A metaanalysis comparing the results of pallidotomy performed using microelectrode recording or macroelectrode stimulation

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Object. There is an active debate regarding whether pallidotomy should be performed using macroelectrode stimulation or the more sophisticated and expensive method of microelectrode recording. No prospective, randomized trial results have answered this question, although personnel at many centers claim one method is superior. In their metaanalysis the authors reviewed published reports of both methods to determine if there is a significant difference in clinical outcomes or complication rates associated with these methods.

Methods. A metaanalysis was performed with data from reports on the use of unilateral pallidotomy in patients with Parkinson disease (PD) that were published between 1992 and 2000. A Medline search was conducted for the key word “pallidotomy” and additional studies were added following a review of the references. Only those studies dealing with unilateral procedures performed in patients with PD were included. Papers were excluded if they described a cohort smaller than 10 patients or a follow-up period shorter than 3 months or included cases that previously had been reported. The primary end points for outcome were the percentages of improvement in dyskinesias and in motor scores determined by the Unified PD Rating Scale (UPDRS). Complications were categorized as mortality, intracranial hemorrhage, visual deficit, speech deficit, cognitive decline, weakness, and other.

There were no significant differences between the two methods with respect to improvements in dyskinesias (p = 0.66) or UPDRS motor scores (p = 0.62). Microelectrode recording was associated with a significantly higher (p = 0.012) intracranial hemorrhage rate (1.3 ± 0.4%), compared with macroelectrode stimulation (0.25 ± 0.2%).

Conclusions. In reports of patients with PD who underwent unilateral pallidotomy, operations that included microelectrode recording were associated with a small, but significantly higher rate of symptomatic intracranial hemorrhage; however, there was no difference in postoperative reduction of dyskinesia or bradykinesia compared with operations that included macroelectrode stimulation.

KEY WORDS • Parkinson disease • pallidotomy • microelectrode recording • dyskinesia • complication • metaanalysis
Metaanalysis of pallidotomy results

### TABLE 1
Summary of outcomes in patients undergoing either pallidotomy technique

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Microelectrode Recording</th>
<th>Macrostimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS motor score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no. of patients</td>
<td>365</td>
<td>198</td>
</tr>
<tr>
<td>% improvement*</td>
<td>34 ± 5</td>
<td>28 ± 7</td>
</tr>
<tr>
<td>dyskinesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no. of patients</td>
<td>302</td>
<td>184</td>
</tr>
<tr>
<td>% improvement*</td>
<td>75 ± 6</td>
<td>80 ± 7</td>
</tr>
</tbody>
</table>

* Not significant.

### TABLE 2
Summary of complication rates in patients undergoing either pallidotomy technique

<table>
<thead>
<tr>
<th>Complication</th>
<th>Microelectrode Recording</th>
<th>Macrostimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>mortality</td>
<td>0.7 ± 0.2</td>
<td>0.4 ± 0.2</td>
</tr>
<tr>
<td>intracranial hemorrhage†</td>
<td>1.3 ± 0.4</td>
<td>0.25 ± 0.2</td>
</tr>
<tr>
<td>visual deficit</td>
<td>1.4 ± 0.4</td>
<td>2.5 ± 0.6</td>
</tr>
<tr>
<td>speech deficit</td>
<td>1.3 ± 0.4</td>
<td>1.9 ± 0.5</td>
</tr>
<tr>
<td>cognitive decline</td>
<td>2.3 ± 0.5</td>
<td>1.3 ± 0.4</td>
</tr>
<tr>
<td>weakness</td>
<td>1.1 ± 0.3</td>
<td>1.6 ± 0.4</td>
</tr>
</tbody>
</table>

† p = 0.012.

* Values are presented as means ± standard errors of the means. If not otherwise specified, the complication rate is not significant.

There was no significant difference (p = 0.54) in the preoperative severity of Parkinsonian symptoms for the two groups as measured by the UPDRS motor score.

**Changes in Dyskinesia**

Studies in which microelectrode recording (302 patients, 13 studies) and macrostimulation (184 patients, eight studies) were analyzed, case reports or preliminary communications and were not believed to reflect the expected outcome of an experienced neurosurgical center in which stereotactic surgery is performed. Follow-up periods shorter than 3 months were excluded because the effects of perilesional edema could not be excluded. Finally, only papers that included complication rates or detailed pre- and postoperative UPDRS scores or dyskinesia severity were analyzed.

