

High-Frequency Stimulation of the Subthalamic Nucleus for the Treatment of Parkinson's Disease—A Team Perspective



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Abstract: Parkinson's disease (PD) is a debilitating neurodegenerative disorder affecting more than 1.2 million people in the United States. Genetic and environmental toxins are believed to be risk factors in acquiring the disease. PD is characterized by tremors, rigidity, bradykinesia, poor gait, and postural instability. These cardinal symptoms improve with medication such as a levo-dopa (L-dopa). However, over time, as the disease progresses, the patient becomes refractory to medication, or medication produces debilitating side effects. When this occurs or when there are worsening of symptoms, neurosurgical treatment is recommended, particularly deep brain stimulating (DBS) electrodes implanted in the subcortical subthalamic nucleus (STN). Over the last 5 years STN DBS has gained acceptance and become the neurosurgical treatment of choice for PD. To achieve maximum beneficial effects with minimum adverse effects from the surgery, the expertise of an integrated team of physicians and nurses is essential. A clear understanding of the different aspects of the procedure, including the risks and benefits of the treatment, assists neuroscience nurses in communicating with the PD patient, and providing the most appropriate, knowledge-based pre- and postoperative care.

Parkinson's disease (PD) is a neurodegenerative disorder affecting over 1.2 million people in the United States. Most patients are older than 50 years, but 10% are younger than 50. The etiology of PD is multifactorial with genetic and environmental factors combining to reduce dopamine levels in the basal ganglia (Baldereschi et al., 2003; Gasser, 2001; Scott et al., 2001; Tsang & Soong,

2003). The disease is characterized by tremors, rigidity, bradykinesia, postural instability, and gait disability. Some of these cardinal symptoms can be improved by medication such as a levo-dopa (L-dopa). However, as the disease progresses, the medication becomes less effective or produces debilitating side effects. The failure of medical therapy to provide long-lasting relief of symptoms, along with improvement in neuroimaging and neurosurgical stereotactic technique, has prompted a resurgence in the surgical approaches for the treatment of PD. One neurosurgical treatment for PD involves high-frequency stimulation of the subthalamic nucleus (STN). This is achieved through a deep brain stimulating (DBS) electrode implanted in the STN, a small structure (10 x 10.7 x 7 mm; Bejjani et al., 2000) buried deep in the sub-cortex.

This neurosurgical procedure is gaining increasing acceptance. Significant improvement in motor symptoms is reported, as well as a significant reduction in dopaminergic medication with a consequent improvement or elimination of L-dopa induced dyskinesias (Krack et al., 2003). As this cost-effective and reversible procedure becomes the standard neurosurgical treatment of choice for PD, nurses play a pivotal role in the management of pre- and postoperative care of PD patients.

This article reviews the preoperative and immediate postoperative aspects of STN DBS and reports on our experiences with this technique. Seventy-eight DBS STN surgeries (i.e., 48 simultaneous bilateral, 22 staged bilateral, and 8 unilateral) were performed at Presbyterian Hospital of Dallas (PHD) with no mortality and no long-term morbidity. Nearly all patients have had their united PD rating scale (UPDRS) lowered by an average 30%; the medication has been reduced by 30%–60%; and four patients are completely off medication. The long-term effects of DBS for motor symptoms continue to be positive, but the progression of the nonmotor symptoms, particularly behavioral ones, continues over time.

The degree of benefit obtained is critically dependent on a number of factors such as (a) selecting the *ideal* patient, (b) timing the surgery, (c) precisely localizing and implanting a DBS electrode at the target site, (d) programming the stimulator to alleviate motor symptoms while reducing adverse effects of stimulation, and (e)

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providing appropriate postoperative care. By careful optimization of all these variables attained by the interaction of a team comprising a neurosurgeon, neurologist, neurophysiologist, anesthesiologist, operating room nurses, nurse practitioners, and outpatient nurses, it is possible to obtain excellent outcomes with few to no immediate adverse effects.

Patient Selection

With the large number of PD patients being considered for DBS, it has become critical that criteria are established that may effectively predict the outcome of the surgery in advance of the neurosurgical treatment. Although no formal criteria have been selected based on long-term outcome studies, factors such as age, cognition, and disease stage play a significant role in predicting who will obtain maximum benefits from the surgery with the least amount of adverse effect.

To determine whether a patient will have a successful outcome following DBS surgery, four factors are considered. First, the patient must be diagnosed with typical idiopathic PD rather than a Parkinsonian syndrome, which has different neuropathologies (Table 1). The typical idiopathic PD patient presents with asymmetrical symptoms, which may become bilateral and with predominant tremor. Typical PD patients exhibit significantly more improvement in their motor symptoms postoperatively with fewer cognitive side effects following the implantation of DBS electrodes in the STN than atypical patients. Atypical PD patients have more symmetrical symptoms, gait disability, and more pre-existing cognitive impairment and dementia than true idiopathic PD (54% vs. 16.5%; Aarsland, Tandberg, Larsen, & Cummings, 1996). These symptoms do not improve with surgery and may result in cognitive and behavioral complications with stimulation (Saint-Cyr, Trepanier, Kumar, Lozanor, & Lang, 2000). Therefore, a correct diagnosis of PD is essential. In general, clinical misdiagnosis of PD ranges from 8% to 25% (Broggi, Franzini, Marras, Romito, & Albanese, 2003). Because the diagnosis of idiopathic PD can only be confirmed definitively at autopsy, the clinical experience of the movement disorder neurologist is the mainstay of patient selection (Rajput, 1993).

The patient's response to L-dopa predicts whether a patient will have a good outcome after DBS surgery. Symptoms that improve with L-dopa will generally respond to DBS with the exception of tremors. The motor symptoms that persist even with medication, except for dyskinesia, are unlikely to benefit from DBS. For this reason, an L-dopa challenge is recommended before surgery. In this test a supramaximal dose of L-dopa, usually 1.5 times the equivalent dose of the morning medication (Deuschl et al., 2002), is given in the morning after an overnight withdrawal of L-dopa (practically defined 'off'). For those patients intolerant of L-dopa, a long-lasting dopamine agonist such as apomorphine is administered in the challenge test. A 33% reduction in the motor section (subscale III) of the UPDRS to the challenge test is an acceptable positive response to dopaminergic stimulation (Fahn & Elton, 1987). Using this approach, it is possible to distinguish those patients who respond well to the medication and therefore will benefit from DBS from those who are not medication-sensitive and are unlikely to respond to DBS after the operation.

Patient age is another consideration for a successful DBS outcome. The consensus is that the younger the patient, the better the surgical outcome. However, only one study has formally evaluated the effect of age on clinical benefits of DBS. In this study, Saint-Cyr et al. (2000) showed that 6 out of 11 patients had cognitive decline 1 year after the surgery; all were older than 69 years, which suggests that older patients are more susceptible to cognitive decline. Most researchers, therefore, use an age of greater than 70 years (Limousin et al., 1998) or greater than 75 years (Alegret et al., 2001) as their exclusion criterion. Several factors are involved in this age cut-off. These include the greater inability of older patients to tolerate the rigor of the surgical procedure. Also, because of a higher incidence of postural instability and freezing in older individuals (Lang & Widner, 2002), older patients who are considered for DBS implantation must be more intensely scrutinized than younger patients.

