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Subthalamic nucleus input-output dynamics are correlated with Parkinson's burden and treatment efficacy.

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Parkinson's disease (PD) is a neurodegenerative disorder affecting motor and non-motor functions caused by the aggregation of misfolded α-synuclein and degeneration of dopamine-producing neurons in the brain. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is an effective treatment for alleviating motor symptoms in advanced PD. The STN plays a central role in the physiology of the basal ganglia, and abnormal STN neural activity, particularly beta oscillations, is strongly associated with PD symptoms. However, the exact relationship between local field potential (LFPs, primarily reflecting the input activity) and the spiking activity (SPK, corresponding more to the output activity or firing of neurons) in the STN, representing STN inputs and output of PD patients, is still unclear.

We explored the differences between LFPs and SPKs in the STN of 146 PD patients (> 25,000 recording sites of electrophysiological data) undergoing DBS procedures. Utilizing the fitting oscillations & one over f (FOOOF) algorithm, we dissected the STN signals into periodic and aperiodic components. We found distinct differences between LFP and SPK activity. LFP showed higher aperiodic exponent values, resembling brown noise, while SPK had lower values, resembling white noise. Additionally, we found a downshift of beta oscillation frequencies in SPK compared to LFP. We employed a battery of regression models to examine the potential of these newly characterized STN physiological features as indicators for PD severity and for the predictions of the effectiveness of treatments. Both R2 and Akaike Information Criterion (AIC) were used to evaluate the goodness of these regression models. STN aperiodic and spiking parameters explained a significant fraction of the variance of PD's burden and treatment efficacy.

Our study offers a non-linear transformation of input to output signals within the STN motor domain, providing new insights into how the STN processes neural information in Parkinson's patients. Notably, these new STN physiological features can be used as biomarkers for PD severity and for predicting treatment effectiveness. We, therefore, suggest that the unique STN input-output dynamics might clarify its role in Parkinson's physiology and can be utilized in future closed-loop DBS therapy.

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Jing Guang did his PhD on visual-motor transformation in the monkey parietal cortex at the Institute of Neuroscience, CAS, Shanghai, China. He is a postdoc fellow at ELSC of HUJI. His research focuses on optimizing the treatment of PD by studying the activity of the basal ganglia during behavior and in the awake, sedated, and asleep states in Parkinsonian monkeys.

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Hagai Bergman investigates the computational physiology of the basal ganglia and their disorders in non-human primates at the HUJI. He is also performing and improving the physiological navigation in deep brain stimulation (DBS) procedures in the Hadassah Medical Center and other medical centers.

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