MAYFIELD CLINIC & SPINE INSTITUTE

Surgery for Parkinson's Disease
advanced level

Overview
The surgical treatment of Parkinson's disease (PD) and other movement disorders prevailed in the 1950s and 60s but declined after effective medications were developed in the late 60s. The return of surgical treatments (pallidotomy and thalamotomy) for movement disorders in the 1990s resulted from advances in the understanding of these disorders, development of sophisticated surgical tools, and the decrease of medication effectiveness, which occurs over time as a result of tolerance or side effects. Even more promising is the development of deep brain stimulation (DBS), which is like a pacemaker for the brain. These surgical procedures can help treat the symptoms caused by the following movement disorders:

- **Parkinson's disease:** tremor, rigidity, and slowness of movement caused by the premature aging and death of dopamine-producing nerve cells in the brain.
- **Essential tremor:** involuntary rhythmic tremors of the hands and arms, occurring both at rest and during purposeful movement. Also may affect the head in a "no-no" motion. Often an inherited condition.
- **Dystonia:** involuntary movements and prolonged muscle contraction, resulting in twisting or writhing body motions, tremor, and abnormal posture. May involve the entire body, or only an isolated area. Spasms can often be suppressed by "sensory tricks," such as touching the face, eyebrows, or hands.

What is Parkinson's disease?
Parkinson's disease (PD) is a slowly progressive, degenerative disease of the brain. It affects nerve cells in areas of the brain called the basal ganglia and substantia nigra (Fig. 1). Nerve cells in the substantia nigra produce dopamine, a neurotransmitter that acts as a chemical messenger in brain circuits important for planning and controlling body movement. For reasons not yet understood, the dopamine-producing nerve cells of the substantia nigra die off prematurely in some individuals.

When dopamine receptors in the striatum are not adequately stimulated, parts of the basal ganglia are either under- or over-stimulated. In particular,

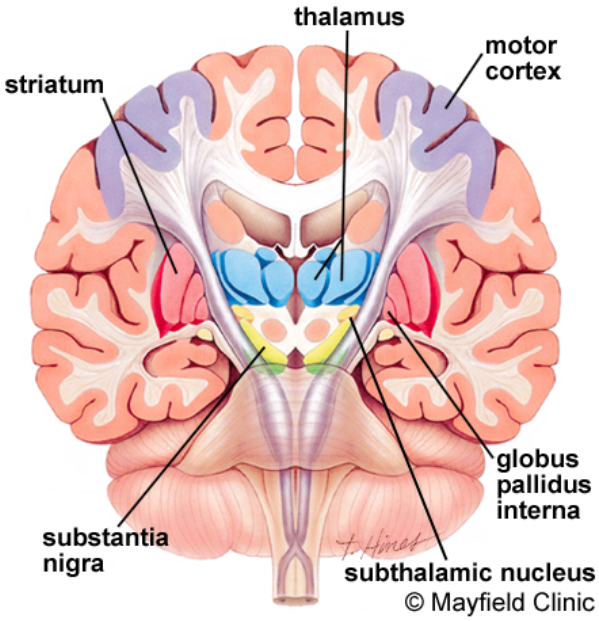

Figure 1. A cross section of the brain. The basal ganglia are responsible for activating and inhibiting specific circuits or feedback loops.

the subthalamic nucleus (STN) becomes overactive and acts as an accelerator on the globus pallidus interna (GPi). The overstimulation of the GPi has an over-inhibitory effect on the thalamus, which in turn decreases its output and causes slowing of motion, and rigidity.

The action of dopamine is balanced by another neurotransmitter called acetylcholine. In PD the nerve cells that produce dopamine are dying. The PD symptoms of tremor and stiffness occur when the nerve cells fire and there isn't enough dopamine to transmit messages. High levels of glutamate, another neurotransmitter, also appear in PD as the body tries to compensate for the lack of dopamine.

When 80% of dopamine is lost, symptoms such as tremor, slowness of movement, stiffness, and balance problems occur. Medications are the first line of treatment to alleviate symptoms of PD. When medical management fails, surgical therapies can be used to treat the symptoms of tremor and rigidity.