Cognitive status is important, and it is prudent to also perform a thorough neuropsychiatric evaluation to rule out dementia, memory disorders, severe depression, and psychiatric disorders. The Core Assessment Program for Surgical Interventional Therapies in Parkinson's disease recommends that a battery of cognitive and behavioral tests (Defer, Widner, Marie, Reny, & Levivier, 1999) be performed to select the best candidates for surgery. Some of these recommended tests were employed to evaluate presurgical levels of depression and dementia, executive functions such as verbal fluency, immediate and delayed memory, reasoning ability, and shift in cognitive strategies. Current data suggest that the presence of these deficits may worsen with DBS. Other exclusion criteria

Table 1. Parkinson's Syndromes and Their Underlying Pathophysiology

Protein Mutation	Parkinson's Syndrome
α -synuclein	Parkinson's disease Diffuse Lewy Body disease
Tau	Fronto-temporal dementia Supranuclear palsy Cortico-basal ganglionic degeneration
Amyloid and Tau	Alzheimer's disease

are abnormal brain scans, defective coagulation and medical comorbidities, instabilities such as uncontrolled diabetes, untreated hypertension, and orthostatic hypotension. The presence of a cardiac pacemaker is also generally considered to be an exclusion criterion unless a computed tomography (CT) can be used in place of magnetic resonance imaging (MRI) to localize the DBS target site. One patient, after medical clearance, had the cardiac pacemaker removed for the STN DBS procedure and then reimplanted after surgery. Conversely, placement of a cardiac pacemaker in patients is not precluded by STN DBS.

Patient Education

After a patient has been selected for DBS surgery, the neurologist and neurology nurse practitioner discuss the beneficial and possible adverse effects of the surgery with the patient and immediate family members. All too often, the patient or a family member, having seen dramatic beneficial effects of the surgery in other patients, has an unrealistic expectation of the surgery. This perception includes an anticipation that all symptoms will be immediately alleviated, an anticipation that there will be no adverse effects, and an anticipation that the patient will be medication free. Therefore, the beneficial effects, as well as risks of DBS and realistic expectation of the surgery, must be equally emphasized so the patient and family have a proper understanding of the surgery.

The patient also receives information on the surgery and a time line on the postoperative programming of the stimulator and neuropsychological testing. The extended time taken for programming is emphasized, sometimes requiring several months after DBS surgery, to achieve an optimization of the stimulation parameters and medication to alleviate motor symptoms while minimizing adverse side effects.

At Presbyterian Hospital of Dallas (PHD), literature and video tapes pertaining to the surgery are given to the prospective patient, who is also encouraged to talk with others who have undergone DBS surgery. With permission, the neurologist and neurology nurse practitioners supply the names and phone numbers of previous patients who have indicated their willingness to talk to potential DBS patients about their positive and negative experience and expectations.

If the patient desires surgery following the meeting with the neurologist, the patient meets the neurosurgeon, who also evaluates the patient for surgery and again discusses (a) the surgical procedure, (b) the patient's expectations of the surgery, and (c) the risks associated with the surgery such as seizures, hallucinations, infection, and stroke. A determination is made whether a unilateral or bilateral implantation is required, based on the patient's symptoms. A unilateral implantation is used if the symptoms are confined to one side only and a bilateral implantation is used if both sides of

the body are involved. After the neurologist and neurosurgeon confer on the patient selection and the patient has requested the surgery, a date is set for surgery.

Preoperative Procedures

Preoperative procedures are similar for all DBS surgeries. A list of all medications, including those obtained over the counter, is obtained, and the patient is instructed not to take any substances that may cause bleeding including aspirin, antiplatelet medications, warfarin (Coumadin), tramadol (Ultracet), or nonsteroidal anti-inflammatory drugs (NSAIDs) as well as over-the-counter supplements such as vitamin E, ginkgo, and ginseng (*Lippincott Nursing Drug Guide, 2003*) for 10 days prior to surgery. Selegeline (Eldepryl) is stopped 7 days prior to surgery to prevent postoperative hypertension, which may be encountered if meperidine (Demerol) is used for pain relief. Preoperative anesthesia assessment of risk is made; the patient's hemoglobin, hematocrit levels, and blood clotting factors are tested; and a chest X ray and electrocardiogram are performed, if needed.

All PD medications are stopped the night before the surgery. This minimizes medication-induced dyskinesia, which may interfere with intraoperative microelectrode recordings and with the assessment of clinical improvement during intraoperative stimulation including the subthalamotomy effect.

Frame Placement

Localization of the STN begins with the placement of stereotactic frame on the patient's head in the operating room. The Leksell G frame (Elekta) is used at PHD, but other frames such as CRW (Radionics) and the COMPASS (Compass International) are also available. The frame is attached rigidly to the skull with sharp titanium pins of appropriate length for the patient's head, under local anesthesia. A mixture of a long-acting 0.25% bupivacaine (Marcaine) and short-acting 2% lidocaine (Xylocaine) is used at PHD. All vital signs are continuously monitored according to the American Society of Anesthesiology standards. The use of ear bars allows for the proper alignment of the frame with the external auditory canals but is reported by patients to be the most uncomfortable portion of the entire surgery. The administration of conscious sedation using midazolam (Versed, < 1.5 mg) or fentanyl (75–100 µg) is recommended. Care is taken to ensure that the x-axis of the frame is perpendicular to the midsagittal plane of the brain and that the y-axis is aligned with an imaginary line connecting the patient's external auditory canal with the inferior orbital rim approximating the anterior commissure-posterior commissure (AC-PC) line. Proper frame alignment is of the utmost importance for targeting the STN, because any deviation from alignment will lead to errors in the stereotactic localization of the STN. Subsequent to frame



Fig 1. Patient, with a stereotactic headframe and an MRI localizer box attached to the frame, ready to undergo MRI. The localizer box is used to add coordinate points to locate the target site in the frame's three-dimensional space.

application, an MRI or CT localizer (fiducial box) is attached to the frame and the patient undergoes either CT or MRI for target localization (Fig 1).

STN Localization

There are differing opinions as to which stereotactic imaging method is most suitable for target determination. CT, MRI, and ventriculography combined with MRI (Krack et al., 2003; Rezai, Hutchison, & Lozano, 1999; Romanelli et al., 2004) are used to determine target coordinates. CT is considered geometrically more accurate and has gradually replaced ventriculography as the standard imaging technique (Krauss & Grossman, 2001). MRI, on the other hand, offers superior anatomic detail of the STN, compared to those seen with CT images, but suffers from nonlinear image distortion. But fusion of

MR and CT images, if available, combines geometric accuracy with anatomic detail.

