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# Electrophysiological Mapping for the Implantation of Deep Brain Stimulators for Parkinson's Disease and Tremor

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**Abstract:** The vast majority of centers use electrophysiological mapping techniques to finalize target selection during the implantation of deep brain stimulation (DBS) leads for the treatment of Parkinson's disease and tremor. This review discusses the techniques used for physiological mapping and addresses the questions of how various mapping strategies modify target selection and outcome following subthalamic nucleus (STN), globus pallidus internus (GPi), and ventralis intermedius (Vim) deep brain stimulation. Mapping strategies vary greatly across centers, but can be broadly categorized into those that use microelectrode or semimicroelectrode techniques to optimize position prior to implantation and macrostimulation through a macroelectrode or the DBS lead, and those that rely solely on macrostimulation and its threshold for clinical effects (benefits and side effects). Microelectrode criteria for implantation into the STN or GPi include length of the nucleus recorded, presence of movement-responsive neurons, and/or distance from the borders with adjacent structures. However, the threshold for the production of clinical benefits relative to side effects is, in most centers, the final, and sometimes only, determinant of DBS electrode position. Macrostimulation techniques for mapping, the utility of microelectrode mapping is reflected in its modification of electrode position in 17% to 87% of patients undergoing STN DBS, with average target adjustments of 1 to 4 mm. Nevertheless, with the absence of class I data, and in consideration of the large number of variables that impact clinical outcome, it is not possible to conclude that one technique is superior to the other in so far as motor Unified Parkinson's Disease Rating Scale outcome is concerned. Moreover, mapping technique is only one out of many variables that determine the outcome. The increase in surgical risk of intracranial hemorrhage correlated to the number of microelectrode trajectories must be considered against the risk of suboptimal benefits related to omission of this technique. © 2006 Movement Disorder Society

**Key words:** subthalamic nucleus; globus pallidus; ventral intermedius; stimulation

The surgical techniques used to implant deep brain stimulators (DBS) vary greatly across centers. Each begins with stereotactic targeting based on one or more imaging modalities (ventriculography, CT, MRI), which is addressed in depth elsewhere in this issue. While a few centers implant the DBS based solely on anatomy,[1,2] the vast majority include some form of physiological mapping to define the optimal site, including microelectrode or semimicroelectrode recording, microstimulation, and/or macrostimulation testing. Factors that call for physiological mapping to refine electrode location following initial anatomical targeting include imaging inaccuracy or distortion (particularly MRI); the need to refine target selection related in part to incomplete understanding of the relationship of anatomy, physiology, and clinical outcome; inaccuracy of frame- or frameless-guided navigation; and/or brain shift due to positioning, loss of cerebrospinal fluid, pressure shifts, and/or pneumocephalus. Here we will discuss the techniques used for physiological mapping and address the questions of how various mapping strategies modify target selection and outcome following subthalamic nucleus

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(STN), globus pallidus internus (GPi), and ventralis intermedius (Vim) deep brain stimulation.

## EQUIPMENT CONSIDERATIONS

### Recording and Stimulating Electrodes

Impedance determines the voltage response of electrodes to current flow during recording and determines the current flow in response to voltage during stimulation. The impedance of the exposed tip of a metal electrode can be understood as resulting from a capacitive reactance (C) in parallel with a resistance (R) and is frequency dependent.[3,4] The impedance is directly determined by the physical characteristics of the electrode. The larger the surface area, the lower the impedance value will measure in the physiological frequency range (usually 1–2 kHz). Thus, impedance is an indicator of the geometry of the electrode tip—surface area and shape—and can determine whether an electrode is a microelectrode, semimicroelectrode, or macroelectrode. For microelectrodes, the preferred tip shape for recording is conical, with a maximal length significantly less than the diameter of the smallest cells (usually 20 μm).[5] Thus, a typical length is 7 to 10 μm, with a 2- to 4-μm diameter at the tip. This length is crucial for allowing the action potential to be detected without short-circuiting the field generated, as would happen with a longer electrode. Moreover, the conical shape allows RC characteristics that are maximally responsive at 2 kHz, which happens to be the frequency of an action potential with a rise time of 0.5 milliseconds. In practice, these electrodes measure between 0.2 and 2 MΩ, although some groups use electrodes up to 10 MΩ.

From the viewpoint of recording neural activity, low-impedance electrodes, also known as macroelectrodes, usually have large tip exposures and are not suitable for detecting single action potentials (spikes). However, because of their large tip exposure and low impedance, they are effective at detecting compound, extracellular potentials corresponding to population activity, whether as multiunit hash activity[4] or as local field potentials.[6–8] In contrast, higher-impedance microelectrodes[5,9] or semimicroelectrodes[10,11] have small enough tips to pick up individual action potentials and allow resolution of single unit or multiple single unit activity, but are poorer at (although not incapable of) providing population background information.[6,9]

The effects of stimulation are determined by the electric field strength (voltage distribution; actually, current density is related to the first derivative of this value, whereas spatial effects on membrane polarization are related to the second derivative[12,13]) resulting from current flow from the electrode tip and are affected by pulse width and frequency,[14–16] as well as local tissue characteristics[15,17] (e.g., impedance, neural elements; reviewed in McIntyre and Thakor[18]). The characteristic of an electrode that determines its electric field properties and effectiveness for stimulation, at a given frequency and pulse width, is its current-carrying capability, governed once again by its surface area and resulting impedance. A lower-impedance electrode passes a greater current at a given voltage. However, higher impedance electrodes can theoretically pass the same amount of current but at proportionally greater voltages. For instance, a 1-MΩ microelectrode delivering 1 mA of current would need to be driven by a 1-kV power source, whereas a 1-KΩ macroelectrode delivers 1 mA from a 1-V power source. Nevertheless, at any given current and radius from the center of the electrode tip, each electrode would produce an identical current density and voltage distribution.[14,19] For example, at the surface of a DBS electrode with a surface area of 6 $mm^2$ (radius, 0.64 mm; length, 1.52 mm), a 3-mA current will produce a current–density of 0.5 $mA/mm^2$; at a distance of 0.64 mm from the center of a microelectrode with a tip surface area of ~0.0015 $mA/mm^2$ (radius, ~10 μm; length, ~25 μm), the current–density will also measure 0.5 $mA/mm^2$.[14]

Current density governs the tissue damaging potential of electrical stimulation.[20] At distances closer to the surface of a microelectrode, current density increases exponentially; thus, currents in the milliamp range will be sufficiently high to cause local tissue damage through heating and hydrolysis.[20] However, since the current density from a milliamp range current at a radius of 0.64 mm from the center of a microelectrode will be identical to that at the surface of a DBS macroelectrode delivering the same current, no more tissue damage would occur than that produced by physical injury due to a DBS macroelectrode. It is not this aspect, therefore, that distinguishes the usefulness of each electrode for providing clinically effective amounts of current, but rather the impracticality of a 1-kV power source necessary to produce 1 mA of current from a 1-MΩ microelectrode and the damage to the insulation of the electrode itself from passing such high levels of current. In practical usage, however, high currents applied to most high-impedance electrodes lead to partial destruction of the insulation at the tip resulting in diminution of the impedance and greater current-carrying capacity.[19] Hence, milliamp current can in practice be delivered from high-impedance microelectrodes, because if the impedance is diminished to 0.1 to 0.2 mΩ, lower voltage is necessary to produce a 1 mA current. For clarity, we will henceforth characterize stimulation in relation to its current range, irre-

spective of the size of the electrode used. Thus, milliamp current, whether delivered from a macro- or microelectrode, is considered macrostimulation because the volume of tissue stimulated and the clinical effects are similar. Microstimulation is considered to be limited to currents $\leq$ 100 μA delivered through microelectrodes.

The effects of current, frequency, and pulse width on neural elements are interdependent. At increasing frequency, the threshold for observing physiological effects occurs at decreasing current intensity, whether it is corticospinal activation, paresthesia, or clinical effects such as tremor suppression that is being examined.[16,21–23] Similarly, at increasing pulse widths, the current threshold also decreases. It is therefore necessary to stipulate the frequency and pulse width when discussing current and voltage thresholds for any given effect of stimulation. Moreover, in addition to the quantitative relationship between frequency and current threshold, there can be a qualitative relationship. For example, whereas the effects of stimulation on the corticospinal tract are quantitatively related to frequency, such that at low frequencies contractions occur which evolve to tetanus or tonic distortions at higher frequencies (white matter tracts easily follow stimulation up to 300 Hz) the effects of stimulation on tremor can be qualitatively different at low frequencies (driving of tremor at $<$50 Hz) compared with higher frequencies (tremor suppression at $>$100 Hz).[22]

### Microelectrodes

Microelectrodes have impedances typically greater than 0.5 MΩ and are usually constructed from tungsten or platinum/iridium, with or without glass coating.[4,5,9] They may be electroplated to decrease their impedance into a favorable range for recording of units. The diameter of the conically shaped microelectrode tip is typically 2 to 4 μm. Because of their high impedance, they are capable of isolating single neural unit activity and thus are useful for precisely defining the properties of individual neurons within thalamic and basal ganglionic nuclei. Background group neuronal activities are relatively diminished due to the high impedance of the electrodes, but can still be seen and measured. Stimulation through microelectrodes is possible as well, but the range of currents that can be used depends on the physical properties of the particular electrode.[9] For example, glass-tipped microelectrodes typically do not withstand sustained trains of stimuli or currents greater than 25 to 50 μA,[24,25] whereas uncoated electrodes can be used to pass currents in the mA range, with limited diminution of impedance (e.g., 6–0.2 MΩ) and the preserved ability to record further single unit activity.[19]

### Semimicroelectrodes

Semimicroelectrodes typically are of the bipolar concentric type, with an external proximal electrode (outer diameter 0.2–0.3 mm) and an internal distal electrode with a ~20-μm tip (interpolar distance of 0.2–0.3 mm). The typical impedance of semimicroelectrodes is approximately 100 kΩ.[10,11] Although they may be capable of isolating single units, semimicroelectrodes most effectively provide information on group neural activity ("neural noise") and local field potentials (e.g., Yokoyama and colleagues[26]). They can report passage from one structure to another if the background activities vary between them. They are also capable of recording evoked group activities, such as from movement of the contralateral limb when located in Vim, STN, or GPi.[27] Stimulation through semimicroelectrodes is performed in the 1- to 10-mA range.

### Macroelectrodes

Macroelectrodes are low-impedance electrodes with larger tips; those used for deep brain physiology have tip diameters that are 1 to 1.5 mm, with 2 to 4 mm of uninsulated exposure. Their surface characteristics are such that they are not useful for recording neural activity, except for field potentials[6] or local tissue impedance.[26] Macroelectrodes that are dedicated to recording and/or stimulation can be used, or alternatively a radiofrequency lesioning electrode or the DBS electrode itself can be used for macrostimulation. A recent addition is the low-impedance shaft of a microelectrode, which allows microelectrode mapping from a high-impedance electrode and macrostimulation through a low-impedance electrode without repositioning. Stimulation through a 1- to 2-kΩ electrode is in the 1- to 10-mA range ($<$20 volts).

