Stereotactic Targeting of the Globus Pallidus Internus in Parkinson’s Disease: Imaging versus Electrophysiological Mapping

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OBJECTIVE: The reintroduction of pallidotomy for the treatment of Parkinson’s disease (PD) has generated various opinions regarding the ideal anatomic or physiological location of the target within the globus pallidus. The role of microelectrode recording guidance in pallidotomy for the treatment of advanced PD is presently under debate. The purpose of this study was twofold. The first goal was to determine the degree of accuracy in the targeting of the globus pallidus internus (GPI) with magnetic resonance imaging (MRI), by comparing these results with the final placement of the thermolytic lesions (as defined by electrophysiological assessment). The second goal was to ascertain the somatotopic arrangement of the GPI in PD.

METHODS: The analysis involved 50 patients with PD who underwent microrecording-guided pallidotomy. The theoretical coordinates for lesioning were calculated after definition of the intercommissural line by MRI. The actual placement of the lesions was determined after mapping of the GPI by microrecording, using stimulation to identify the sensorimotor region and its somatotopic organization.

RESULTS: In most cases, the lesions were placed posterior and lateral to the targets chosen by MRI. Mapping by microrecording revealed differences of 2.3 ± 1.55 mm and 3 ± 1.9 mm in the mediolateral and anteroposterior coordinates, respectively. The actual lesion overlapped the theoretical target for only 45% of the patients. The somatotopic organization of the GPI was analyzed. Most of the units with sensorimotor activity or tremor-related activity were in the lateral portion of the nucleus. Upper limb and axial units were in the most lateral region and mainly in the ventral one-third of the nucleus. Lower limb responses were recorded mainly in the dorsal one-third of the nucleus. Tremor-related cells were found throughout the sensorimotor region of the nucleus.

CONCLUSION: These results indicate that lesion targeting based on MRI alone is not sufficiently accurate to guarantee placement of the lesion in the sensorimotor region of the GPI. (Neurosurgery 45:278–289, 1999)

Key words: Microrecording, Pallidal somatotopy, Pallidotomy, Parkinson’s disease

Pallidotomy has been revived as a surgical procedure for the treatment of advanced Parkinson’s disease (PD). Pallidal lesions alleviate mainly bradykinesia, rigidity, and tremor during the “off” period and abolish dyskinesia induced by chronic treatment with levodopa (3, 10, 23, 25, 28, 42). Improvements after the stereotactic procedure are mainly on the side contralateral to the operation, with less alleviation on the ipsilateral side. Pallidotomy as a neuroablative surgical procedure is the subject of a continuing debate regarding target localization. Some teams consider anatomic localization by imaging and macroelectrical stimulation to be sufficient, and others think that physiological localization is necessary to yield the best possible results.

The first aim of this study was to investigate the discrepancies between the final, electrophysiologically determined lesions in the globus pallidus internus (GPI) and the targets that had been previously chosen by magnetic resonance imaging (MRI). In addition, we define the somatotopic
organization of the GPi and discuss its importance for pallidotomy.

PATIENTS AND METHODS

Fifty patients (29 men and 21 women; mean age, 52.28 yr; age range, 42–74 yr) with advanced PD (average duration of disease, 19.2 yr) were subjected to microelectrode-guided pallidotomy. Seventeen operations were performed in the right hemisphere and 33 in the left. All surgical procedures were unilateral, on the side opposite that on which the signs were more severe.

Patients selected for surgery were identified as having idiopathic PD according to the Brain Bank Criteria (13), with initially positive responses to levodopa. All patients exhibited major complications, such as motor fluctuations and dyskinesia, related to chronic treatment.

Patients were excluded from surgery if they exhibited cardiac or pulmonary disease, uncontrolled arterial hypertension, evidence of atypical parkinsonism (with signs of upper motor neuron disease and cerebellar involvement), unresponsiveness to levodopa treatment, or dementia. The age of the patients was a relative criterion for exclusion, with an upper limit of 75 years being established.

Image acquisition

A Leksell Model G stereotactic frame was positioned after administration of local anesthesia, and MRI was performed (0.5 T; General Electric Medical Systems, Milwaukee, WI). Images were acquired using a T1-weighted inversion recovery sequence (3-mm-thick axial and sagittal slices; repetition time, 1500 ms; inversion time, 650 ms; field of view, 22–25 cm) and T2-weighted (3-mm-thick slices) and T1-weighted (1.8-mm-thick slices, with no interslice gap) spin echo sequences to localize the anterior and posterior commissures (192 × 192 matrix). The software of the MRI instrument measured the distance between the anterior and posterior commissures with respect to the center of the frame. These data were transcribed to a digitized sagittal stereotactic map of the Schaltenbrand-Bailey atlas (34). The atlas image was then adjusted to fit the intercommissural distance for the patient. The initial target chosen was a point 20 to 22 mm lateral to the midline (when the third ventricle was wider, the target was more lateral), 2 to 3 mm in front of the center of the intercommissural line, and 5 to 6 mm below the line described by Laitinen (26) and Laitinen et al. (27).