### Measurements of Outcomes and Complications

There is a general consensus among movement disorder specialists (supported by this analysis) that pallidotomy significantly reduces contralateral dyskinesia and, to a lesser extent, reduces bradykinesia, 7,36,37,42,49 Other potential benefits include a reduction in tremor, 6,12,19,31,44,49 pain, 29 and difficulties in gait 50 and balance. 30,40 We selected dyskinesia and the UPDRS motor score as outcome measurements. A summary of data from papers providing this information is presented in Table 1. The dyskinesia scores obtained from studies involving microelectrode recording6,20,21,32,38,45,47,49,51,52,55,58,60,63 and macrostimulation studies 7,12,18,27,35,46,56,57 were analyzed. Because different scales were occasionally used, data were reduced to a common value, that is, the percentage of improvement in the severity of dyskinesia (difference between preoperative and postoperative dyskinesia scores divided by the preoperative value). When multiple follow-up time points were given, we chose the value closest to 1 year. Too few papers existed in which longer follow-up periods were reported for us to select a longer time point. The UPDRS motor score was the most commonly reported assessment of motor outcome for both microelectrode recording studies 6,20,21,32,38,45,47,49,51,52,55,58,60,63 and macrostimulation studies 7,12,18,27,35,46,56,57 Most patients were studied during the off medication period (>12 hours after their last dose of antiparkinsonian medication), although in some papers the timing of testing was omitted. The percentage of improvement in the UPDRS motor score was calculated in the same manner as that for dyskinesia.

A summary of mortality and morbidity events for the two methods of pallidotomy is presented in Table 2. Incidences of mortality and morbidity following microelectrode recording2–6,11,16,21,45,47,49,51,55,58,61,62,64 and macrostimulation7,8,12,14,18,23,27,28,30,31,33,36,37,39,46,56,57 were tabulated. Morbidity events were categorized as intracranial hemorrhage, persistent visual deficit (dysarthria, dysphasia, or hypophonia), persistent cognitive decline, persistent weakness (facial or limb hemiparesis), or other rare problems (seizure, infarction, infection, abandonment of the procedure, or a persistent neurological deficit not included earlier). We excluded temporary complications such as lethargy, confusion, or weakness that improved quickly (potentially with resolution of postoperative edema). We excluded asymptomatic hemorrhages found on routine postoperative imaging because this would provide a bias against those groups that looked for this problem. The primary measurements for complications were the rates of mortality, intracranial hemorrhage, visual deficit, speech deficit, cognitive decline, and weakness. Rates were calculated by dividing the number of patients who died or in whom a complication developed by the number of patients beginning the procedure. A single patient with multiple complications was counted in each category in which a complication occurred (that is, a hemorrhage resulting in weakness was included in both categories of complications). Any patient who died was excluded from the morbidity calculations.

### Statistical Analysis

A metaanalysis was performed on the data following the methods outlined by Hedges and Olkin. 29 Sample sizes of individual studies were used as weights in combining data for each variable separately across microelectrode and macrostimulation trials. Tests of homogeneity (Q-tests) were conducted and pooled estimates for the two methods of pallidotomy were compared. 29 Confidence intervals were derived with additional precision by using the two roots of the quadratic equations given by Fleiss. 37 The preoperative UPDRS motor score was used to compare the two groups of patients before treatment to ensure that patients in whom microelectrode recordings were performed during pallidotomy did not significantly differ in the severity of their Parkinsonian motor symptoms compared with the group undergoing pallidotomy with macrostimulation.

### Results

There was no significant difference (p = 0.54) in the preoperative severity of Parkinsonian symptoms for the two groups as measured by the UPDRS motor score.
ies) were used were sufficiently homogeneous (p = 0.68 and p = 0.67, respectively) to allow a comparison (Table 1). There was no significant difference in the percentage of improvement in dyskinesia between the two groups (p = 0.64). The mean improvement following pallidotomy with microelectrode recording was 75 ± 6% (95% CI 64–87%). The mean improvement following pallidotomy with macrostimulation was 80 ± 7% (95% CI 65–94%).

Changes in UPDRS Motor Score

Studies in which microelectrode recording (365 patients, 14 studies) and macrostimulation (198 patients, 10 studies) were used were sufficiently homogeneous (p = 0.64 and p = 0.99, respectively) to allow a comparison (Table 1). There was no significant difference in the percentage of improvement in UPDRS motor scores between the two groups (p = 0.44). The mean improvement observed following pallidotomy with microelectrode recording was 34 ± 5% (95% CI 24–45%). The mean improvement following pallidotomy with macrostimulation was 28 ± 7% (95% CI 14–42%).

Operative Complications

Operations in which microelectrode recording was performed were associated with more than five times the rate (p = 0.012) of intracranial hemorrhage compared with operations in which macrostimulation was performed. The rate of intracranial hemorrhage associated with microelectrode recording was 1.3 ± 0.4% and that associated with macrostimulation was 0.25 ± 0.2%. Although the mortality rate was almost double for procedures that included microelectrode recording, it did not reach statistical significance (p = 0.38). The rates for each of the other morbidities are presented in Table 2. There was no significant difference in the rates of visual deficit (p = 0.11), speech deficit (p = 0.35), cognitive decline (p = 0.1), or weakness (p = 0.34). The difference in estimated rates were all small. If larger numbers of patients had been available to increase the statistical power, these small differences would not likely translate into a significant clinical difference.

