

# State of The Art: Deep Brain Stimulation in Parkinson's Disease

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*Surgical therapy for Parkinson's disease has a long history beginning in the 1930s with empirical exploration of different brain targets, such as resection of the primary motor cortex or extirpation of the caudate. Recently, there has been a renaissance of functional neurosurgery for the treatment of advanced Parkinson's disease, particularly deep brain stimulation (DBS). To date, DBS of the globus pallidus interna and subthalamic nucleus has been reported to relieve motor symptoms and levodopa-induced dyskinesia in patients with advanced Parkinson's disease. DBS also has different advantages over pallidotomy and subthalamotomy, including reversibility, decreased risk of reoperation and decreased morbidity. In addition to well-experienced neurologists and neurosurgeons, a multidisciplinary team approach is fundamental and critical to ensure success in the DBS procedure in individual patients. With the advances in neuroimaging, neurophysiology and localization techniques, it is increasingly likely that there will be more surgical targets in the future that can also improve cardinal features of Parkinson's disease, or even nonmotor manifestations of this condition.*

**Keywords:** Deep brain stimulation, Parkinson's disease, Globus pallidus interna, Subthalamic nucleus

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Surgical options for movement disorders are rapidly expanding and include ablative procedures, deep brain stimulation (DBS) and transplantation. Although functional neurosurgery for the treatment of Parkinson's disease (PD) has been performed since 1921, neurosurgery was considered an "outmoded" therapy for PD when levodopa was first introduced approximately 30 years ago. In the early 1990s, multiple factors have led to the resurgence of interest in the surgical treatment of PD including dissatisfaction from long-term medical therapy for PD, greater understanding of the pathophysiology of PD and improving techniques, especially advanced neuroimaging and neurophysiological recording resulting in more precise localization of the basal ganglia (BG). Therefore, knowledge about basal ganglia structures and connectivity is critically important to the understanding of

the pathophysiology underlying Parkinson's disease as well as the basis of surgical treatment.

The term *basal ganglia* refers to masses of gray matter deep within the cerebral hemispheres. The term is debatable because these masses are nuclei rather than ganglia, and some of them are not basal, but it is still widely used. Anatomically, the basal ganglia (BG) consists of the caudate nucleus, the putamen (PUT), and the globus pallidus (GP). The internal capsule (IC) runs between the nuclei comprising the basal ganglia, thus imparting a striped appearance. The caudate nucleus, putamen and globus pallidus are collectively termed corpus striatum. The caudate nucleus and putamen develop together and contain similar cells and are termed the striatum. Lateral to the IC, the putamen and globus pallidus abut each other to form a lens-shaped mass termed lenticular nuclei. A medial medullary lamina divides GP into two portions being globus pallidus externa (GPe) and globus pallidus interna (GPi). Functionally, the BG, their interconnections and neurotransmitters form the extrapyramidal

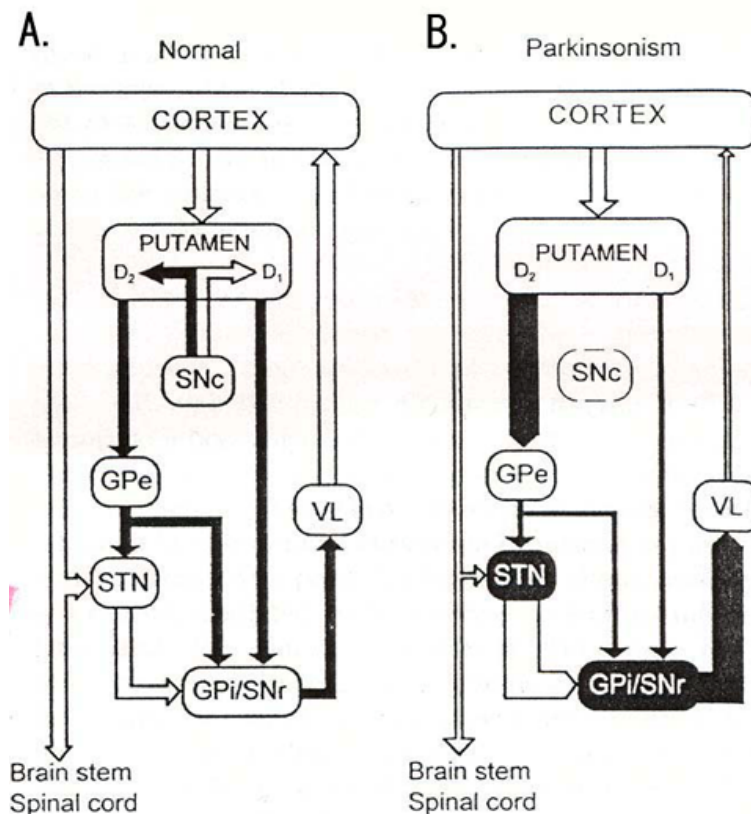
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system, which includes midbrain nuclei such as substantia nigra (SN) and the subthalamic nucleus (STN). The subthalamus is the wedge-shaped subdivision of the diencephalons located ventral to the thalamus and lateral to the hypothalamus. It contains three nuclei: the zona incerta dorsolaterally, the prerubral field dorsomedially, and the subthalamic nucleus ventrally. The fibrous offshoot of the IC that separates the STN from the overlying zona incerta is called lenticular fasciculus. The substantia nigra is the largest nuclear mass of the midbrain consisting of two parts; a more dorsal part that is compact (SNc) and a more ventral part that is reticular (SNr).

