LONG TERM SAFETY AND EFFICACY OF UNILATERAL DEEP BRAIN STIMULATION OF THE THALAMUS FOR PARKINSONIAN TREMOR

K E Lyons, W C Koller, S B Wilkinson, R Pahwa

Abstract

The objective was to investigate the long term safety and efficacy of unilateral deep brain stimulation (DBS) of the VIM nucleus of the thalamus in Parkinson’s disease. Twelve patients with Parkinson’s disease underwent unilateral DBS of the thalamus for medication resistant tremor between 1994 and 1997. Patients were evaluated using the motor section of the unified Parkinson’s disease rating scale (UPDRS) in the medication on state at baseline, 3 months, 12 months, and yearly thereafter. Three patients were lost to follow up. Nine patients had follow up evaluations greater than 24 months and were included in the analyses. The last postsurgical follow up occurred on average 40.0 (SD 17.2) months after surgery. Tremor scores were significantly improved with stimulation on at the long term follow up compared with baseline. There was no significant change in UPDRS motor scores at long term follow up compared with baseline. There was no significant change in any stimulus parameters from 3 months to the long term follow up. Two patients had asymptomatic intracerebral haemorrhages and one patient had a subcutaneous haematoma over the implantable pulse generator site. Stimulation related adverse reactions were mild and easily controlled with changes in stimulus parameters. Two patients had replacement of the implantable pulse generator due to normal battery depletion, one patient had lead repositioning due to migration, and one patient had the lead extension wire replaced due to erosion.

In conclusion, unilateral DBS of the thalamus has long term efficacy for treatment of tremor due to Parkinson’s disease.

Methods

PATIENT SELECTION

Twelve patients with Parkinson’s disease received unilateral DBS of the thalamus for medication resistant tremor at the University of Kansas Medical Center from 1994–7. The tremor had to cause significant disability despite pharmacological treatment. No patient had surgery outside of the study. Tremor had to be 3 or 4 in severity on a tremor rating scale of 0 to 4 in which 0 was equal to no tremor and 4 was severe tremor. All patients gave informed consent.

SURGICAL PROCEDURE AND PROGRAMMING

The procedure has been described in detail previously.1 Electrode model 3387 with an interelectrode distance of 1.5 mm was used for all patients. The implantable pulse generator model Itrel II was programmed to yield the greatest tremor suppression with the fewest side effects. Stimulation parameters and contact selection were programmed by telemetry, using a Medtronic Model 7432 console.
Table 1 UPDRS scores (medication on, stimulation on) and stimulation variable settings (mean (SD))

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 Months</th>
<th>12 Months</th>
<th>Long term follow up</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS Tremor</td>
<td>7.2 (1.4)</td>
<td>1.3 (1.1)</td>
<td>2.2 (1.3)</td>
<td>0.9 (1.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>UPDRS Motor</td>
<td>40.7 (13.9)</td>
<td>29.2 (7.2)</td>
<td>32.4 (12.7)</td>
<td>35.6 (11.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Amplitude (V)</td>
<td>3.2 (0.6)</td>
<td>3.6 (0.5)</td>
<td>3.6 (0.7)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Pulse width (µs)</td>
<td>76.7 (40.0)</td>
<td>90.0 (42.4)</td>
<td>80.0 (26.0)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Rate (Hz)</td>
<td>155.0 (25.6)</td>
<td>166.7 (22.6)</td>
<td>158.3 (24.0)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Polarity</td>
<td>9 Unipolar</td>
<td>8 Unipolar</td>
<td>3 Unipolar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results

The motor section (part III) of the unified Parkinson's disease rating scale (UPDRS) was performed with medications on at baseline and with medications on and stimulation on post surgery at 3 months, 12 months and yearly thereafter.

Statistical Analysis

Wilcoxon signed rank comparisons for non-parametric data were used to compare UPDRS scores at baseline and follow up evaluations. Analysis of variance (ANOVA) was used to compare stimulation parameters across visits. Significance was set at p<0.05.

Discussion

Our study shows that thalamic stimulation is effective for the long term management of tremor in Parkinson’s disease; however, other Parkinson’s disease symptoms such as bradykinesia, rigidity, and gait and balance abnormality are not improved with thalamic stimulation. In our study, seven patients (58%) indicated global improvement compared with baseline, one patient indicated no change (8%), and three patients (25%) reported good long term tremor control; however, due to the progression of their other parkinsonian symptoms, they have become almost completely disabled. Therefore, great caution should be taken in evaluating the patient’s complete symptom profile before determining the most appropriate DBS target site. As a large percentage of patients with Parkinson’s disease have medication resistant tremor, thalamic stimulation may be the surgery of choice for patients with tremor predominant Parkinson’s disease with little evidence of other disabling parkinsonian signs.

Long term follow up studies of thalamic stimulation in Parkinson’s disease have been minimal. Blond et al. reported on 10 patients with Parkinson’s disease with a mean follow up period of 19.4 months. In nine of the 10 patients tremor suppression was maintained and one patient required thalamotomy due to loss of tremor control. Akinesia was unchanged in their patients and the authors thought that it was difficult to evaluate rigidity due to the severe tremor. Side effects were minimal.

www.jmp.com
Albanese et al\(^5\) described 27 patients with Parkinson’s disease who received thalamic stimulation. Six of their patients had bilateral implantation and 21 had unilateral implantation. The mean follow up was 0.9 years. Tremor scores improved by 73% in the upper limbs and 62% in the lower limbs. A slight reduction in rigidity was reported in three patients and moderate relief of bradykinesia in three patients. Complications included one intracranial haemorrhage, one skin erosion, one electrode breakage, two local infections, two lead replacements, and three catheter disconnections. Similarly, Hariz et al\(^6\) reported 22 patients with Parkinson’s disease who received DBS of the VIM nucleus of the thalamus with a mean follow up of 21 months. There was a significant improvement in the motor section of the UPDRS and particularly on the tremor items of the UPDRS. Kumar et al\(^7\) reported on 11 patients with Parkinson’s disease with a mean follow up of 16.2 months who had significant improvements in the contralateral arm and leg rest tremor but no overall improvement on the motor portion of the UPDRS or other symptoms of Parkinson’s disease.

In our study, after an average of 40 months, there were no significant changes in stimulus parameters compared with the 3 month visit. Similarly, Albanese et al\(^8\) reported some change in stimulation parameters during the first 2 to 3 months after surgery but they did not report any changes over long term follow up. Hariz et al\(^9\) showed significant increases in stimulation parameters for up to 1 year; however, after 1 year of stimulation parameters seemed to stabilise. By contrast, Kumar et al\(^10\) reported that this was necessary to increase the current intensity over time to control tremor. These inconsistent findings related to changes in stimulus parameters could be related to variability in disease progression, the development of tolerance, or individual differences in initial programming parameters used.

We conclude that for patients with tremor predominant Parkinson’s disease, thalamic deep brain stimulation provides long term clinical benefit for tremor. Deep brain stimulation of the thalamus was found to be a relatively safe procedure for the treatment of parkinsonian tremor. Surgical induced and stimulation induced adverse effects were mild and were quickly resolved. However, there were many device complications. Forty per cent (5/12) of our patients required additional surgical procedures to maintain good tremor control.

This work was supported in part by the Parkinson’s Association of Greater Kansas City.