

## Automated deep brain stimulation programming based on electrode location: a randomised, crossover trial using a data-driven algorithm.

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Within the recent years, neuroimaging has made rapid advances to inform the field of deep brain stimulation (DBS). Increasing quality of imaging data, along with specialized processing pipelines such as Lead-DBS, have allowed to precisely reconstruct electrode placement and establish reproducible links between stimulation sites and clinical improvements following DBS across various diseases.

At the same time, DBS devices have become more advanced allowing to distribute electric current independently across up to eight (directional) contacts and novel electrode designs with 16 contacts in clinical testing. While this extends possibilities to adjust stimulation, it widens the space of possible settings and a thorough exploration of the parameter space based on clinical trial-and-error becomes a challenging, if not impossible endeavor.

Here, we prospectively applied the settings suggested by our recently developed DBS programming algorithm, StimFit, in a cohort of 35 PD patients and compared the motor benefit to patients' standard of care (SoC) treatment in a randomized double-blind cross-over design. Mean absolute difference of motor outcome between both conditions was  $-1.6 \pm 7.1$  (95% CI: [-4.0, 0.9]) establishing non-inferiority of StimFit at the pre-defined margin of -5 points ( $p = 0.004$ ). Importantly, SoC often involves multiple adjustments over weeks and months, whereas programming with StimFit was realized within one hour per patient.

Algorithms leveraging the interrelation between electrode location and clinical outcome to guide DBS programming could support clinical practice and play a major role in the future of DBS. StimFit suggests parameter settings for PD patients treated with STN-DBS based on electrode location in a fully automated manner. The data-driven algorithm identifies settings which maximize predicted motor symptom control while accounting for potential stimulation-induced side-effects. Our results hold promise for more efficient and streamlined DBS programming procedures that are informed by offline computations based on population data to reduce programming time and patient burden. Future technical innovations, like

the integration of clinical or demographic data, or electrophysiological features could further improve model accuracies – and ultimately outcome – of guided or automated programming procedures. Additional prospective studies are required to assess the effects of software-assisted DBS programming on non-motor domains and long-term quality of life and to evaluate how such solutions could be embedded in clinical practice. ■



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Jan Roediger is a physician with focus on DBS and movement disorders at Charité – Universitätsmedizin Berlin. He is a fellow of the Einstein Center for Neurosciences MD/PhD program and a research assistant in the Kühn lab. His research focuses on prospective and translational applications of image analysis and spatial statistics in the field of DBS.



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Andrea Kühn is the head of the Movement Disorders and Neuromodulation Unit at Charité Berlin and the Spokesperson of the CRC TRR 295. Her research on basal ganglia electrophysiology has majorly contributed to the understanding of the pathophysiology of movement disorders and the mechanisms of action of DBS.