Localization of the STN can be made using a direct and an indirect method. Direct targeting of the STN involves the direct visualization of the STN and its nuclear boundaries from specific MR T2-weighted coronal or axial fast spin echo inversion recovery pulse sequence images (Bejjani et al., 2000; Rezai et al., 1999; Starr, 2002; Zonenshayn et al., 2000). The indirect method of target localization with CT and MRI is based on coordinates obtained from a standardized human atlas such as the stereotactic atlas of Schaltenbrand and Wahren (1977), with respect to anatomical landmarks, namely, the anterior commissure (AC) and the posterior commissure (PC; Fig 2). In this indirect method of targeting, CT or MR images (1- to 2-mm width slices) are imported into stereotactic surgical targeting software. The SurgiPlan software (Elekta) is used at PHD, because the x, y, and z coordinates can be verified by hand calculations. Other frequently used software packages include Framelink (Medtronic-Sofamor-Danek) and Stereoplan (Radionics). The stereotactic coordinates of the STN are obtained with reference to the midpoint of the AC-PC line: that is, 3 mm posterior to the midpoint of the AC-PC line (y axis), 12 mm lateral from the midline (x axis), and 4 mm below the AC-PC line (z axis; Fig 3). However, because of the small size of the nucleus, its oblique orientation, its variation in its spatial position, and individual variability in the length of AC-PC, the final STN coordinates may be somewhat imprecise. Therefore, relying on this method of targeting alone may result in the misplacement of the DBS electrodes.

There is much debate about the accuracy of targeting the STN using MRI alone. Dormant et al. (1994) and Patel et al. (2003) assert that MRI-guided stereotactic targeting

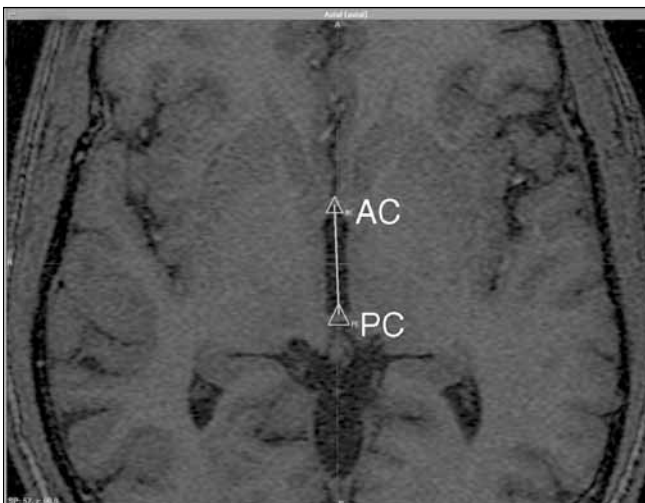


Fig 2. MRI imaging: identification of the anterior commissure (AC) and posterior commissure (AC-PC) on an axial MRI section of the brain.

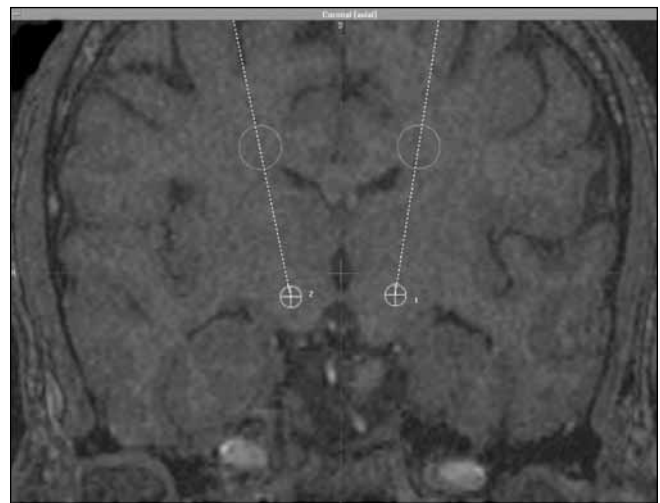


Fig 3. The stereotactic bilateral location of the subthalamic nucleus (cross-hair circles) is shown on a coronal section. The dashed lines indicate the planned trajectory of the electrodes.

alone can be used for the precise localization of the STN with confidence, while others report discrepancies often more than 3 mm between the theoretical coordinates obtained by defining the AC-PC intercommissural line by MRI and the final site of electrode location (Bejjani et al., 2000; Cuny et al., 2003; Guridi et al., 2000; Starr, 2002; Sterio et al., 2002; Zonenshayn et al., 2000). Discrepancies may result from common MRI geometric image distortion, imperfect visualization of the target structure and brain shifts that occur when the dura is first opened for electrode placement. Because of these errors, many centers perform intraoperative neuronal recordings to confirm the position of the target site physiologically.

Lead Placement

After imaging is completed, the patient is brought to the operating room (OR). While the patient is in a semisitting position, the patient's head is shaved, thoroughly cleansed, and prepped for surgery. For some, this hair loss is traumatic; others adapt readily. At PHD, patients are encouraged to wear a cap or scarf if hair loss is embarrassing and then counseled that the lost hair will grow back quickly.

The patient's head frame is attached to the operating table to immobilize the head. Because the patient will be in this position and awake for the next 3–4 hours, every attempt is made to make the patient as comfortable as possible. This includes use of a padded operating table, an indwelling urinary catheter, and warming blankets. Because of immobility, the patient will often experience cramping during the procedure. When this occurs, the circulating nurse, who is present at the bedside to provide comfort, massages the cramping area.

Midazolam and/or fentanyl are administered on an "as needed" basis for the patient's comfort. The use of propofol is avoided

because it increases the incidence of dyskinesia (Krauss, Akeyson, Giam, & Jankovic, 1996). In addition, a prophylactic intravenous dose of fosphenytoin (Cerebyx) is administered to avoid postoperative seizures. A scalp incision is made and a burr hole is drilled just anterior to the coronal suture and 3 cm lateral to the midline suture on the desired side. Oxygen levels and blood pressure are continuously monitored prior to passing an electrode into the brain to prevent hemorrhage. A diltiazem (Cardizem) drip is used at PHD to closely control the blood pressure.

The brain is mapped using a platinum/iridium microelectrode aimed for the STN. It is lowered into the brain using the stereotactic coordinates calculated from the MRI or CT images. Extracellular recordings are