The basal ganglia are components of circuits that include the cerebral cortex and thalamus. These circuits originate in specific cortical areas; pass through separate portions of the basal ganglia and thalamus and project back to the frontal cortical area from which they took origin<sup>(1,2)</sup>. The cortical sites of origin of these circuits define their presumed function and include “motor”, “oculomotor”, “associative” and “limbic”. The

motor circuit is particularly important in the pathophysiology of PD<sup>(3)</sup>. This circuit originates in pre- and postcentral sensorimotor areas, which project to the putamen. In each of these circuits, the striatum and subthalamic nucleus serve as the input stage of the basal ganglia and globus pallidus interna (GPi) and substantia nigra pars reticulata (SNr) serve as output stations. Between input and output structures, two major projection systems; direct and indirect pathways have been identified, arising from separate neuronal populations in the striatum (Fig.1). The direct pathway originates from striatal neurons that contain GABA plus the peptide substance P or dynorphin (DYN) and project monosynaptically to the GPi/SNr<sup>(4)</sup>. The indirect pathway arises from striatal neurons that contain GABA and enkephalin (ENK) and whose influence is conveyed to the GPi/SNr polysynaptically through relays in the GPe and STN. Although main neurotransmitter of all striatal output neurons is GABA, the projection from the STN to the GPi/SNr is glutamatergic and excitatory.



**Fig. 1** Drawing diagram of the basal ganglia-thalamocortical circuit. Green arrows: excitatory connections, Red arrows: inhibitory connections. Changes in the widths of the arrows indicate changes in the relative activity of the pathway presented. Wider lines indicate increased activity and vice versa

At the striatal level, dopamine appears to facilitate transmission along the direct pathway and to inhibit transmission along the indirect pathway, these two opposite effects being mediated apparently by D1 and D2 dopamine receptors respectively. The imbalance between the activity in the direct and indirect pathways and the resulting alterations in the GPi/SNr are thought to account for the hypokinetic features of PD (Fig. 1). Bradykinesia or akinesia in PD is postulated to result from increased GABAergic inhibition of thalamic premotor neurons caused by excessive excitatory drive from the STN to the GPi/SNr. The loss of striatal dopamine that characterizes PD is thought to cause a disinhibition of GABA/ENK neurons at the origin of the indirect pathway, which leads to a marked hypoactivity of the GPe, followed by a disinhibition of the STN.

Surgery for movement disorders has been used since 1906 with a cortical resection by Victor Horsley for athetosis<sup>(5)</sup>. Since then, the development of surgery for PD can be separated into two main stages. In the first stage (1912-1947), that of open functional neurosurgery, the surgeon has to gain access to the surgical target structure by cutting away the superficial nervous tissue layers. In the second stage (from 1947), the 'closed' stereotactic functional neurosurgery stage, the superficial tissue layers are preserved. A burr hole is drilled through the skull and with a thin electrode, the calculated target structure

can then be reached with the least possible tissue damage. With the long term treatment of patients with dopaminergic medications, the complications of mainly motor fluctuations and dyskinesias have become evident in the majority of patients. Therefore, the indication for surgical treatment nowadays is aimed to alleviate a severe and highly disabled motor state (Table 1). Currently, there are three types of approaches to surgery for PD; ablative surgery, deep brain stimulation (DBS) and restorative therapies. Both ablative surgery and DBS procedure attempt to compensate for, rather than correct, the biochemical defect in PD. On the contrary, the restorative therapies of intracerebral cell transplantation or growth factor infusion, attempt to correct the biochemical defect of PD by replacing lost dopaminergic neurons or promoting the survival of host dopaminergic cells. However, the restorative therapies are still experimental and restricted to a few research centers.

