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Imaging-informed brain simulations predict personalized DBS response

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Introduction: Deep Brain Stimulation (DBS) is a successful symptom-relieving treatment for Parkinson's disease (PD). However, the introduction of advanced directional DBS electrodes significantly expands the programming parameter space, rendering the traditional trial-and-error approach for DBS optimization impractical and demonstrating the need for computational tools. Our recently developed DBS model using The Virtual Brain simulation tool was able to reproduce multiple biologically plausible effects of DBS in PD (Meier et al., 2022), though a link with clinical outcome data was still missing.

Methods: In the current work, we extended our virtual DBS model toward higher resolution for the stimulus input, incorporating streamlines around the electrode and the electric field calculation, adapting a previous approach by (An et al., 2022). The region-based whole-brain simulations were set up with The Virtual Brain applying the generic two-dimensional oscillator as neural mass model and an averaged connectome from the Human Connectome Project S1200 release as underlying structural network. We simulated DBS of N=14 PD patients with available empirical data on monopolar ring and directional contact activations of N=392 different electrode settings (in total over all patients, with varying amplitudes between 0 and 3mA) of the 'SenSight'electrode with corresponding motor task outcome (Busch et al., 2023). The motor task involved maximum-velocity pronation-supination movements of the lower arm, with the movement velocity recorded using a handlebar-like device held in the patient's hand. To predict the motor task outcome for each individual setting, we fitted a linear model based on the first three principal components of the N=392 time-averaged DBS-evoked simulated responses.

Results: The whole-brain simulations are now sensitive to the exact three-dimensional location of the activated contact and the tested amplitude. Our prediction model based on the simulated or so-called sweet dynamics demonstrated a correlation between predicted and empirically observed motor task improvements due to DBS of r=0.386 (p<10-4) in a leave-one-setting-out cross-validation (Figure 1A-B). Benchmarking revealed a trend toward better predictions with our sweet dynamics than imaging-based static methods such as the sweet spot (r=0.16, p<0.05) and sweet streamline (r=0.26, p<10-4) approaches (Hollunder et al., 2024). Furthermore, our model outperforms the traditional trial-and-error method in predicting optimal clinical settings for individual patients, e.g. achieving an over 60% likelihood of identifying the optimal contact within the first two suggested contacts compared to a 25% likelihood for the trial-and-error method (Figure 1C).

Conclusions: We identified the sweet dynamics that show improved motor task outcome for individual electrode settings of PD patients. These simulated DBS-evoked responses can be used to find the optimal electrode settings via a novel network-dynamics-based computational method. In the future, the developed framework can be used to optimize the electrode placement and settings in silico in individual patients prospectively. Our study showcases the potential benefit of whole-brain simulations for improving clinical routine.

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