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Surgical Treatment for Parkinson's Disease: Professionals Edition

When should one refer a patient for surgical treatment?

For most patients with Parkinson's disease, levodopa and other medications are effective for maintaining a good quality of life. As the disorder progresses, some patients develop significant motor fluctuations. Often, wearing off and dyskinesias can be managed with changes in the medication regimen (see Medications for Parkinson's disease). When medication adjustments do not alleviate motor fluctuations or when side effects from medications cause significant problems, surgical treatment of Parkinson's disease may be considered. Two recent studies have shown advantages of deep brain stimulation over best medical therapy in appropriated selected patients with Parkinson's disease (Deuschl et al 2009, and Follett et al 2010). Selection criteria for these studies included levodopa responsiveness and persistent disabling fluctuations. Patients were excluded for atypical syndromes, dementia, and continuing drug or alcohol abuse.

What are the different types of surgery for Parkinson's disease?

The different types of surgery for Parkinson's disease are summarized in the table below. Thalamotomy and pallidotomy were the first surgical procedures developed and are brain lesioning procedures. To perform them, the surgeon uses a small heat probe to destroy a small region of brain tissue that is abnormally active in Parkinson's disease. No instruments or wires are left in the brain after the procedure, which produces a permanent effect on the brain. In general, it is not safe to perform lesioning on both sides of the brain. Thalamic surgery is generally reserved for patients with essential tremor and is not recommended for patients with Parkinson's disease. Pallidotomy is the standard ablative procedure.

Neurosurgical procedures for Parkinson's disease

<i>Procedure</i>	<i>Effect of Procedure</i>
Lesioning Procedures	
Thalamotomy (thalamus)	Proven benefit for tremor only
Pallidotomy (globus pallidus)	Proven benefit for tremor, rigidity, bradykinesia, and levodopa-induced dyskinesias. Bilateral procedures are not recommended.
Subthalamotomy (Subthalamic nucleus)	Under development; may reduce tremor, rigidity, bradykinesia, and levodopa-induced dyskinesias. Not recommended for bilateral use.

Deep Brain Stimulation Procedures	
Thalamic (thalamus) stimulation (Vim DBS)	Reduces tremor but not the other signs of Parkinson's disease; approved by U.S. Food & Drug Administration (FDA) in 1997
Pallidal (globus pallidus) stimulation (GPi DBS)	Reduces tremor, rigidity, bradykinesia, dyskinesias, and gait disorder; approved by FDA in 2002
Subthalamic nucleus stimulation (STN DBS)	Reduces tremor, rigidity, bradykinesia, dyskinesias, and gait disorder; approved by FDA in 2002

Deep brain stimulation (DBS) surgery involves placing a thin metal electrode into either the globus pallidus or subthalamic nucleus. A programmable pulse generator is implanted subcutaneously beneath the clavicle. A subcutaneous extension wire connects the pulse generator to the brain electrode. The stimulator can be adjusted during a routine office visit by a physician or nurse. Unlike lesioning, DBS does not destroy brain tissue. Instead, it reversibly alters the function of the brain tissue in the region of the stimulating electrode. Although DBS is a major advance, it is a more complicated therapy that may demand considerable time and patience before its effects are optimized.

What are the possible brain targets for DBS?

There are now three possible target sites in the brain that may be selected for placement of stimulating electrodes:

- the globus pallidus (GPi),
- the subthalamic nucleus (STN),
- the thalamus (the specific region is the ventro-intermediate nucleus or Vim)

As part of the basal ganglia circuitry, these anatomic locations play a critical role in the control of movement. The effects of stimulating these brain regions are indicated in the Table. Thalamic (Vim) stimulation is only effective for tremor, not for the other symptoms of Parkinson's disease. Stimulation of the globus pallidus or subthalamic nucleus, in contrast, may benefit not only tremor but also other parkinsonian symptoms such as rigidity, bradykinesia, dyskinesias, and gait problems. For most patients with Parkinson's disease, DBS of the globus pallidus or subthalamic nucleus are more appropriate choices than thalamic DBS because stimulation at these targets affects a broader range of symptoms. A recent study compared the outcomes of 300 patients who were randomized to deep brain stimulation of either the globus pallidus interna or subthalamic nucleus (Follett et al 2010). Two years after surgery, there was no clear advantage to either location. Patients undergoing subthalamic stimulation required a lower dose of dopaminergic agents than did those undergoing pallidal stimulation. One component of processing speed declined more after subthalamic stimulation group, and the level of depression worsened somewhat after subthalamic stimulation and improved after pallidal stimulation. Serious adverse effects occurred at similar rates.

How does DBS work?

In Parkinson's disease, loss of dopamine-producing cells leads to excessive and abnormally patterned activity in both the GPi and the STN. "Pacing" of these nuclei with a constant, steady-frequency electrical pulse corrects this excessive and abnormal activity. DBS does not act directly on dopamine producing cells and does not affect brain dopamine levels. Instead, it compensates for one of the major secondary effects of dopamine loss, the excessive and abnormally patterned electrical discharge in the GPi or the STN. The mechanism by which the constant-frequency stimulation pulse affects neuronal function has not been determined.

How is the surgery performed?

The procedure for implanting a brain electrode varies somewhat from one medical center to another. Typically these operations are performed with the patient awake, using only local anesthetic and occasional sedation. The basic surgical method is called stereotaxis, a method useful for approaching deep brain targets through a small skull opening. For stereotactic surgery, a rigid frame is attached to the patient's head just before surgery and an MRI is obtained with the frame in place. The images of the brain and frame are used to calculate the position of the desired brain target and guide instruments to that target with minimal trauma to the brain.