Surgical procedure

With the patient in a semi-sitting position, after local anesthesia had been administered, a 14-mm burr hole (20 mm lateral to the midline and anterior to the coronal suture) was made. After coagulation of the dura and cortex, a guide tube was introduced for recording. A special instrumental configuration had been developed for neuronal recording; a microstereotactic head-stage with x-y coordinates had been adapted to fit the stereotactic head-frame. The initial target coordinates were centered at 100 and 100 on the head-stage, and subsequent adjustments in the mediolateral (x) or anteroposterior (y) planes were made by withdrawing the guide carrier and adjusting the coordinates of the x-y stage, without changing the angles of the stereotactic arc. This procedure allows a rapid and precise change in coordinates; all tracks or trajectories under study are parallel to the sagittal plane atlas and exhibit similar recording characteristics. Microrecording was performed by using platinum/iridium-coated microelectrodes, with tip diameters of 2 to 4 μm (impedance, 0.2–1.0 MΩ at 1000 Hz). The electrode was placed in a stainless steel carrier tube (26 gauge) attached to a hydraulic microdrive (25-mm total length; David Kopf Instruments, Precision Designs for Research, Tujunga, CA), which was connected to the head-stage. This allowed the microelectrode to be moved, by micrometers or more (when not recording), by a course drive. The electrode carrier and the inner guide tip were set at 45 mm from the target.

A high-impedance preamplifier for recording was attached to the microdrive assembly. The preamplifier was connected to standard electrophysiological equipment for amplification, filtering, and discrimination of the electrophysiological signals (Neurosysterm-2; Atlantic Research System, Atlanta, GA). The electrode could also be used for microstimulation. The recorded signals from single cells or units were displayed and analyzed on an oscilloscope screen, transmitted to a signal audio-amplifier for neuronal electromyographic recording, and stored on tape for subsequent off-line analysis.

Recording tracks were made in the parasagittal plane at an angle of 45 to 60 degrees with respect to the horizontal plane of the frame. To record neuronal activity throughout the striatum, the globus pallidus externus and GPi were monitored. After passing through the most ventral portion of the GPi, the microelectrode traversed the ansa lenticularis and then entered the optic tract or internal capsule. The optic tract was identified by a high-frequency audio signal coinciding with a light stimulus and by the reporting of phosphene by the patient (Fig. 1).

During the recording phase, the globus pallidus externus was identified by two different patterns of discharge. A majority of units (70–80%) exhibited periods of high-frequency discharge separated by pauses. A few units discharged at low frequency, with brief high-frequency bursts. In the GPi, the majority of neurons were identified by a high-frequency and tonic discharge pattern.

To determine the somatotopic arrangement of the sensorimotor area of the GPi, neuronal activity was first recorded for 30 to 60 seconds with the patient at rest; responses to passive manipulation and active movements of the limbs (wrist, elbow, shoulder, ankle, knee, and hip on the contralateral and ipsilateral sides, with respect to the surgical procedure), neck, and orofacial region were then assessed. The neck, paraver-

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tebral, and abdominal musculature was passively tested with pressure (no active movements could be undertaken), and orofacial movements were assessed as jaw opening and closing, tongue protrusion, and ocular movements. The units that showed conspicuous changes in their firing rates (judged on-line by the investigator) in response to passive and active movements of the contralateral joints were labeled as kinesthetic cells. After a unit was well isolated and clearly recognized as kinesthetic for a given body part, the investigator completed testing of the remaining body regions. For practical reasons, it was not possible to test all studied units for both passive and active movements. For patients who exhibited resting tremors during the procedure, neurons discharging in synchrony with the tremors, which were identified by visual inspection of the limbs and simultaneous surface electromyographic recording in the contralateral limbs, were classified as tremor-related cells. The precise locations of only clearly isolated and stable units in each recording track were noted; these locations were subsequently compared with the atlas, to define the topographic features of the sensorimotor region and its somatotopic arrangement. High-quality recording for these analyses was performed for 18 patients. Recording data from the remaining 32 patients were used for topographic definition of the GPi during surgery but not for off-line analysis. Generally, recording tracks were maintained in the same sagittal plane until the internal capsule was detected. A final track was then obtained in a more lateral plane (usually 2–3 mm), with maintenance of the same rostrocaudal coordinate. With this template, the GPi is shorter than in previous tracks, indicating the outer limit of the GPi. Microstimulation (10–100 µA, 300 Hz, 0.2–0.5 ms) was also used to establish the boundaries of the GPi (especially the optic tract and internal capsule). Three to five recording tracks were generally sufficient for mapping of the GPi sensorimotor area (Fig. 1).