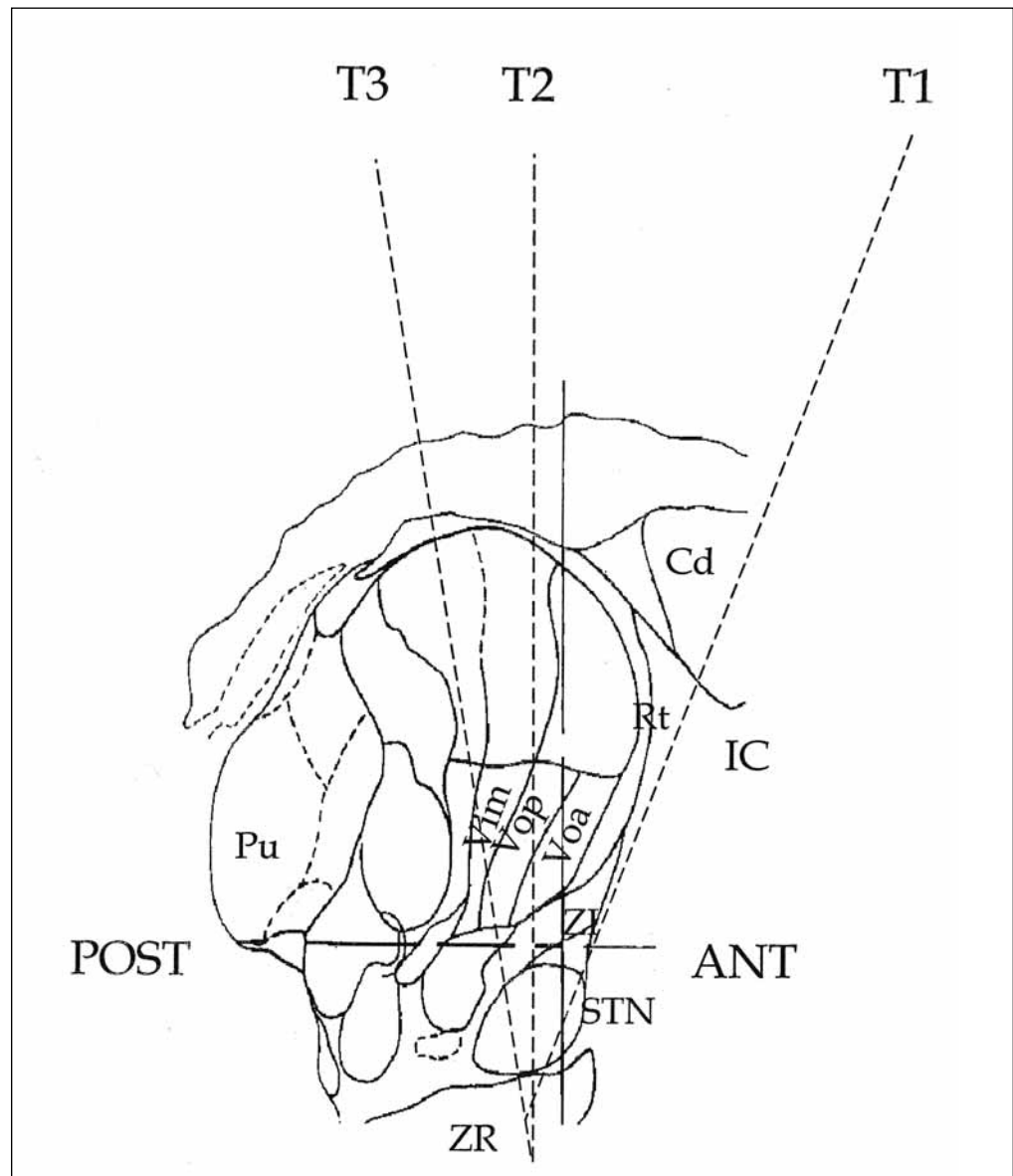


Fig 4. Diagrammatic representation of a sagittal section 12 mm lateral to midline (based on Schaltenbrand & Wahren [1977] stereotactic atlas). Depending on the position of the burr hole and the angle of the electrode trajectories, the electrode passes may be at T1, T2, or T3.

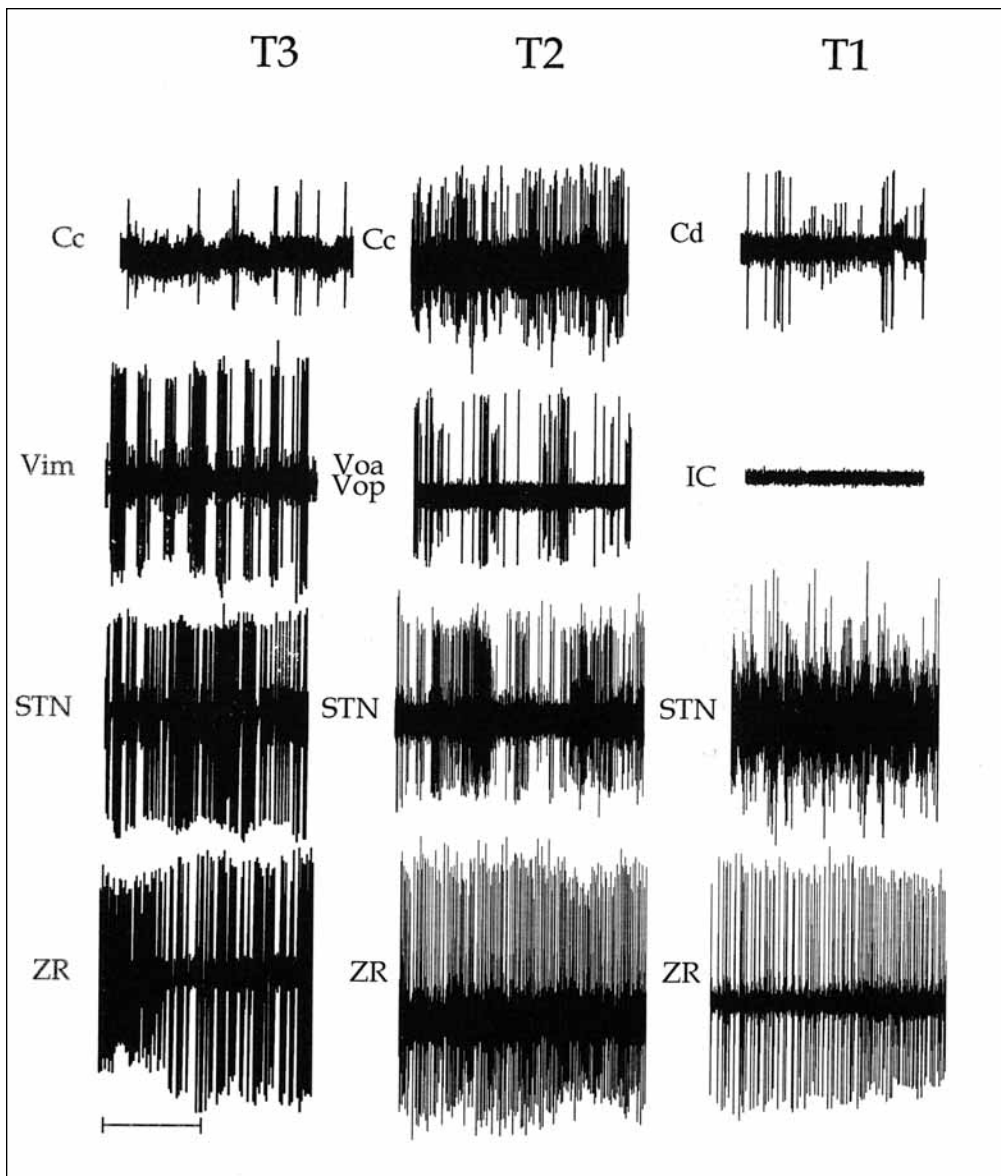


Fig 5. Discharge patterns of neurons encountered in electrode trajectories T1-T3. The time bar equals 1 second in all traces except in the ZR traces where the bar equals 0.25 seconds. Abbreviations are as follows: ANT = anterior, Cd = caudate, IC = internal capsule, POST = posterior, Pu = pulvinar, Rt = reticular thalamic nucleus, STN = subthalamic nucleus, VIM = ventral intermediate thalamic nucleus, VOA = ventro-oralis anterior thalamic nucleus, VOP = ventro-oralis posterior thalamic nucleus, ZI = zona incerta, ZR = zona reticulata.

performed, and neuronal activity is displayed on an oscilloscope and played on an audio monitor. This technique is based on the premise that neurons in one nucleus may be differentiated from neurons in neighboring nuclei by their electrophysiological “signatures” (Figs 4 and 5). Thus, neurons in the STN are distinguished from neurons in the thalamus, zona incerta, and substantia nigra reticulata (SNR) by their discharge rate and discharge pattern.