Am I a candidate for surgery?

If you have PD, you should consider surgery when your medicine becomes insufficient in controlling your symptoms, if you experience severe ups and downs ("off-on" fluctuations), or if your tolerability of the medication is poor and you develop side effects, including dyskinesias (excessive wiggling of the torso, head, and/or limbs). You should **not** consider surgery if you have severe depression, advanced dementia, or an unstable medical condition, or if you have symptoms that are atypical for PD and that may represent atypical parkinsonism or "Parkinson's plus," such as progressive supranuclear palsy or multiple system atrophy. It is important to understand that surgery will **not** eliminate your need for medication; it will help make your symptoms less severe so that lower doses may be used.

Before determining whether surgery is an option, your condition will be thoroughly evaluated and assessed. A neuropsychologist will assess your thinking and memory and a neurologist will review your current medication regimen and evaluate your physical condition using the Hoehn and Yahr scale and the Unified Parkinson Disease Rating Scale (UPDRS), which examine:

1. mentation, mood, and behavior
2. activities of daily living
3. motor function
4. motor complications (wearing off and dyskinesias)

What surgical options are available?

Several surgical options are available for the treatment of PD and other movement disorders. Each procedure targets a specific structure in the brain that is causing the uncontrollable symptoms. Because the left side of the brain controls the right side of the body and vice versa, these procedures may need to be performed on both sides of the brain. Pallidotomy and thalamotomy are currently performed less often given the safety and efficacy of deep brain stimulation:

Deep Brain Stimulation (DBS)

In deep brain stimulation (DBS), an electrode is implanted in the desired area of the brain (subthalamic nucleus, globus pallidus, or thalamus), and then connected to a pulse generator/battery that is implanted under the skin below the collarbone (Fig. 2). The generator sends electrical signals to regulate activity in the desired structure in the brain. DBS works like a pacemaker to the brain. The doctor can control the stimulation parameters with an external computer, which programs the pacemaker. Because DBS does not permanently destroy any structure of the brain, it is reversible if the symptoms change as the disease progresses or if future therapies require preservation of these structures.

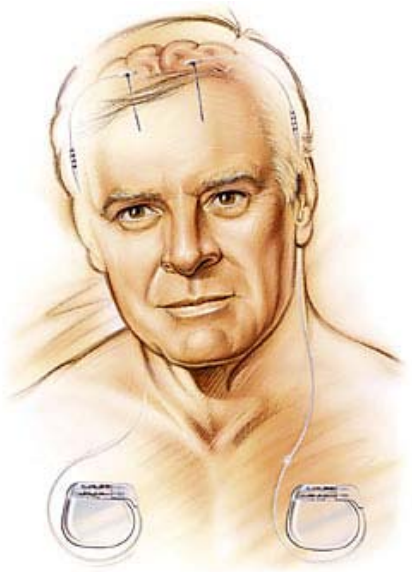

Figure 2. A deep brain stimulator electrode is placed in the desired structure of the brain. The electrode is connected to a battery implanted under the skin below the collarbone. The patient is able to turn the generator off and on with a handheld control magnet. (illustration: Medtronic Inc.)

Subthalamic nucleus and globus pallidus stimulation control slowness of movement, tremor, rigidity and can also improve dyskinesias in patients with PD. Globus pallidus stimulation can help patients with different forms of dystonia as well. Thalamic stimulation is mostly used for patients with essential tremor or other types of tremor.

Pallidotomy

The structure targeted is the internal portion of the globus pallidus (GPi), which is about the size of a tic tac deep inside the brain. The surgeon carefully destroys the GPi by passing a high-frequency energy current through it and heating it to a desired temperature. The procedure is mostly used to relieve dyskinesias caused by higher doses of medication.

Thalamotomy

The structure targeted is the posterolateral part of the thalamus, which lies almost in the center of the brain. The surgeon destroys the structure by passing a high-frequency energy current through it and heating it to a desired temperature. The procedure relieves the symptoms of tremor but given its limited effect on rigidity and dyskinesia, is only used in certain cases.