## Microelectrode Stage and Drive Equipment

There are several systems available to guide and drive electrode insertion into the brain, and the choice of which system to use is related to the mapping strategy. Essentially, there are fixed and adjustable electrode holders. The fixed holders include multielectrode holders as well as single electrode holders that are part of any stereotactic frame but that must be modified to hold and advance the microelectrode. The most popular multielectrode holder has a central channel surrounded by four peripheral channels situated 2 mm anterior, posterior, medial, and lateral. Anywhere from one to five microelectrodes can be advanced simultaneously.[28] To achieve other positions than the five initial ones, an offset device is used.

If only a single-channel electrode holder is used, different positions are attained by adjusting the frame itself, which may not be as accurate. The adjustable type of holder refers to an "X–Y" micropositioner—an additional stage that can be fitted to the guide of any stereotactic frame—which provides movements in the X (medial/lateral) and Y (anterior/posterior) directions without manipulating the frame itself.[25] This stage allows precise and variable movements in 1 mm or greater increments. It can also be coupled to a single- or multichannel electrode guide.

There are advantages and disadvantages to either system. The advantage of using an X–Y stage over a prefabricated multielectrode holder is that movements can easily be made to any position (e.g., 2 mm lateral, 1 mm anterior), and the number of tracks can be tailored to the developing map. On the other hand, when only one electrode is advanced at a time, variability between tracks may be introduced. The advantage of the multielectrode holder is that, without manipulation of the frame or even of a micropositioner, the electrodes are more likely to traverse strictly parallel trajectories. Moreover, simultaneous passage of the guide cannulae may "fix" the brain tissue, maintaining an accurate spatial relationship between them. Finally, if multiple amplifiers and microdrives are available, then the tracks can be recorded simultaneously, which, although complicated, might decrease time for mapping. On the other hand, the number of electrode tracks, and the theoretical risk associated with them, is increased if all five electrodes are used simultaneously. Also, if a track is desired aside from the prefabricated ones (such as 2 mm lateral and 2 mm anterior), the offset must be used, which is cumbersome.

## SURGICAL CONSIDERATIONS

Certain surgical considerations can affect the results of electrophysiological mapping. The entire surgical procedure usually is performed with the patient awake in order to aid in examining movement responsiveness in neuronal populations during micro- or semimicroelectrode recording and allow for detailed examination of the effects of stimulation with respect to clinical benefits and adverse effects. In exceptional circumstances, however, the surgery may be performed under general anesthesia. The awake patient is operated on while in the *off* medication condition to facilitate intraoperative recording and stimulation testing, and because dyskinesia can adversely affect surgical manipulations. In addition to local anesthetic, conscious sedation with short-acting benzodiazepine, narcotic, and/or propofol can be used during frame application, MR and/or CT imaging (to facilitate acquisition of a movement-free scan and to allay anxiety), and even during mapping if necessary. Used judiciously, these agents do not impair the ability to record neural activity (single or multiple units),[29–35] although discharge frequency, pattern, and ability to observe motor driving may be altered. Stimulation testing is best done with no sedation, or minimal sedation with narcotic or benzodiazepine, as propofol can have antiparkinsonian actions that may interfere with examination of the effects of stimulation on symptoms.[36]

Patient positioning in the operating room can affect electrophysiological mapping results. First, patient comfort must be ensured as much as possible due to the anticipated length of the procedure, especially in bilateral surgeries. Neutral head positioning is necessary for the maintenance of an adequate airway throughout the procedure. A nearly supine position is recommended; although semisitting may be thought to minimize loss of cerebrospinal fluid and the resultant brain shift, in fact, this may increase pneumocephalus due to negative pressure created during inspiration. The brain shift that results from gravity and pneumocephalus in the semisitting position may adversely affect electrophysiological mapping results. Other effective techniques for minimizing loss of cerebrospinal fluid include fashioning electrode tracks that avoid the lateral ventricle and the use of some form of fibrin sealant within the burr hole. Some centers avoid opening the dura, penetrating it sharply with the recording electrodes.

During each electrode penetration, care must be taken to avoid the deflection of the electrode by the bone, dura, or even the pia, which can also be opened sharply (this also minimizes the chance of causing a subdural hematoma from depressing the brain and tearing a bridging vein).

## ELECTROPHYSIOLOGICAL MAPPING STRATEGIES

Mapping strategies can be broadly categorized into those that use microelectrode or semimicroelectrode techniques to optimize position prior to implantation of a macroelectrode or the DBS lead, and those that rely solely on macrostimulation and its threshold for clinical effects (benefits and side effects).

### Microelectrode Mapping Approaches

Microelectrodes or semimicroelectrodes are used to characterize precisely the target nucleus and its boundaries prior to insertion of a macroelectrode/DBS electrode. The physiological characteristics of the target (STN, GPi, Vim, other), including the firing rate and pattern of its neurons, and those of surrounding struc-

tures, allow its positive identification. Moreover, the nature of the evoked responses of its neurons, e.g., movement-evoked responses, further allows characterization of the topography within the nucleus, thus for example defining the sensorimotor region of the STN or GPi. One or more electrode tracks are required. Fewer tracks are necessary when positive identification of the target is all that is required, whereas more tracks are necessary when the position within the nucleus, in relation to subterritories of the nucleus or its borders, is being characterized. In the former, as few as one track may be possible, whereas in the latter, a minimum of three tracks may be required to define an anterior and lateral margin.

In addition to recording through the micro- or semimicroelectrode, microstimulation through the same electrode is sometimes used (typically up to 100 μA; 0.2–0.7 ms; 200–300 Hz). The restricted spread of currents of <100 μA (some centers limit to 40–50 μA due to breakdown of glass insulation on the electrode) limits the capacity to evoke therapeutic responses, so microstimulation is generally not useful for testing for clinical benefits. The exception to this is tremor; in the thalamus, microstimulation in the region of tremor cells leads to tremor suppression at currents of 50 to 100 μA.[9] In STN and GPi, tremor suppression may be seen with microstimulation but is less reliable.[24,37] (Limited effects from microstimulation are not seen when milliamp current is delivered from the microelectrode. As discussed above, this is considered macrostimulation, as the current density at a given distance from the electrode tip is the same regardless of the tip diameter.) Microstimulation is useful, however, for determining whether the electrode is within a structure that produces side effects, such as the internal capsule, optic tract, or medial lemniscus, where low-threshold current reliably evokes responses. It should be emphasized that the limited diffusion of current is such that failure to evoke side effects from microstimulation (≤100 μA) when stimulating within a nucleus (GPi, STN, Vim) does not predict that macrostimulation in the milliamp range in the same region will be safe from side effects. Thus, microstimulation can be useful in mapping but cannot replace macrostimulation to establish a safe location for the DBS electrode.

Several different strategies can be used when mapping with microelectrodes. The mapping strategy associated with the use of an X–Y stage is typically to determine the next track position based on the accrued results (serial approach; e.g., Starr and colleagues[24] and Vitek and colleagues[25]). Most centers will perform tracks in one plane first (e.g., the sagittal plane) and then move laterally or medially in increments of 1 to 3 mm. The number of electrode passes varies from center to center (Tables 1–3); some limit the number to 1 to 2, while others will perform more passes to gather more information about the boundaries of the target structure. In contrast, the multielectrode holder involves a strategy in which all five microelectrodes are typically (although not exclusively) advanced simultaneously (they are separated by 2 mm), and the best position is selected based on the results of mapping within that volume (e.g., Pollak and colleagues[19] and Bejjani and colleagues[38]). Locations other than those provided by the initial five channels are rarely used. A compromise approach involves inserting one to three initial electrodes through the holder and adding further ones as indicated.[39,40]

### Macroelectrode Stimulation Approach

Macroelectrodes are used almost exclusively for stimulation, although impedance monitoring can be performed[41] or field potential changes can be detected through macroelectrodes as well. Virtually all groups use some form of macrostimulation prior to settling on a final location for the DBS. Macrostimulation can be delivered through a dedicated electrode (often a radiofrequency lesioning-type electrode), the DBS electrode, the low-impedance shaft of the microelectrode, or through microelectrodes when stimulating in the milliamp range. At increasing voltages/currents, the relative effects of macrostimulation on the production of side effects vs. the amelioration of clinical signs and symptoms are carefully determined. From this ratio, it can be determined whether the electrode is satisfactorily located. If there is an insufficient therapeutic window between benefits and side effects, then the electrode can be repositioned. When used following microelectrode mapping, however, the map should have been sufficiently defined that movements of the macro-/DBS electrode are less necessary. Hence, many centers aim to perform macrostimulation along just one track, the optimal one defined by microelectrode mapping (Tables 1–3). How successful this approach is at minimizing the number of passes with the larger electrode is difficult to ascertain, however, as this information is omitted from most reports. Additionally, several centers actually macrostimulate along multiple tracks through the low-impedance shaft of the microelectrode carrier (e.g., Bejjani and colleagues[38]) or a semimicroelectrode (e.g., Limousin and colleagues[42]), or by passing higher (milliamp) current through the microelectrode itself.[19] Since the diameter of the microelectrode shaft is <1 mm, this approach to macrostimulation inflicts less direct tissue injury than passing a true macroelectrode. Moreover, when the microelectrode itself is used for macrostimulation, the stun or microlesioning effect from larger-diameter electrodes is minimized, im-

**TABLE 1.** *Neurophysiological approach to the subthalamic nucleus*

| Location | Formula | Atlas | Direct | Microrecording | Microstimulation | Macrostimulation | Intraoperative confirmation | Strategy |
|---|---|---|---|---|---|---|---|---|
| Amsterdam[70] | X (V, M and/or C) | | | No | No | Macro | ND | ND |
| Bristol, United Kingdom[72] | | X | X | No | No | Macro | | Single |
| Cologne[73,120] | X (V, C, M) | | X (M) | No | No | Macro | Stx X-ray | Serial |
| Miumbai[69] | X (M, C) | | X | No | No | Macro | No | Single |
| Oxford, United Kingdom[8,109] | X | | RN | No | No | Macro; DBS | None | Single |
| Rome (Università Cattolica)[71] | X (V) | | | No | No | DBS | No | Single |
| Vicenza[62] | X (V, C, M) | | | No/yes | ND | ND | ND | Five-track |
| Portland[92,117] | X (M) | | | No→yes | No | Macro | ND | ND |
| Cuba[27] | X (M, C) | X | | Semi | No | Semi; Macro | | Serial |
| Hamamatsu[26] | X (V) | | | Semi | No | Macro | | ND |
| Torino[56] | X (M, C) | X | | Semi | No | Macro; DBS | Fluoro | Serial |
| Turin[126] | X (M, C) | | | Semi | No | DBS | No | Single |
| Barcelona[61] | X (C) | | | Yes | Yes | DBS | | Serial |
| Birmingham, United Kingdom[55] | X | | X | Yes | No | DBS | Fluoro | Serial |
| Bordeaux[60] | X (V and M) | | X | Yes | No | DBS | Stx X-ray | Five-track |
| Grenoble[51,121] | V | X | X | lga | Yes (mA) | No | Stx X-ray | Five-track |
| Heidelberg[74] | X (M) | | | Yes | Yes | DBS | ND | Serial |
| Kiel[122,123] | X (M, C) | | X | Yes | Yes (mA) | DBS | Fluoro | Five-track |
| Liverpool[64] | | | X (M) | Yes | No | DBS | No | Serial |
| Milano (Priori)[40] | | | X (M, C) | Yes | No | Cannula | | 1-2 electrodes (in five-track) |
| New York (New York University)[48,68] | X (M) | X | X | Yes | No | DBS | Stx X-ray | Serial |
| Palo Alto[54] | X (M, V) | X (M, V) | | Yes | Yes | | Stx X-ray | Serial |