Electrode trajectory T3 of Fig 5 shows that cortical neurons were encountered greater than 30 mm from target.

before encountering the STN. In general, caudate neurons were slow, irregularly discharging neurons. The characteristic feature of this trajectory was the absence of any neuronal activity but the presence of small amplitude monophasic spikes in the internal capsule. This was in contrast to the high amplitude baseline activity observed when the electrode entered the STN.

Recordings begin approximately 50 mm above the STN, which allows for a complete sampling of neuronal activity from the caudate, through the thalamus to the

The majority of these neurons were generally slow (4–8 Hz) and irregularly discharging in clusters. Thalamic neurons, particularly ventral intermediate thalamic nucleus (VIM) neurons, characteristically discharged with a burst frequency of 4–5 Hz corresponding to the tremor frequency. Neurons in the STN discharged either with a regular, irregular, or bursting discharge pattern, which may or may not be synchronous with the tremor frequency. Neurons in the zona reticulata (ZR) consistently discharge with a high frequency and regular discharge pattern.

Electrode trajectory T2 of Fig 5 shows both ventro-oralis anterior thalamic nucleus (VOA) and ventro-oralis posterior thalamic nucleus (VOP) neurons discharged in an irregular clustering pattern. A second, smaller population of these VOA and VOP neurons (not shown) tonically discharge with a higher frequency. In general, it is difficult to distinguish between the VOA and VOP as well as the dorsal and ventral tiers of the thalamic nuclei solely on their electrophysiological properties.

Electrode trajectory T1 of Fig 5 shows that the most anterior electrode trajectory traversed the caudate nucleus and the internal capsule

STN and SNR. The distance over which neurons characteristic of the STN are encountered is used to determine the width of the STN and to determine whether a second electrode pass is needed.

At least 4 mm of STN recordings are obtained at PHD. If this distance is less than 4 mm or if no neurons characteristic of the STN are encountered, a second electrode pass is made. The coordinates of the second tract are based on observations on neuronal discharge rate and pattern encountered at certain depths of the first electrode pass combined with knowledge of anatomical structures at this level of the brain. For example, if little to no neuronal activity is recorded throughout the electrode tract or if the first encounter of STN neurons is high, the electrode is too anterior and/or too lateral. If the first encounter of the STN neurons is low in the electrode pass or there is a small distance between the ventral border of the thalamus and the STN, the electrode is too posterior. However, if no sensorimotor-related STN neurons are encountered at depths corresponding to the position of the STN, the electrode is too medial. The circulating nurse plays a key role in manipulating the patient's limbs to determine the effect of limb movement on STN neuronal activity. When a patient displays tremors, STN neurons discharging in bursts at a tremor frequency of 4–5 Hz are encountered. When a second pass is required, the aforementioned observations are used to determine the coordinates of the second pass. On occasion, the recording electrode has had to be moved by as much as 2 mm to localize the STN. This represents a 30% difference when compared with the overall size of the STN, which emphasizes the importance of intraoperative recordings in localizing the STN.

The benefits and risks of using microelectrode recording (MER) can be related to the number of electrode passes made to localize the STN. Although MER can optimize the targeting of the STN, the use of too many electrode passes (e.g., more than 3) or an inexperienced neurosurgical team may be detrimental to the clinical outcome. Other factors (e.g., the type of microelectrodes used, the recording equipment utilized, and the depth at which recordings are commenced) vary among centers and do not determine the final clinical outcome.

The safety and risks involved with the use of intraoperative recording to localize the STN continue to be subject to debate. Hariz (2002), in reviewing the literature on MER use, concluded that the technique does not necessarily improve targeting and that *not* using MER is at least five times safer than using it. Others (Pollak et al., 2002; Priori et al., 2003) contend that intraoperative mapping is mandatory because of MRI targeting error and the deviation produced when a microelectrode is inserted into the brain. The consensus is that although MER does lead to a more precise localization of the target site, there is no doubt that multielectrode passes are associat-

ed with a greater hemorrhage risk. In one study (DBS for PD study group, 2001), patients with mean of 2.9 ± 1.8 passes experienced no hemorrhage ($N = 83$), while those with 4.1 ± 2.0 passes to localize the STN, experienced hemorrhage ($N = 13$). At PHD, staff have been able to locate the STN in 78% of STN DBS surgeries ($N = 62$) with one electrode pass; 15% of the surgeries ($N = 12$) have required 2 passes; and 5% ($N = 4$) required 3 passes. With (a) careful and precise targeting using MR or CT images, (b) a good knowledge of the anatomical structures in the vicinity of the STN, and (c) an acceptance of 3.5 mm or greater as the width of the STN, the number of electrode passes made to locate the STN may be kept to a minimum, thus avoiding hemorrhage and infection.

Localization of the STN is also dependent on the verbal patient feedback. The patient is awake during the intraoperative testing stage. For this reason, administration of midazolam or fentanyl should be made only on an as needed basis for the comfort of the patient. Because the sedative effect of these drugs can be cumulative, the use of these drugs can interfere with the patient's cooperation during the surgery and also prolong the recovery period. Difficulty in waking postoperatively has been treated occasionally using flumazenil (Romazicon) and naloxone (Narcan) to reverse the midazolam and fentanyl effects respectively in the recovery room.

After the precise location of the STN is defined, the microelectrode is removed from the guide tube and replaced by a quadripolar DBS lead (Medtronic model 3387) at the same coordinates. The quadripolar lead has four platinum-iridium contacts (#0, #1, #2, and #3), which are 1.5 mm in length, separated by 1.5-mm spaces, which span a length of 10.5 mm covering approximately the entire length of the STN and ventral thalamus. Some neurosurgeons prefer using the DBS lead in which the contacts span a distance of 7.5 mm (Medtronic model 3397). In either case, the ventral tip of the caudal contact zero (0) is set at the depth at which the microelectrode exited the STN as defined by the absence of neurons and a decrease in background activity. A lead holder assembly is attached to the frame, to stabilize and secure the DBS electrode and cannula. A stylet-coupled cannula is then inserted to the target site under fluoroscopic guidance. Subsequently the DBS electrode is lowered to the target and the cannula is removed.

The mere passage of an electrode through the STN may suppress motor symptoms or induce adverse temporary changes because of a "microlesion" effect. Many patients note the immediate cessation of tremor or the relaxation of the limb and the ability to move limbs faster while in the OR.

