Subthalamic Stimulation in Parkinson Disease
With or Without Anesthesia?

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Objective: To study the effects of general anesthesia on the postoperative outcome of patients with Parkinson disease (PD) who underwent surgery using bilateral placement of stimulating electrodes within the subthalamic nucleus (STN).

Design: Retrospective analysis.

Setting: Hopital de la Salpetriere, Paris, France.

Patients: Fifteen PD patients who underwent bilateral implantation of electrodes within the STN received general anesthesia because of severe anxiety, poorly tolerated off-period dystonia, or respiratory difficulties. These patients were compared with 15 patients matched for age, disease duration, and parkinsonian motor disability who underwent the same neurosurgical procedure under local anesthesia.

Main Outcome Measure: Motor disability scores.

Results: After surgery, the severity of parkinsonian motor disability was markedly improved in both groups of patients. Compared with patients who were under local anesthesia during the operation, the residual parkinsonian motor score under stimulation (with "on" or without "off" levodopa) and the intensity of stimulation were higher in patients who were under general anesthesia during the operation.

Conclusions: Although the improvement of parkinsonian motor disability is greater in PD patients who receive local anesthesia during surgery, general anesthesia can be performed in patients unable to tolerate prolonged states without levodopa.

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BILATERAL STIMULATION OF the subthalamic nucleus (STN) is one of the most effective treatments for advanced levodopa-responsive forms of Parkinson disease (PD). The success of the postoperative clinical outcome depends on the quality of the inclusion of patients and the optimal targeting and electrophysiological recording of the STN. Surgery is usually performed with the patient under local anesthesia, which allows the intraoperative, stimulation-induced improvement of parkinsonian signs and dyskinesias to be evaluated. However, general anesthesia is sometimes used for patients with severe anxiety or painful off-period dystonia who are unable to tolerate the operation while under local anesthesia. To evaluate the effects of general anesthesia on postoperative outcome in PD patients, we retrospectively compared 15 patients who received general anesthesia with 15 matched patients who were under local anesthesia during the operation.

METHODS

Of the 105 consecutive PD patients who underwent bilateral placement of stimulating electrodes within the STN at the Hôpital de la Salpêtrière, Paris, France, between May 1997 and December 2002, 15 (11 men, 4 women; mean ± SD age, 59.0 ± 8.0 years; mean ± SD disease duration, 13.4 ± 3.7 years) received general anesthesia rather than local anesthesia during the procedure because of severe anxiety (n = 9), painful dystonia (n = 5), respiratory difficulties while without ("off") levodopa (n = 3), or an unexplained loss of consciousness during the positioning of the stereotactic frame with the patient under local anesthesia (n = 1) (some patients had ≥1 condition). All experienced severe PD (Hoehn and Yahr6 stage while off levodopa, ≥3) and levodopa-related motor complications (Table). These patients were compared with 15 PD patients (9 men, 6 women) matched for age (mean ± SD age, 58.0 ± 6.1 years), disease duration (mean ± SD disease duration, 13.5 ± 2.6 years), and parkinsonian motor disability who underwent the same procedure while under local anesthesia (Table).

The neurosurgical procedure was performed as previously described, except the pa-
After Surgery

Telemetry with a view to continuous stimulation. The therapeutic contacts were fine-tuned by programmable pulse generator (ITREL II, n=9; Kinetra, n=21; Medtronic). The optimal functional target was defined not only by STN electrophysiological recordings but also by the effectiveness with which the lowest-intensity stimulation decreased parkinsonian signs without inducing adverse effects. In the latter group, the definitive electrodes were implanted along the central trajectory in 29 cases and along the medial trajectory in 1 case. In the local anesthesia group, the optimal functional target was defined not only by STN electrophysiological recordings but also by the effectiveness with which the lowest-intensity stimulation decreased parkinsonian signs without inducing adverse effects. In the latter group, the definitive electrodes were implanted along the posterior (n=3), medial (n=1), lateral (n=1), and central (n=25) trajectory. In the general anesthesia group, computed tomography was systematically performed after surgery to rule out the existence of any postoperative complications. Within 3 days, the electrodes were connected to a subcutaneous programmable pulse generator (ITREL II, n=9; Kineta, n=21; Medtronic). The therapeutic contacts were fine-tuned by telemetry with a view to continuous stimulation.

