stimulation amplitude, potentially improving therapeutic outcomes while minimizing adverse effects such as dyskinesia.

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Varvara Mathiopoulou is a Doctoral Student in the Movement Disorders and Neuromodulation Unit at Charité – Universitätsmedizin Berlin. She has been working on chronic recordings of local field potentials from the STN in PD patients, with a focus on beta and gamma band activity as biomarkers for closed-loop DBS.

Prof. Andrea Kühn

Andrea Kühn is the director of the Movement Disorders and Neuromodulation Unit at Charité Berlin and the ReTune Spokesperson. Her research on basal ganglia electrophysiology has majorly contributed to the understanding of the pathophysiology of movement disorders and the mechanisms of action of DBS.

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