After the quadripolar DBS lead is placed, it is tested by connecting it to a hand-held pulse generator, which is used to change the desired lead contacts, pulse width, amplitude, and the frequency of stimulation. In this situation, testing is used mainly to determine the voltage thresholds for possible adverse effects rather than the

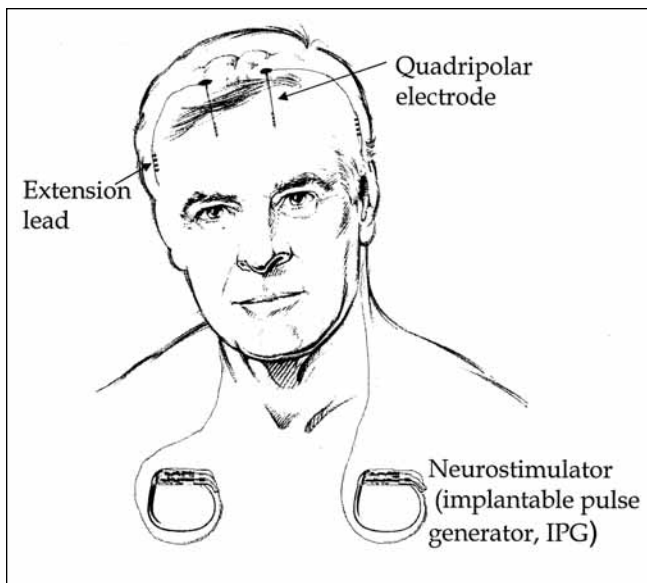


Fig 6. *Diagram of the Activa Therapy Implanted Components consisting of a quadripolar DBS electrode (model 3387), extension lead and the neurostimulator (implantable pulse generator, IPG). The DBS electrode contains four cylindrical platinum/iridium contacts that are 1.5 mm in length and separated from the neighboring contact by an insulated distance of 1.5 mm. (Courtesy of Medtronic, Inc.)*

beneficial effects, which may require several days to become apparent.

In the awake patient, stimulation between the ventral contact 0-, and the most dorsal contact 3+ (i.e., length span of 10.5 mm) is started at 0 V with a pulse width of 60 microseconds and a frequency of 130 Hz, and slowly increased to 3 V. If voltage thresholds below 3 V induce dysarthria or facial muscle contraction, this indicates the DBS electrode is too close to the internal capsule, the largest fiber bundle carrying information from the cortex. If the patient reports the presence of paresthesias, this indicates the DBS electrode is too medial or posterior. The presence of eye deviation indicates the electrode placement is too ventral. If such adverse effects are seen, stimulation between another pair of electrode contacts is tested. Stimulation between contacts that produce the least side effects and maximum beneficial effects is finally used. Following satisfactory testing of the DBS lead, the stimulation is turned off and the lead disconnected. The DBS lead is then anchored to the burr hole, under fluoroscopic guidance, using a burr hole ring-and-cap system. Information on electrode placement and which contacts produce the least adverse effects are relayed to the neurologist and/or the nurse responsible for programming the stimulator for later use.

Regarding bilateral implantation, assuming both right and left sides of the brain are symmetrical, MER on the second side is not performed at PHD. This, and the fact

that the target site is located with 1–2 electrode passes, shortens OR time and enables implantation of bilateral DBS electrodes and bilateral neurostimulators (i.e., implantable pulse generators, IPG; Fig 6) in the chest at one sitting. Some centers prefer staged surgeries, implanting bilateral DBS electrodes at one sitting and the neurostimulators approximately 3 weeks later, under general anesthesia. The latter decreases the time the patient is in the OR at one sitting. In addition, staged surgeries may have significantly better reimbursement.

If bilateral leads are to be placed, a second quadripolar DBS lead is lowered on the contralateral side under fluoroscopic control, at the x, y, and z coordinates. Perfect superimposition of both leads—such that only one lead and the four contacts are seen—indicate the symmetrical placement of both DBS leads (Fig 7). The macrostimulation procedure is repeated to ensure that no adverse effects occur at low voltage thresholds and the subsequent placement and anchoring of the lead is again conducted under fluoroscopic guidance.

The distal ends of both DBS leads are then tunneled under the scalp and the subsequent bilateral placement of the lead extender and neurostimulators are conducted under general desflurane (Suprane) inhalation anesthesia. The implantation of the neurostimulator is conducted with the patient in a supine position. A horizontal incision is made below the clavicle and a subcutaneous pocket is made to house the Soletra neurostimulator (Medtronic, Inc). The distal end of the DBS lead is connected to an extension wire from the patient's head and then tunneled to the infraclavicular opening. The distal end of the extension is connected to the neurostimulator, which is then sutured to the pectoralis fascia to prevent migration. There may be a bulge in the chest and women who want to wear low-cut garments should be made aware of this possibility. Implantation of the neurostimulator in the abdomen is a possibility and should be discussed with the neurosurgeon.

A neurostimulator is similarly implanted on the contralateral side (Fig 7). A new stimulator is now available (Kinetra, Medtronic, Inc.) that may be implanted unilaterally to control bilateral DBS electrodes. Standard wound closure is performed and all wounds are irrigated with antibiotic solutions.

Postoperative Care

Postoperative care requires continuous patient assessment to prevent aspiration and detect weakness, decreased alertness, arrhythmia, trauma, seizures, and acute behavioral changes. If the patient has difficulty waking because of the cumulative effect of midazolam or fentanyl given during the surgery, flumazenil and naloxone hydrochloride, respectively, are used to reverse the sedative effect of the drugs.

Some patients have marked choreiform movement as they wake from surgery. This may last several hours. A