| Number | A/P angles | M/L angles | Important criteria for DBS implantation | Outcome reduction in UPDRS *off* | Levodopa response | Neurophysiolgocial findings |
|---|---|---|---|---|---|---|
| ND | ND | ND | Clinical effects | 49% (b/l, n = 20, 6 m) | 59% | |
| | Oblique | Oblique | Postimplantation M | 61% (b/l, n = 16, 12 m) | 56% | Single track in every patient |
| ND | 70 | 35 | Clinical effects | 60% (b/l, n = 16, 12 m) | 73% | |
| ND | ND | ND | Clinical effects | 53% (b/l, n = 23, 12 m) | | |
| ? | Oblique | | LFP coherence with EMG | ND | ND | |
| ND | ND | ND | Clinical effects | 41% (b/l, n = 7, 12 m) | 57% | |
| 5 | ND | ND | Length of STN, borders | 38% (b/l, n = 7, 3 m); no change in 22 patients without MER | | |
| ND | ND | ND | Clinical effects | 48% (b/l, n = 10, 12m) | 51% | Randomized comparison to GPi |
| 7. (5-15) | 40-65 | 0-15 | Multiunit activity; clinical effects | NR | NR | STN lesions; 82% of first tracks in STN; change = 1.25, 1.53, 0.67 mm |
| ND | ND | ND | NP findings NOS | ND | ND | Somatopy with semi-mr; clinical effects not informative because sx were freezing and PIGD |
| 1.3 (1-3) | 58-63 | 14-20 | NP findings NOS; clinical effects | 61% (b/l, n = 14, 12 m) | 65% | STN 4.2 mm long; MER correction: 0.7 mm (X), 0.5 mm (Y), 0.9 mm (Z) |
| ND | ND | ND | ND | 57% (b/l, n = 14, 3 m) | 66% | |
| 2.8 (1-8) | | 2 cm | Driving | 67% (b/l, n = 15, 6 m) | 51% | Moved 0.4 mm (X), 1.6 mm (Y), 0.8 mm (Z) in 26/30 sides; 11/30 not in STN in first track |
| 1.2 (1-3) | | | Center of STN activity | ? | | 4.65 mm average length; adjusted in 90% but most were depth; 0.42, 1.0, 0.88 moved; 2 mm in 35%; one track in 40, two in 12, three in 2; with better M: 79% one track |
| | | | Driving, frequency; clinical effects | ND | 72% | Used average of three imaging methods: final location 2.61, 2.85, 3.92 from M (i), V (i), direct; 14/28 electrodes modified by EP |
| | | | Driving; length of tracks; clinical effects | 60% (b/l, n = 24, 12 m) | 70% | STN 42 Hz; SNr 30 Hz; arm/leg in 40% of tracks; rarely orofacial; most had dyskinesia; two to three but sometimes five tracks good |
| Mos 1 (1-3) | 45-60 | 8-16 | Clinical effects | 40% (b/l, n = 11, 6 m) | 55% | GPi: 14% |
| | ND | ND | NP findings NOS; clinical effects | 51% (b/l, n = 48, 6 m) | 58% | |
| | ND | ND | NP findings NOS; clinical effects | 48% (b/l, n = 17, 10 m) | | 74% first track in STN; 1.7 mm target adjustment; 4/50 > 3 mm |
| 1.7 (1-3) | 55-60 | 12-15 | NP findings NOS; clinical effects | ND | ND | MER determined final DBS position in 17% of electrodes |
| 3.4 first side, 1.8 second | 39-68 | 0-18 | Longest, most lateral, and central (A/P) track | ND | ND | Always have cellular response laterally; STN 47 ± 12 Hz; STN 5.4 ± 1.1 mm; MER modified composite target by 1.27 mm (up to 5-6 mm) |
| | Oblique | Oblique | ND | ND | ND | Somatotopy in STN |

**TABLE 1.** (*Continued*)

| Location | Formula | Atlas | Direct | Microrecording | Microstimulation | Macrostimulation | Intraoperative confirmation | Strategy |
|---|---|---|---|---|---|---|---|---|
| Pamplona/San Sebastian/ Atlanta[46,53,65,125] | | X (M) | | Yes | Yes (<100 μa) | DBS | Yes | ND |
| Paris[38,57] | | X | X | Yes | No | Cannula; DBS | Stx X-ray | Five-track |
| Philadelphia[59,67] | | X | X | Yes | No | DBS | No | Serial |
| Rome, (Università "Tor Vergata")[39] | | X (V, C, M) | | Yes | Yes | DBS | | Three-track |
| San Francisco[24] | X (M) | | X | Yes | Yes | DBS | No | Serial |
| Toronto[37,45, 116, 124] | | X (M) | X | Yes | Yes (100 μa) | DBS | Yes | Serial (dual electrode) |
| Toulouse[66] | X (M) | | X | Yes | No | Macro | Fluoro | Five-track |

A/P, anterior/posterior; b/l, bilateral; C, CT; fluoro, fluoroscopy; M, MRI; macro, macroelectrode; MER, microelectrode recording; M/L, medial/lateral; ND, no data; NOS, not otherwise specified; NP, neurophysiology; NR, not reported; semi, semimicroelectrode; s/m, sensorimotor; Stx, stereotactic; V, ventriculography; X, X-ray.

proving assessment of the clinical benefits of macrostimulation.[19] This latter approach is often coupled to the use of the multielectrode holder, yielding comparative information on the therapeutic window from macrostimulation along up to five separate tracks.

Some groups use macrostimulation without prior microelectrode mapping, relying solely on the ratio of benefits to side effects to determine if the electrode is satisfactorily positioned. The map so developed is by nature less precise, but may be sufficient as it mimics the potential side effects of macrostimulation using the chronic DBS electrode, which is an advantage over microstimulation in the microamp range. When a large macroelectrode such as the lesioning probe or the DBS is used in this manner, only one pass is typically performed, although again this is rarely documented in the literature (Tables 1–3). However, the introduction of the macroelectrode will generally lead to a stun or microlesion effect that, although generally transient, often is significant enough to preclude a correct evaluation of the beneficial effects of stimulation on the target symptoms. This is not the case when using microelectrodes, even with several parallel tracts, and this is a strong argument in favor of using microelectrodes rather than macroelectrodes for stimulation, provided stimulation in the milliamp range is possible. Alternatively, macrostimulation can be performed along several tracks using a semimicroelectrode to minimize brain trauma.

## MAPPING STRATEGIES FOR SPECIFIC TARGETS

### Subthalamic Nucleus

#### Anatomy

The STN is a complex, biconvex lens–shaped, triply oblique structure (see Kopell and colleagues in this issue). Measurements are difficult to apply given the com-

| Number | A/P angles | M/L angles | Important criteria for DBS implantation | Outcome reduction in UPDRS *off* | Levodopa response | Neurophysiolgocial findings |
|---|---|---|---|---|---|---|
| ND | 45-60 | 0 | NP findings NOS; clinical effects | 74% (b/l, n = 15, 12 m) | 73% | STN 33 Hz (13-117 Hz); 64% of first tracks in STN; 47% in s/m region; 32% cells activated - all in d/l; somatotopy; 25/36 DBS > 1.5 mm and 16/36 > 3.0 mm from theoretical target in X and/or Y axis; mean X deviation 1.52 mm (0-4): 11 medial, 13 lateral; mean Y deviation 2.31 mm (0-7): 22 anterior, 8 posterior |
| | 62-80 | 21-32 | Longest track; clinical effects | 67% (b/l, n = 23, 6 m) | 77% | 19/24 in central track; STN: 39 ± 24 Hz; dyskinesia predictive of outcome; STN length: 4.42 mm (0-7) |
| | ND | | 4.5 mm length; clinical effects | 42% (b/l, n = 39, 12 m) | 56% | 1.8 mm in axial plane adjustment: −2-2 mm lateral; −2-4 mm A/P |
| ND | 85-90 | 10-15 | NP findings NOS; clinical effects | 54.5% (b/l, n = 8, 2 m) | 51% | Compared to GPi in same patients |
| 3.2 (1-6) | | 10 | > 4 mm track with driving; > 2 mm from borders; bipolar threshold for AE > 2v | 45% (b/l, n = 10; 12 m) | 54% | First track in STN 96%; 53% of tracks s/m; moved lead (3) if low thresholds for Aes; MR target adjustment: X, 0.45 mm (0-2); Y, 0.96 mm (0-3); Z, 1.07 mm (0-5); change of 2 mm or more in 25% |
| 6 (2-9) | ND | 3 cm lateral | NP findings NOS; clinical effects | 51% (b/l, n = 25, 12 m) | 54% | 96% of MR cells in rostrodorsal STN; no consistent somatotopy: 37 ± 17 Hz (25-45 Hz); 26% movement-related (activated); 4% inhibited |
| | | 15-25 | NP findings NOS; clinical effects | ND (only *on* given) | | Central track 46% |

plex shape in each axis, but its maximal length is 13.2 mm rostrocaudally and 8 to 9 mm mediolaterally (see Fig. 1 in Bejjani and colleagues[38]). STN is bordered on its anterior and lateral sides by the corticobulbospinal tract, while posteromedially lies the prelemniscal radiation and the red nucleus. The dorsal border of STN is with Forel's field H2 (the lenticular fasciculus) anteriorly, and field H1 (thalamic fasciculus) posteriorly, with the thalamus dorsal to the latter. The ventral border is formed by the substantia nigra reticulata (SNr). STN is organized into motor, limbic, and associative regions.[43] In the axial plane, the STN slopes from anteromedial to posterolateral, parallel to the cerebral peduncle below. Whereas the limbic region lies in the anteromedial portion, the sensorimotor region of STN lies in the posterolateral portion, and within this area it lies dorsally. Some mapping strategies are directed toward locating the motor region by confirming the presence of movement-evoked neural responses (and bursting activity synchronous with tremor, when present), which are organized somatotopically within STN.[24,44–47]

## Targeting and Approach

This is the subject of another article in this issue. In brief, various imaging techniques and target determination strategies (direct and/or indirect) may be used to pick the initial target for the microelectrode or macroelectrode (Table 1). This provides the starting point for electrophysiological mapping and obviously its initial accuracy ultimately determines the number of tracks necessary to refine the target.