There are currently three targets for ablative surgery and DBS; the globus pallidus interna (GPi), the subthalamic nucleus (STN) and the motor thalamus (Vim)<sup>(6)</sup>. Surgical destruction of portions of the GPi is called pallidotomy. Pallidotomy has been shown in many studies to be effective for most Parkinsonian motor signs. Destruction of the motor thalamus, called thalamotomy, continues to be performed in selected cases of Parkinsonian tremor or severe essential tremor.

**Table 1.** General considerations on patient selection for movement disorders surgery (Modified from Kumar R, Lang A<sup>(10)</sup>)

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- 1) Patients must have significant disability in performance of activities of daily living or tasks necessary for employment, despite maximal drug therapy.
  - 2) Patients should be in reasonable good health without any specific contraindications to the neurosurgical procedure and have the physical and mental stamina to provide feedback while awake during a procedure. These procedures are usually performed with the patients awake. Patients who are medically ill or debilitated or who have unstable cardiac, pulmonary, renal or liver function, severe hypertension or cancer are poor candidates for surgery. The need for chronic anticoagulation is not necessarily contraindicate surgery although careful perioperative management is required.
  - 3) Patients' biological age, life expectancy and expected duration of benefit should justify the risks of surgery. However, there is not exact age limitation for the procedures.
  - 4) Patients and families should have reasonable expectations of the outcome of surgery.
  - 5) Patients should have a good understanding of the risks of surgery, including especially the risk of hemorrhage or ischemic stroke which may result in serious neurologic disability or death.
  - 6) There should be no controlled psychiatric illness, especially anxiety or mood disorder, which may cause intraoperative patient decompensation that may compromise patients' feedback during the procedure.
  - 7) Patients must not be demented or have significant cognitive impairment. In addition to inability to provide feedback during surgery, demented patients may pose difficulty to program postoperatively as well as lacking insight into their own motor status or inability to manage their own stimulation. Surgery may also worsen cognitive function, especially in patients with pre-existing cognitive deficits.
  - 8) Pre-operative MRI should not reveal severe cerebral atrophy or extensive white matter T2 lesions, which may increase the risk of cerebral hemorrhage.
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The theoretical mechanism for ablative surgery is relatively easy to understand. Destruction of a nucleus eliminates excessive or abnormally patterned activity from that nucleus. On the other hand, the mechanism of action of DBS is still unclear and much more complex than that of lesioning<sup>(7,8)</sup>. Theoretically, a stimulating electrode can activate or inactivate nearby neurons or axons, depending on their morphology, distance from the electrode, baseline discharge rate and exact stimulating parameters. Stimulation could either directly activate cells or axons by depolarization but could also inactivate cells or axons by depolarization blockade. In terms of surgical targets, interruption of activity in the motor region of the GPi should decrease the inhibitory influence of basal ganglia output nuclei on the motor thalamus and restore thalamocortical activity. The STN; however, may be an even more attractive target than the GPi as the STN affects the function of both basal ganglia output nuclei; SNr and GPi. Therefore, interruption of STN activity may potentially alleviate more motor symptoms than interruption of GPi activity alone. Clinically, chronic stimulation of the motor thalamus has well-documented efficacy for tremor, similar to that of thalamotomy. GPi or STN DBS is an exciting new procedure that seems to improve most Parkinsonian motor signs and is probably replacing ablative procedures. Until now, the exact target locations as well as indications for each of these procedures have not been standardized.

#### **Patient Selections and Methods of Assessment:**

Patient selection is one of the most important tasks necessary to ensure a successful outcome from movement disorders surgery. A multidisciplinary team including a neurologist, neurosurgeon and neuropsychologist is often necessary to comprehensively evaluate a patient's suitability for surgery. In general, surgery should be considered for PD in patients with severe medication-refractory motor fluctuations and levodopa-induced dyskinesias, disabling medication-refractory tremor or marked medication intolerance making medical management unsatisfactory. Caution should be noted with respect to hallucinations or other psychiatric symptoms occurring on a low dose of dopaminergic medications as this is often a forewarning sign of subsequent dementia. More comprehensive criteria are provided in Table 1.