Lesioning procedure

The lesioning electrode probe (tip of probe, 2 mm; diameter, 1.1 mm; Radionics, Burlington, MA) was advanced as far as the dorsal border of the GPi, and macrostimulation was performed at selected intervals (2 mm) until the optic tract was reached. The stimulation frequency was 300 Hz (pulse width, 0.2 ms), and the safety stimulation thresholds were 0.7 to 1 mA for the optic tract and 0.3 to 0.5 mA for the internal capsule (Grass S48 stimulator; Medical Instruments, Quincy, MA). These parameters allowed the pallidotomy to be performed approximately 1 mm above the optic tract and 2 mm anterior to the internal capsule, without producing any permanent deficits. The temperature of the lesioning probe was 60°C, 70°C, and then 80°C, each for 60 seconds (radiofrequency generator RFG-C; Radionics). This procedure produced cylindrical lesions of approximately 3 mm in diameter, with variable lengths of 4 to 7 mm (43). The volumes of the lesions, as calculated in the operating room and later confirmed by MRI, were approximately 100 to 150 mm³ (volume = 4/3π × r₁ × r₂ × r₃, where r₁ is the anteroposterior radius, r₂ is the ventrodorsal radius, and r₃ is the mediolateral radius). When the most caudally placed lesion was thought to miss the entire sensorimotor region, as defined above, a second or third lesion was made in a more rostral location. The average time for the procedure was 3.5 hours.

Fifty patients underwent surgery, and 50 GPi analyses, with a total of 285 recording trajectories or tracks, were performed. The mean number of recording tracks for mapping during guided pallidotomy was 4.92 (range, 3–11). The mean number of lesions was 2.3 (range, 1–3) for each patient. A few days (3–5 d) after surgery, control MRI was performed. The images were used to reconstruct the coordinates of the lesion, taking into consideration the data recorded during the mapping procedure. In MRI analysis, the lesions were measured in T1- and T2-weighted scans (2-mm-thick slices, with no interslice gaps) in the axial plane only. The high-intensity signal was measured. Therefore, the coordinates of the initial lesion corresponded (by definition, on the basis of the method used) to the most lateral and posterior region of the GPi explored in each operation. Taking this as a reference, we extrapolated the laterality of the recording tracks for each patient, dividing the GPi into three sagittal templates (L-17, L-20, and L-22 or greater) according to the Schaltenbrand-Wharen atlas (35).
The L-22 plane was the lesion template, the L-20 plane generally coincided with the first track recorded, and the L-17 plane was more medial than the initial recording track. This procedure was used for all patients, regardless of the actual distance between the lesion and the midline or the mediolateral extent of the sensorimotor pallidum. It must be noted that these three planes may not correspond exactly to the actual laterality values for every patient and should be used as relative references. The dorsoventral distribution of the GPI was determined by subdividing the GPI into three equal axial planes, taking the level of the optic tract (as established by recording and microstimulation) as the initial reference.

The coordinates chosen after MRI and digitized sagittal stereotactic mapping corresponded to the first recording track and are defined as the “theoretical coordinates.” The coordinates of the most ventrolateral and posterior lesions, which were chosen according to the microrecording and stimulation findings, are regarded as the “final coordinates.” Deviations from the target coordinates were calculated using absolute values for the three coordinates of the space, regardless of their relative positions. We compared the degree of matching between the two coordinate sets, to assess the accuracy of targeting by imaging alone. This calculation does not take into account the locations of other lesions (usually more anteriorly placed) that were subsequently made. Our strategy was to lesion the sensorimotor portion of the GPi as extensively as possible.

RESULTS

Clinical results

The effects of pallidotomy in this group of patients after 1 year of follow-up monitoring (for 35 patients) have been presented at different meetings and reported in detail elsewhere (15, 29, 30). In summary, the most significant improvement was in contralateral dyskinesia (90%, \( P < 0.01 \)). Contralateral pallidal lesions decreased the mean “off” motor Unified PD Rating Scale score by 33.7% (\( P < 0.01 \)) 1 year after surgery. Significant improvements were also observed in contralateral tremors (72%) and rigidity (67%) (\( P < 0.01 \)). Bradykinesia scores were improved by 46% (\( P < 0.01 \)). Axial signs were improved, but these results were less predictable. Two cases involved major complications (hemorrhage) that were directly related to surgery. One patient died 2 months after surgery, and the other experienced a good recovery. Neither of these patients belonged to the group of 18 patients who were studied in detail intraoperatively and are described below. Antiparkinsonian drug administration was decreased by 5% after surgery (not significant). The results of the pallidal lesions after 1 year of follow-up monitoring are shown in Table 1.