Transplantation

In transplantation, fetal tissue (either human or pig) is implanted in a structure called the caudate nucleus, which then sprouts and secretes necessary substances that are lacking in PD. Transplantation is not FDA-approved and is only performed as part of a clinical trial, as it is considered experimental.

What happens before treatment?

During your office visit, the neurosurgeon will discuss with you the procedure's benefits and risks, answer your questions, and have you sign consent forms.

Patients are admitted to the hospital the morning of the procedure. No food or drink, including your Parkinson's medication, is permitted after midnight the night before surgery. Several routine tests (e.g., blood test, electrocardiogram, chest X-ray) are performed, and an IV line is started in your arm. An anesthesiologist will explain the effects of anesthesia and its risks.

What happens during treatment?

The procedure involves five main steps. The entire process takes 5-7 hours; the operative procedure generally takes 3–4 hours.

Step 1. attach stereotactic frame

The procedure is performed stereotactically, which requires attaching a frame (or halo) to your head. The pin sites are injected with local anesthesia to minimize discomfort. You will feel some pressure as the pins are tightened. A metal cage, which looks like a birdcage, is placed on the frame (Fig. 3).

Step 2. MRI or CT scan

You will undergo an imaging scan using either computerized tomography (CT) or magnetic resonance imaging (MRI). The rods of the "bird cage" show up on the scan and help the surgeon create "landmarks" that will aid in the exact targeting of the desired brain structure. The cage is removed after the scan, but the frame remains in place to secure the head during surgery.

Step 3. perform a craniotomy

Next, you will be taken to the operating room (OR). You will be positioned on an OR table, and the stereotactic frame will be secured to the table. This prevents any small movements during this very precise procedure. You will remain awake throughout the procedure, and no sedatives will be given as they can mask the Parkinson's symptoms, whose source the surgeon is trying to find within the brain. Next, a local anesthetic is injected in a site at the top of your head. A small skin incision is made and a hole, about the size of a quarter, is drilled into the skull.

Step 4. insert electrode to the target

Through the small hole a recording electrode is inserted into your brain. Based on calculations from the MRI scan, the electrode is inserted to a specific depth and angle inside the brain. The accuracy of the electrode placement is confirmed by a number of tests. These tests can include flashing lights, commands to lift your arms or legs, and counting numbers. In addition, the surgical team will listen for the correct nerve cells with the aid of a computer program that allows them to hear the cell

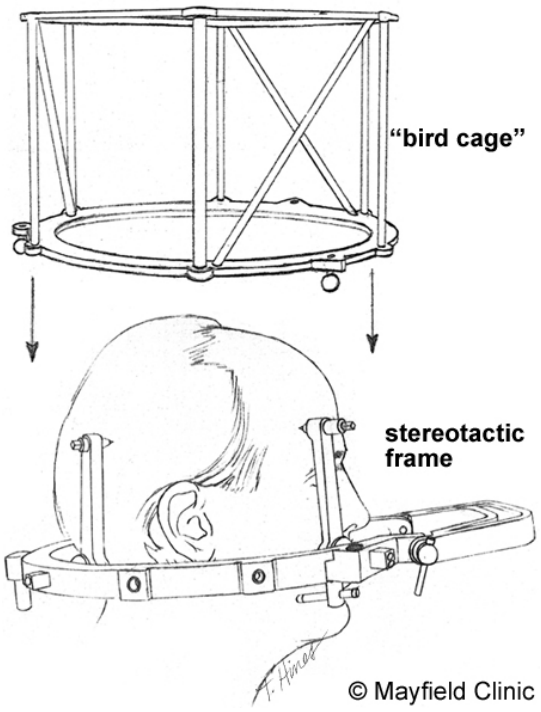

Figure 3. A stereotactic frame is attached to the patient's head with four pins. A metal "birdcage" is placed on the frame during the MRI scan.

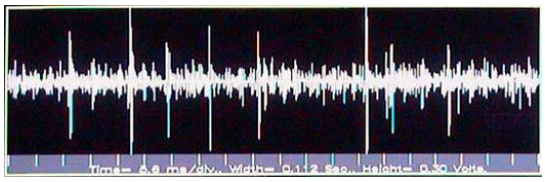

Figure 4. The surgeon locates the specific nerve cells by listening and observing their waveforms.