Although surgery is considered late in the course of disease after chronic treatment with levodopa, the timing of surgery should be assessed with respect to when the advantages of surgery outweigh the risks

of surgery and the risks of medical treatment. Patient quality of life based on personal, professional, and social factors are important factors that the patient must use to judge the risk/benefit ratio of surgery. On the other hand, the surgery should not be 'too delayed' until the patient's quality of life is severely compromised because of physical disability and loss of independence. A more recent study suggested that STN DBS may alter the course of PD by potentially reducing excitotoxic glutamatergic outflow from the STN to a number of targets, especially SNr although there is currently no clinical data to suggest that this procedure is neuroprotective<sup>(9)</sup>.

Individual evaluation of a possible surgical candidate by each member of multidisciplinary team is critically important in selecting appropriate candidates for surgery<sup>(10)</sup>. A neurologist must ensure that the underlying diagnosis is correct, maximal medical therapy has been provided and the patients still have significant disability. A neurosurgeon should evaluate the patients' general health with regards to surgical risks, neurosurgical contraindications and full discussion with patients and families on possible complications. Neuropsychological evaluation is mandatory in all cases of surgery. The CAPIT (Core Assessment Program for Intracerebral Transplantation), initially developed to evaluate potential candidates for brain grafting, has been adapted for other types of surgeries including ablative and DBS procedures in some centers<sup>(10,11)</sup>. The protocol comprises four clinical rating scales: UPDRS (United Parkinson's Disease Rating Scale), Hoehn & Yahr (H&Y) Staging, Dyskinesia Rating Scale and Self-Reporting Questionnaire, certain timed tests, and number of clinical and imaging evaluations, inclusion and exclusion criteria for patient selection, and definition of 'off', 'on' periods and levodopa responsiveness. However, the CAPIT protocol does not include assessment of cognitive functions and quality of life. Cognitive abnormalities in keeping with the underlying diagnosis of PD should not be a contraindication to the procedure. However, significant deficits that are not normally seen in uncomplicated PD require further evaluation. The authors find it very useful to have regular meetings of the entire multidisciplinary team to discuss results of the evaluation of each patient and make a final recommendation regarding a patient's suitability for surgery as well as types of procedure, which may be most appropriate.

Candidates for surgical treatment of PD are those individuals who have idiopathic PD without

**Table 2.** Patients with following clinical conditions tend to respond poorly to surgical treatment

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- 1) Atypical parkinsonism, e.g. Parkinsonism-plus syndromes
  - 2) Severe brain atrophy or ischemic changes
  - 3) Significant psychiatric illnesses
  - 4) Dementia, more than expected in uncomplicated PD
  - 5) Alcohol abuse
  - 6) Terminal illness or systemic diseases
  - 7) Severely debilitated PD
  - 8) Advanced age (should not be an absolute contraindication)
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evidence of multiple system involvement, such as absence of tremor, the presence of supranuclear gaze palsy, dysautonomia, pyramidal signs, and poor response to levodopa, which may suggest a neurodegenerative disease other than PD. These patients respond poorly to surgical interventions (Table 2)<sup>(12)</sup>. The elderly with severe brain atrophy may pose technical difficulties during surgery and the presence of severe ischemic changes greatly increases operative risk. Patients with severe depression, dementia, or other behavior disorders are usually poor candidates for surgery as their outcome may be difficult to assess. In addition, the lack of insight and poor judgement could impair their full understanding of the relative risks and benefits of surgery. Patients with terminal illness are usually excluded because of limited life span and higher surgical risk of complications. Although the patient's physical and mental health, rather than age is the primary consideration in selection of suitable candidates, most surgeons do not operate on patients above 80 years of age<sup>(11)</sup>.