### TABLE 1. Results of Pallidotomy (35 Patients) after 1 Year of Follow-up Monitoring

<table>
<thead>
<tr>
<th>Score</th>
<th>Range</th>
<th>Basal</th>
<th>1-yr Follow-up</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>UPDRS score</td>
<td>0–108</td>
<td>49 (15.5)</td>
<td>32.46 (11.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tremor, contralateral</td>
<td>0–4</td>
<td>1.37 (1.2)</td>
<td>0.7 (0.16)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Rigidity, contralateral</td>
<td>0–4</td>
<td>2.27 (0.7)</td>
<td>0.84 (0.45)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Bradykinesia, contralateral</td>
<td>0–4</td>
<td>2.74 (0.7)</td>
<td>1.33 (0.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Axial signs</td>
<td>0–4</td>
<td>2.18 (0.9)</td>
<td>1.36 (0.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dyskinesia, contralateral</td>
<td>0–4</td>
<td>2.5 (1.1)</td>
<td>0.07 (0.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tremor, rigidity, and bradykinesia, ipsilateral</td>
<td>0–36</td>
<td>13.1 (6.2)</td>
<td>14.18 (5.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Tremor, rigidity, and bradykinesia, contralateral</td>
<td>0–36</td>
<td>19.0 (5.1)</td>
<td>7.68 (3.6)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* The results of our study showed that, 1 year after surgery, the most significant improvement was the reduction of dyskinesia; this was maintained for 1 year of follow-up monitoring. Pallidotomy significantly improved “off” contralateral Unified Parkinson’s Disease Rating Scale (UPDRS) motor performance, by 33.7% (\( P < 0.01 \)). The alleviation of contralateral tremor and rigidity was more significant than that of bradykinesia (\( P < 0.01 \)). The improvement in axial signs was less predictable but was significant. The calculated median preoperative and postoperative group scores were compared using the Wilcoxon rank test. NS, not significant.

* Numbers in parentheses are standard deviations.

### SOMATOTOPIC ORGANIZATION OF THE GPi

The distributions of the lesion coordinates in the three stereotactic planes are shown in Figures 2 and 3. The difference between the theoretical target and the final target in the \( x \) coordinate (mediolateral plane) was between 6 mm lateral and 3 mm medial, with a mean of 2.3 ± 1.55 mm (Fig. 2A). The deviation in the \( y \) coordinate (anteroposterior plane) showed a range of 3 mm anterior to 8 mm posterior, with a mean of 3 ± 1.9 mm (Figs. 2B and 3). The mean deviation in the \( z \) coordinate (dorsoventral plane) was 1.6 ± 1.11 mm, ranging from 4.0 mm dorsal to 5.0 mm ventral (Fig. 3).

In most cases, the coordinates of the final target were located posteriorly and laterally, with respect to the initial target established by imaging (Fig. 3). The estimated extension of the final lesion included the theoretical target in only 45% of the procedures (Fig. 4).

### ACCURACY OF TARGETING BY MRI

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rons of 368 assessed units showed changes in their firing rates with contralateral movements (kinesthetic cells), and 35 units were tremor-related cells. The somatotopic distribution of the kinesthetic neurons is shown in Table 2. Distal joints (wrist, fingers, and ankle) of the contralateral limbs showed a greater percentage of responses than did proximal joints (elbow, shoulder, and hip), with 57% in the lower limb and 55% in the upper limb. Some neurons showed changes in their firing rates in response to stimulation of several segments or joints and were labeled as “multiunits.” There were 5 multiunits for the lower limb and 10 for the upper limb.

The dorsoventral distribution of the neurons with sensorimotor responsiveness, according to the body part activated to elicit neuronal discharges, is summarized in Table 2 and Figure 5. The leg representation was found dorsally in the nucleus, so that 50% of leg-related units were in the most dorsal one-third of the GPi (Fig. 6). Units correlated with facial, jaw, and axial movements were ventral in the GPi, with 68.7% being in the ventral one-third of the nucleus (Fig. 7). For the upper limb, 66% of neurons were in the ventral two-thirds of the GPi (Fig. 8).

With respect to the mediolateral organization, 81 units (62%) were located in the most lateral plane (L-22) and 52 units (37%) were isolated in the L-20 plane (Fig. 5), which often coincided with the first recording track (the theoretical target). Nine neurons with “driving” were found in the L-17 plane, a template that was usually medial to the initial recording track. Neurons corresponding to the upper limb were distributed between the L-20 and L-22 planes, predominating in the most lateral template (60% of the neurons were recorded in the L-22 plane) (Fig. 8). Face and jaw units and the
few neurons corresponding to the neck and trunk were found primarily in the L-22 plane (Fig. 7). The lower limb was equally represented in the three lateral planes, but it is noteworthy that all neurons in the L-17 plane belonged to the leg (Fig. 6).