Once the target is set, the entry point is determined. Most centers have chosen to orient their tracks in a double oblique manner for several reasons. First, a lateral-to-medial orientation in the coronal plane (up to 30°, with 10°–15° being the most common; Table 1) avoids the ventricle, which minimizes brain shift due to loss of

**TABLE 2.** *Neurophysiological approach to the globus pallidus*

| Location | Formula | Atlas | Direct | Microrecording | Microstimulation | Macrostimulation | Intraoperative confirmation | Strategy |
|---|---|---|---|---|---|---|---|---|
| Berne[114] | X (M) | | | Yes | Yes | DBS | | Serial |
| Bordeaux[86] | X (V/M) | | | Semi (in 2/7) | No | DBS | Stx X-ray | Serial |
| Buenos Aires[98] | | | | Yes | Yes | Macro | | Serial |
| Clermont-Ferrand[99,131] | | | X (M, V) | No | No | Macro | Stx X-ray | Single |
| Dusseldorf[101,120] | X (V, C) | | | No | No | Macro | Stx X-ray | Serial |
| Ghent[100] | X (V, C) | | | No | No | Macro | | Serial |
| Grenoble[95,115] | X (V, M) | X | | Semi | | Semimicro | Stx X-ray | Five-track |
| Heidelberg[74] | X (M) | | | Yes | Yes | DBS | ND | Serial |
| Kansas City[93] | X (C) | | | Yes | Yes | Macro | | Serial |
| Lausanne[119] | X (M) | | | No | No | Macro | ND | Single |
| Pamplona/San Sebastian[65] | X (M) | | | Yes | Yes | DBS | Yes | Serial |
| Paris[94] | | | X (M) | Yes | No | Cannula; DBS | Stx X-ray | Five-track |
| Portand[92,117] | X (M) | | | No→yes | No | Macro | ND | ND |
| Rome (Stanzione)[118] | | X (V, C, M) | | Yes | Yes | Macro; DBS | | Five-track |
| Rome (Stanzione)[39] | | X (V, C, M) | | Yes | Yes | Macro; DBS | | Five-tracks |
| Toronto[116] | | X (M) | | Yes | Yes | DBS | Yes | Serial |

Abbreviations are as in Table 1.

cerebrospinal fluid, possible intraventricular hemorrhage, and deflection of the electrode by the ependymal lining of the ventricle. This also places the entry point more lateral with respect to the sagittal sinus and the veins draining into it, thereby theoretically minimizing the risk of venous complications. Second, the anterior-to-posterior orientation in the sagittal plane (angles with respect to the intercommissural line range from 40° to 90°, with 45°–60° most common; Table 1) ensures entry through the precoronal region, thus sparing the motor cortex from injury, both direct and related to venous injury. Finally, the double oblique track happens to be closer to the long axis of the STN, maximizing the length of electrode within the target nucleus.

## Physiological Findings During Mapping

**Microelectrode Findings.** Recording begins at various distances from the STN target, from several millimeters (level of AC–PC line; Fig. 1B) to up to 40 mm (Fig. 1A), depending on whether striatal and/or thalamic activity is recorded. Findings depend on the obliquity of the planned tracks. When the entry is more lateral, the track misses the striatum or thalamus, residing completely within the corona radiata and internal capsule (Fig. 1B). When recording begins more proximally (~40 mm above target) and with more medial entry points, the caudate is encountered with its characteristic pattern of phasically active units (although some tonically active

| Number | A/P angles | M/L angles | Important criteria for DBS implantation | Outcome reduction in UPDRS *off* | Levodopa response | Neurophysiological findings |
|---|---|---|---|---|---|---|
| 1-3 | ND | ND | 1 mm above ventral border of GPi | 41% (b/l, n = 10, 12 m) | 46% | |
| ND | ND | ND | Clinical effects | 35% (u/l, n = 7, 12 m) | 32% | |
| ND | ND | ND | NP findings NOS; clinical effects | 29% (u/l, n = 6, 3 m) | 39% | |
| | ND | ND | Clinical effects | 36% (b/l, n = 4; u/l, n = 1, 6 m) | 75% | |
| ND | ND | ND | Clinical effects | 68% (b/l, n = 11, 12m) | Invalid | |
| 2.4 (1-9) | ND | ND | Clinical effects | 50.7% (3 m); + 8.3% (> 24 m; u/l, n = 26) | 60% | |
| | ND | ND | NP findings NOS; clinical effects | 39% (b/l, n = 5, 6 m) | 67% | |
| Most 1 (1-3) | 40-52 | 3-10 | Clinical effects | 14% (b/l, n = 5, 6 m) | 50% | |
| ND | ND | ND | NP findings NOS; clinical effects | 24% (b/l, n = 3; u/l, n = 2, 3 m) | 56% | |
| ND | ND | ND | Clinical effects | 50% (b/l, n = 6, 12 m) | 42% | |
| ND | 45-50 | ND | NP findings NOS; clinical effects | ND | ND | 16/21 DBS > 1.5 mm, 9/21 > 3.0 mm from calculated target; mean X deviation 1.5 mm (0-3.5 mm; all 10 lateral); mean Y deviation 2.35 (0-7 mm; 2 anterior, 15 posterior) |
| Five on first side, one on second side | Oblique | Oblique | NP findings NOS; clinical effects | ND | ND | |
| ND | ND | ND | NP findings NOS; clinical effects | 39% (b/l, n = 10, 12 m) | 52% | |
| | 70-80 | 5-15 | Apo-responsive cells; clinical effects | 50% (b/l, n = 6) | 46% | |
| | 70-80 | 5-15 | NP findings NOS; clinical effects | 43.1% (b/l, n = 8, 2 m) | 51% | |
| ND | ND | ND | NP findings NOS; clinical effects | 27% (u/l, n = 4; b/l, n = 4) | ? | |

units may also be encountered).[24] Below this, the internal capsule is entered, from which occasional fibers may be recorded. More anterior tracks will pass in front of the thalamus, next encountering the zona incerta (ZI), in which small infrequent neurons may be recorded with low tonic firing rates,[37] or even bursting neurons (25–45 Hz).[48] Fibers in this region may also be detected, corresponding to the fields of Forel. More posterior tracks pass into the thalamus, approximately 7 mm above the STN. The shell of the thalamus contains the reticular nucleus with its characteristic bursting pattern discharges (15 ± 19 Hz).[37] Within the thalamus, the ventral basal complex is encountered next, the cells of which have a more tonically active pattern and fire at an average of 28 Hz.[37,48–50] These cells are easily distinguished from the STN itself as their firing rate is significantly lower, and the overall background of the thalamus is substantially quieter. After 1 to 2 mm, in which neurons corresponding to ZI may be recorded, the STN is entered, characterized by an abrupt increase in background activity. Usually, the background changes prior to encountering individual units, which can actually be difficult to resolve because of the dense cellularity of the nucleus. Nevertheless, individual units can be isolated, which fire with a tonic and irregular discharge pattern with occasional bursts. Mean firing rates have been reported in the 34- to 47-Hz range, with standard deviations in the 25 Hz range, indicating a large variance in the frequency of individual units recorded.[24,37,38,46,48,50–52] Another much less frequently (<10%) encountered type of

**TABLE 3.** *Neurophysiological approach to the ventral intermediate nucleus*

| Location | Formula | Atlas | Direct | Microrecording | Microstimulation | Macrostimulation | Intraoperative confirmation | Strategy |
|---|---|---|---|---|---|---|---|---|
| Amsterdam[132] | | X (V) | | No | No | Macro | | |
| Grenoble[22,28] | X (V, M) | | X (M) | Yes | Yes | No | Stx X-ray | Five-track |
| Houston[112] | X (C) | | | No | No | DBS | No | Serial |
| Jacksonville[108] | X (M) | | | Yes/no | No | DBS | Fluoro | Serial |
| Kansas City[129] | X (C) | | | No | No | Macro | | |
| Lille[111,128] | X (V) | | | No | No | DBS | Stx X-ray | Single |
| New York (BI)[110] | X (M) | | | Yes | | DBS | | Serial |
| Toronto[49,133,134] | X (M) | X (M) | X (M) | Yes | Yes | DBS | Fluoro | Serial |
| Vienna[127] Zurich[130] | X (V) | | | No | No | Macro DBS | | |

Abbreviations are as in Table 1.

unit fires with a regular bursting pattern at 4 to 6 Hz, which may be synchronous with tremor if present.[37,51,53] These may be found more dorsolaterally and are usually movement-responsive.[46] Neurons firing with a pausing pattern (30 Hz; range, 12.7–65.4 Hz) similar to those seen in the globus pallidus externus have also been described.[53]

STN units are routinely tested for movement responsiveness to active and/or passive manipulation. The somatotopy of the STN has been well characterized in nonhuman primates, but is the subject of some controversy in patients. Nevertheless, several reports demonstrate a consistent somatotopy within STN. From 40% to 53% of tracks contain movement-responsive units ("driving"), which tend to be found more dorsolaterally.[24,44–46,51] From 26% to 42% of recorded units respond to movement.[45,46,51] Lower extremity units tend to be found more medially to upper extremity units (usually separated by just 1–2 mm) and slightly more posteriorly.[24,46,47,54] Cells with receptive fields in distal muscle groups are much more rare than proximal groups. Orofacial responsive units (tongue, jaw, orbicularis) are encountered much less frequently (perhaps related to sampling bias and/or the difficulty in examining trunk responsiveness) and tend to be found more ventrally.[46,54]

Below the STN, the electrode traverses into SNr, with a variable separation from STN (0.5–3 mm). Neurons in SNR have a more regular and tonic pattern than those in STN, lacking bursting and tremor or motor driving.[37,38,46,48,51] The mean firing rate of SNr neurons in most reports is higher than those in STN, ranging from 50 to 70 Hz,[37,38,48] but a lower mean rate has also been noted ($30 \pm 13$; range, 8–80 Hz).[51] However, given the large variance in the firing rates of both STN and SNr neurons, the absolute firing rate of any given unit is not sufficient to distinguish between the two nuclei. Rather, the pattern of neuronal activity (burstiness), motor responsiveness, and background activity offer greater reliability in determining electrode location.

