Deep brain stimulation improves gait velocity acutely in patients with Parkinson’s disease

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Background
• Deep brain stimulation (DBS) in patients with Parkinson’s disease (PD) is highly effective for appendicular symptoms (tremor, rigidity, bradykinesia, dyskinesia), but gait response is less predictable. Here we hypothesize that subthalamic nucleus (STN) and globus pallidus internus (GPI) DBS treatment exerts acute and chronic effects on gait and that the effects are related to the location of the active contact in the targeted nucleus.

Objectives: To systematically investigate the acute (5 minutes) and chronic (1 month) effects of DBS of STN and GPI on gait velocity in patients with PD.

METHODS
• Quantitative gait metrics were collected at initial DBS programming visit and at follow-up data, 14 (52%) improved, 9 (33%) had no change, and 4/27 (15%) worsened compared to baseline (Fig 2).
• Acute clinically meaningful improvement (>5 cm/sec) was seen in 23/33 patients (69%). For 27 patients who had chronic follow up data, 14 (52%) improved, 9 (33%) had no change, and 4/27 (15%) worsened compared to baseline (Fig 2).
• Lead-DBS software was used to visualize all active contacts in a normalized brain space (MNI).

RESULTS – Gait Velocity

<table>
<thead>
<tr>
<th>N</th>
<th>STN</th>
<th>GPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>65.2±8.7</td>
<td>60.5±9.5</td>
</tr>
<tr>
<td>Gender</td>
<td>30W/30M</td>
<td>0W/16M</td>
</tr>
<tr>
<td>Dx duration (yrs)</td>
<td>12.6±8.0</td>
<td>12.0±10.6</td>
</tr>
<tr>
<td>Bilateral</td>
<td>23</td>
<td>11</td>
</tr>
<tr>
<td>Unilateral</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Second side</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

• 2 patients were non-ambulatory at all timepoints

• DBS activation resulted in statistically significant improvement at the acute and chronic time point (Fig 2).

RESULTS – Active contact localization

- Chi-square analysis of active contact quadrant (DL, DM, VL, VM) and velocity change was not significant for either left or right brain hemispheres in either STN or GPI.

METHODS – DBS lead contact localization

- The rapid improvement is consistent with immediate reduction of pathologic beta-band neural activity. The lack of significant change between baseline and OFF would argue against a practice effect but a placebo effect cannot be excluded.

CONCLUSIONS
• On a group level, gait velocity increased statistically significantly within minutes of DBS initiation. This effect was reduced but still significant at 1 month follow up.
• Very few patients demonstrated deterioration (4/27) with acute and/or chronic stimulation.
• The rapid improvement is consistent with immediate reduction of pathologic beta-band neural activity. The lack of significant change between baseline and OFF would argue against a practice effect but a placebo effect cannot be excluded.
• Sustained improvement may require reorganization of underlying neuronal networks which was not observed in all patients. This could be due to suboptimal stimulation settings (lower amplitude) at the initial programming. Longer follow with optimization of the DBS settings is necessary to determine the effect of chronic DBS therapy.
• There was no effect of target nucleus or active contact location (nucleus quadrant) on gait velocity.