PATIENT PAGE

Does deep brain stimulation help early or mild Parkinson disease?

Steven Karceski, MD

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What did the authors study?

In "Effects of deep brain stimulation on rest tremor progression in early stage Parkinson disease,"[1] Dr. Hacker and coauthors studied the effects that deep brain stimulation (DBS) has when it is used early in the course of Parkinson disease (PD).

DBS is a system to help symptoms of PD. There are 3 main parts of this system. The first is a lead—a series of coiled wires—that have a tiny electrode on the end. These electrodes are surgically implanted deep in brain tissue. The lead is connected to an extension wire that is attached to a battery-powered electrical stimulator that is placed in the chest or abdomen. The stimulator sends electric currents into the brain.

There are many reasons why a study like this is important. First, DBS is used in addition to medications for PD. Second, it is almost always used when PD is in its middle or late stages. In other words, DBS is considered only when a person's PD has advanced to the point where medications are either no longer working or are working in a less-than-optimal way.

Part of the reason that DBS is used late in the course of PD is that a deep brain stimulator is invasive. In order for DBS to be used, an electronic device must be surgically implanted. Electrodes are most often placed in the subthalamic nucleus, a group of nerve cells in the brain that are affected by PD. DBS is not new. For many years, DBS has been used to send a small electrical impulse to the cells of the subthalamic nucleus, thereby reducing or stopping the tremor (and other symptoms) that occurs in PD.

Although not new, DBS has not been applied to early PD. What Dr. Hacker wanted to know was this: What if DBS was used earlier? How does it affect PD? More specifically, could DBS change the course of PD? It is known that PD is a slowly progressive illness. We have medications that treat the symptoms of PD, but we do not have a treatment that slows or stops the progression of PD. In other words, even with treatment, the PD gradually gets worse. What if early DBS slowed the course of PD? That would mean that a person would live with minimal or no symptoms for longer. It may also mean that a person would need less medication over time.

How did the authors perform the study?

Studying the effects of DBS in early PD is challenging. First, there is no placebo. It is not ethical to implant people with placebo device in order to study the effects of a device. Instead, the authors chose to study the effects of usual medications (which they called optimal drug therapy [ODT]) vs a combination of ODT plus the DBS. However, they realized that they could not measure the PD while the person was on treatment, because the treatments suppress the symptoms of PD. Knowing that the treatments (both DBS and medications) stay in the system for a short time, they decided that at 6-month intervals, they would stop all treatments for 1 week. At the end of the week (of no treatment), they would then measure symptoms of PD, like the person's tremor.

In order to minimize any bias, the authors videotaped the patients at the end of the week without treatment. They sent the videos to a doctor for review. This doctor did not know what treatments the person may have had, and gave each person's video a score. The score was based on the Unified Parkinson's Disease Rating Scale, part III (UPDRS-III). To further reduce bias, the person who received the videos did not know when in the course of the person's PD the video had been taken. In short, the assessor reviewed each video independently, using the UPDRS-II rating scale.

The researchers studied 28 people, all of whom had early PD. The duration of illness was short: the patients had been taking medications for PD for 6–48 months before entering the study. The people were 50–75 years old. They could not have another neurologic illness like dementia (Alzheimer disease)—that way, the researchers could eliminate the possible effects that another neurologic illness might have on PD. The patients stopped their PD treatments for 1 week at the following time points: 6 months, 1 year, 18 months, and 2 years, which was the end of the study. In other words, each patient would have had 5 videos: 1 that was done before the study treatment occurred and 1 from each of the 6-month time periods.

What did the study show?

When assessing the videos, the most accurate measurements occur with regards to tremor. In the DBS group, over 2 years (24 months), there was a minimal change in the severity of tremor. This was in comparison to the medication-only group (ODT group), where the tremor severity scores worsened. In fact, when comparing the 2 groups, the risk of tremor worsening was 2.6 times higher in the ODT group.

In PD, the tremor usually starts in one limb (one arm or leg), and spreads to affect other limbs. The researchers looked at this as well: how often does a new tremor occur? In the DBS group, the number of affected limbs either stayed the same or went down slightly. This was in comparison to the ODT group, where PD was observed to double. In other words, if the tremor affected one limb, at the end of 2 years, it now affected two. Another way of thinking about this is that there was a new tremor in about half (46%) of the DBS group over a 2-year period. For the medication-only group, 86% developed a new tremor.