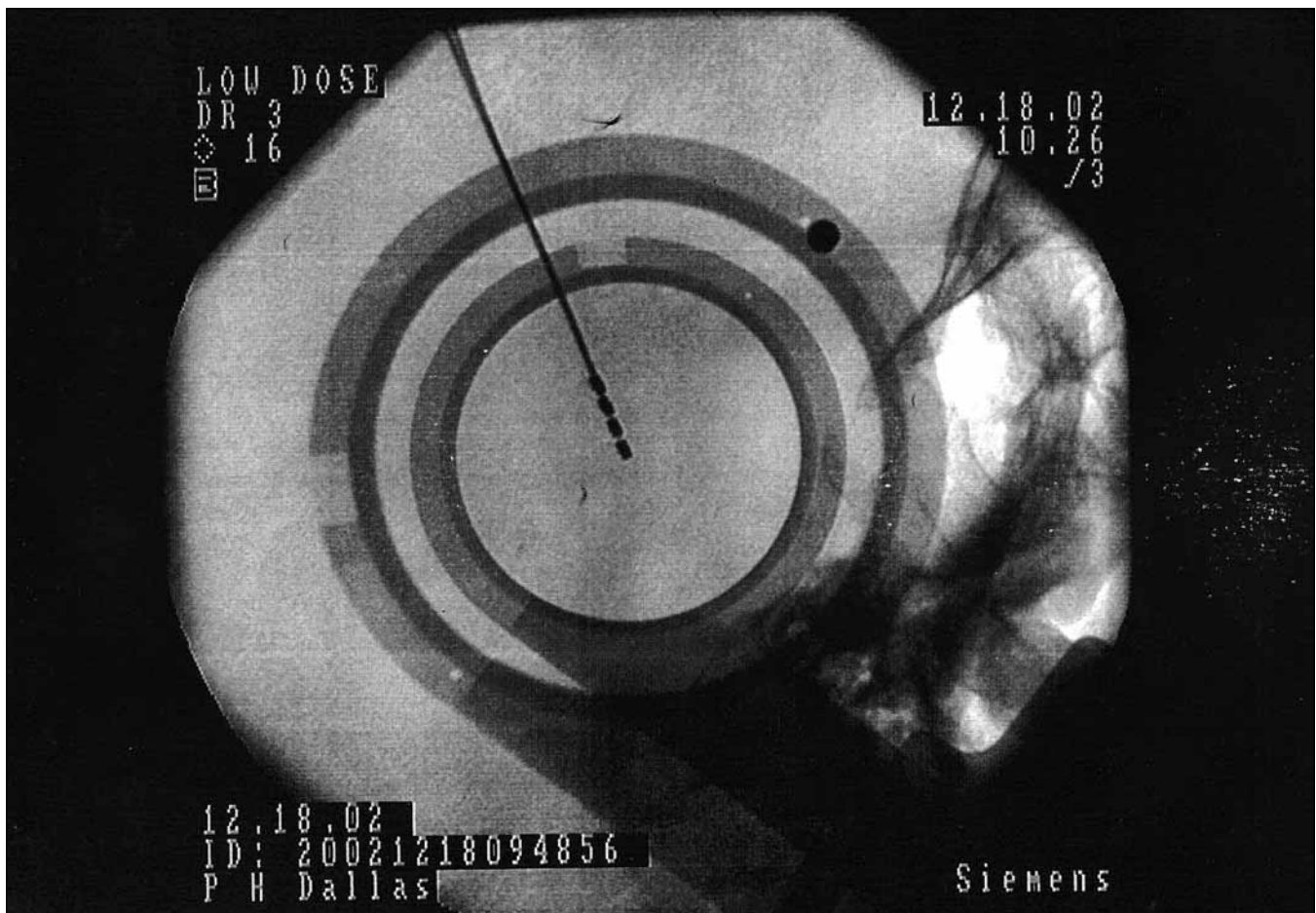


Fig 7. Intraoperative stereotactic radiograph of DBS electrodes in the subthalamic nucleus. Note the complete overlap of the bilaterally placed DBS electrodes and the 4 contacts. The anchoring of the DBS electrode is monitored via fluoroscopy to avoid movement of the electrode. The tips of the DBS electrodes are at target, which is also the center of the stereotactic ring.

small amount of choreiform movement is generally acceptable and indicates the correct placement of the electrode. Hemiballismus, involuntary movements of a sudden, violent and flailing nature are rarely seen. If an intracranial hemorrhage is suspected, a CT scan of the head must be obtained. If the patient is agitated and exhibits psychosis, lorazepam (1–2 mg, every 4 hours) is administered intravenously or quetiapine (25–100 mg) may be taken orally once a day.

Criteria for Discharge from the Recovery Room

Following recovery from anaesthesia, the patient is transferred to the intensive care unit or step-down unit. Anti-PD medication is usually restarted at a reduced amount after the patient is alert and able to swallow. If the patient is unable to swallow, a low dosage of diphenhydramine (Benadryl) is administered intravenously every 6 hours. Postoperative care generally consists of frequent checking on the patient, monitoring of vital signs, and ensuring there is no aspiration. Turning the patient is important because many PD patients have difficulty turning in bed due to muscle rigidity, especially when off the medication.

A CT scan of the head is performed the day after surgery to discover any possible intracerebral hemorrhage and also to confirm lead placement. If the stimulator is turned off and the voltage set to zero, the patient may also have an MRI if necessary. Hemocrit and electrolytes levels are also compared with preoperative values. When stable, the patient can be transferred to the acute care unit.

Motor symptoms may be alleviated immediately after surgery because of the microlesion and edema created by irritation of tissue produced by the mere passage of the electrode into the STN. As this effect wears off, which may last from 1 to 14 days, motor symptoms will return. At the discretion of the neurologist, the patient may restart medication, although the dosage may be significantly lower. Generally, the stimulator is turned on approximately 2 weeks after surgery. However, if the patient experiences tremors that cannot be controlled by medication without dyskinesia, the stimulator can be programmed soon after the surgery, so medication may be reduced to a tolerable level.

The patient may be medically stable but may experience transient confusion, hallucinations and agitation, poor responsiveness, or seizures because of sensitivity to

narcotics and general anesthesia and the process of being taken off the anti-PD medication. Confusion may be controlled by reducing the dosage of carbidopa/levodopa and by avoiding dopamine agonists and amantadine, because of its anticholinergic effect. If the patient is agitated or aggressive, oral or intravenous valproate may be administered (250 mg, every 4 hours). If the patient becomes paranoid or experiences delusions and hallucinations, quetiapine, an atypical antipsychotic, may be used. Potent antipsychotics such as haloperidol should be avoided because of the extrapyramidal side effects. Benzodiazepines such as lorazepam can be used but may cause excessive sedation. Obsessive compulsive behavior, such as picking at the surgical site, may be treated with small doses of quetiapine.

After the patient is on the neurology ward, early ambulation is encouraged to avoid deconditioning. PD patients may be at risk for falls because of the disease, low blood pressure, and medication-related confusion. Therefore blood pressure monitoring for any orthostatic change is essential. As the subthalamotomy effect wanes, which may take between 1 and 14 days, the patient's medication may require adjustment but care must be taken to neither under nor over medicate. Although the majority of the patients may go home, those who are older and with more advanced disease may require inpatient rehabilitation to improve their motor skills with help from a physical therapist. Stimulator programming for these patients will begin in the hospital. If the patient goes home, hydrocodone (Vicodin 50 mg/500 mg) is prescribed for pain on an "as needed" basis and the programming will start as an outpatient at the time of suture removal. Darvocet-N 100 is prescribed if the patient is allergic to codeine.

Summary

Ultimately, the success of any particular patient's DBS surgery may not be attributed to any one factor. However, early and vigorous involvement of a dedicated team, especially highly trained nursing staff in pre- and post-operative care is essential. Careful coordination of all team members performing the surgery itself, programming and balancing of stimulation and medication also contributes greatly to the likelihood of a successful outcome with minimum to no immediate adverse effects. Finally the patient's own positive attitude and a focus on enhancing care and understanding from family, friends, support groups, and the community are also essential for an excellent outcome.