In summary, the majority of cells with sensorimotor responses in the GPi were found in the L-20 plane or beyond. The face representation was mainly lateral and ventral. The leg was dorsal and present in the three sagittal templates. Neurons related to the arm were mainly lateral and were found in the ventral two-thirds of the GPi.

Thiry-five tremor-related cells were recorded and identified in these patients. Oscillatory or rhythmic neuronal activity was not detected in patients in whom tremor was not present at the time of surgery. The somatotopic distribution of tremor-related cells is summarized in Figures 5 and 6. These cells were evenly distributed in the three sagittal planes and showed the same somatotopic pattern as kinesthetic units. Tremor-related units were recorded throughout the dorso-ventral extent of the GPi.

**DISCUSSION**

There is now renewed interest in the therapeutic possibilities of pallidotomy and deep-brain stimulation of the palli-
dum and subthalamic nucleus in PD. This enthusiasm could rapidly fade if the surgical technique used fell below required standards. In this regard, our findings are directly relevant to the issue of ensuring the outcome of surgery in PD.

Targeting

We observed a relative discrepancy between the coordinates of the lesion defined by imaging (theoretical target) and those finally chosen for the lesion (final target). Such a difference has several practical consequences with respect to the goal of obtaining the best possible results and minimal side effects with pallidotomy.

The preferred method for subcortical target localization is the subject of an ongoing debate in the field of functional neurosurgery (9, 21). For PD in particular, the classic approach has consisted of defining the coordinates by using ventriculography and, more recently, computed tomography or MRI of the brain as imaging methods plus macrostimulation with the lesioning probe as a means of functional assessment. The reintroduction of pallidotomy for the treatment of PD has evolved with the physiological definition of the sensorimotor region of the GPi, mainly using the microrecording-guided technique (3, 28, 31, 38, 42). Pallidotomy is now widely used throughout the world, but there is no agreement regarding the necessity of using microrecording (9, 21, 42). Essential to this argument is the question of whether definition of the target is only anatomic (imaging) or requires physiological confirmation. Our findings support the latter view.

It might be argued that our results are explainable because the MRI resolution achieved in this study was inadequate for the purpose of defining the GPi. According to this view, the application of MRI with higher magnetic fields might reduce the degree of variability (14). However, Lozano et al. (31), using 1.5-T MRI, observed a similar degree of error, suggesting that imaging quality is not the only or crucial factor involved in the inaccuracy discussed here. Hiner et al. (18) reported that microrecording led to a change in the final placement of the lesion in 70% of patients, and Azizi et al. (2) showed that, in 25% of the cases, the theoretical coordinates were more than 5 mm away from the final site of the lesion. Tsao et al. (40) recently reported that, in 13 of 25 patients, hypothetical lesion positions were located in such a way that the lesion center would not have remained in the globus pallidus without microelectrodes. Vitek et al. (43) indicated that, in their most recent experience, there were overall differences of 2.2 and 1.3 mm in the rostrocaudal and mediolateral planes, respectively, between the target location determined by MRI and the final coordinates of the lesion determined by microrecording. It seems, therefore, that a certain degree of
variability between imaging-derived and physiologically specified targets is the rule in basal ganglia surgery.

**Sources of errors**

Stereotactic frames have provided extreme levels of mechanical precision for surgical localization, but the procedure is not completely accurate because the errors of localization are additive (32). Errors arise from two main sources, namely imaging and individual variations. Imaging errors introduce distortion during the image-acquisition phase and exist with any method used for targeting identification. Positive-contrast ventriculography is associated with imaging distortion because of anterior shifting of the third ventricle; in addition, ventriculography prolongs hospital stays and may be accompanied by unpleasant side effects (16). Computed tomography and MRI are noninvasive techniques and provide direct observation of brain structures, but both introduce distortion during the imaging procedure. The accuracy of the computed tomography-guided stereotactic system is dependent on the computed tomographic scan slice thickness, the interslice spacing, and the size of the target itself (5). MRI has been widely reported to introduce distortion resulting from inhomogeneities in the magnetic field and nonlinear magnetic field gradients (24, 37). The stereotactic frame itself, with its metal components, may introduce errors or distortion during image acquisition (44).

The second source of error lies in individual anatomic variations. Hawrylyshyn et al. (17) reported that the thalamocapsular border shifts in accordance with the width of the third ventricle. The thalamic border is more lateral when the ventricle is wider. Kelly et al. (22) reported that the theoretical target did not coincide with the final target, as established by physiological findings, for 75% of patients subjected to thalamotomy. Variability is greater in the pallidum than in the thalamus, because the pallidum is farther away from the midline and has a more complex shape. Another factor to be considered is the possibility of brain shifting after opening of the dura and during surgery. There may be variations between the brain position when the patient is in the supine position during image acquisition and that when the patient is in a semi-sitting position during surgery. This effect may be particularly important in older patients, who have wider subarachnoid spaces and cisterns.