Patients were evaluated within the month before and 6 months after surgery. Before surgery, the motor disability score (Unified Parkinson’s Disease Rating Scale [UPDRS] Part III) was assessed while the patient was in the off-levodopa condition as defined by the Core Assessment Program for Surgical Intervventional Therapy (ie, after at least a 12-hour interruption of antiparkinsonian medication) and in the best “on”-levodopa condition after the administration of a single supra-threshold dose of levodopa. The axial score, defined as the sum of the following motor subscores: speech, arising from chair, posture, gait, and postural stability (items 18, 27, 28, 29, and 30 of the UPDRS Part III), was assessed in the same conditions. After surgery, parkinsonian motor disability scores were evaluated in 4 conditions: (1) not receiving stimulation and off levodopa, after a night without treatment and after the stimulation had been switched off for at least 1.5 hours; (2) receiving stimulation and off levodopa, after the stimulation had been switched on for at least 1 hour; (3) not receiving stimulation and on levodopa, after a suprathreshold dose of levodopa; and (4) receiving stimulation and on levodopa. The percentage of improvement in parkinsonian motor disability was determined with respect to the preoperative off-levodopa condition. Levodopa-related complications were evaluated using the UPDRS Part IV (levodopa-induced dyskinesias and motor fluctuations; parts A and B, respectively).

Results are presented as mean (SD) values. Clinical data before and 6 months after surgery were compared using the Wilcoxon signed-rank test for nonparametric data. We used a nonparametric Mann-Whitney test to compare the postoperative outcome between the 2 groups of patients (P<.05).

RESULTS

Six months after surgery, the parkinsonian motor score (UPDRS Part III, axial score) under stimulation with or without levodopa was significantly improved compared with the preoperative state (off levodopa) in both groups. Parkinsonian motor disability (UPDRS Part III) under stimulation alone (residual score: receiving stimulation, off levodopa) or under stimulation and medication (receiving stimulation and on levodopa) was significantly lower in the local anesthesia group. The postoperative axial score under stimulation alone or under stimulation and levodopa tended to be lower in the local compared with the general anesthesia group, although this was not statistically significant (P=.07 and P=.06, respectively). The postoperative levodopa-equivalent dosage was significantly reduced in both groups of patients. The se-

Clinical Characteristics of Patients 1 Month Before and 6 Months After Surgery

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>General Anesthesia Before Surgery</th>
<th>Local Anesthesia Before Surgery</th>
<th>General Anesthesia After Surgery</th>
<th>Local Anesthesia After Surgery</th>
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<tbody>
<tr>
<td>Motor disability (UPDRS Part III)</td>
<td></td>
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<tr>
<td>“Off” levodopa</td>
<td>47.1 ± 15.4 10.4 ± 5.7 (78)</td>
<td>39.9 ± 13.9 9.4 ± 5.2 (78)</td>
<td>17.0 ± 8.6 (63)†</td>
<td>10.9 ± 7.2 (74)‡</td>
</tr>
<tr>
<td>“On” levodopa</td>
<td></td>
<td></td>
<td>8.9 ± 4.5 (79)††</td>
<td>5.3 ± 4.7 (87)t‡</td>
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<tr>
<td>Receiving stimulation, off levodopa</td>
<td></td>
<td></td>
<td>3.5 ± 2.4 (54)†</td>
<td>2.5 ± 3 (68)†</td>
</tr>
<tr>
<td>Receiving stimulation, on levodopa</td>
<td></td>
<td></td>
<td>2.5 ± 1.8 (63)†‡</td>
<td>1.5 ± 1.8 (78)†</td>
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<tr>
<td>Axial score</td>
<td></td>
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<tr>
<td>Off levodopa</td>
<td>9.4 ± 4.8 2.5 ± 1.4 (73)</td>
<td>8.5 ± 3.5 2.4 ± 1.9 (74)</td>
<td>1.1 ± 1.7 (85)†</td>
<td>2.3 ± 2.6 (79)†‡</td>
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<tr>
<td>On levodopa</td>
<td></td>
<td></td>
<td>1 ± 1.5 (63)†</td>
<td>1.1 ± 1.7 (79)†</td>
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<tr>
<td>Receiving stimulation, off levodopa</td>
<td></td>
<td></td>
<td>0 (100)†</td>
<td>0.73 ± 1.3 (87)†‡</td>
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<td>Receiving stimulation, on levodopa</td>
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<td>Levodopa-induced complications</td>
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<tr>
<td>UPDRS Part IV</td>
<td>8.4 ± 2.8</td>
<td>11.1 ± 2.3</td>
<td>1.1 ± 1.7 (85)†</td>
<td>2.3 ± 2.6 (79)†‡</td>
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<tr>
<td>Dystokinesias (part A)</td>
<td>4.1 ± 1.6</td>
<td>6.3 ± 2.7</td>
<td>1 ± 1.5 (63)†</td>
<td>1.1 ± 1.7 (79)†</td>
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<tr>
<td>Motor fluctuations (part B)</td>
<td>3.5 ± 1.4</td>
<td>3.6 ± 1.4</td>
<td>0 (100)†</td>
<td>0.73 ± 1.3 (87)†‡</td>
</tr>
<tr>
<td>Levodopa equivalents, mg/d</td>
<td>1449 ± 398</td>
<td>1507 ± 465</td>
<td>310 ± 350 (78)†</td>
<td>392 ± 440 (76)†‡</td>
</tr>
</tbody>
</table>

