PAPER OF THE MONTH 05/2022

TRR 295 ReTune

Toward therapeutic electrophysiology: beta-band suppression as a biomarker in chronic local field potential recordings.

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NPJ Parkinsons Dis. 2022 Apr 19; 8(1): 44. doi: 10.1038/s41531-022-00301-2. PMID: PMC9018912

Subthalamic beta band activity has previously been suggested as a biomarker for Parkinson's disease that could be used as a feedback signal for adaptive deep brain stimulation (aDBS) algorithms. Beta band activity was shown to be suppressed through both DBS and dopaminergic medication, and suppression of beta band activity was correlated with motor symptom severity. Most of this research has been conducted in local field potential recordings acutely after the surgical implantation of DBS leads. To date, most aDBS studies have been restricted to a controlled laboratory setting and the translation to chronic therapeutic use has not yet been achieved. With the novel Percept implantable pulse generator (IPG), subthalamic electrophysiological data can be streamed chronically, even years after implantation. As with this novel device there is the potential for long-term adaptive stimulation for the first time, it is of importance to investigate beta band activity as a chronic biomarker.

In the present study, 10 Parkinson's disease patients from three DBS centers, implanted with the novel Percept IPG were included. At the three months' follow-up or during an outpatient clinic visit, a monopolar review recording was performed. During OFF medication state, stimulation was increased in a stepwise manner (0.5 mA) for each hemisphere separately. On each stimulation step, motor performance was objectified in accelerometer recordings of a finger tapping task. In the main analysis, we only included bradykinetic patients (10 STN). Local field potential (LFP) data were preprocessed and transformed to the time frequency domain; accelerometer data were synchronized to the LFP recordings and analyzed regarding velocity. Mean resting state activity was averaged over ~30 sec on each stimulation step. A linear mixed effects model was fitted to associate frequency band activity and velocity/stimulation amplitude.

We could show that in chronic recordings, beta band activity is suppressed in a dose-dependent manner. Moreover, at the individual stimulation amplitude with the best clinical effect, suppression was specific for the beta frequency band. Low beta band suppression was a strong predictor for velocity improvement, and the relation between stimulation amplitude and low-beta suppression was confirmed. Overall, this study shows that beta band activity is a strong, chronic biomarker modulated through therapy and reflecting motor symptom severity in bradykinetic patients. We could show that this effect is frequency specific and dose-dependent, supporting the chronic implementation of aDBS and use of electrophysiology for clinical parameter optimization.

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Lucia Feldmann is a clinician scientist (Postdoctoral researcher/medical doctor) in the Movement Disorders and Neuromodulation Unit of Prof. Andrea A. Kühn at Charité Berlin. Her research focuses on the exploration of chronic biomarkers for aDBS in intracranial local field potential recordings in Parkinson's disease patients. She is co-funded by the Berlin Institute of Health as a Junior Clinician Scientist.

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RETUNE
CRC TRR 295 Berlin-Würzburg