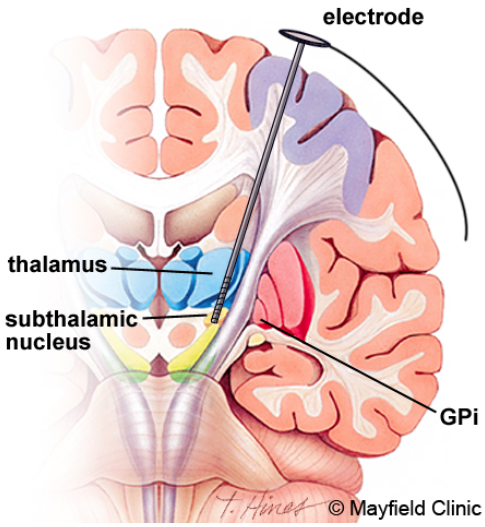

Figure 5. The electrode is placed accurately in the specific brain target, in this illustration the subthalamic nucleus (STN).

firing and see its waveform frequency (Fig 4). This is the most time-consuming part of the procedure and the most critical. Your patience and cooperation will help the surgical team do their job.

Step 5. Destroy or stimulate the target cells
In pallidotomy and thalamotomy, the surgeon locates the nerve cells to be destroyed, then eradicates them with a heating current. The electrode is then removed.

In DBS, once the exact nerve cells are located, the surgeon replaces the recording electrode with a permanent DBS lead (Fig. 5). A test stimulation is performed, and the surgeon, with the patient's help, will determine how well the stimulation suppresses the PD symptoms. The exact calibration of the stimulator parameters will occur later at the follow-up office visit.

The lead is attached to an extension wire that must be passed under the skin of the scalp, down the neck, to the generator, which will be implanted under the collarbone. For this part of the procedure you will be given general anesthesia. A small incision is made near the collarbone and the neurostimulator is implanted. The neurostimulator/battery will be visible as a small bulge under the skin, but it is usually not seen under clothes.

What happens after the procedure?

After the operation you may take your regular dose of Parkinson's medication immediately. You are kept under close observation in the intensive care unit overnight. Most patients are usually discharged home the next day. Approximately 10 days after the procedure your sutures will be removed during an office visit. If you had DBS surgery, the neurostimulator will be programmed and your medication dosage will be adjusted. It is important that you work with the neurologist and nurse to adjust your medications and refine the programming of the stimulator.

Which procedure is right for me?

If tremor is the primary problem, then DBS or thalamotomy offers the best chance for tremor control; however, pallidotomy can also be effective. If control of other symptoms, such as rigidity, dyskinesia, or walking, is needed, then pallidotomy or DBS can be effective. The effect of DBS varies with the location of the implanted electrode. Unlike pallidotomy and thalamotomy, DBS is a potentially reversible procedure; however, it carries a slightly higher risk of infection, along with the inconvenience of interference with some magnetic and high-frequency fields. For these and other reasons, you should discuss with your doctor which surgery would best fit your needs.

What are the results?

Pallidotomy and thalamotomy
Preliminary studies demonstrate that postoperative improvement lasts several years in most patients. Because PD is progressive, however, some of your symptoms may return, and other symptoms might appear after surgery.

Other surgical options can be discussed if your symptoms reappear; however, this is determined individually based on the location and size of the old lesion/stimulation, the nature of symptom recurrence, and your general medical health.

DBS of the thalamus
Studies have shown that this procedure may significantly reduce tremor in about two-thirds of PD patients. Tremor may not be eliminated and may continue to cause some impairment.

DBS of the globus pallidus (GPi)
This procedure is most useful in treatment of dyskinesias (involuntary wiggly movements) as well as other tremors. With DBS of the GPi, patients experience on average a 33% improvement in symptoms during "off" state (without the effect of levodopa) and 26% improvement during "on" state (under such effect). Their medication "on" time increased from 28 to 64%[1].

