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Modulation of DBS-induced cortical responses and movement by the directionality and magnitude of current administered.

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Therapeutic effects of STN-DBS vary widely across people with Parkinson's disease (PwP), which may be partially attributable to the large parameter space required to be individually titrated to optimize clinical outcomes. Some parameters that may augment STN-DBS efficacy are the magnitude and directionality of current administered to the STN, albeit clinicians currently lack reliable biomarkers for indexing effective parameter settings. One proposed mechanism underlying clinical outcomes related to STN-DBS is an antidromic activation of the hyperdirect pathway (HDP), which subsequently suppresses pathologically elevated beta (~15-30 Hz) synchrony in the basal ganglia-cortical loop to improve motor function. To date, electrophysiological studies of STN-DBS have identified the presence of medium-latency (i.e., ~2-10 ms) evoked cortical responses likely reflective of HDP-related activation of the basal ganglia-cortical loop based on its conduction speed, topography and specificity to STN-DBS as opposed to alternative stimulation strategies in PwP (e.g., pallidal-DBS). Similarly, pathologically-elevated beta oscillations, as well as elevated STN-cortical beta coherence has been well characterized in PwP, and can be suppressed to augment movement during therapeutic regimens of STN-DBS. However, the comprehensive impact of these neurophysiological markers for indexing DBS programming efficacy in PwP has yet to be evaluated.

Herein, monopolar stimulation paradigms of the left STN were administered to 20 PwP during MEG and standardized movement protocols (i.e., Unified Parkinson's Disease Rating Scale Item 3.4). MEG data were imaged in the time-frequency domain using minimum norm estimation, and peak vertex time series were extracted to directly quantify neural dynamics evoked and induced by STN-DBS as a function of varying parameter settings (i.e., best/worst directional contacts, clinical amplitude ± 50%) using linear mixed-effects models. Finally, using mediation analyses, we probed a well-theorized mechanism of action of STN-DBS (i.e., HDP-related improvements in motor function through levels of cortical beta synchrony).

Our results indicated that DBS parameters significantly modulated neural and behavioral outcomes, with clinically-effective contacts eliciting significant increases in ipsilateral sensorimotor medium-latency evoked responses, reductions in induced beta power, and better movement profiles compared to suboptimal contacts, often regardless of the magnitude of current applied. Finally, HDP-related improvements in finger tapping performance were fully mediated by the level of cortical beta power. This effect was further exacerbated by the clinical efficacy of DBS parameters tested. Together, these data suggest that DBS-evoked and induced cortical responses, as well as quantitative assessments of movement may provide novel mechanistic and clinical insight for characterizing optimal DBS programming strategies necessary for alleviating motor symptoms in PwP in the future.

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