### Technical Aspects of Surgery

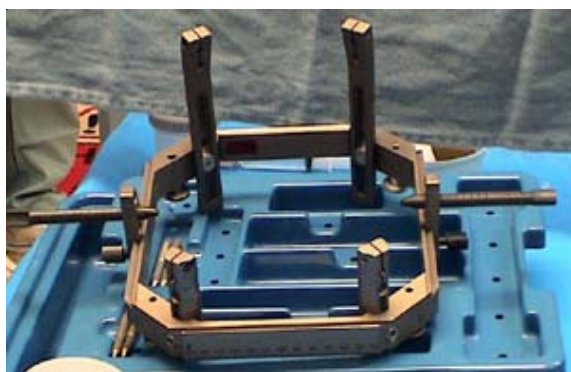
Current surgical therapies for PD are based on the concept of stereotactic surgery, in which the three-dimensional (x,y,z) coordinates of a point in the brain (the target) are established relative to a frame ("localizing ring") secured to the patient's head<sup>(13)</sup>. In addition, other methods have been used to further determine target location before lesioning or stimulator placement including microelectrode mapping and macrostimulation. The initial target is chosen by direct or indirect methods. Ventriculography is the gold standard of imaging for functional neurosurgery. With the advent of modern imaging, target localization with high resolution MRI is highly accurate compared with ventriculography. The indirect method identifies the paraventricular structures in relation to anterior commissure (AC) and posterior commissure (PC). The

indirect target used in posteroventral GPi is 3-5 mm ventral to AC-PC, 19-21 mm lateral to AC-PC line, and 2-3 mm anterior to the midcommissure point (MCP). The indirect target for STN is 11-13 mm lateral to midline, 3-4 mm posterior to MCP and 3-5 mm ventral to AC-PC line. Another method of indirect targeting uses an atlas-based method, commonly Schaltenbrand-Wahren atlas. Direct targeting uses high resolution MRI directly targets at dorsolateral STN. Various techniques were reported by using MRI for direct targeting such as red nucleus (RN), angle formed by internal capsule (IC) and the substantia nigra (SN)<sup>(14,15)</sup>.

Most centers, with the exception of those performing radiosurgical ablations, use physiological confirmation of the target by macrostimulation. Several centers use microelectrode recording and microstimulation to guide placement of the DBS electrode before final confirmation of the lead placement by macrostimulation. The target, which can be motor thalamus, GPi or STN is identified on the radiographic study, usually in relation to intracerebral landmarks such as the anterior and posterior commissures (AC, PC respectively) (Fig. 2). Then the coordinates of the target are calculated in relation to the frame (Fig. 3). The operation is typically performed under local anesthesia and is usually well tolerated by patients. The surgeon makes a small opening (3-10 mm in diameter) in the calvarium and passes a small guide cannula toward the target according to the calculated coordinates to the depth approximately 15 mm above target. Recording, stimulation and/or lesioning electrodes can be inserted through this cannula. The microdrive is used to move the microelectrode toward the target. Proper localization can then be confirmed by using microelectrode recording techniques to study stereotypical neuronal activity at the target site and by observing response to focal electrical stimulation of the brain at the target site, which produces specific motor and sensory responses that can be assessed while the patient is awake<sup>(16,17)</sup>. In general, striatal neurons have very low (0-10 Hz) spontaneous discharge rates. GPe neurons have higher spontaneous rates and typically discharge in burst or pausing patterns. GPi neurons have higher and more regular mean spontaneous discharge rates than do GPe neurons<sup>(17,18)</sup>. Cell with slower activity, border cells, are typically found in the white matter laminae surrounding the GPe and GPi. The optic tract can be identified by light-evoked fiber activity, below the inferior margin of the GPi. Cells in GPi can be responsive to joint movements, usually respond to the movement of one or of a small number



**Fig. 2** Imaging-guided localization of the subthalamic nucleus on sagittal and coronal images



**Fig. 3** Leksell's stereotactic frame

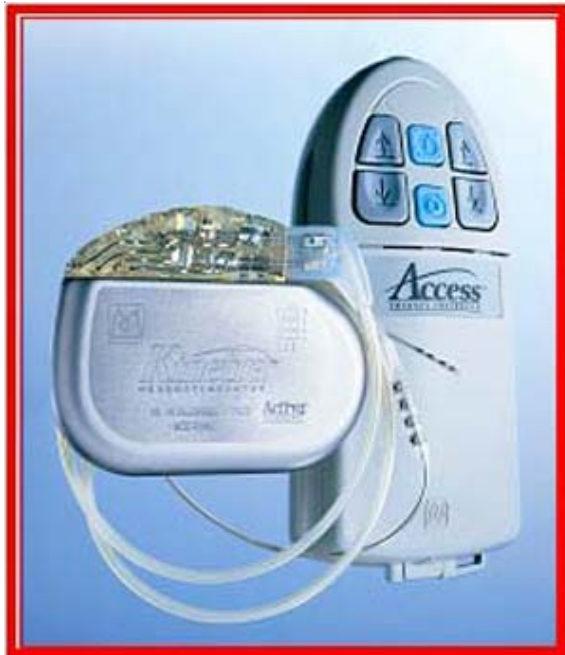
of joints in a restricted region on the contralateral side of the body. STN cells have a characteristic electrophysiology with extremely high background noise and individual cells are difficult to isolate<sup>(16,19)</sup>. The discharge patterns will then change abruptly when the micro-electrode passes through the inferior border of the STN into the SNr.

