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DBS-evoked cortical responses index optimal contact orientations and motor outcomes in Parkinson's disease.

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Although subthalamic deep brain stimulation (STN-DBS) is an effective treatment for alleviating motor symptoms in patients with Parkinson's disease (PD), some patients are still left without experiencing optimal clinical benefits. Moreover, clinicians currently lack reliable biomarkers for optimizing DBS parameters, which may contribute to less effective and efficient treatment. One proposed parameter that could aid STN-DBS efficacy is the orientation of the current administered (e.g., segmented vs. ring-shaped contacts). However, the precise neurophysiological markers underlying optimal DBS contact orientations and subsequent clinical outcomes are not well understood, albeit recent work proposes the evaluation of stimulation-evoked cortical responses as potential markers of STN-DBS clinical efficacy. For example, previous studies suggest that short, medium, and long-latency cortical responses evoked by STN-DBS are largest when undergoing clinically-effective stimulation settings (e.g., larger stimulation amplitudes, longer pulse widths, clinically-effective contacts), which may be reflective of the corticospinal tract, hyper-direct pathway, and orthodromic polysynaptic activation of the basal ganglia-cortical loop, respectively.

Herein, we expand upon previous intracranial and scalp-based work in this area by analyzing whole-brain magnetoencephalographic (MEG) recordings of 24 patients with PD. Specifically, patients completed a monopolar stimulation paradigm of the left STN during MEG and during standardized movement protocols assessed outside the scanner. MEG data underwent source reconstruction using minimum norm estimation, and peak vertex time series were extracted to interrogate the directional specificity of STN-DBS current administration on accelerometer metrics of fine hand movements using linear mixed-effects models. Importantly, we hypothesized that clinically-effective contact orientations would elicit larger sensorimotor evoked responses and, further, better behavioral performance during finger tapping paradigms compared to non-optimal contacts. Moreover, we hypothesized that larger sensorimotor evoked responses would be predictive of behavior in a contact-dependent manner across the sample.

Our results indicated that long-latency DBS-evoked responses in the ipsilateral sensorimotor cortex (SM1) were largest when applying current via optimal contact orientations compared to other non-optimal contacts tested. Similarly, optimal contact orientations yielded smoother movement profiles (i.e., slower execution-related tap acceleration, greater tapping consistency, and frequency), which were differentially predicted by SM1 responses in a contact-dependent manner. Moreover, we observed that reported side effects were consistent with the anatomical direction of the current administration, which was concomitant with lower therapeutic windows (i.e., minimal stimulation amplitude required to elicit clinical benefits vs. side effects) during non-optimal stimulation paradigms in our sample. Taken together, these data suggest that DBS-evoked cortical responses and quantitative assessments of movement may provide novel clinical insight for characterizing the optimal DBS programming strategies necessary for alleviating motor symptoms in patients with PD in the future.

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