Discussion

Microelectrode recording during stereotactic neurosurgery allows the recognition of neuronal firing patterns.43,59 These patterns, which are unique to different nuclei within the basal ganglia, can be recognized and used to help localize the tip of the electrode. Although the equipment and methodology for microelectrode recording varies between institutions, most microelectrodes are typically very sharp (approximately 1–4 mm in diameter) and are often passed several times through the target area to map it. The need for microelectrode recording during stereotactic surgery is hotly debated.22,24 Advocates report improved target localization and research opportunities that are unavailable during macrostimulation. Persons who do not favor this method cite the increased operative time required as well as the expense and complexity of the technique. Within the United States, this debate intensified when Medicare announced it would not fund pallidotomy without microelectrode recording. This decision was soon changed. (No Food and Drug Administration–approved microelectrode recording systems were available at the time.) Macroelectrodes are more blunt (1–2 mm in diameter); they allow measurement of tissue impedance, but cannot record neuronal firing patterns. Brief pulses of current can be sent through the uninsulated tip to test the patient’s response to stimulation (macrostimulation). If the tip is placed too close to the optic tract or internal capsule, patients will report phosphenes or paresthesia. The newer lesion generators also allow high-frequency stimulation at the macroelectrode tip, can mimic the response to a lesion before it is made.

Our metaanalysis did not demonstrate any significant differences in improvements in dyskinesias or UPDRS motor scores in patients with PD who underwent unilateral pallidotomy procedures with either microelectrode recording or macrostimulation. There was a significantly higher rate of symptomatic intracranial hemorrhage following operations involving microelectrode recording (1.3 ± 0.4%) compared with those involving macrostimulation (0.25 ± 0.2%). The hemorrhage rate was still quite low and similar to rates following brain biopsy (1.2%).15 This increased risk of hemorrhage following microelectrode recording has been reported.1 It may be due to the increased number of electrode passes that occur when using this method or to the sharper tip of the microelectrode, which may pierce vessels instead of pushing them aside. Insufficient data on the number of electrode passes utilized for each method were available for statistical analysis. The hemorrhage rate in centers in which microelectrode recordings are performed during pallidotomy did not appear to be biased toward those in which fewer cases were performed. When centers were ranked by the number of cases reported, those in the lowest one third reported a lower hemorrhage rate than those in the highest one third. The most common cause of death following pallidotomy was intracranial hemorrhage with its associated complications. The hemorrhage rate associated with microelectrode recording, which was five times higher than that associated with macroelectrode stimulation, did not, however, translate into a statistically higher rate of mortality.

There was no significant difference in the rate of visual complications between the two methods. One strength of microelectrode recording is its ability to define the lower border of the pallidum and the location of the optic tract; however, this did not translate into reduced visual field deficits.

Several assumptions we made about the data may weaken the strength of this metaanalysis. First, we assumed that the two groups being compared were homogeneous. There was no significant difference between groups with respect to their UPDRS off-medication scores, but insufficient data were available to test for possible differences in patient age, disease duration, medications, or UPDRS on-medication scores. Second, we assumed that the published reports represented what was actually occurring in the specific clinics. There may be a tendency not to report complications or deaths, but this probably would be equally prevalent between those centers using either method. Third, we assumed that the outcome measures reviewed are relevant. One could argue that additional outcome measures, such as activities of daily living, could also be important, but reports of these were too infrequent to test. When multiple follow-up testing was performed, we selected the scores closest to 1 year. This time was selected as a compromise between the longest available follow-up period and the fol-
low-up duration that was most frequently reported. There may be a change in benefit over time.33 but too few groups have published results beyond 1 year to allow a reliable comment. Fourth, we assumed that centers reporting microelectrode recording used this method in all their patients undergoing pallidotomy. It has been our experience (and those in many other centers) that complication rates fall over time to a stable level once the learning curve is passed. This concept is likely true for both methods.

At our center there is no financial bias toward either method. Although the results of this metaanalysis do not definitively answer the question of whether microelectrode recording or macrostimulation should be used during unilateral pallidotomy, it does cast doubt on the current dogma that microelectrode recording is worth the added time it requires. This study also highlights the increased risk of hemorrhage associated with the use of microelectrode recording. This risk, however, remains small. A prospective, randomized trial is needed to answer the question definitively. Finally, these results cannot be extrapolated to surgical procedures involving other brain targets such as the subthalamic nucleus.

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