Once the proper target is confirmed, the surgical intervention is then performed. In ablative procedures, the most common technique for lesion generation is that of radiofrequency (RF) thermocoagulation. Acutely, RF lesioning produces a central zone of coagulation necrosis surrounded by edema. In the brain, temperature greater than 45 °C produces permanent tissue destruction. For DBS procedures, a stimulation electrode is passed through the guide cannula into the target site to provide chronic electrical stimulation of surrounding tissue. The intracranial end

of the electrode has four platinum-iridium contacts, 1.5 mm in length, separated by 1.5 mm (Medtronic, Inc., Model 3387) or 0.5 mm (Medtronic, Inc., Model 3389). This is connected to a battery-operated, programmable pulse generator, which is implanted subcutaneously in the infraclavicular area (Fig. 4). Any single or two contacts may be used for monopolar or bipolar stimulation. The pulse width, stimulation amplitude, and the stimulation frequency, as well as the choice of active contacts and stimulation mode can be adjustable by the physician, using an external programming unit (Fig. 4, 5). Implantation of the pulse generator and extension wire is typically performed under general anesthesia. Once discharged, the patient may turn the stimulator 'on' or 'off' at home or at office using an external magnet (Fig. 6).

#### **What is the best operation for PD?**

In the three different surgical targets discussed, lesioning and stimulation techniques seem to produce similar effects. Thalamic lesioning and DBS are of approximately the same efficacy for tremor with significant improvement at over 80%<sup>(20)</sup>. The lesioning of the STN or GPi also have similar beneficial effects as stimulation. Posteroventral pallidotomy series demonstrated 14-70% improvement in 'off' state UPDRS motor scores following surgery<sup>(21-24)</sup>. In patients treated with pallidal stimulation, turning on the stimulator in the 'off' state improved UPDRS motor scores by 21-35%. However, DBS carries the obvious advantage of being reversible and adjustable and less tissue is destroyed (Table 3). In addition, stimulation is also programmable in order to maximize benefits and minimize



**Fig. 4** A pacemaker-like device containing battery and microelectronic circuit, which is implanted subcutaneously near the clavicle and generates electrical signal that are delivered by the extension lead to the targeted structure deep in the brain. (With permission from Medtronic)



**Fig 6.** Access Review Therapy Controller. The patient can place this compact controller over the neurostimulator and presses buttons to turn the neurostimulator ON and OFF (With permission from Medtronic)



**Fig. 5** Physician programmer. Physicians use the programmer to adjust the stimulation parameters noninvasively (With permission from Medtronic)

adverse effects. The effects of DBS are easy to document objectively, because of varying status of the stimulator ('on' or 'off'), its effect can be readily studied in a double-blinded fashion. Furthermore, DBS preserves options for the patient in the event that in the future, practical and effective therapies emerge from current trials of restorative techniques, for example cell transplantation or growth factor administration. These advantages make bilateral procedure more practical and safe. On the contrary, the hardware for DBS is quite costly and may be associated with complications including hardware infections, breakage and battery changes. In addition, many follow-ups are often required to adjust stimulation setting requiring a large effort by both physicians and patients. DBS procedure may not be appropriate in patients who live far from surgical centers. Although most studies suggested that lesioning and stimulation are equally efficacious, the authors recommend that the choice of stimulation or lesioning should be individualized depending on resources available at the surgical center and a variety of patient specific factors.