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References

- Aarsland, D., Tandberg, E., Larsen, J.P., & Cummings, J.L. (1996). Frequency of dementia in Parkinson's disease. *Archives in Neurology*, 53(6), 538-542.
- Alegret, M., Junque, C., Valldeoriola, F., Vendrell, P., Pilleri, M., Rumia, J., et al. (2001). Effects of bilateral subthalamic stimulation on cognitive function in Parkinson's disease. *Archives in Neurology*, 58, 1223-1227.
- Baldereschi, M., Di Carlo, A., Vanni, P., Ghetti, A., Carbonin, P., Amaducci, P., et al. (2003). Lifestyle-related risk factors for Parkinson's disease: A population-based study. *Acta Neurologica Scandinavica*, 108, 239-244.
- Bejjani, B., Dormont, D., Pidoux, B., Yelnik, J., Damier, P., Arnulf, I., et al. (2000). Bilateral subthalamic stimulation for Parkinson's disease by using three-dimensional stereotactic magnetic resonance imaging and electrophysiological guidance. *Journal of Neurosurgery*, 92, 615-625.
- Broggi, G., Franzini, A., Marras, C., Romito, L., & Albanese, A. (2003). Surgery of Parkinson's disease: Inclusion criteria and follow-up. *Neurological Sciences*, 24 (Suppl. 1), S38-S40.
- Cuny E., Guehl, D., Burbaud, P., Gross, C., Dousset, V & Rougier, A. (2002). Lack of agreement between direct magnetic resonance imaging and statistical determination of a subthalamic target: The role of electrophysiological guidance. *Journal of Neurosurgery*, 97, 591-597.
- Deep Brain Stimulation for Parkinson's Disease Study Group. (2001). Deep brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. *New England Journal of Medicine*, 345, 956-963.
- Defer, G.L., Widner, H., Marie, R.M., Reny, P., Levivier, M. and the Conference Participants. (1999). Core assessment program for surgical interventional therapies in Parkinson's disease (CAPSIT-PD). *Movement Disorders*, 14, 572-584.
- Deuschl, G., Fogel, W., Hahne, M., Kupsch, A., Muller, D., Oechsner, M., et al. (2002). Deep-brain stimulation in Parkinson's disease. *Journal of Neurology*, 249, 36-39.
- Dormont, D., Zerah, M., Cornu, P., Parker, F., Aubert, B., Sigal, R., et al. (1994). A technique of measuring the precision of an MR-guided stereotaxic installation using anatomic specimens. *American Journal of Neuroradiology*, 15, 365-371.
- Fahn, S., Elton, R. & UPDRS Development Committee. (1987). Unified Parkinson's disease rating scale. In S. Fahn, C. Marsden, D. Calne, M. Goldstein (Eds.), *Recent developments in Parkinson's disease*, (vol 2., pp.153-163). New York: Macmillan.
- Gasser, T. (2001). Genetics of Parkinson's disease. *Journal of Neurology*, 248, 833-840.
- Guridi, J., Rodriguez-Oroz, M.C., Lozano, A.M., Moro, E., Albanese, A., Nuttin, B., et al. (2000). Targeting the basal ganglia for deep brain stimulation in Parkinson's disease. *Neurology*, 55, S21-S28.
- Hariz, M. (2002). Safety and risks of microelectrode recording in surgery for movement disorders. *Stereotactic and Functional Neurosurgery*, 78, 146-157.
- Krack, P., Batir, A., Van Blercom, N., Chabardes, S., Fraix, V., Ardouin, C., et al. (2003). Five-year follow up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *New England Journal of Medicine*, 349, 1925-1934.
- Krauss, J.K., Akeyson, E.E., Giam, P., & Jankovic, J. (1996). Propofol-induced dyskinesias in Parkinson's disease. *Anesthesia & Analgesia*, 83(2), 420-422.
- Krauss, J.K., & Grossman R.G. (2001). Principles and techniques of movement disorders surgery. In J.K. Krauss, J. Jankovic, R.G. Grossman (Eds), *Surgery for Parkinson's disease and movement disorders* (pp. 74-109). Philadelphia: Lippincott Williams & Wilkins.
- Lang, A.E., & Widner, H. (2002). Deep brain stimulation for Parkinson's disease: Patient selection and evaluation. *Movement Disorders*, 17(Suppl 3), S94-S101.

- Limousin, L., Krack, P., Pollak, P., Benazzouz, A., Ardouin, C., Hoffmann, D., et al. (1998). Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. *New England Journal of Medicine*, *339A*, 1105-1111.
- Lippincott nursing drug guide*. (2003). Philadelphia: Springhouse Publishers.
- Patel, N.K., Plaha, P., O'Sullivan, K., McCarter, R., Heywood, P., & Gill, S.S. (2003). MRI directed bilateral stimulation of the subthalamic nucleus in patients with Parkinson's disease. *Journal of Neurology Neurosurgery and Psychiatry*, *74*, 1631-1637.
- Pollak, P., Krack, P., Fraix, V., Mendes, A., Moro, E., Chabardes, S., et al. (2002). Intraoperative micro- and macrostimulation of the subthalamic nucleus in Parkinson's disease. *Movement Disorders*, *17*(3), S155-S161.
- Priori, A., Egidio, M., Pesenti, A., Rohr, M., Rampini, P., Locateli, M., et al. (2003). Do intraoperative microrecordings improve STN targeting in stereotactic neurosurgery for Parkinson's disease? *Journal of Neurosurgical Sciences*, *47*, 56-60.
- Rajput, D.R. (1993). Accuracy of clinical diagnosis of idiopathic Parkinson's disease. *Journal of Neurology Neurosurgery and Psychiatry*, *43*(8), 938-939.
- Rezai, A.R., Hutchison, W., & Lozano, A.M. (1999). Chronic subthalamic nucleus stimulation for Parkinson's disease. In S.S. Rengachary, R.H. Wilkins (Eds), *Neurosurgical operative atlas*. (pp. 195-207). Park Ridge, American Association of Neurological Sciences.
- Romanelli, P., Heit, G., Hill, B.C., Kraus, A., Hastie, T., & Bronte-Stewart, H.M. (2004). Microelectrode recording revealing a somatotopic body map in the subthalamic nucleus in humans with Parkinson's disease. *Journal of Neurosurgery*, *100*(4), 611-618.
- Saint-Cyr, J.A., Trepanier, L.L., Kumar, J., Lozano, A.M., & Lang, A.E. (2000). Neuropsychological consequences of chronic bilateral stimulation of the subthalamic nucleus in Parkinson's disease. *Brain*, *123*, 2091-2108.
- Schaltenbrand, G., & Wahren, W. (1977). *Atlas for stereotaxy of the human brain*. Chicago: Year Book Medical Publishers, Inc.
- Scott, W.K., Nance, M.A., Watts, R.L., Hubble, J.P., Koller, W.C., Lyons, K., et al. (2001). Complete genomic screen in Parkinson's disease. *Journal of the American Medical Association*, *286*, 2239-2244.
- Starr, P.A. (2002). Placement of deep brain stimulators into the subthalamic nucleus or globus pallidus internus: Technical approach. *Stereotactic and Functional Neurosurgery*, *79*, 118-145.
- Sterio, D., Zonenshayn, M., Mogilner, A.Y., Rezai, A.R., Kiprovski, K., Kelly, P.J., et al. (2002). Neurophysiological refinement of subthalamic nucleus targeting. *Neurosurgery*, *50*, 58-69.
- Tsang, F., & Soong, T.W. (2003). Interactions between environmental and genetic factors in the pathophysiology of Parkinson's disease. *International Union of Biochemistry and Molecular Biology Life*, *55*(6), 323-337.
- Zonenshayn, M., Rezai, A.R., Mogilner, A.Y., Beric, A., Sterio, D., & Kelly, P.J. (2000). Comparison of anatomic and neurophysiological methods for subthalamic nucleus targeting. *Neurosurgery*, *47*, 282-294.

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