A Case Control Series of Thalamic DBS in Patients with Demyelinating Neuropathy and Medication Refractory Tremors

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BACKGROUND

Essential tremor (ET) is one of the most common movement disorders and up to 55% of tremors are refractory to standard pharmacotherapy.

Deep brain stimulation (DBS) to the ventral intermediate nucleus (VIM) nucleus can be an effective treatment for refractory ET.

13-40% of patients with VIM DBS are reported to develop tolerance to continuous stimulation, but the reasons are not understood.

Observed phenomena of tolerance include:

- Tumor rebound: a temporary increase in tremor intensity over the pre-operative state after switching off DBS.
- Habituation: a loss of sustained tremor control over a short duration of follow-up.
- Late therapy failure: loss of tremor control up to 1 year after stable tremor control with DBS.

We have reviewed a group of patients with medication refractory tremors (MRT) and co-morbid demyelinating peripheral neuropathy (PN) in whom we have had difficulty achieving sustained long term tremor control due to accelerated tolerance.

We aim to describe the long term management of VIM DBS patients with MRT-PN compared to those with uncomplicated ET.

METHODS

Patients with MRT-PN were identified through our clinical practice and DBS database.

A control group was established from a database search of patients implanted with VIM DBS from 2003-2006 at the PDCMDC (n=50).

Inclusion criteria: >10 years of diagnosed ET with at least 1 family member affected and 4 continuous implant years of follow-up.

Exclusion criteria: Other etiologies of tremor, evidence of PN on exam, diabetes or other conditions associated with PN, and possible parkinsonism.

A retrospective chart review was conducted to record patient demographics, frequency of programming visits, degree of amplitude adjustments and symptoms of tolerance; data obtained was analyzed using descriptive statistics.

PATIENT CASE HISTORIES

Patient 1: 77 y/o with bilateral moderate to severe postural & kinetic tremor with history of restless legs syndrome (RLS) and hypothyroidism incidentally found to where he was noted to have frequent visits due to habituation.

Patient 2: 64y/o with tremors “his whole life” underwent R VIM DBS and could not tolerate DBS off due to severe tremor rebound.

Patient 3: 70y/o with moderate to severe postural and kinetic tremors in the left hand with history of RLS and cervical stenosis underwent R VIM DBS. He was lost to follow-up for 22 months and returned to our care in 2006 with a new L VIM DBS where he was noted to have frequent visits due to habituation.

Patient 4: 54y/o with 15-year history of minimal tremors in R hand and acute worsening 3-6 months prior to presentation when he was diagnosed with CIDP.

Patient 5: 74y/o with new onset mild to moderate bilateral postural tremors 2 years prior to evaluation underwent DBS for medication refractory tremors. He noted robust tremor improvement for 2-3 days after each programming session. He had frequent visits due to habituation and could not tolerate DBS off due to severe tremor rebound.

RESULTS

Table 1: VIM-PN Group Demographics

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>G</th>
<th>H</th>
<th>Post &amp; kinetic Duration</th>
<th>PN</th>
<th>Diagnosis</th>
<th>Evaluation of PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>77</td>
<td>M</td>
<td>R</td>
<td>10+ years</td>
<td>Y</td>
<td>DPN</td>
<td>EMG: 2007, minimal</td>
</tr>
</tbody>
</table>

Table 2: Control Group Demographics

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>G</th>
<th>H</th>
<th>Post &amp; kinetic Duration</th>
<th>PN</th>
<th>Diagnosis</th>
<th>Evaluation of PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>55</td>
<td>M</td>
<td>R</td>
<td>15+ years</td>
<td>Y</td>
<td>DPN</td>
<td>EMG: 2007, minimal</td>
</tr>
</tbody>
</table>

RESULTS (continued...)

- All patients in the MRT-PN group noted improvement of tremors with any & Δ in amplitude.
- A cycling of amplitude over time was observed.

DISCUSSION

- All patients in the MRT-PN group developed tremor habituation and severe rebound to continuous DBS resulting in suboptimal long term tremor control while the uncomplicated ET group did not.
- A few case reports have suggested successful short term (6-9mos) suppression of neuropathic tremors in subjects with severe acquired autonomic or essential demyelinating PN.
- The diagnosis of ET in patients with PN, particularly demyelinating subtypes, which are often associated with phenomenologically identical tremors, may be difficult.
- It is possible that our MRT-PN patients have co-morbid neuropathologic tremors.
- Neuropathic tremors are theorized to be secondary to abnormal cerebellar processing of distorted muscle spindle input due to slowed peripheral conduction. Altered sensory feedback due to deafferentation may underlie the tremor pathophysiology and abnormal response to VIM DBS.
- We suggest that the presence of demyelinating PN is a risk factor for suboptimal tremor control due to high risk of tolerance and is a relative contraindication to continuous stimulation to the VIM nuclei.

The observation of short term tremor suppression with parameter adjustment changes DBS as an option for treatment of patients with demyelinating PN or neuropathic tremors. Future studies should be directed at alternate targets and/or new methods of stimulation delivery.

REFERENCES


Figure 1: Visits per Implant Year

![Graph showing visits per implant year]