Although the accuracy of targeting without microelectrode guidance may be quite good for a high proportion of patients who undergo pallidotomy, the findings reported in this and other studies suggest that there is a high incidence of changes in the final lesion locations, indicating that macrostimulation alone does not provide sufficient information for lesioning. Macrostimulation allows determination of the boundaries of the nucleus with tonic or clonic movements and phosphenes, indicating that the tip of the electrode is close to the capsule and optic tract, respectively. However, macrostimulation does not indicate whether the electrode is within the GPi, as in the eight cases showing false-positive stimulation among our patients. We suggest that precise mapping with a microelectrode guide is the best way to create a lesion with sufficient probability of improving the long-term outcome. Although this report suggests improved accuracy with these recording techniques, there is no consensus demonstrating their clinical benefits.

**Importance of defining the sensorimotor region of the GPi**

The current use of pallidotomy for the treatment of PD aims to define the sensorimotor region of the GPi while sparing the associated regions (1, 7). This is based on experimental evidence indicating that the basal ganglia are somatotopically organized in monkeys (7, 12) and that only inactivation of the sensorimotor region of the GPi led to alleviation of parkinsonism induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine in monkeys (45). Finally, there is current clinical evidence indicating that only lesions of the posteroverentral and lateral GPi are associated with clear-cut motor benefits; dorsomedial lesions produced no improvement or only transient improvement (43) (JL Vitek, personal communication). The GPi in patients with PD has a somatotopic organization that is similar to that described in monkeys (38, 43).

Microrecording is the only effective method for investigating the somatotopic organization of the GPi. In monkeys made parkinsonian with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, the number of cells responding to active and passive movements of the limbs is significantly increased, regardless of whether the somatotopic arrangement is preserved, as has been analyzed in detail (4, 7, 11, 12). Filion et al. (12) showed that, in monkeys, the parkinsonian state is correlated with a larger number of units responding to movement of several body parts. This characteristic may account for the variability encountered in human studies. In patients with PD, the proportion of cells with responses to passive and active limb movements varies from 19 to 46% (36, 38, 43). This large range may be attributable to bias in the selection of the cells. Our own results (38% of cells with sensorimotor responses) agree with those reported for monkeys and are probably near the actual values. The somatotopic organization of the GPi in patients with PD has been analyzed by a few groups, with varying findings. Vitek et al. (43) reported an organization similar to that described for monkeys. The majority of neurons with sensorimotor responses were found in the posterolateral region of the GPi (L-18 or L-19 of the Schaltenbrand-Bailey atlas [34]). The leg was preferentially represented dorsomedially, with respect to the arm and face. The jaw representation was found more ventrally. On the other hand, Taha et al. (38) described arm neurons in two cluster groups distributed rostrocaudally (i.e., a rostral segment 5 mm above the pallidal base and a caudal segment 1.5 to 3 mm above the pallidal base), whereas leg kinesthetic units were located more centrally (3–4.5 mm above the pallidal base). In this study, we found that arm-related neurons were located mainly in the ventromedial region and caudolaterally of the nucleus. The leg-related cells were mainly dorsal and extended mediolaterally throughout the nucleus, reaching as medially as 17 mm from the midline in the atlas of Schaltenbrand and Wharen (35). A large majority of axial and face-related units were found ventrally and laterally (more than 20 mm from the midline). Our results, therefore, are in keeping

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with the findings for monkeys (6, 8) and the observations by Vitek et al. (43) for patients with PD. The somatotopic arrangement confirmed here in the parkinsonian state is valid, we think, for practical intraoperative purposes and as a general reference regarding the organization of the GPi in human subjects. We did not use any test designed to detect possible internal segregation of motor neurons according to their cortical projection areas, as indicated by Hoover and Strick (19) in normal monkeys. Therefore, we suggest that in PD the somatotopic arrangement of the GPi can be summarized as follows: the majority of cells are located posterolaterally in the nucleus and, within this region, the leg is more dorsal than the arm and the face, which (with the jaw) is mainly ventral.

**Tremor-related cells**

Cells with tremor-related activity were present only in the sensorimotor region of the GPi and showed a somatotopic distribution similar to that of the kinesthetic cells discussed above. The existence of tremor-related cells in the GPi was first described by Umbach and Ehrhardt (41) and was more recently analyzed by Hutchinson et al. (20), who found these cells approximately 3 to 6 mm above the optic tract but provided no additional details regarding their somatotopic arrangement. We found tremor-related cells within the sensorimotor region of the GPi, with no specific clustering for their distribution (Figs. 5 and 6).

