

Resting State Functional Connectivity Changes with Subthalamic Nucleus Deep Brain Stimulation in a Parkinson's Disease Patient

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Introduction

The purpose of this study was to compare resting state functional connectivity in a Parkinson's Disease (PD) patient between on and off subthalamic nucleus deep brain stimulation (STN-DBS) conditions using low-frequency BOLD fluctuations (LFBF), also known as functional connectivity MRI (fcMRI). STN-DBS in PD has been shown to be efficacious in reducing the cardinal motor symptoms of bradykinesia, rigidity, and tremor. However, the exact mechanism of DBS and its effect on basal ganglia and thalamo-cortical functional connections remain under investigation. Assessing the functional connectivity of the basal ganglia and their cortical projections while in the resting state during continuously-on and -off DBS can provide greater insight into how functional networks are affected by DBS.

Methods

A whole brain T1-weighted MPRAGE and two whole-brain resting state echo-planar (EPI) scans with 137 repetitions each, 31 axial slices of 4mm isotropic voxels, were acquired from a PD patient with unilateral left-sided STN-DBS implantation. The first EPI scan was acquired with DBS continuously on and the second with DBS off, both while resting with eyes closed. Scan protocols and data preprocessing, including spatial filtering as well as corrections for slice-common noise, physiologic noise, and rigid body motion, were performed following previously described methods [1]. A priori defined regions of interest (ROI) were drawn for bilateral caudate head, putamen, globus pallidus, and thalamic nuclei on the MPRAGE and transformed into EPI space for both on and off condition scans. Seed-based correlation analyses were done to generate whole brain z-score maps of significant correlation to each reference ROI.

Results

Compared to the DBS OFF condition, resting state functional connectivity with DBS ON showed significantly decreased bilateral connectivity for putamen and globus pallidus as well as increased connectivity of putamen and thalamus to left and right supplementary motor areas (SMA) and cingulate cortex. Also in the DBS ON condition, left putamen and globus pallidus were more negatively correlated with parieto-occipital regions of cuneus and precuneus. (See figure). These effects were apparent with right-sided seed regions as well but were more prominent in the left-sided seed regions.

Discussion

This case study of a unilateral STN-DBS PD patient demonstrates stimulation-associated changes in resting state functional subcortical and thalamo-cortical connections. Unilateral stimulation appears to interrupt bilateral functional connectivity of the globus pallidus and putamen and strengthen connectivity of the thalamus and putamen to cortical regions. Past studies have shown that STN-DBS alters basal ganglia output and prevents the relay of synchronized globus pallidus interna oscillations to cortex [2]. Our results suggest that STN-DBS similarly affects resting state connectivity in the basal ganglia by interrupting the synchrony of contralateral pallidal thalamic and putamenal nuclei. Such changes in baseline connectivity may lead to a normalization of thalamo-cortical connections, particularly thalamic output to the SMA. This finding is consistent with results of previous studies showing functionally hypoactive SMA in dopamine deficiency states and STN-DBS-associated restoration of SMA function with improved motor function [3]. The precuneus and occipital cortices have been found to increase in activity with DBS STN [4], consistent with known preferential activation of these areas during resting states [5]. Reversed patterns of task-related functional connectivity activation and deactivation in posterior cingulate cortex and precuneus have also been noted in PD patients compared to healthy controls [6].

Acknowledgements: This work was supported by the National Institutes of Health (NIH) under grant NS052566-01A1.

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