Habituation and Rebound to Thalamic DBS in Long-Term Management of Tremor Associated with Demyelinating SensoryMotor Peripheral Neuropathy

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RESULTS

Table 1: Clinical Characteristics of Patients with MRT-PN

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Handedness</th>
<th>Diagnosis</th>
<th>Family history</th>
<th>Duration (years)</th>
<th>DBS Implant (year)</th>
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<tbody>
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<td>57</td>
<td>M</td>
<td>R</td>
<td>ET</td>
<td>Y</td>
<td>5</td>
<td>2002</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>R</td>
<td>ET</td>
<td>N</td>
<td>&gt;20</td>
<td>2006</td>
</tr>
<tr>
<td>82</td>
<td>M</td>
<td>R</td>
<td>ET</td>
<td>Y</td>
<td>&gt;20</td>
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<tr>
<td>82</td>
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<td>R</td>
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</table>

Table 2: Clinical Characteristics of Patients with ET without clinical habituation

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Handedness</th>
<th>Diagnosis</th>
<th>Family history</th>
<th>Duration (years)</th>
<th>DBS Implant (year)</th>
</tr>
</thead>
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<td>N</td>
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<td>2006</td>
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</tbody>
</table>

Figure 1: Number of Visits/Implant Year

Figure 2: Change in Amplitude per Visit

Figure 3: Video 1: Tremor habituation. In the 1st segment, P1’s is shown 3 months after last programming session when settings were optimized. He reported tremors worsened within 1 week adjustment. In 2nd segment, a minor reduction in pulse width (15%) and frequency (15%) to right VM and 0.1V increase to left VM resulted in marked improvement of rest, postural and kinetic components of his tremor. In 3rd segment, bilateral DBS has been turned “off” for 30 minutes, with marked worsening of tremors consistent with tremor rebound.

Figure 4: Video 2: Tremor rebound. In the 1st segment, P4 is shown at baseline, before DBS. The 2nd segment shows P4 after 37 months of continuous stimulation. The 3rd segment is with bilateral DBS “off” for 5 minutes. The patient experiences tremor that is significantly worse compared to his pre-operative state, consistent with rebound.

DISCUSSION

• 5/6 MRT-PN cases developed tremor habituation and severe rebound to continuous DBS vs. 0/7 in the control group.

• Typical ET progression is unlikely to explain symptoms.

• Previous case reports have described short-term (6-12mo) tremor suppression with VIM DBS in patients with tremor and various acquired autoimmune and genetic demyelinating neuropathies. Our series differs because all of our MRT-PN patients likely had ET, and were followed for a longer period of time.

• DBS may reduce tremor severity in ET by masking burst-driven inputs to the thalamus, suggesting that tremor habituation in ET results from resetting the oscillatory frequency of thalamic neurons.

• A cycling of settings was transiently beneficial in MRT-PN, suggesting that central oscillators are only temporarily “re-set.”

• Tolerance is likely a stimulation-induced phenomenon and the presence of demyelinating PN in our MRT-PN increases the risk for tolerance. MRT-PN may represent a relative contraindication to VIM DBS.

• Limitations include: lack of detailed homogenous tremor assessments due to retrospective study, lack of formal neuropsychological evaluations on all patients and MRI was not performed systematically. We did not include all patients with habituation or rebound, therefore it is possible that some factors not identified in the analysis may contribute to tolerance.

• Alternatives such as the subthalamic area,12,13 should be explored in patients similar to ours with MRT-PN. Temporal irregular stimulation,13,14 as opposed to continuous stimulation, or even closed-loop systems based on brain sensing15 may also show promise with respect to addressing risk of tolerance.

REFERENCES