DBS of the subthalamic nucleus (STN)
This procedure has an effect on most of the motor features of PD, including bradykinesia, tremor, and rigidity. With DBS of the STN, patients experience on average a 51% improvement in symptoms during "off" state and 25% improvement during "on" state. Their medication "on" time increased from 27 to 74%[1].

What are the side effects?

Side effects related to the procedure occur in less than 1 in 20 cases. They include seizures, infection, and a 1% chance of bleeding in the brain. The target site is very close to the optic tract, and injury to the tract can cause partial blindness.

Side effects related to the DBS device are infection, movement of the electrode out of position, and breakage of the lead that connects the electrode to the pulse generator. Also, the battery implanted under the collarbone must be replaced every 3 to 5 years.

Living with a DBS

Cellular phones, pagers, microwaves, security doors, and anti theft sensors will not affect your stimulator. Be sure to carry your patient identification card when flying, since the device is detected at airport security gates.

Sources & links

If you have any questions, please call the Mayfield Clinic at 800-325-7787.

Support

Local support groups in Ohio, Kentucky, Indiana, and Michigan can be found through the Tristate Parkinson's Wellness Chapter at 513-948-1100 or 800-840-2732. For all other states, contact the American Parkinson Disease Association at 800-223-2732. A support group setting enables patients and their families to share experiences, receive support, and learn about advances in treatments and medications.

Sources

1. Deep-Brain Stimulation for Parkinson's Disease Study Group: Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. N Engl J Med 345:956-63, 2001
2. Favre J, Burchiel KJ, Taha JM, Hammerstad J: Outcome of unilateral and bilateral pallidotomy for Parkinson's disease: Patient assessment. J Neurosurg 46(2):344-355, 2000
3. Andaluz N, Taha JM, Dalvi A: Bilateral pallidal deep brain stimulation for cervical and truncal dystonia. J Neurol 57: 557-558, 2001
4. Taha JM, Janszen MA, Favre J: Thalamic deep brain stimulation for the treatment of head, voice, and bilateral limb tremor. J Neurosurg 91:68-72, 1999

Links

The National Parkinson Foundation
www.parkinson.org
Parkinson's Disease Foundation www.pdf.org
Movement Disorder Information & Education
www.wemove.org
Michael J. Fox Foundation www.michaeljfox.org
Parkinson's Institute www.thepi.org
American Parkinson Disease Association
www.apdaparkinson.org
Essential Tremor Foundation
www.essentialtremor.org
Medtronic Inc.
www.medtronic.com/neuro/parkinsons/activa_qa.html

Glossary

basal ganglia: a mass of nerve cell bodies (gray matter) located deep within the white matter of the cerebrum. Has connections with areas that subconsciously control movement.
bradykinesia: slowness of movement, impaired dexterity, decreased blinking, drooling, expressionless face.
caudate nucleus: part of the basal ganglia involved with voluntary control of movement.
dopamine: a neurotransmitter that passes messages from neuron to neuron across synapses.
dyskinesia: abnormal involuntary movements that may be caused by either high or low levels of anti-parkinson medication in patients with PD.
electrode: a conductor that carries electrical current.
globus pallidus interna (GPi): nuclei in the brain that regulate muscle tone; part of the basal ganglia.
neuron: basic unit of the nervous system, composed of a cell body, dendrites, and axon; also called a nerve cell.
neurotransmitter: a chemical substance that allows electrical impulses to be transmitted from one nerve cell to another across synapses. Some neurotransmitters include acetylcholine, noradrenaline, dopamine, serotonin, gamma-aminobutyric acid, and glutamate.
posterolateral: behind and to one side.
stereotactic: use of three-dimensional coordinates to precisely locate deep brain structures.
substantia nigra: an area of the brain where dopamine is produced.
synapse: the tiny gap between two nerve cells; the release of neurotransmitters enables impulses to cross these gaps. Some brain cells have more than 15,000 synapses.
thalamus: a relay station for all sensory messages that enter the brain; part of the basal ganglia.

updated > 2.2009
reviewed by > Alberto Espay, MD