**Table 3.** DBS Surgery: Advantages and disadvantages over ablative procedures

Advantages	Disadvantages
<ul style="list-style-type: none"><li>- Reversible</li><li>- Adjustable setting</li><li>- Less tissue is destroyed.</li><li>- Does not exclude patients from future therapies</li><li>- Benefits are easy to document objectively.</li></ul>	<ul style="list-style-type: none"><li>- Expensive</li><li>- Requires expertise and training</li><li>- Available only in major medical centers</li><li>- Time consuming for both physicians and patients for programming and frequent visits</li><li>- Hardware problems can occur as well as infections</li></ul>

Comparing between GPi and STN surgery, there is little published data on direct efficacy comparison of the two procedures. However, both STN and GPi surgery can improve all of the cardinal features of PD, including tremor, bradykinesia, and rigidity in addition to improving levodopa-induced dyskinesias<sup>(25-28)</sup>. Nonrandomized studies suggest that bilateral STN DBS may improve off-period parkinsonism to a slightly greater degree than bilateral GPi DBS<sup>(28-30)</sup>. However, it is probably too premature to exclude GPi as an appropriate target for DBS<sup>(31)</sup>. STN DBS predominantly reduces dyskinesias because of reduction in concomitant drug therapy while GPi DBS or lesioning directly suppresses dyskinesias<sup>(30)</sup>. The STN may be a preferable target in that it is small and easily seen on MRI, has low spatial variability between patients and has good correlation of response to intraoperative stimulation and postoperative benefit. Unlike GPi surgery, bilateral STN DBS allows a marked reduction in antiparkinsonian medications<sup>(25)</sup>.

#### **How to avoid the complications from movement disorders surgery?**

With improvement and refinement of surgical, neurophysiologic and neuroimaging techniques, the results of surgical intervention in the treatment of PD have markedly improved. It is critical; however, that only the most suitable candidates are selected. The importance of good clinical judgement in the diagnosis, selection and optimization of treatment can not be overemphasized. These surgeries, unlike other neurosurgical procedures, are not 'life-saving' operations and the patients still have other choices of treatment if they do not undergo surgery. Furthermore, it is a 'blind' operation performed deep in the brain with local anesthesia on an awake patient. Therefore, careful preoperative work-ups, reliable intraoperative physiological monitoring and investigations as well as detailed information about the patient are critically important to avoid any complications, which can be life-threatening with these procedures.

General, non-target specific complications with these procedures are similar to other stereotactic or device-implanted neurosurgical operations and will not be mentioned here. The authors will discuss those potential side effects and complications that are more or less specific to the specific nucleus or pathways that have been lesioned, stimulated or even missed at surgery. It is very important to mention that these specific side effects, although occurring, are generally transient and will disappear after a few weeks after surgery when the edema resolves or when the stimulations are modified. In addition, the occurrence or not of a complication does not always parallel the success of surgery on the symptom on which the patient has been operated<sup>(32)</sup>. These possible complications should be informed and discussed with the patient preoperatively or even intraoperatively and every attempt should be made in order to avoid its occurrence and minimize its impact on the patient's disability.

Many complications of thalamotomy are fortunately transient, lasting for a few weeks to a month. Leg hypotonia is not uncommon, especially if the lesion encroaches the subthalamic area or zona incerta. A too anterior or too medial thalamotomy can result in contralateral inattention and or apraxia. In thalamic DBS procedure, development of tolerance and appearance of tremor rebound when turning off stimulation are common<sup>(33)</sup>. In most patients with thalamic DBS procedure, stimulation will usually need incremental increase of current parameters to maintain initial effect on tremor. Thalamic DBS if placed too posteriorly may result in sensory paresthesia in fingers and lips. If placed too laterally, it can precipitate dysarthria, muscle cramps and gait disturbances. Fortunately, these symptoms usually subside with a reduction in current voltage or pulse width. Occasionally, low-frequency proximal tremor or ataxia can be observed following thalamic stimulation. Bilateral thalamotomy should be avoided at all costs. Up to 50% of dysarthria, in addition to balance and memory problems, has been reported. On the other hand, bilateral thalamic DBS can be safely performed.



In general, the risks of pallidotomy are less than those of thalamotomy. Unlike thalamotomy, many of pallidotomy complications may not become evident until days or weeks following surgery<sup>(32)</sup>. The risk of cognitive impairment is usually seen if the lesion is too medial, anterior and dorsal in the pallidum as it involves in the striatolimbic fibers. Weight gain, which can be a favorable side effect, is very common following pallidotomy, which can be secondary to a reduction in violent dyskinesias. Optic tract injury may also occur during pallidotomy as it lies just inferior and medial from posteroventral pallidum. Careful macrostimulation and microrecording in order to judge the proximity of the lesioning can avoid this complication. Delayed stroke is a possible, although rare, complication of pallidotomy, leading to hemiparesis or dysarthria in most cases<sup>(34)</sup>. Complications specific to pallidal DBS are usually rare, mostly reversible, and very much dependent on electrode contacts and stimulation parameters. Increased drooling is a common complication following bilateral pallidotomy as well as worsening dysarthria or dysphonia.