Then, the patient is taken to the operating room. At that point sedative medication is given and a patch of hair on top of the head is shaved. After local anesthesia of the scalp, an incision is made on top of the head behind the hairline and a small craniotomy (1.5 cm) is performed. At this point, all intravenous sedatives are turned off so that the patient becomes fully awake.

To maximize the precision of the surgery, some surgical teams employ a brain-mapping procedure in which fine microelectrodes are used to record brain cell activity in the region of the intended target to confirm that it is correct, or to make very fine adjustments of 1 or 2 mm in the intended brain target if the initial target is not exactly correct.

Once the target site has been confirmed by microelectrode recording, the permanent DBS electrode is inserted. After the DBS electrode is inserted and tested, the patient is sedated. The electrode is anchored to the skull with a plastic cap, and the scalp is closed with sutures. The patient then receives a general anesthetic for the placement of the pulse generator in the chest wall and positioning of a connecting wire between the brain electrode and the pulse generator unit. This part of the procedure takes about 40 minutes and is sometimes performed at a second operation.

Would both sides of the brain be done at once or separately?

DBS on one side of the brain mainly affects symptoms contralaterally. Many patients have symptoms bilaterally. DBS leads can be placed on one side or both sides on the same operating day. The decision to place one or two stimulators in one operating day is made according to a patient's symptoms and general health. For elderly patients, or patients concerned about a longer operation, it may be best to stage the procedures a few weeks or months apart.

What are the benefits of DBS surgery?

The major benefit of surgery for Parkinson's disease is that it improves the off-medication state so that it is more like the on-medication state. In addition, it may reduce levodopa-induced dyskinesias. The procedure is most beneficial for patients with Parkinson's disease who cycle between states of immobility ("off" state) and states of better mobility ("on" state). Surgical treatments "smooth out" these fluctuations so that there is better function during of the day. Symptoms that improve with levodopa (slowness, stiffness, tremor, gait disorder) may also improve with DBS. Symptoms that do not respond at all to levodopa usually do not improve significantly with DBS. Following DBS of the STN, there may be a reduction, but not elimination, of antiparkinsonian medications. At present, we believe that DBS only suppresses symptoms and does not alter the underlying progression of Parkinson's disease. In addition to improvements in motor function, recent studies show improvements in quality of life measures for subjects randomized to DBS compared to those randomized to best medical therapy (Deuschl et al 2006; Weaver et al 2009).

What are the risks of DBS surgery?

The most serious potential risk of the surgical procedures is a cerebral hemorrhage, producing a stroke. This risk varies from patient to patient, depending on the amount of brain atrophy and the general medical condition, but the average risk is about 2%. If stroke occurs, it usually occurs during or within a few hours of surgery. The effects of stroke can range from mild weakness that recovers in a few weeks or months to severe, permanent weakness, intellectual impairment, or death.

The second most serious risk is infection, which occurs in about 4% of patients. If an infection occurs, it is usually not life threatening, but it may require removal of the entire DBS system. In most cases, a new DBS system can be re-implanted when the infection is eradicated. Finally, in 10-20% of patients, hardware may break or erode through the skin with normal usage, requiring it to be replaced.

In the first few days after surgery, it is normal to have some temporary swelling of the brain tissue around the electrode. This may produce no symptoms, but it can produce mild disorientation, sleepiness, or personality change that lasts for up to 1-2 weeks.

What factors predict whether a patient will obtain benefit from surgery?

Improvement after surgery correlates with preoperative levodopa responsiveness and younger age. Patients with dementia or atypical parkinsonism do not typically benefit from surgical treatments.

Can patients control the DBS device themselves?

Following DBS surgery, the patient is given the Medtronic Access Review unit, a hand-held battery-operated unit that can be used to determine if the device is on or off, to turn it on or off, and to check battery life. The device may also be programmed to allow patients to adjust

stimulation parameters according to limits set by the programming physician. Normally, in DBS for Parkinson's disease, the device is left on all the time. The newest generation of DBS devices offers a rechargeable system (using external charging pads for those subjects who require high power settings and stimulators with longer battery life.

Is DBS surgery covered by health insurance?

Medicare and many private insurers now cover DBS for Parkinson's disease.

Are "restorative therapies" available?

Many patients inquire about "restorative" therapies, a category of procedures that includes transplantation of fetal cells or stem cells, growth factors, or gene therapy. The goal of most of these procedures is to correct the basic chemical defect of Parkinson's disease by increasing the production of dopamine in the brain. Although theoretically very attractive, more experimental work must be done in order to make these therapies practical and effective. Phase 1 have been conducted for 3 different gene therapies and phase 2 studies have either been completed or planned to test these therapies against sham surgical control subjects. There have been no studies of stem cell treatments for PD thus far.

Summary

The surgical treatment options for patients with Parkinson's disease are expanding. DBS surgery offers important symptomatic relief in patients with moderate disability from Parkinson's disease who still retain some benefit from antiparkinsonian medications and who are cognitively intact. Patients who fluctuate between "on medication" and "off medication" states are usually good surgical candidates. The major risk is a 2% risk of stroke, due to bleeding in the brain. DBS requires regular neurological follow-up and periodic battery changes. It reduces, but does not eliminate, symptoms of Parkinson's disease. The time to consider DBS surgery is when quality of life is no longer acceptable on optimal medical therapy as administered by an experienced neurologist.

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