Recognition of GPi somatotopy and the distribution of tremor-related cells may have practical implications for producing optimal results with pallidotomy. Not all patients who undergo surgery have the same clinical characteristics. In a relatively large proportion of patients, the clinical motor signs and dyskinesia predominate in one body segment (for example, the leg). In such instances, our experience indicates that failure to determine the location of neurons related to that body part may yield suboptimal benefits. In keeping with this suggestion, Taha et al. (39) reported that the efficacy of pallidotomy in the treatment of tremors was significantly greater for patients in whom tremor-related cells were recorded at the time of surgery.

**CONCLUSION**

The only approach to definitively establish whether microrecording is critical for the achievement of optimal results after pallidotomy involves a prospective randomized study. Such a trial is unlikely to be performed with this methodology. The clinical benefits obtained for our patients and those of other groups using similar methods are not substantially different, at first glance, from those reported by teams not using microrecording. This is clearly true for the antidysskinetic effects of pallidotomy, but a closer analysis of the published data suggests that patients with lesions in the sensorimotor pallidum retained their benefits, including alleviation of axial symptoms, whereas patients with lesions outside the sensorimotor GPi region lost their benefits (43).

In accordance with the aforementioned technical limitations of stereotactic procedures and the experimental and clinical data indicating the functional organization of the basal ganglia, we think that pallidotomy should be performed with precise delineation of the sensorimotor region. This approach requires functional definition of the GPi motor territory, which is not possible with either imaging alone or imaging and macrostimulation together. Placement of the lesion on the basis of MRI and macrostimulation findings without microelectrode recording is considered, according to the results presented here, to be insufficient for adequate lesioning of the GPi in patients with PD.

We confirmed that the somatotopic arrangement of the GPi in patients with PD is similar to that found in monkeys; the leg representation is located in the most dorsal and medial planes with respect to the arm, face, and jaw, which are found more ventrally and laterally in the sensorimotor region of the nucleus. A similar distribution was found for cells with tremor-related activity. We think that verifying this organization in each patient by microrecording is the best way to achieve optimal clinical results with pallidotomy.

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COMMENTS

This is another article demonstrating the advisability of electrophysiological recording during deep-brain stereotactic surgery.
surgery, especially for far-midline targeting. Whether imaging distortion, individual anatomic variability, or individual functional variability among patients with Parkinson’s disease (PD) prompts the use of physiological mapping is a matter of discussion. Perhaps all three play a role in the variations observed, in almost every case, between the predetermined target and the final target of posteroventral pallidotomy, but the last, i.e., the functional variability of the globus pallidus internus (GPI) among individual patients with PD, is probably the most important. Unfortunately, there is no way to demonstrate changes in the somatotopic arrangement of the sensorimotor area of the GPI in normal subjects versus patients with PD, as implied in the Discussion. Therefore, we must consider imaging distortion and individual anatomic variations. Although I am primarily in agreement with the authors, I am not sure that positive-contrast or even air ventriculography should be completely disregarded as adequate imaging techniques for stereotactic functional neurosurgery; together with microelectrode recording, these techniques were adequate in the era before computed tomography and magnetic resonance imaging (MRI). However, for correction of individual anatomic variations, microelectrode recordings are unsurpassed.

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Guridi et al. describe their stereotactic targeting of the GPI. Their anatomic versus electrophysiological mapping and their description of the somatotopic organization of the GPI and tremor-related cells are very similar to our work (2–4). Although it is most rewarding to see one’s own work corroborated by others in a well-performed study, I have a few additional points to discuss.

The somatotopic arrangement described here is identical to that which we have observed (3, 4). This arrangement is not like that seen in the thalamus or sensorimotor cortex. It is crude at best and in PD one cell may respond to multiple joints, which is probably not true in the normal state. As Hoover and Strick (1) have observed in monkeys, there may be several somatotopic maps with different cortical projections. We find that mapping of somatotopic features is quite helpful for determining laterality. It is also useful for evaluating the effectiveness of lesioning. If we do not observe much improvement in the leg, we perform more medial lesioning. This type of information should be helpful to stereotactic neurosurgeons regardless of whether they use microelectrodes.

Anatomic versus electrophysiologic localization techniques continues to be controversial. Regardless of published reports describing anatomic versus electrophysiologic variants, the value of microelectrodes remains unproved. Whether the same type of corrections can be made with macrostimulation remains very difficult to ascertain. I think that microelectrodes are extremely useful, but I have no proof. When performed by experienced neurosurgeons, I think that macrostimulation alone may be sufficient in the thalamus, where there are good electrophysiologic end points. For other targets, such as the pallidum, macrostimulation is much less useful and the importance of microelectrodes emerges. The findings obtained using microelectrode recording clearly help define the target and can yield more precise initial anatomic targeting (2).