Limitations of the study

First, this was a small study. The Food and Drug Administration has already approved a much larger, multicenter study to better assess these findings. Second, there were symptoms of PD that the videos could not measure. For instance, many people with PD also develop stiffness. The medical term for this is rigidity. Rigidity is something that a doctor will find when he or she examines a patient. However, it cannot be seen. Instead, rigidity is something that is felt. The doctor assess the stiffness of a person's arms or legs by moving the person's limbs, and feels the severity of the stiffness. In this study, the authors were unable to assess whether DBS had an effect on the person's rigidity.

What does this mean?

There are many ways to interpret a study like this. First, the study findings need to be confirmed in a larger trial. If both trials show the same thing, it may mean that early use of DBS is an effective way to manage PD. Not only would DBS reduce the symptoms of PD, but it may also decrease the speed at which PD progresses.

PATIENT PAGE

About Parkinson disease

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What is Parkinson disease?

Parkinson disease (PD) is named after James Parkinson. He first described the illness in 1817. PD mostly causes problems with moving around. PD causes a person to move very slowly; this is called bradykinesia. A person with PD appears stiff or rigid. A person often develops a slightly stooped posture, and will begin to have a very characteristic walking pattern. Patients may shuffle their feet, and take very small, frequent steps (called festination). At times, a person with PD may appear to suddenly freeze up or be unable to move for a short period of time. When a person has PD, he or she often will have one or more of these symptoms.

A tremor of the hands is common. In fact, tremor is the most characteristic physical finding in PD. The tremor is called a pill-rolling tremor. It gets its name because of how the tremor appears. Many years ago, pharmacists used to make their own tablets. In order to make the medications into a pill, they would roll the medicine into a small round ball. In order to roll a small ball, the hand has to move in a very specific way. This hand movement looks similar to the tremor in PD.

What causes PD?

In PD, the underlying problem has to do with a neurotransmitter called dopamine. A small number of very specific brain cells make dopamine. These brain cells reside in an area of the brain called the substantia nigra. The substantia nigra is in a deep part of the brain called the brainstem. Though only a few cells make dopamine, these cells send the neurotransmitter to many different regions of the brain. Changes in dopamine levels therefore can have widespread effects within the brain.

When we are young, our brains make plenty of dopamine. As we get older, this amount decreases. In PD, the amount of dopamine becomes critically low. In PD, these changes occur very slowly: the amount of dopamine gradually decreases over time. The gradual loss of dopamine causes the gradual worsening of movement. In early PD, as in this study, the symptoms may be mild.

Treatment of PD

Understanding the link between dopamine and PD has led to the development of many treatments. The answer seems simple enough: take dopamine. However, the body does not allow dopamine to cross over into the brain, where it is needed. This is why people with PD take levodopa. Levodopa can cross over into the brain. The brain converts the medication into dopamine.

There are many other treatments for PD. For the most part, these treatments are aimed at increasing the amount of dopamine in the brain. Some treatments help to keep the dopamine where it is needed most. Other treatments, like the DBS, are aimed at the system of brain cells that function together to create smooth, graceful movements. Electrical impulses, when applied to this delicate network of brain cells, reduce tremor and improve a person's mobility.

Every person is different. A physician may not know which treatment is best for a specific person. This is because there is no blood test or scan that would help a doctor to know which treatment option will work the best. Studies are limited: they can tell us which medicines work, but they do not tell us which ones work best for a specific person. It is studies like this that help doctors to know not only which treatments work, but when these kinds of treatments need to be used, in the course of an illness, in order to help a person feel as well as he or she can, for as long as possible.

A person with PD can become frustrated if the first treatment does not work. To make things even more complicated, some people may need a combination of treatments in order to feel well. In these instances, several treatments may need to be tried before the best treatment plan can be found.

Additional resources

Brain & Life
brainandlife.org/

American Parkinson Disease Association
apdaparkinson.org/

Michael J. Fox Foundation for Parkinson's Research
michaeljfox.org/

Parkinson's Foundation
parkinson.org/

Reference

1. Hacker ML, Delong MR, Turchan M, et al. Effects of deep brain stimulation on rest tremor progression in early stage Parkinson disease. Neurology 2018;91:e463–e471.