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Differential modulation of movement speed with state-dependent deep brain stimulation in PD.

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In recent years, closed-loop deep brain stimulation (DBS) approaches have shown that the ongoing state of a patient can critically influence the effects of stimulation. Most studies to date have focused on neural states, such as oscillatory power and phase. The role of a patient's motor state, however, has remained largely unexplored, which limits the capacity to leverage DBS's timing precision for optimal therapeutic effect. Bradykinesia, characterized by reduced movement speed, is one of the cardinal symptoms of Parkinson's disease (PD). Results in rodents have inspired the hypothesis that the effects of DBS on bradykinesia may depend on the speed of the patient at the time of stimulation. To investigate this hypothesis, we translated a speed-adaptive optogenetic rodent study into a speed-adaptive paradigm performed by PD patients treated with DBS in the subthalamic nucleus (STN). This unique setup allowed us to selectively stimulate particularly fast or slow movements and examine speed-dependent stimulation-induced modulations of future movement speed.

We found three key insights: First, the speed during DBS differentially modulated future movement speed. DBS during fast movements provided a stronger anti-bradykinetic effect, thus a less pronounced speed decline, compared to DBS during slow movements. On a finer time scale, we found that stimulation shifted the speed of the subsequent trial toward the speed of the stimulated movement, compatible with a reinforcement effect of STN stimulation.

Second, fMRI-connectomics revealed a whole-brain network underlying the speed-dependent effect, with stronger functional connectivity producing greater speed-dependent modulation. The network encompassed cortical, thalamic, and basal ganglia regions, with the supplementary motor area and putamen as key hubs, and is consistent with previously reported networks mediating the clinical effects of continuous DBS.

Third, using intracranial cortical electrophysiology in a single patient, we observed a stimulation-induced increase in post-movement cortical beta activity, a signal previously linked to motor adaptation, suggesting that movement-adaptive STN-DBS modulates cortical processes related to motor learning.

Together, our results suggest that stimulation of more vigorous motor behavior could potentially provide a more effective alleviation of bradykinesia than stimulation applied during less vigorous motor states. This has important implications for the development of future DBS control algorithms and motivates speed-adaptive approaches to maximize therapeutic efficacy. In a single patient, we provide proof of principle that continuous movement speed can be decoded from sensorimotor electrocorticography signals, supporting the feasibility of fully embedded, movement-dependent DBS systems in the future.

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Alessia Cavallo is a PhD student in the Movement Disorders and Neuromodulation Unit at the Charité in the lab of Julian Neumann. She develops closed-loop behavior-adaptive DBS algorithms to elucidate basal ganglia functioning and advance treatment options for patients with Parkinson's disease.

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