I think that most investigators would agree that electrophysiological confirmation is useful. The ultimate anatomically based lesioning method is radiosurgery, for which thalatomy and pallidotomy results have been mediocre. There has been one exception (5), but those results were only short term (unbiased data were obtained for only 6 months) and were not as good as the best results obtained using electrophysiologically monitored lesioning, whether with microelectrodes or macroelectrodes alone.

In summary, I think that the information obtained in this study should be quite useful for all stereotactic neurosurgeons. Finally, I strongly agree with the authors that, in addition to a randomized trial, long-term comprehensive evaluation of patients is essential for assessment of the relative merits of these techniques.

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The article summarizes a single-center experience involving the treatment of 50 patients with advanced PD who underwent unilateral stereotactic pallidotomy. The target for each lesion was chosen using stereotactic MRI and was then refined using intraoperative micerecording. The authors showed that the difference between the initial MRI target and the final lesion location varied between 4 and 8 mm in each direction. Only 45% of all patients experienced overlap between the MRI target and the actual lesion, which is very close to the recently published results of Tsao et al. (4), in which 52% of hypothetical lesions were found to be outside the globus pallidus.

These results are similar to the findings of our group and several other groups (1–4). They confirm the usefulness and importance of intraoperative micerecording in the delineation of major surrounding structures and the selection of the final target location. The authors also present a review of their findings on the somatotopic representation of the GPI. Unfortunately, the GPI is not divided into separate sections that are
responsible for various parts of the body; instead, these areas are overlapping and interwoven. However, surgeons may aim more laterally and ventrally for arm targeting and more medially and dorsally for leg targeting. Whether improved resolution of MRI scanners and/or the use of intraoperative imaging for target confirmation will eventually decrease or eliminate the need for microrecording is not clear. The issue of individual variability cannot be ignored.

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Guridi et al. present a study of 50 patients who underwent microelectrode recording-guided pallidotomy. The value of the study is twofold; it relates the imaging-derived target to the final electrophysiologically determined target and it addresses the issue of somatotopy in the globus pallidus. Both of these issues are directly relevant to the performance of pallidotomy and, ultimately, to the outcome of this procedure.

The authors present emphasize that the use of imaging alone for localization is insufficient. On the basis of their recordings, the authors needed to adjust their pallidotomy targets to optimize the lesioning and to avoid inappropriate lesion placement. Their analysis of the somatotopy of kinesthetic representation in the GPi is quite interesting. Although there are data regarding the somatotopic representation in the GPi of normal primates, analysis of somatotopy in the GPi in the parkinsonian state (for example, in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine model) has not been performed. As described by Filion et al. (1), the issue of GPi somatotopy in the dopamine-deficient state is quite complex. Pallidal neurons in PD respond to multiple joints rather than single joints, the responses are exaggerated, and several neurons adopt reciprocal responses, i.e., they become excited in one direction and inhibited in the opposite direction. Additional neurons may respond to both ipsilateral and contralateral limb movements, as reported for patients with PD by Lozano et al. (4). This is perhaps the underlying basis for the bilateral improvements seen after pallidotomy or pallidal stimulation.

Another important finding concerning GPi organization is that the GPi is parceled along functional territories, and even the motor circuit is further subdivided in subcircuits. The work of Hoover and Strick (3) has shown that there are multiple motor representations in the pallidum, corresponding to pallidal outflow to various motor areas, including the supplementary motor area, the premotor area, the motor cortex, and the dorsolateral prefrontal cortex. There is somatotopic representation within each of these subcircuits. This suggests that there are multiple clusters of somatotopy that are concatenated within the GPi, rather than general areas for the arm, leg, and face, as Guridi et al. suggest. In addition, because in the parkinsonian state (at least in primates) defocusing of receptive fields and exaggerated responses are observed, it is unlikely that the GPi of patients with PD has such discrete arm, leg, and face areas as the authors suggest. Nevertheless, the somatotopic model in PD and the multiple representation of motor subcircuits lead us to several testable hypotheses. It could be predicted that, if somatotopy is indeed functionally relevant, then discrete lesions within the pallidum might provide benefit to one limb or one body part and not others. Additional lesions in a motor subcircuit might improve some aspects of parkinsonian disability and not others. Indeed, recent work by Gross et al. (2) suggests that certain parkinsonian features respond differentially as a function of the location of the pallidotomy lesion within the GPi. Not all pallidotomies are equal.

The main points of this work are that there is still much to learn regarding the functions and organization of the globus pallidus and that imaging is an important component of localization but is currently insufficient for determining the ultimate target. It is only when the imaging results are congruent with physiological features and functional findings that functional neurosurgeons can be confident that localization is optimal.

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