Central tracks through STN are long and contain movement-responsive neurons. The maximal length of STN recorded varies from patient to patient and depends also on the approach angles, but ranges from 4.2 to 5.4 mm.[38,48,55–57] Tracks through the STN that are toward the posterior, lateral, or medial border are shorter in length, and those more posterior and/or medial lack movement-responsive neurons. When trying to determine in which direction such a track is eccentric from the center of STN, the characteristics of the rest of the recording track are useful. The absence of the thalamus above STN suggests a more anterior and/or lateral location, unless the approach is from a more lateral entry point, which will typically miss the thalamus. If thalamus is present but the STN length is short, the track may be posterior or medial. The absence of SNr below suggests a lateral location. Additional tracks may be run to optimize the microelectrode findings and/or to determine the location of the anterior and lateral borders of the STN when the

| Number | A/P angles | M/L angles | Important criteria for DBS implantation | Outcome reduction in UPDRS *off* | Neurophysiolgocial findings |
|---|---|---|---|---|---|
| | | | Clinical effects | 91% (21 PD, 7 ET, 5 other) at 6 m | |
| | | 0 in 184; 6-10 in 15 | NP findings NOS; clinical effects | Good to exc reduction in 83% of PD (n = 111e), 59% of ET (n = 36e) at last follow-up | |
| 1.29 (1-4) | ND | ND | Clinical effects | Marked exc in 87% with PD (n = 45); 93% with ET (n = 42) | |
| ND | Axis of Vim | 10 | Clinical effects | Significant tremor reduction | Without MER: 57% central track |
| | | | Clinical effects | 100% PD (n = 19), 84% ET (n = 10) at 3 m | |
| One in 12; two in 2 | Oblique | 5-10 | Clinical effects | 80% PD (n = 10); 75% ET (n = 4) at average 17 m; suppression of dyskinesia in PD | Electrodes may be in CM-Pf |
| 2.4 (1-5) | ND | ND | NP findings NOS; clinical effects | TRS 3→0 | With M targeting, only laterality is adjusted |
| ? | | 0 | NP findings NOS; clinical effects | 7/8 PD, 3/5 ET good to exc at 12 m | |
| | | | Clinical effects | 82%, n = 23 PD, 4 ET | |
| | | | Clinical effects | 70-100% effect in 40 PD, 18 other | |

approach is to implant the DBS a fixed distance from these landmarks. Using the five-channel multielectrode holder, usually two to three but up to all five tracks may contain units characteristic of the STN.[51]

These findings are mirrored in semimicroelectrode recordings (Fig. 2), where the overall background of the STN provides a sharp contrast to that of the internal capsule and/or ZI above and the SNr below.[26,27] Movement responsiveness can be detected with semimicroelectrode recordings as well. Several reports have explored the use of local field potentials to characterize the STN using semimicroelectrodes or macroelectrodes.[6–8]

Microstimulation (≤100 μA; 200–300 Hz; 0.1–0.5 ms), when used (Table 1), can be performed through the microelectrode as the track is being run[37,46] or performed only to look for side effects when the electrode is outside of STN[24] (see below for discussion of microstimulation in the mA range in STN). Microstimulation at the site where tremor-related neurons were recorded can induce tremor arrest with a short latency (<200 ms).[37,46] Currents greater than 50 μA are usually necessary. This effect is limited to specific body segments in accordance with the somatotopic arrangement. The use of a wider pulse duration (>0.5 ms) usually spreads the antitremor effect to other body regions after a longer delay (1–2 s).[46] Restricted current spread with microstimulation (≤100 μA) limits the evocation of side effects from stimulating within STN and thus does not predict that macrostimulation at the same site will be free from adverse effects. However, microstimulation within surrounding structures will sometimes evoke side effects specific for those regions, such as muscle contractions, paresthesias, or ipsilateral eye movements from stimulating within corticobulbar tract, medial lemniscus, or third nerve fascicles, respectively.[37,58] Again, the ability to elicit these effects is limited by the current spread from microstimulation.

**Microelectrode Criteria for Macroelectrode/DBS Implantation.** The constellation of findings is determined by the location of the track. The ideal track through the STN passes through ≥ 4 mm of the nucleus (from a double oblique angle) and encounters movement-responsive units corresponding to the arm and/or leg. For some groups, this constellation of findings suffices for proceeding to macroelectrode/DBS electrode implantation,[59–61] while others define the anterior, lateral, and/or posterior borders of STN and place the DBS ≥ 2 mm from them.[24,48,55,62]

The predictive value of the above criteria for the optimal site of DBS implantation has been subjected to analysis. The length of STN encountered did not predict the optimal electrode location in and of itself (based on outcome).[57] The presence of movement-related units is thought to be important by most, but not all, centers, and most centers examine for this and rely on its presence to indicate an adequate site for implantation.

**Macrostimulation.** Following microelectrode mapping, or in many centers in lieu of it, macrostimulation is

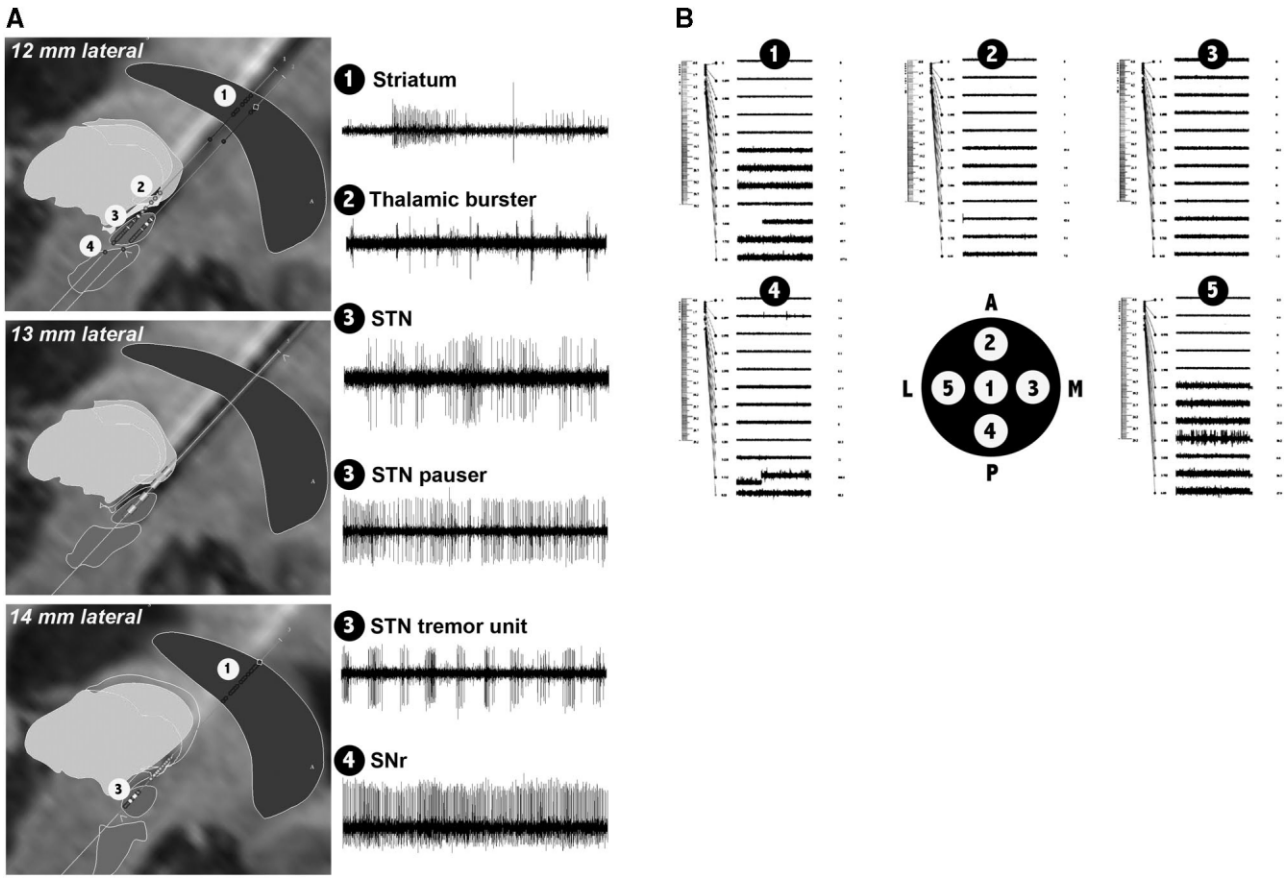


**FIG. 1.** Microelectrode mapping of the subthalamic nucleus. Typical data from microelectrode mapping using two different approaches. **A:** Serial-track approach. Reconstructions (in the plane of the electrode tracks) are shown from three tracks passing from the striatum (40 mm above target) to the STN, the first two at 12 mm lateral and the third at 14 mm lateral. Typical cell recordings indicative of the striatum, thalamus, STN (phasic cell, pauser cell, and tremor-responsive cell) and SNr are shown. Movement-responsive cells driven by leg movements were found at 12 mm lateral, whereas arm-responsive driving was found at 14 mm lateral. The DBS was implanted between the two planes at 13 mm lateral followed by clinical testing. **B:** Five-simultaneous-track approach. Five simultaneous parallel tracks, separated by 2 mm, were run with a tungsten microelectrode through the Ben gun five-channel microelectrode holder, and recordings were obtained over approximately 12 mm (from 5 mm above the AC–PC line to the SNr). Recordings over 8 mm, at approximately 100 μm intervals, are shown from the white matter into the STN and then into SNr. Recordings typical of the STN are seen in Tracks 1 and 5, where both single unit activity is seen and elevation of the overall background activity. The SNr is seen below the STN. Microelectrode mapping is used in conjunction with constant current (milliamp range) stimulation and detailed evaluation of clinical effects to chose the final position for the DBS electrode.

performed with either the microelectrode using current in the milliamp range, the uninsulated tip of the inner guide cannula through which the microelectrode was passed, a dedicated macroelectrode (e.g., a radiofrequency lesioning electrode), or the DBS electrode. The thresholds for side effects and clinical effects are carefully assessed.

Within the internal capsule, orofacial and/or appendicular contractions are noted, as are contraversive eye movements. Within the thalamus, various effects have been reported (e.g., vegetative effects) in some instances, and a mild reduction in distal muscle tone ventrally.[63] Stimulation within ZI and the fields of Forel can produce a decrease in rigidity at relatively low voltage thresholds.[63] Stimulation in the STN produces the maximal clinical effects intraoperatively, however, and they are obtained at the lowest thresholds. Therefore, the benefits obtained in the ZI, especially the antiakinetic effects, are likely to reflect current diffusion to the dorsal (sensorimotor) part of the STN. Stimulation within SNr is generally without clinical effects, although some have observed decreases in rigidity and worsening of bradykinesia.

When stimulating with a macroelectrode within or nearby to STN with either a mapping electrode, the shaft of the microelectrode, the DBS, or even a microelectrode at high currents (mA range), clinical effects are produced at their lowest voltage thresholds and side effects at higher threshold (Fig. 3).[19] Current spread outside the nucleus in

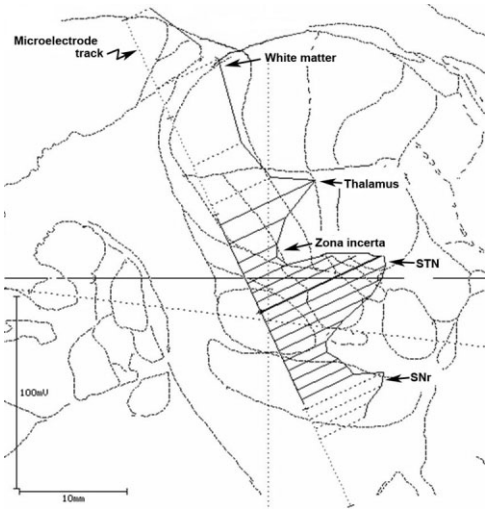


**FIG. 2.** Semimicroelectrode mapping of the subthalamic nucleus. A typical semimicroelectrode recording track into the STN. Superimposed on the track (indicated by arrow) is a representation of the amplitude of the integrated electrical activity at serial points along the track. The changes in electrical amplitude are consistent with traversing of the microelectrode from the white matter into the thalamus, the zona incerta, the STN, and then the SNr. The integrated electrical activity within the STN is substantially greater than that in surrounding structures, facilitating its identification. Modified from Lopez-Flores and colleagues.[27]

an anterior or lateral direction produces stimulation of the corticogeniculate fibers (contraction of the lower part of the face contralateral to stimulation or bilateral lid closure, the so-called apraxia of eyelid opening), corticobulbar fibers (dysarthria), and/or the corticospinal tract (contraction of the upper limb, mainly intrinsic hand muscles, more frequently than the lower limb). Diffusion to supranuclear oculomotor fibers will induce conjugate controversive eye deviation. Current spread posteriorly activates the fibers of the medial lemniscus, producing paresthesias that are usually transient. Medially, current spread can also produce paresthesias and other subjective complaints such as dizziness, nausea, breathing difficulties, and anxiety, as well as objective vegetative signs such as ipsilateral sweating, mydriasis, and/or flushing. Ventromedial current spread may activate the fibers of the third nerve, producing ipsilateral medial eye deviation, mydriasis, and/or lid retraction.[19,24]