Abbreviation: UPDRS, Unified Parkinson’s Disease Rating Scale.

*Values are the mean ± SD (percentage of improvement compared with the drug-free condition before surgery).
†P<.05 when compared with the preoperative off-levodopa condition, Wilcoxon signed rank test.
‡P<.05 when compared with the patients under general anesthesia during the operation, Mann-Whitney test.

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verity of levodopa-related complications was markedly reduced in both groups of patients but remained significantly higher in the local anesthesia group (UPDRS Part IV, motor fluctuations) (Table).

Although the frequency and pulse width of stimulation did not differ between the 2 groups, the intensity of stimulation was significantly higher in the general compared with the local anesthesia group for the right side (general anesthesia: 2.85 ± 0.42 V; local anesthesia: 2.52 ± 0.32 V; \( P = .02 \); left side, general anesthesia: 2.81 ± 0.54 V; local anesthesia: 2.71 ± 0.31 V; \( P = .19 \)).

No adverse reactions to the use of propofol were observed. One patient who needed an endotracheal intubation had a transient pulmonary atelectasis. No other intraoperative or postoperative complications were observed.

**COMMENT**

Although this is a retrospective study, we think that the results are valid. First, the patients who were under general anesthesia during the operation were carefully matched for age, disease duration, severity of parkinsonian motor disability, and response to levodopa treatment. Second, the clinical criteria used to select patients for neurosurgery were scrupulously respected in the 2 groups: age younger than 70 years, excellent response to levodopa treatment, advanced form of the disease, presence of disabling motor fluctuations and levodopa-induced dyskinesias (Table), and absence of contraindications such as cognitive or psychiatric impairment. Third, the intraoperative characteristics of STN neuronal activity were recorded in all patients whether or not they received general anesthesia. Therefore, apart from general anesthesia, the only difference between the general vs local anesthesia patients was the absence of intraoperative assessment of parkinsonian motor disability and of stimulation-induced dyskinesias.5,10

The severity of parkinsonian motor disability assessed postoperatively was more important in the general compared with local anesthesia patients. The results suggest that the bilateral targeting of the STN was less precise in the absence of intraoperative clinical assessment in the general anesthesia group. This is confirmed by the fact that the intensity of stimulation tended to be higher in general anesthesia patients. Such a conclusion is not unexpected, since the definitive electrode implanted was the central one in almost all cases (29 of 30) in the general anesthesia group and in only 83% of the cases in the local anesthesia group (25 of 30). This suggests that the long-term clinical benefit of neurosurgery will not be optimal in a nonnegligible fraction of patients who received general anesthesia during the operation. Although this study needs to be replicated prospectively in a larger population of patients, the results nevertheless suggest that STN stimulation can be performed with general anesthesia in patients with severe off-period dystonia or anxiety who receive general anesthesia during neurosurgery because they would not tolerate undergoing the operation while under local anesthesia.

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**Author contributions:** Study concept and design (Drs Malte‡te, Navarro, Welter, and Agid); acquisition of data (Drs Malte‡te, Navarro, Welter, Roche, Bonnet, Houeto, Mesnage, Pidoux, Dormont, and Cornu); analysis and interpretation of data (Drs Malte‡te, Navarro, Welter, Dormont, Cornu, and Agid); drafting of the manuscript (Drs Malte‡te and Agid); critical revision of the manuscript for important intellectual content (Drs Navarro, Welter, Roche, Bonnet, Houeto, Mesnage, Pidoux, Dormont, Cornu, and Agid); statistical expertise (Dr Malte‡te); obtained funding (Drs Malte‡te and Cornu); administrative, technical, and material support (Dr Dormont); study supervision (Drs Welter, Bonnet, Dormont, and Agid).

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**REFERENCES**