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Surgical Treatment: Patient Edition

When should one consider surgical treatment?

For most people who have Parkinson's disease, levodopa and other medications are effective for maintaining a good quality of life. As the disorder progresses, however, some patients develop variability in their response to treatment, called "motor fluctuations." During an "on" period, a person can move with relative ease, often with reduced tremor and stiffness. "Off" periods describe those times when a person is having more difficulty with movement. A common time for a person with Parkinson's disease to experience an "off period" is just prior to taking the next dose of levodopa, and this experience is called "wearing off."

Another form of motor fluctuation is uncontrolled abnormal movement of the face, body or a limb, which is called "dyskinesia." For most people with Parkinson's disease, wearing off and dyskinesias can be managed with changes in medications (see Medications for Parkinson's disease). However, when medication adjustments do not improve mobility or when side effects from medications cause significant problems, surgical treatment may be considered.

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. The first surgical procedures developed were the "ablative" or "brain lesioning" procedures. Examples of lesioning surgery include thalamotomy and pallidotomy. In lesioning, a 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 and it 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.

Overview of neurosurgical procedures for Parkinson's disease

Procedure	***Effect of Procedure***
Lesioning Procedures	
Thalamotomy (thalamus)	Proven benefit for tremor only
Pallidotomy (globus pallidus)	Proven benefit for tremor, rigidity, bradykinesia, and levodopa-induced dyskinesias. Not recommended for use on both sides of the brain.

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, dyskinesia, and gait disorder; approved by FDA in 2002
Subthalamic nucleus (STN DBS)	Reduces tremor, rigidity, bradykinesia, dyskinesia, and gait disorder; approved by FDA in 2002

Most surgical teams now prefer an alternative treatment called deep brain stimulation (DBS). DBS surgery involves placing a thin metal electrode (about the diameter of a piece of spaghetti) into one of several possible brain targets and attaching it to a computerized pulse generator, which is implanted under the skin in the chest (much like a heart pacemaker). All parts of the stimulator system are internal; there are no wires coming out through the skin. To improve control of symptoms, the stimulator can be adjusted during a routine office visit by a physician or nurse using a programming computer held next to the skin over the pulse generator. Unlike lesioning, DBS does not destroy brain tissue. Instead, it reversibly alters the abnormal function of the brain tissue in the region of the stimulating electrode. Although deep brain stimulation is a major new 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), and the thalamus (the specific region of thalamus is called "Vim" (ventro-intermediate nucleus). These structures are small clusters of nerve cells that play critical roles 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 (muscle stiffness), bradykinesia (slow movement), 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.

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 nearby brain cells has not been determined.

How is DBS 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 though a small skull opening. For stereotactic surgery, a rigid frame is attached to the patient's head just before surgery, after the skin is anesthetized with local anesthetic. A brain imaging study (usually 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.

After frame placement, MRI, and calculation of the target coordinates on a computer, 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 giving local anesthetic to the scalp to make it completely numb, an incision is made on top of the head behind the hairline and a small opening (1.5 centimeters, about the size of a nickel) is made in the skull. 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. The brain mapping produces no sensation for the patients, but the patient must be calm, cooperative, and silent during the mapping or else the procedure must be stopped. The brain's electrical signals are played on an audio monitor so that the surgical team can hear the signals and assess their pattern. Since each person's brain is different, the time it takes for the mapping varies from about 30 minutes to up to 2 hours for each side of the brain. The neurological status of the patient (such as strength, vision, and improvement of motor function) is monitored frequently during the operation, by the surgeon or neurologist.

Once the target site has been confirmed by microelectrode recording, the permanent DBS electrode is inserted. After the DBS electrode is inserted and tested, intravenous sedation is resumed to make the patient sleepy. The electrode is anchored to the skull with a plastic cap, and the scalp is closed with sutures. Either at this time or at a second operation, the patient receives a general anesthetic and is completely asleep for the placement of the pulse generator in the chest and positioning of a connecting wire between the brain electrode and the pulse generator unit. This part of the procedure takes about 40 minutes.

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

DBS on one side of the brain mainly affects symptoms on the opposite side of the body. Many patients have symptoms on both sides. DBS leads can be performed on one side or both sides of the brain 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 perform the procedures a few weeks or months apart.

What are the benefits of DBS surgery?

The major benefits of surgery for Parkinson's disease are

- improved movement in the off-medication state (increases on time)
- reduced levodopa-induced dyskinesias
- possible reductions in medications

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 throughout 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, it may be possible to reduce antiparkinsonian medications. At present, we believe that DBS only suppresses symptoms and does not alter the underlying progression of Parkinson's disease.

What are the risks of DBS surgery?

The most serious potential risk of the surgical procedures is bleeding in the brain, producing a stroke. This risk varies from patient to patient, depending on the overall 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.

Some additional risks are:

- 4% risk of infection, usually not life threatening, that may require removal of the entire DBS system
- 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
- Breakage or erosion of hardware through the skin with normal usage, requiring it to be replaced

What makes a patient a good candidate for surgical treatment?

Deciding whether a person is a good candidate for surgical treatment is best determined by an evaluation with a neurologist or neurosurgeon familiar with the surgical treatment of Parkinson's disease. In reviewing the outcome of many people who have undergone surgical treatment, the people who derive the most benefit have

- good general health
- normal intellectual and memory function for their age
- benefit (however short) from levodopa

Can patients control the DBS device themselves?

Following surgery, the patient is given a stimulator control 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. Some control units also allow the patient to alter the intensity of stimulation but further programming is usually performed in the physician's office. Normally, the device is left on all the time. The next generation of DBS devices allows some stimulators to be recharged while implanted using an external charging pad.

Is DBS surgery covered by health insurance?

Medicare and almost all private insurers in California now cover DBS for Parkinson's disease. Insurance approval is sought prior to hospital admission.

Other surgical treatments: restorative therapies

Many patients inquire about the "restorative" therapies, a category of procedures that includes:

- transplantation of fetal cells
- transplantation of stem cells
- infusion of growth factors
- gene therapy which may be used to deliver growth factors or enzymes to the brain

The goal 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, much more laboratory work must be done in order to make cell transplantation therapies practical and effective. At this time, the restorative therapies are experimental and are not available as treatment. Several gene therapy studies are being conducted to determine whether they are safe and beneficial.

Summary

There are more medical and surgical treatment options for patients with Parkinson's disease than ever before. Deep brain stimulation surgery offer important symptomatic relief to 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 is a more complex therapy requiring 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.