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TRR 295 ReTune

Subthalamic beta bursts correlate with dopamine-dependent motor symptoms in 106 Parkinson's patients.

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Parkinson's disease (PD) is a hypokinetic movement disorder that has been linked to prolonged bursts of beta oscillations (13-30 Hz) in basal ganglia nuclei. Recordings from human basal ganglia nuclei have traditionally been limited to a brief intra- or post-operative interval following deep brain stimulation (DBS) surgery. Accordingly, cohort sizes were relatively small, specifically with respect to studies reporting the temporal dynamics of subcortical beta oscillations and their association with motor symptom severity in PD. Here, we report subthalamic recordings from the dopamine-depleted (OFF) and substituted state (ON) of 106 PD-patients, the largest cohort to date.

We could replicate findings from smaller cohorts by revealing a significant correlation of subthalamic oscillatory power between 13-20 Hz, corresponding to the lower beta band, and motor symptom severity in the OFF-state (R=0.21, P=.03). Reduction of subthalamic beta power (13-20 Hz) reflected the motor symptom improvement with dopaminergic medication (R=0.36, P=.001), but did not explain the remaining motor symptoms in the ON-state. In the temporal domain, the increased beta power in the OFF-state was related to a shift towards longer bursts of beta activity (OFF = 579.1 ± 469.1 ms; ON = 358.6 ± 230.2 ms; P < .001). Similar to beta power, the averaged beta burst duration correlated with motor symptom severity in the OFF-state (R=.18, P=.05), as did its shortening with motor symptom alleviation by dopaminergic medication (R=.26, R=.008). Specifically, the amount of beta bursts > 700 ms was associated with motor symptom severity (R=.56, P<.001).The correlation between beta features and symptom severity was primarily driven by bradykinesia scores (R=.3, P=.04), as tremor scores did not correlate with neither beta power nor beta burst duration. It was moreover frequency-specific, as high beta frequencies (20-35 Hz) did not correlate with motor symptoms. Combining both features, power and burst duration, did not increase the explained variance, indicating that averaged power and burst duration capture similar pathophysiological characteristics of PD. Of note, there is an ongoing debate whether the exact methodological approach used to define beta burst critically influences the correlation to motor symptom severity. Here, we compared two commonly used methods: One based on the 75th percentile of the beta amplitude distribution, the other based on the noise floor of the individual recording. Both methods yielded qualitatively similar results with respect to motor symptom association but differed in absolute beta burst durations.

Taken together, this study demonstrates that subthalamic beta activity is a reliable and robust biomarker of bradykinetic symptoms in the dopamine-depleted state across a large number of PD patients. This is encouraging with respect to control-algorithms for demand-adapted application of DBS that are currently tested in international clinical trials. However, capturing motor symptom severity in the dopamine-substituted state will probably require a more complex combination of spectral and temporal features.

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Roxanne Lofredi is a neurology resident at Charité with a focus on movement disorders and clinician scientist funded by the Berlin Institute of Health. She is a postdoc in Andrea Kühns Lab and her research focuses on the oscillatory signatures and DBS-effects on voluntary and involuntary movement patterns in PD and dystonia patients.

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Andrea Kühn is the head of the Movement Disorders and Neuromodulation Unit at Charité Berlin and the Spokesperson of the CRC TRR 295. 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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