

From Biomarkers to Neuromodulation: Integrating Longitudinal MRI and Real-Time fMRI Neurofeedback in Parkinson's Disease

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Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease, characterized by degeneration of dopaminergic neurons, resulting in motor and non-motor symptoms (1). PD is the second most common neurodegenerative disease worldwide, with an estimated 25.2 million people projected to be living with the disease by 2050 (2). Although pharmacological therapies provide symptomatic relief, accurate early diagnosis and effective long-term treatment remain major challenges. Therefore, there is a need to better understand PD and find alternative treatment options. Deep Brain Stimulation (DBS) is a neurosurgical intervention that modulates specific neural circuits to reduce motor symptoms in PD (3). However, its invasive nature has stimulated interest in non-invasive approaches such as real-time functional Magnetic Resonance Imaging (rt-fMRI) neurofeedback (NF). This study investigates whether rt-fMRI neurofeedback can help PD patients learn to self-regulate neural activity within the putamen to reduce symptom severity. In parallel, data from the TRACK-PD study, a longitudinal ultra-high field 7T MRI imaging study are used to characterize structural and functional brain changes associated with disease progression. Together, these studies aim to improve understanding of PD by combining longitudinal MRI biomarkers with putamen-targeted neurofeedback, ultimately informing both earlier diagnosis and the development of imaging-based therapeutic approaches.

Methods

The neurofeedback study is a multicenter randomized controlled trial including 60 PD patients. Participants were randomized to either an experimental group receiving fMRI neurofeedback (NF) training or a control group engaging in mental imagery without feedback. Inclusion criteria included an official diagnosis of Parkinson's disease, disease stage 1–3 on the Hoehn and Yahr scale, and age 18 years or older. At the baseline assessment, the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) in the medication on state, the Hospital Anxiety and Depression Scale (HADS), and the distal finger tapping test (DFT) were administered. The experimental group had four weekly NF sessions (~1.5 hours each), using motor imagery with real-time visual feedback to increase putamen activity. The control group performed the same motor imagery tasks but without feedback. Participants also practiced daily self-regulation at home. Symptom assessments were repeated after the final MRI session and at a 1-month follow-up, with the MDS-UPDRS as the primary outcome. Secondary outcomes included putamen activation and whole-brain activation changes during and after neurofeedback training, effects on non-motor symptoms, and the association between neurofeedback success and distal finger tapping performance.

The TRACK-PD study included 106 recently diagnosed (≤ 3 years since diagnosis) PD patients and 45 healthy controls at baseline. Longitudinal whole-brain structural and functional MRI data, together with clinical, cognitive, and neuropsychiatric assessments, were collected. The longitudinal imaging data will be analyzed to investigate anatomical and functional alterations associated with Parkinson's disease. Findings related to the putamen will provide complementary information for interpreting the neurofeedback intervention.

Results

The neurofeedback trial is still ongoing. Preliminary findings from a preceding feasibility study demonstrated that patients with Parkinson's disease could significantly increase putamen activity during rt-fMRI neurofeedback accompanied by activation of widespread cortical and subcortical motor networks (4). Analyses of the TRACK-PD imaging data are currently ongoing.

Conclusions

Preliminary evidence suggests that PD patients can voluntarily modulate putamen activity through rt-fMRI neurofeedback, highlighting the putamen as a promising target for non-invasive neuromodulation. Complementary longitudinal MRI data from the TRACK-PD study will provide additional insight into structural and functional brain changes associated with PD and support the identification of imaging biomarkers of disease progression, while providing a broader neurobiological context for putamen-targeted neurofeedback. Together, these studies illustrate how advanced MRI may contribute to both improved diagnosis and the development of non-invasive neuromodulation strategies for Parkinson's Disease.

References (optional, maximum 6)

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