At voltage levels below those that produce any of the above side effects, the effects of more chronic stimulation on clinical signs and symptoms are assessed. Resting tremor is a variable sign and it is therefore difficult to assess stimulation-related changes in it. Rigidity evaluation is difficult as rigidity varies with activation maneuvers or with changes in vigilance, but in expert hands it can be reliably assessed.[24] Bradykinesia is also difficult because it is greatly influenced by patient cooperativeness and motivation and is subject to placebo effects. The effect of stimulation on gait is not possible to evaluate intraoperatively. Stimulation of the sensorimotor STN induces dyskinesias mainly contralateral to stimulation in parallel with improvement in akinesia. The appearance of dyskinesia is not considered a side effect; rather, it is a predictor of positive outcome. The relative levels at which clinical benefits are observed as compared to side effects is critical for determining the correct position of the lead. However, many patients exhibit few signs to evaluate following mapping and DBS electrode implantation, called the stun or microlesion effect, and in this case sole reliance on the physiological map and the thresholds for side effects may be necessary.[24,26,48]

The predictive value of intraoperative stimulation was analyzed by Houeto and colleagues.[57] Decrease in rigidity was not correlated with outcome because it had in fact decreased in nearly all patients. Decrease in segmental akinesia intraoperatively correlated with improvement in this score postoperatively. The finding of dyskinesia with stimulation intraoperatively predicted improvement on

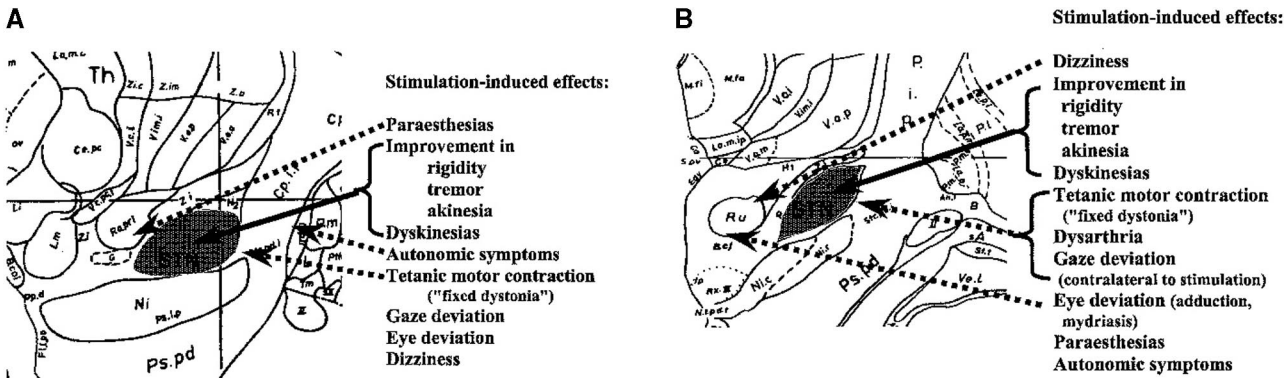


**FIG. 3.** Stimulation testing in the subthalamic nucleus. The clinical effects associated with macrostimulation in and around the STN in the sagittal (**A**) and the coronal (**B**) planes. Reproduced from Pollak and colleagues.[19]

several postoperative parameters, as has been observed by others.[19] Not all patients experience dyskinesia with stimulation, however.[24] Those patients who do not have dyskinesia in response to levodopa do not readily display dyskinesia with stimulation.

### Modification of Target Based on Electrophysiological Mapping

The distance and direction of refinement of initial targeting is related to the accuracy of the initial imaging and target calculation, as well as the technique and accuracy of the mapping procedure. One measure of both the inadequacy of the initial imaging, target calculation, and stereotactic technique, and the subsequent ability of physiological mapping to "correct" these errors, is the amount of correction of the electrode position following mapping. (This assumes that this correction brings the electrode to the most efficacious location; see below for a discussion of this assumption.) Both microelectrode mapping techniques and macrostimulation techniques can be used to correct the electrode position. However, none of the five groups that relied solely on macroelectrode/DBS mapping to position the electrode optimally reported how many tracks were necessary to accomplish this, nor the amount of correction, if any, that was needed (Table 1), the assumption being that the anatomically chosen track produced sufficient benefits and tolerable adverse effects without modification. In contrast, there is plenty of data regarding modification of the electrode location following microelectrode mapping. The first track, or the central track for those groups using a multielectrode holder, was in the STN from 63% to 96% of the time,[24,27,38,61,64] with 47% in the sensorimotor region.[65] Microelectrode mapping led to modification of the target in 17%,[40] 21%,[38] 32%,[55] 50%,[60] 54%,[66] and 87%[61] of patients and in 69% of electrodes.[65] Target adjustments following microelectrode mapping ranged from an average of 1.27 to 3.94 mm,[60,64,65,67,68] $\geq$ 2 to 3 mm in 8% to 35% of cases,[24,55,64] and as much as 5 to 6 mm.[68] Adjustments averaged 0.64 mm (0.4–1.25 mm) in the X direction, 1.12 mm (0.5–1.6 mm) in the Y direction, and 0.86 mm (0.67–1.07 mm) in the Z direction.[24,27,56,61,64,65]

### Relationship of Mapping Strategy to Outcome

There is thus ample evidence that physiological mapping with microelectrodes leads to significant adjustment of the DBS target in STN. In contrast, in those centers that use macroelectrodes alone, there is little or no documentation of modification of the target from the anatomical one. In the absence of class I prospective, randomly assigned, and blinded comparisons of the two approaches, we are left to compare outcomes across centers that use mapping vs. those that do not and across centers using different mapping strategies. With the understanding that this approach is subjected to serious confounding factors, such as selection and reporting bias, and inconsistencies across centers with regard to outcome analysis, we will examine the question of whether outcomes differ across centers as a function of physiological mapping strategy.

**Does the Use of Mapping Improve Outcome?** In fact, all centers used some form of mapping following target selection, in as much as macrostimulation testing even with the DBS is a form of mapping, when implanting STN DBS leads. There are thus insufficient data available to determine whether any mapping at all, as opposed to pure anatomical targeting without modification based on intraoperative evaluation, is necessary for good results from STN DBS.

**Is One Form of Mapping Superior to Another?** Only 5 of 28 groups relied solely on macroelectrode stimulation and clinical testing after STN DBS insertion.[69–73] Of these, only one[71] did not reach a reduction of motor *off* Unified Parkinson's Disease Rating Scale (UPDRS) scores that was comparable to the levodopa response, if reported. For the remainder of the groups that used a microelectrode (n = 18) or semimicroelectrode (n = 4) mapping technique (Table 1), 2 of 13 failed to reach this benchmark.[59,74] Even so, each of these three groups reported at least a 40% reduction of motor *off* scores. With the absence of class I data, and in consideration of the large number of variables that impact clinical outcome, it is not possible to conclude that one technique is superior to the other in so far as motor UPDRS outcome is concerned.

**Does the Use of More Tracks Improve Outcome?** In those reports using a serial approach to mapping, an average of 1 to 7.2 tracks was required to complete mapping (Table 1). Seven of the 22 groups using micro- or semimicroelectrode mapping utilized the multielectrode holder and thus used five tracks in every case. Is use of a greater number of tracks associated with improved outcome because of increased accuracy of DBS implantation? Those using five or greater tracks achieved a 57% reduction in motor *off* scores, while those using three or less achieved a 51% reduction. Although there does not seem to be any obvious clinical advantage to using more tracks to complete the mapping process, limitations in the quality of the data prevent any definitive conclusions to be formed on this issue.

### Physiological Mapping of the STN: Discussion

Although most centers spend considerable amount of time mapping the target in order to optimize outcome, the analysis of the existing literature is not very helpful in guiding those teams that wish to start DBS. Laitinen and Hariz[41] compared microrecording with macrostimulation and impedance measuring in pallidal and thalamic surgery and concluded that microrecording, in their hands, was not very useful as it was too time-consuming and did not add much to accuracy. In contrast, others put a very high emphasis on microrecording[9,24,25,51,68,75,76] and/or microstimulation in the mA range.[19] Outcomes of different groups, however, cannot be compared based on presence/absence of microrecording only. One must not forget that mapping technique is only one out of many variables that determine the outcome (some others being patient selection, quality of imaging techniques, the surgeon, and neurological follow-up), and certainly the fact that a team uses microrecording is not in and of itself deterministic. Moreover, as reflected in Table 1, there are many different approaches to microrecording, and some may be more effective than others.

The only way to minimize the multiple other variables would be a randomized comparative study of using or not using microrecording by a single team to reduce the numbers of variables. So far, the benchmark is a measure of surgical outcome compared to the levodopa response. However, for many papers, the numbers of patients is small and the follow-up relatively short (Tables 1–3). Another benchmark may be long-term outcome. The 5-year outcome based on the technique used in Grenoble[77] was more favorable than the short-term outcome of other groups (Table 1). Such variance cannot be explained by a difference in a single variable such as microrecording.

The microrecording debate[78] finally remains open. Even if the authors believe that the use of microrecording is a useful tool in order to improve targeting accuracy, it has to be acknowledged that there is an increase in surgical risk as the number of cerebral hematomas is correlated to the number of trajectories.[79–82] The question that is most difficult to resolve is which prevails: the risk of side effects related to the technique or the risk of suboptimal outcome related to omission of the same technique. Future studies will have to address this question.

## Globus Pallidus

### Anatomy

The motor region of the internal segment of the globus pallidus (GP) is the target for DBS in PD and dystonia. GP forms part of the lenticular nuclei, which describes its shape in the coronal plane, the narrow point being medially situated. The external segment (GPe) forms the lateral border of GPi, and medially, the dorsal border. The posterior limb of internal capsule forms the posteromedial border (oriented obliquely from anteromedial to posterolateral). The ansa lenticularis, the main outflow of GPi, lies below GPi coursing medially and anteriorly. Below this white matter lies the optic tract coursing posterolaterally toward the lateral geniculate nucleus. The putamen is separated from GPe by the external medullary lamina, and GPe is separated from GPi by the internal medullary lamina. There is a variably present lamina (lamina incompleta) that separates the external and internal segments of GPi itself. Each of these laminae is surrounded by cells called border cells, which are related to the large acetylcholinergic cells of the nucleus basalis that underlies the anterior portion of the globus pallidus.[25]

### Targeting and Approach

The details of targeting the globus pallidus are covered by Rezai and colleagues in this issue. In brief, a combination of MRI, CT, and/or ventriculography may be used to determine the initial target within GPi, using indirect and/or direct methods. Typically, the initial track for microelectrode targeting is chosen toward the back end of the posterolateral GPi (the motor region), where the boundaries of GPi with the optic tract (ventral) and internal capsule (posterior) can be determined. Because the pallidal target lies more lateral and anterior than STN, the coronal angle of the tracks necessary to avoid the ventricle can be less oblique, or even strictly parasagittal (0°–15° in the reviewed series; Table 2). As with STN, the sagittal angle is anteriorly inclined both to avoid the motor cortex and to produce an angle away from the internal capsule for the DBS lead. These considerations produce a track that traverses the striatum, corona radiata, GPe, and GPi. Anterior tracks pass through the bottom of GPi into the ansa and then optic tract, whereas posterior tracks pass through the back of GPi into the internal capsule.

