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Clinical Brain Computer Interface for adaptive neuromodulation in Parkinson's disease as regular clinical care: a protocol

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Background: In Parkinson's disease (PD), spectral power of beta oscillations (13-30 Hz) in the subthalamic nucleus (STN) local field potentials (LFPs) are linked to motor symptom severity. Beta power typically decreases after levodopa intake or deep brain stimulation (DBS) and can guide adaptive DBS (aDBS), which adjusts stimulation in real-time using closed-loop control. Furthermore, 7 Tesla MRI connectivity analysis ensures precise brain-electrode placement in the STN motor subdivision for optimal beta signal localization. aDBS may alleviate adverse effects associated with continuous DBS (cDBS) or combined medical treatment ("ON-related adverse effects") and address insufficient efficacy while medication is wearing off ("OFF episodes"). The Medtronic BrainSense™ technology in the Percept™ DBS neurostimulator supports aDBS implementation as a clinical brain-computer interface (BCI).

Methods: Starting January 2025, Amsterdam UMC will evaluate aDBS in regular clinical care through a single-blinded, n-of-1 trial design to establish its efficacy for individual PD patients. Inclusion criteria include daily OFF periods (>2 hours), ON-related adverse effects (>2 hours), or inadequate symptom control during the ON state due to stimulation-induced adverse effects. Stimulation adverse effects, often affecting speech or gait, are assessed via the Unified Parkinson's Disease Rating Scale (UPDRS). For each patient, 7T MRI connectivity (T2-weighted imaging and DWI probabilistic tractography) confirms electrode placement relative to the STN motor subdivision. Electrode contacts within this subdivision are used for LFP analysis and the aDBS algorithm. Eligible patients implanted with the Medtronic Percept™ system (~300) will be screened, with aDBS initiated for approximately 1 patient weekly. Beta power frequencies for the aDBS algorithm will be identified using cluster-based permutation tests and Cohen's d analysis of LFP spectral densities recorded during OFF- and ON-levodopa states. Participants will undergo 1-week periods of aDBS and cDBS in a blinded, randomized order over a 2-month evaluation phase. The primary outcome is the change in duration (hours/day) and intensity (VAS) of primary symptoms and adverse effects. Secondary measures include UPDRS, PDQ-39, BDI, SAS, and ISI scores. Therapy preference will be assessed via satisfaction VAS scales.

Discussion: This accumulated, n-of-1 study will provide important clinical evidence for and experience with the use of STN beta power-based commercial BCI technology in the management of advanced PD.

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