Use of functional MRI to understand modulation of chronic pain in Parkinson Disease patients with DBS

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Disclosures

This project was funded in part by GE Global Research Center. Dr. Pilitsis receives funding from Medtronic, Boston Scientific and Abbott. Grant support is given to Dr. Pilitsis from Medtronic, Boston Scientific, Abbott, GE Global Research, Jazz Pharmaceuticals and NIH (1R01CA166379). Julia Prusik receives grant support from Jazz Pharmaceuticals. Ileana Hancu, Eric Fiveland, Radhika Madhaven, and Suresh Joel are employees of GE Global Research Center. Dr. Eric Molho receives clinical trial grants from NIH/PSG, CHDI/HSG, Civitas Therapeutics, Kyowa Hakko Kirin, MJF/PSG, and Bristol-Myers Squibb/Biogen. He is on the speaker’s bureau for Neurocrine Biosciences, Acadia Pharmaceuticals, is a consultant for Neurocrine Biosciences and is supported by the Riley Family Chair in Parkinson’s Disease.
Introduction

Parkinson’s disease (PD) is the second most prevalent neurodegenerative disease affecting over 10 million people worldwide.

PD is characterized by a loss of dopaminergic neurons impairing the basal ganglia which regulates fine motor control.

Figure 1. Depicts the current accepted pathway in both a normal condition (A) and PD condition (B). In (A) there is a balance between the direct and indirect pathways leading to correct motor control. In B) the depletion of dopamine triggers the indirect pathway to become dominant, impairing the motor cortex.
Introduction

One of the main non-motor symptoms of PD is chronic pain affecting 80% of PD patients. Deep brain stimulation (DBS) is a treatment option that is able to treat both motor and non-motor symptoms. However the mechanism of action is unknown.

Conditional DBS labeling allows patients to undergo an MRI with their DBS turned on.

This allows for the possibility to visualize blood oxygen level dependent (BOLD) changes to better understand DBS and how it may treat chronic pain.
Methods

Two cohorts were utilized: subjects whose chronic pain was treated by DBS and control subjects who had chronic pain and did not have DBS. All subjects completed the Kings Parkinson’s Disease Pain Scale (KPDPS), a numerical rating scale (NRS) and UPDRS-III scoring. Control subjects underwent one fMRI scan with a noxious mechanical stimuli. DBS subjects underwent 2: 1. DBS ON with stimuli, 2. DBS Off with stimuli.

Model-based voxel-wise General Linear Model (p=0.005, cluster voxels =50) and a group analysis were used to determine regions altered by DBS using SPM12. A 2-sample t-test was performed on all areas of interests, KPDPS and NRS pain scales.

Figure 2. The homemade mechanical stimuli that was applied for 15 seconds on and 30 seconds off during fMRI scanning.
Results

Table 1 shows patient demographics in the tremor and AR cohorts including: sample size, number of females and males, mean age and location of implantation.

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Control</th>
<th>Treated with DBS</th>
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<tbody>
<tr>
<td>Females, males</td>
<td>N=5</td>
<td>N=2</td>
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<tr>
<td>Mean age (range)</td>
<td>62 (51-74)</td>
<td>62.7 (61-63)</td>
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<tr>
<td>Average KPDPS score</td>
<td>33.8±12.82</td>
<td>2.0±2.0</td>
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Figure 3. Example of an individual control and DBS patient.
A) A control subject with activation observed in the S1, and M1 when the mechanical stimuli was applied. B) A DBS patient with DBS off and activation patterns similar to that of the control patient. C) The same DBS patient with DBS turned on, the S1 and M1 now show deactivation (p=0.05).
Results

Figure 4. Comparisons of the control and DBS subjects. An ANOVA was performed on t-values generated by the GLM to compare regions of interest between the control and DBS subjects. There was no difference in the thalamus (A), S1 (B) or M1 (C) although there appears to be a large difference in S1 and M1 between DBS ON and DBS OFF (p=0.10, 0.11, respectively). The lack of significance is most likely due to the small n.
Figure 5. Group analysis of the controls and DBS cohorts  A) The control cohort shows activation observed in the S1. B) The DBS cohort with DBS off showed activation similar to that of the group cohort with S1 activation. C) When DBS was turned on, S1 deactivation was observed.
Results

Figure 6. Comparisons of group control and DBS subjects at ROIs. Graphs show the mean t-values produced by the group analysis for the three regions of interest. These values were placed onto previously generated plots to show that they were within the standard deviation of the individual analysis. In these preliminary findings there is an observational difference between DBS ON and OFF.
Discussion

Control subjects and results from DBS OFF produced similar findings with activation in the S1 and M1, with no activity present in the thalamus. With DBS ON however, the thalamus became activated and the S1 became deactivated. These preliminary results suggest that DBS is able to deactivate the S1 to alleviate chronic pain.

Figure 7. The pathway depicted may be the possible pathway that is altered by DBS to reduce chronic pain. Signals from both the basal ganglia and the spinal cord enter VL-VPL the transitional zone. Both nuclei send efferents to the M1 and S1. When DBS is applied it would interrupt the glutamate release in the S1 deactivating the pathway reducing pain.