### Physiological Findings During Mapping

**Microelectrode Findings.** Depending on how far above the putative target one begins, tracks toward the GPi may begin with recording within the corona radiata, followed by entry into the putamen (≥22 mm lateral), or more medially with recording in the caudate and passage into the anterior limb of the internal capsule (≤20 mm lateral; Fig. 4). The neurons of the caudate or putamen are phasically active, but rarely tonically active units

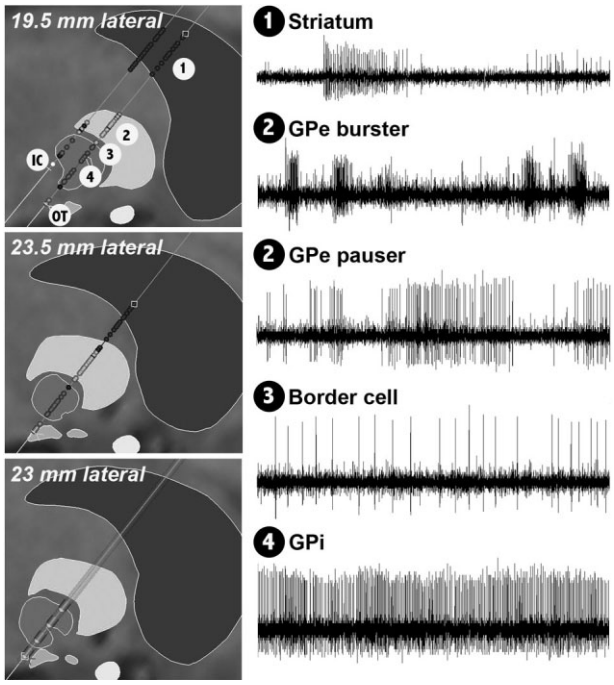


**FIG. 4.** Microelectrode mapping of the globus pallidus. Serial-track approach to microelectrode mapping of the globus pallidus. Three serial tracks were run from the striatum (40 mm above target) to the optic track (OT) or the internal capsule (IC) through GPe and GPi. The first two tracks were in the 19.5 mm plane (based on postoperative reconstruction in the plane of the electrode track). The third track was 4 mm lateral to the first plane to define the laterality of the planes and also showed GPi. The DBS electrode was implanted in the 23-mm plane 4 mm anterior to the pallidocapsular border, and macrostimulation was performed for clinical effects.

with a low frequency (4–6 Hz) may be encountered.[25] Passage through the external medullary lamina surrounding GPe is marked by border cells that are tonically active lower-frequency units (34 ± 19 Hz),[25,76,83,84] but which can alternately enter a burst-firing mode. The GPe contains two types of units: most are higher-frequency units (50 ± 21 Hz) that are tonically active but with frequent short pauses, and less commonly lower-frequency units (18 ± 12 Hz) punctuated by high-frequency bursts.[25,76,85] Between GPe and GPi lies the internal medullary lamina, surrounded by border cells. In Parkinson's disease, units within GPi have a high tonic frequency (82 ± 24 Hz) with few pauses compared to GPe.[25,76,85] Other patterns that may be seen include units firing in phasic bursts at a frequency of 4 to 6 Hz, often in synchrony with tremor when present. The overall background activity is also elevated in GPi. Within the sensorimotor (posteroventrolateral) region of GPi driving of the unit discharges is elicited by passive and/or active limb movements, often by multiple joints, sometimes bilaterally (38%–46% of neurons).[25,84] The subject of the somatotopy of GPi has been controversial. Those groups that show a somatotopy find that leg-related driving is seen medial and dorsally to arm and face, with jaw-related driving more ventral.[25,84]

After traversing border cells at the bottom of GPi and the fibers of the ansa lenticularis, the optic tract is encountered (~1.5 mm below GPi). Light flashes delivered to the eyes produce evoked discharges within the fibers of the optic tract in 87% of patients[25] that can be appreciated aurally more easily than visually. Microstimulation (2–20 μA) or macrostimulation of these fibers produces phospenes in the central or contralateral visual field that are perceived by most patients (75%).[25,76] The posterior limb of the internal capsule lies posterior to GPi, and microstimulation of its fibers (≤100 μA, 200–300 Hz) produces orofacial or contralateral motor contractions.

GPi can also be mapped with a semimicroelectrode, but the distinction between GPe and GPi is less readily discerned.[86,87] Visual evoked potentials can be obtained, however, that discern the optic tract below GPi.

**Microelectrode Criteria for Macroelectrode/DBS Implantation.** Formulaic and/or atlas-based indirect targeting of GPi may be insufficient due to patient-to-patient anatomical variations, such as the width of the third ventricle, which compounds stereotactic and intraoperative issues that can lead to mistargeting.[88,89] MR imaging can lead to marked discrepancies in stereotactic targeting of up to 1 cm.[90] To compensate for these issues, the goals of physiological mapping are to define a long run through GPi, consistent with a track that is not too lateral and close to GPe; to elicit driving of GPi units consistent with the posterolateral sensorimotor region; and to define a safe distance from the internal capsule posteriorly and the optic tract inferiorly. Generally, it is difficult to garner all of this information without at least two tracks in the initial parasagittal plane. Although the relative height of GPi and GPe and the presence of driving responses yield clues to the laterality of the mapped plane, this can be deceiving,[89] necessitating one or two tracks laterally.[25,65,91] Nevertheless, some groups limit the number to one or two tracks.[92,93] Conversely, several groups routinely use the five-track multielectrode holder.[39,94,95]

**Macrostimulation.** At the completion of, or in lieu of, microelectrode mapping, the macroelectrode is positioned greater than 2 mm medial to GPe, ≥ 3 to 4 mm anterior and lateral to the pallido–capsular border, at the ventral border of GPi (or >2 mm rostral to optic tract if microrecording is not used to define GPi; e.g., Starr and colleagues[96]). Macrostimulation is then performed to determine the voltage thresholds for clinical benefits, corticobulbar and corticospinal side effects, and, at the low-

est contact, visual phospenes. An adequate therapeutic window is sought, but in many cases clinical benefits from the stun effect of the electrode tracks preclude accurate clinical assessment, and it is therefore important to pay careful attention to the thresholds for side effects. In fact, visual side effects are rarely a problem because the most ventral contact is a safe distance from the optic tract when placed at the ventral border of GPi, and stimulation through the most ventral contact with the DBS electrode is unusual. Motor effects, however, are common, but again thresholds are lower, more posteroventrally within a track.

Absolute recommendations for tolerable current and voltage thresholds are difficult to make because the more important parameter is the ratio of clinical benefits to side effects. Moreover, current and voltage thresholds are frequency- and pulse width–dependent. Nevertheless, using the DBS in bipolar mode with parameters similar to those used for chronic stimulation (e.g., frequency 130–185 Hz, pulse width 60–90 μs), voltage thresholds for capsular activation that are less than 4 volts are likely to limit therapeutic benefits. Starr and colleagues[96] found that stimulation thresholds for motor effects between 5 and 10 volts at 185 Hz, 90 μs, correlated with a location of the active electrode 3 to 5 mm from the pallido–capsular border. Laitinen and Hariz[41] recommended thresholds of 8 to 10 mA at 6 Hz and 5 mA at 60 Hz (pulse width 1 ms) prior to radiofrequency pallidotomy with a 1.8 mm diameter × 2 mm electrode, but these thresholds may differ when implanting a DBS electrode (although 5 mA would correspond to ~5 V with a typical DBS contact impedance of ~1 kΩ). When lower thresholds for motor side effects occur, this can be attributed to current spread posteriorly and/or medially, necessitating readjustment to a more anterior or lateral location.

### Modification of Target Based on Electrophysiological Mapping

All of the 15 groups reporting the implantation of GPi DBS electrodes for PD used macrostimulation (including microstimulation with stimulation intensity in the mA range) during mapping, whereas 11 of 14 additionally used microelectrode (n = 9) or semimicroelectrode (n = 2) mapping techniques (Table 2). Most used a serial approach, requiring from one to three tracks (with some outliers), although three groups used the five-simultaneous-track approach. The reports reviewed here do not describe in detail the neurophysiological criteria that were used to determine the final target based on mapping, such as how far anterior/lateral to the internal capsule, medial to the lateral border of GPi, or rostral to the optic tract the electrodes were implanted. There is only one report describing how far the final target was modified from the initial target.[65] This type of information is available for stereotactic and neurophysiological techniques used during pallidotomy for PD,[84,89,91] but may not be precisely applicable to GPi DBS. Although each group used macrostimulation to check for clinical effects and side effects, they never reported whether the final position of the DBS lead was revised as a consequence of the clinical results of macrostimulation testing in the operating room. However, Guridi and colleagues[65] analyzed the results after microelectrode mapping in GPi. Sixteen of 21 leads were more than 1.5 mm (the estimated radius of the region that the DBS current may reach) from the initial target, in the X direction (n = 3), Y direction (n = 10), or both (n = 3). In 43%, the discrepancy was more than 3 mm. Mean deviation in the X direction was 1.5 mm (0–3.5 mm) and 2.35 mm in the Y direction (0–7 mm). Unfortunately, this report contains no clinical outcome data.

### Relationship of Mapping Technique to Outcome

Differences in outcome related to the physiological technique used during surgery are difficult to ascertain due to the retrospective and confounded nature of such analyses. A meta-analysis of series of pallidotomies done with microelectrode recording vs. macrostimulation as the sole technique failed to reveal a difference in outcome, but suggested an increase in hemorrhagic complications.[78,97] If the benchmark of achieving at least 80% of the reduction in motor *off* UPDRS scores compared to that seen with levodopa is used, 5 of 9 reports using microelectrode mapping failed to meet this benchmark,[74,92,93,95,98] as compared to two of three reports not using some form of microelectrode mapping.[99,100] One of the most serious failures used microelectrode mapping (14% reduction in motor UPDRS),[74] while another did not (8.3% increase in the motor score).[100] The best outcome ever reported was based on macrostimulation only (57% decrease in UPDRS motor *off* scores),[101] but the benefit was lost in the long term, illustrating the importance of using long-term results as a benchmark as well. It is not possible to argue for or against a role for microelectrode mapping based on these studies.

