Effect of stimulation of the subthalamic nucleus on oral control of patients with parkinsonism

Michèle Gentil, Pedro Garcia-Ruiz, Pierre Pollak, Alim-Louis Benabid

Abstract

Objectives—To assess the oral system of parkinsonian patients treated with chronic stimulation of the bilateral subthalamic nucleus (STN) to evaluate precisely the effectiveness of this procedure on the articulatory organs.

Methods—Load sensitive cantilevers were used to sample ramp and hold force contractions generated by the upper lip, lower lip, and tongue. The subject was given the instruction to produce forces as rapidly and as accurately as possible in response to the target signal (ranging from 0.25 to 2 N), which appeared on a screen. Maximal force of each effector organ was also measured. Fourteen healthy control subjects and 10 patients participated in this study. After an overnight fast the patients were evaluated in the morning under two conditions: during bilateral stimulation and 1 hour after stopping STN stimulation.

Results—During STN stimulation, dynamic and static control of the articular- 

tory organs were improved: the maximal strength of the articular organs, their accuracy to reach the target, and the precision of the hold phase increased. In addition, the reaction time and the rise time of the ramp phase decreased. Patients' speech as assessed by the item 18 of the unified Parkinson's disease rating scale (UPDRS) was greatly improved by electrical stimulation of the STN.

Conclusions—Improvement of oral control of the stimulated patients suggests that STN stimulation modulates neuronal structures involved in speech. However, more patients have to be evaluated for a fuller understanding of the effect of this surgical procedure on speech.

Keywords: parkinsonism; surgical therapy; subthalamic nucleus; oral control (speech)

Although the advent of levodopa has revolutionised the treatment of Parkinson's disease, long term dopaminergic therapy is often complicated by motor fluctuations difficult to control and levodopa induced dyskinesias. Recent advances in the knowledge of basal ganglia physiology 1,2 have led to great interest in functional neurosurgical procedures for Parkinson's disease. In particular, since 1993 STN stimulation has been used to treat patients with disabling Parkinson's disease and severe motor fluctuations.3 Stimulation of the STN is effective for the main signs of parkinsonism—bradykinesia, rigidity, and tremor—and greatly improves parkinsonian motor disability.4 The importance of STN input in the control of non-primary motor areas which have a dominant role in the control of movements in parkinsonian patients has been demonstrated.5 Although the effect of STN stimulation on limb control is known, the precise effect of STN stimulation on oral control is not. Quantitative data relative to speech in patients treated with STN stimulation have not been obtained. It is important to evaluate speech in patients treated with STN stimulation because we know that other surgical procedures have detrimental effects on speech; the risk of speech dysfunctions was particularly high with bilateral thalamotomy, surgical intervention used earlier to treat tremor.6,7 Dysarthria was also seen in patients with electrical stimulation of the ventral intermediate nucleus (VIM) of the thalamus, a valuable therapeutic procedure against the tremor of Parkinson's disease.8,9

Force has been considered as one of the likely variables controlled by the nervous system in producing motor behaviour.10 The usefulness of force transducers for evaluating impairments in the control of lip, jaw, and tongue muscles in patients with motor speech disorders has been shown in several investigations.11–13 The evaluation of non-speech oral strength has been recognised as a worthwhile tool to assess the effects of therapies on speech.14 To estimate the effectiveness of bilateral STN stimulation on the oral system in parkinsonian patients, we investigated force measurements of the articular organs, especially the lips and tongue, and we evaluated speech with item 18 of the UPDRS, under two conditions: during stimulation and 1 hour after stopping stimulation.

Methods

SUBJECTS

We studied 10 patients with Parkinson's disease (six men and four women) who underwent bilateral stereotaxic electrode implantation into the STN for chronic high frequency stimulation. At the time of surgery their mean (SD) age was 49 (9) years and the mean duration of symptoms was 11 (40) years. Evaluations of the oral system were performed within a period from 3 months to 3 years after surgery. The selection criteria were the speech impairment of the patients perceptually evaluated—without medication and without stimulation—as moderate or marked, as well as the patients' consent. Dysphagia was not present in these patients. In addition, 14
healthy subjects with a mean age of 56 (SD 7) years served as control subjects. This study was approved by the Grenoble University Hospital ethics committee.