STN DBS is usually performed bilaterally, if not in one session. Transient increase in dyskinesias has been reported although most STN procedures will later lead to a decrease in levodopa doses improving the symptoms. Blepharospasm is also a common complication, seen in up to 25% of cases. As the medial part of the STN is involved in cognition, confusion, psychiatric symptoms and memory impairment can occur with the stimulation in this area<sup>(35-37)</sup>. Regardless of which part of STN has been targeted, postoperative confusion is not that uncommon. The authors conclude that STN is probably not a preferred target if the patients already presents with any memory or cognitive decline preoperatively. Hypersalivation has been reported in bilateral STN stimulation.

Although the fundamental defect in the parkinsonian brain is the loss of dopaminergic cells of the SNc, this abnormality results in electrophysiologic imbalance throughout the motor thalamus and basal ganglia. Alteration of neuronal activity, either by ablative surgery or DBS, at different target sites, can improve parkinsonian symptoms and signs in careful selected cases. The importance of good clinical judgment in the diagnosis, selection and optimization of treatment by a multidisciplinary team can not be overlooked. It is critical to select the right surgery for the right patient. Ablative procedures can provide substantial clinical benefits although the current trend is toward DBS surgery. At Chulalongkorn University

Hospital, the authors have established a comprehensive movement disorders program, which also includes a DBS initiative. The authors employ a multidisciplinary approach, comprising of a neurologist, neurosurgeon, psychiatrist, neuropsychologist, neuroradiologist, and movement disorders nurse when evaluating patients for DBS. So far, the authors have performed both STN and GPi DBS in patients with PD and dystonia. There were no immediate complications and the initial results confirmed the efficacy of both procedures. Surgical treatments for Parkinson's disease, although can be very effective, do not permanently correct the underlying pathogenesis of PD and should be reserved for aspects of PD that are not controlled by medication treatment.

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## การผ่าตัดรักษาโรคพาร์กินสันด้วยการฝังอิเล็กโทรด และกระตุ้นด้วยไฟฟ้า

รุ่งโรจน์ พิทยศิริ, ถิรเดช ศรีกิจวิไลกุล, ชัยชน โฉวเจริญกุล, กัมมันต์ พันธุมจินดา, สุรัชชัย เคารพธรรม

การรักษาโรคพาร์กินสันด้วยการผ่าตัดมีมานานตั้งแต่ปี พ.ศ. 2473 เช่นการผ่าตัดส่วนของ Primary motor cortex ออก เพื่อลดอาการแข็ง หรือสั่นในโรคพาร์กินสัน ในช่วงที่ผ่านมา เทคนิคในการผ่าตัดได้มีการเปลี่ยนแปลงไปมาก รวมถึงการพัฒนาในการผ่าตัดด้วยวิธี Deep brain stimulation (DBS) ในผู้ป่วยโรคพาร์กินสัน ในปัจจุบันการผ่าตัดแบบ DBS ในส่วนของ Globus pallidus interna และ Subthalamic nucleus ได้เป็นที่ยอมรับว่าได้ผลดีและชัดเจนในผู้ป่วยโรคพาร์กินสัน ช่วยลดอาการยุกยิก แข็งเกร็ง สั่น และช่วยเพิ่มเวลาการตอบสนองของยานอกเหนือจาก อายุรแพทย์ และศัลยแพทย์ระบบประสาท การรักษาด้วยการผ่าตัดแบบ DBS ในปัจจุบันต้องอาศัยบุคลากรจากหลาย ๆ ฝ่าย ดังเช่น รังสีแพทย์ จิตแพทย์ นักจิตวิทยา และพยาบาล ที่มีความรู้ ความเชี่ยวชาญในเรื่องของการ ผ่าตัด แบบ DBS ที่จะทำงานร่วมกัน เพื่อให้การผ่าตัดเป็นผลสำเร็จ และมีผลดีที่สุดด้วยความก้าวหน้าทางการแพทย์ และการวิจัยในปัจจุบัน มีความเป็นไปได้เป็นอย่างดีว่าจะมีการใช้ตำแหน่งการผ่าตัด รวมถึงวิธีการผ่าตัดใหม่ ๆ ที่จะช่วยรักษาอาการโรคพาร์กินสัน ให้ดีขึ้นกว่าที่ได้ผลในปัจจุบัน