## Vim Thalamus

### Anatomy

The detailed thalamic nuclear and connectional anatomy, and the terminology to describe it, are complex, controversial (see Krack and colleagues[102] and Macchi and Jones[103] for review) and beyond the scope of this

article. There is general agreement that the physiologically characterized kinesthetic region of the ventrobasal thalamus, corresponding to the area that receives cerebellar afferents, is the target for deep brain stimulation for tremor. This area incorporates Vim and ventro–oralis posterior (Vop),[104,105] ventral lateral nucleus (VL),[104] and VL posterior nucleus.[103] Posterior to the cerebellar receiving area lies the principal sensory nucleus receiving medial lemniscal and spinothalamic sensory afferents, called ventral caudalis (Vc)[105] or ventral posterior lateral nucleus (VPL). Anterior to the cerebellar receiving area lies the region that receives afferents from the basal ganglia (GPi, SNr), incorporating ventro–oralis anterior (Voa),[104,105] ventral anterior nucleus (VA),[104] and VL anterior and VA.[103] Ventrally lies the medial lemniscus itself. Dorsally, Vim is bordered by the dorsal region of the ventral tier nuclei (e.g., dorsal intermedius [Dim]). The medial border of Vim is with Vim.i, which is anatomically similar to Vim but receives proprioceptive afferents with receptive fields in the face region. Laterally, Vim is bordered by the posterior limb of the internal capsule. Organization within Vim is strictly somatotopic, with face followed by hand followed by leg from medial to lateral.

### Targeting and Approach

Various means to select the initial target are used but all are based on indirect means since Vim cannot be distinguished from surrounding structures on MRI (see Rezai and colleagues in this issue). As with STN, a double oblique (anterior, lateral) approach is necessary if the ventricle is to be avoided, but some groups take a parasagittal (transventricular) approach (angles range from 0 to 10°; Table 3). The anterior angle of approach may be important since it determines whether more proximal contacts on the DBS move anteriorly with respect to Vim (Fig. 5). For this reason, several groups implant the electrode in parallel with the border of Vim and Vop. Conversely, a more sloped angle traverses borders between nuclei, which facilitates mapping, but places more rostral contacts more anteriorly away from Vim. Similarly, a coronal angle that is too lateral-to-medial places rostral contacts closer to internal capsule.

### Physiological Findings During Mapping

**Microelectrode Findings.** The initial track generally traverses initially through Voa/Vop, where tonically active units are encountered (mean firing rate 18 ± 3 Hz in PD),[49] which are driven by voluntary (active) movements of the contralateral upper or lower extremity (Fig. 5).[9] Passive driving is much less robust in Voa/Vop. As the electrode passes caudally and toward Vim, units are encountered (25.8 ± 3.5 Hz)[49] that are progressively more activated by passive kinesthetic movements of the joints rather than by active movements. The strict somatotopic map in the thalamus places face receptive fields medially, with the representation of the fingers lateral to face. Upper extremity representation is found ventromedial and lower extremity dorsolateral. Hence, a typical dorsolateral-to-ventromedial track is likely to encounter leg followed by arm kinesthetic receptive fields. The dorsal shell of Vc is next encountered, which also contains proprioceptive receptive fields, but is more exquisitely activated by palpation of the muscle belly; its distinction from Vim is a matter of controversy.[103,106] Finally, caudal progression into Vc itself yields units with well-defined cutaneous receptive fields activated by very light touch in a narrow somatotopic region. Care must be taken during microelectrode recording to search for receptive fields, including in the orofacial region, as they can in a short span move from one body region to an adjacent one. As the electrode passes through the ventral border of the thalamus, it enters into the fibers of the medial lemniscus.

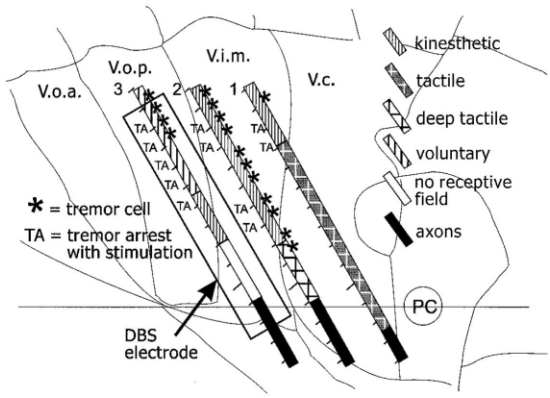


**FIG. 5.** Microelectrode mapping of the ventral intermedius nucleus. Typical microelectrode map during implantation of DBS into the Vim nucleus of thalamus. Three electrode tracks were performed to define the location of Vim and Vc prior to positioning the DBS electrode. Courtesy of W. Hutchison, University of Toronto.

Semimicroelectrode recordings are also informative and can yield similar information with respect to single unit, multiunit, and group discharges, but are better for the latter.[9,87,107] The background activity in Vim is very high, with large amplitude spikes, as compared to that in Vop, which has low background and small spikes (see Ohye and Narabayashi[10]), with a clear border between them. Rhythmical discharges associated with tremor can be seen in Vim and Vop.[10,11] Vc also has high background and large spikes and can only be distinguished from Vim by the presence of cutaneous tactile receptive fields.

Microstimulation is generally performed through the microelectrode as the track is being run.[9,107] Within Vop and Vim, microstimulation with currents up to 100 μA can lead to partial or complete tremor suppression of the somatotopically corresponding body region. Sometimes microstimulation within Vim or the dorsal shell of Vc produces mild localized paresthesia corresponding to the receptive field of the corresponding units. Microstimulation in Vc itself produces paresthesia at very low current thresholds (e.g., 1–5 μA) that precisely correspond (except in cases of deafferentation) to the receptive field of the sensory unit. It is useful to microstimulate when the receptive field of an isolated unit is unknown to determine where to look for activation. Microstimulation below the thalamus within the medial lemniscus produces paresthesia that are more widespread (e.g., face, arm, and trunk) and at higher current thresholds (e.g., 25 μA) compared to Vc.

### Microelectrode Criteria for DBS Implantation

The DBS electrode is implanted into the region containing neurons with kinesthetic receptive fields corresponding to the hand, 2 to 4 mm anterior to the border with the sensory Vc nucleus. A single track that is well placed may yield all the information necessary for macroelectrode implantation, as is the case when the electrode traverses caudally into the distal upper extremity region of Vim. It is also useful to have a more posterior track to define precisely the border of Vim with Vc so as to place the DBS at a safe distance (>2 mm) from Vc. Moreover, good responses are described as occurring anterior to the region of Vc with cutaneous receptive fields in the lateral digits.[22]

### Macroelectrode Stimulation

Following microelectrode mapping, or in lieu of it, the macroelectrode is inserted and stimulation testing performed. First and foremost, the voltage or current threshold for the suppression of tremor is determined. Complete or near-complete suppression is sought, which may occur with currents as low as 0.2 mA,[22] but should occur with less than 1 to 2 mA. Paresthesia is usually produced in the caudal region closer to Vc, but can be elicited in Vop as well. When the electrode is within Vim and a safe distance from Vc (2–3 mm), these paresthesias habituate within 10 seconds.[22] It is mandatory to obtain tremor suppression in the absence of sustained paresthesia, as this will limit patient satisfaction. Often, this is not the case with the most ventral DBS contact but the next contact up should satisfy these criteria; if not, the electrode should be repositioned anteriorly by 1 to 2 mm. Often, macrostimulation will produce complete tremor suppression in the upper extremity and the paresthesia produced will be orofacial due to the close proximity of these regions in the onion skin–shaped thalamus. Orofacial paresthesia is acceptable so long as it abates completely at a voltage level that produces tremor arrest, or patient satisfaction will be jeopardized. However, strong consideration should be given to repositioning the electrode 1 to 2 mm laterally, which, considering the oblique posterolateral slope of the Vim/Vc border, will both move the electrode away from the face region of Vc and position it relatively more anteriorly with respect to Vc.

### Modification of Target Based on Electrophysiological Mapping

Of 10 centers reporting their results, only 4 centers currently use microelectrode mapping, 1 of the ten having stopped using it after a time[108] (Table 3). Two centers used the five-track multielectrode holder, and one reported that in only two of their five cases did they use the central track.[109] Two centers used serial electrode tracks, one reporting that they used one to five tracks (mean = 2.4 tracks) and only needed to adjust the lateral coordinate.[110] Those centers not using microelectrodes directly implanted the DBS electrode or a macroelectrode. Generally, one track sufficed in the majority of cases (12 of 14 in one center[111]; 1–4; mean, 1.29 in one center[112]; 57% in one center[108]).

### Relationship of Mapping Technique to Outcome

There is no discernable difference in the outcomes reported by groups using or not using microelectrode mapping to implant DBS electrodes in patients with tremor.

## ELECTROPHYSIOLOGICAL MAPPING UNDER GENERAL ANESTHESIA

Although several centers implant DBS leads for dystonia under general anesthesia for reasons of increased risk associated with awake surgery in a stereotactic frame for some of these patients, only rarely is DBS done under general anesthesia for patients with PD or tremor, because of their psychological constitution or psychiatric disease. In such cases, general anesthesia can be considered, accepting the risk of suboptimal outcome. Microelectrode mapping of the globus pallidus has been done under general anesthesia in dystonic patients, although there is some question as to whether pallidal firing rate is affected.[98–100] Notably, it has been possible to observe movement-evoked responses from pallidal neurons in anesthetized patients. Visual evoked potentials can be obtained under general anesthesia to map the optic tract below GPi.[29,31,32] Although stimulation testing for cap-

sular effects can be carried out, the assessment of subjective side effects such as paresthesia or visual phosphenes and the effects of stimulation on clinical symptoms cannot be examined.[32] In Parkinson's disease, there is only one report of the use of general anesthesia coupled to microelectrode mapping. Maltete and colleagues[113] used the five-microelectrode holder to map the STN in a cohort of 15 patients under general anesthesia and compared them to a group done under local anesthesia. The investigators noted no marked difference in the microelectrode recording obtained under general anesthesia as compared to the local anesthetic group, but no further details of the observation were provided. The central track was used in 29 of 30 electrodes under general anesthesia, as compared to 25 of 30 performed awake, likely reflecting a lack of electrode adjustment based on the effects of stimulation on clinical findings. However, in this small group, outcome was only marginally affected (64% decrease in UPDRS motor *off* scores with general anesthesia vs. 73% decrease in the awake group).

## CONCLUSION

Electrophysiological mapping is an essential part of implantation of DBS leads for Parkinson's disease and tremor. Several techniques are available, including microelectrode and semimicroelectrode recording, microstimulation, and macrostimulation. Each one in experienced hands leads to outcomes that appear satisfactory, but given the lack of class I evidence it is impossible to know the relative benefits or risks of each technique. Most studies lack detailed information that allows their comparison to other studies, such as number of tracks performed. Broad dogmatic statements regarding the superiority of one technique over another are thus not possible to substantiate with reliable data. Efforts in the future should be directed at addressing the benefits and risks of alternative techniques with prospectively acquired, detailed comparative studies. In as much as the primary goal of each approach is to maximize outcome, the use of benchmark outcome data, such as benefit derived from DBS with respect to the maximal levodopa response, is encouraged. Complete documentation of the complications of each approach is also mandatory.

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