FORCE TASK TESTING AND MOTOR EXAMINATION
Load sensitive devices (Neuro Logic Inc, Bloomington, IN, USA) were used to sample compression forces generated by the upper and lower lips and tongue. The device slid along a jaw yoke that was encapsulated in a malleable dental impression block and placed between the molars. On the screen of the oscilloscope put in front of the subject—who was seated on a dental chair in a Faraday cage—the target and the actual force transducer waveforms were displayed on line. The target levels were 0.25, 0.5, 1, and 2 N, corresponding to forces within speech range. The subject was given the instruction to generate forces from baseline as rapidly and as accurately as possible in response to the target signal which appeared on the screen. The rapid phase of force increase to reach the target was followed by a stabilisation to the target level for 3 seconds. We recorded for each articulatory organ 10 consecutive contractions at each of the four target levels, which were randomised, and two maximal forces. The patients were evaluated in the morning after a period of at least 10 hours without medication and under two conditions: during bilateral STN stimulation, and 1 hour after stopping STN stimulation.

Before each force examination, the motor disability of the patients was assessed by means of the UPDRS, part 3, items 18–31, using a 0 (no impairment) to 4 (severe impairment) scale, maximum score=108.21. In particular, speech was evaluated with item 18 of the UPDRS: 0=normal; 1=slight loss of expression, diction, and/or volume; 2=monotone, slurred but understandable, moderately impaired; 3=marked impairment, difficult to understand; 4=unintelligible.

MEASURES AND DATA ANALYSIS
Maximal voluntary forces of the lips and tongue were measured, as well as the following four variables of the ramp and hold force task (fig 1): (1) reaction time, defined as the time interval from the time the target signal appeared on the screen until the force had reached 10% of peak force; (2) peak force during the force ramp—that is, the highest force level occurring in the 1 second period immediately after 0.1 N; (3) rise time—that is, the time during the ramp phase (10% to 90% of peak); (4) mean and SD of force output during the last 3 seconds of the hold phase. The first three variables estimated dynamic fine force control, and the last one, static force control. These variables were quantified from the digitised records of each articulatory organ for each subject.

The data were submitted to sequential one way analyses of variance (ANOVA) and Tukey tests (p<0.01) to characterise the significant difference between the three groups of subjects: controls and unstimulated and stimulated patients. Two sample t tests were also used to estimate significant differences between two groups of subjects. To estimate the precision of certain variables in relation to the target, such as mean amplitude of peak force or mean amplitude during the hold phase, we calculated for each trial the difference between the amplitude of the actual variable and that of the target force, then we evaluated the mean difference for comparison between the patients.

### Results
The motor disability and speech assessment of the patients with and without stimulation are presented in table 1. The UPDRS mean motor score greatly decreased in the stimulated patients, who improved their motor performance by 42% to 87%. All the items of the

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**Table 1 Motor examination of patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>UPDRS Without stimulation</th>
<th>% Improvement</th>
<th>Speech (item 18)</th>
<th>Without stimulation</th>
<th>With stimulation</th>
<th>Without stimulation</th>
<th>With stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>11</td>
<td>56</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>19</td>
<td>69</td>
<td>2</td>
<td>0</td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td>64</td>
<td>20</td>
<td>55</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>9</td>
<td>64</td>
<td>2</td>
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<tr>
<td>5</td>
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<td>16</td>
<td>71</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>62</td>
<td>36</td>
<td>42</td>
<td>3</td>
<td>2</td>
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<td></td>
</tr>
<tr>
<td>7</td>
<td>48</td>
<td>14</td>
<td>70</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>27</td>
<td>5</td>
<td>82</td>
<td>3</td>
<td>2</td>
<td></td>
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</tr>
<tr>
<td>9</td>
<td>36</td>
<td>6</td>
<td>83</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td>6</td>
<td>87</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

UPDRS= Unified Parkinson’s disease rating scale, part 3, item 18-31.
For any articulatory organ, mean reaction time of the stimulated patients was shorter than that of the unstimulated patients but this difference was only significant for the tongue ($t=2.79$, $p<0.01$). In addition, the patients exhibited a larger variability than the controls as indicated by the large SD.

Figure 3 shows the precision of peak force of the upper lip, lower lip, and tongue at the 2 N and 1 N target levels in the stimulated and unstimulated patients.

Two sample $t$ tests showed that no significant difference was seen between the two periods of the hold phase. Results are reported for the first period. Table 2 shows the mean amplitude of the force of the upper lip, lower lip, and tongue during the first period of the hold phase in the control subjects and stimulated and unstimulated patients, at each target level. The control subjects were very close to the target, and this precision was steady as indicated by the relatively low SD. The stimulated patients were significantly closer to the target and consequently more precise than the unstimulated patients for the three articulatory organs, as

<table>
<thead>
<tr>
<th>Target Level</th>
<th>Upper Lip</th>
<th>Lower Lip</th>
<th>Tongue</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 N</td>
<td>0.24 (0.04)</td>
<td>0.25 (0.04)</td>
<td>0.26 (0.04)</td>
</tr>
<tr>
<td>0.50 N</td>
<td>0.47 (0.05)</td>
<td>0.50 (0.04)</td>
<td>0.49 (0.06)</td>
</tr>
<tr>
<td>1 N</td>
<td>0.97 (0.08)</td>
<td>0.99 (0.07)</td>
<td>0.98 (0.07)</td>
</tr>
</tbody>
</table>

**Table 2** Mean amplitude of the force (SD) (N) during the first period of the hold phase.

UL=Upper lip; LL=lower lip; T=tongue. Values in parentheses are SD.
shown by two sample t tests—that is, for the upper lip at 0.5 N (t = 2.68, p < 0.01), 1 N (t = 3.37, p < 0.01), and 2 N (t = 3.32, p < 0.01); for the lower lip at 1 N (t = 3.62, p < 0.01) and 2 N (t = 5.70, p < 0.01); and for the tongue at 0.5 N (t = 3.14, p < 0.01), 1 N (t = 7.09, p < 0.01), and 2N (t = 7.83, p < 0.01). Moreover, the hold phase of the unstimulated patients was not so steady as that of the stimulated patients as indicated by the greater SD.

Discussion

Bilateral stimulation of the STN greatly improved motor control in this group of patients, who were studied without medication. The 42% to 87% improvement in the global motor evaluation of the UPDRS part 3 reflects the good sensitivity of the parkinsonian syndrome to STN stimulation. In the same way, the item dysarthria of the UPDRS was improved. However, the use of a qualitative five point scale to estimate precisely speech disorders is inadequate and electrophysiological measurements of the speech organs turned out to be necessary. We examined the production of lip and tongue force of the patients under two conditions: without and with bilateral stimulation, considering the difference between both conditions as an index of the influence of the bilateral STN stimulation. Stimulation favourably influenced the patients’ articulatory organs. In stimulated patients we noted a large increase in maximal voluntary force of the lips and tongue, which approached that of the control subjects. These results agree with those of a study relative to the limbs of the control subjects. These results confirm the antiakinetic effect of STN stimulation, previously shown in several studies.5 26

Mean reaction times of the stimulated patients were shorter than those of the unstimulated patients. These findings confirm the antiakinetic effect of STN stimulation, previously shown in several studies.5 26

The hold phase of the control subjects was accurate and steady. The unstimulated patients had difficulty in maintaining a given contraction with the articulatory organs. Milner-Brown et al27 reported that, even when voluntarily attempting to maintain a force, some motor units in patients with Parkinson’s disease stop firing for prolonged periods or fire at abnormally low frequencies. In addition we cannot exclude the possibility that the disturbance in constant force may be due to a dysfunction of the integration of proprioceptive inputs.28 Hold phase accuracy of the stimulated patients was greater than that of the unstimulated patients.

In conclusion, bilateral STN stimulation influences both oral and limb systems. We noted an improvement in force of the articulatory organs and concomitant improvement in speech assessment. However, when using excessively high stimulation parameters or with incorrect electrode location, speech may be worsened by STN stimulation. Consequently, it may be helpful in determining whether a speech problem is related to stimulation. The mechanism of action of STN stimulation is unknown, although it is probable that it modulates neuronal structures involved in speech. Further speech investigations in a large number of patients are warranted to clarify the role of STN stimulation on parkinsonian dysarthria. A better knowledge of the impact of this surgical procedure on speech is very important given that dysarthria may greatly reduce the ability of the parkinsonian patients to function fully in society.