Deep brain stimulation at two different targets gives similar motor benefits in Parkinson's

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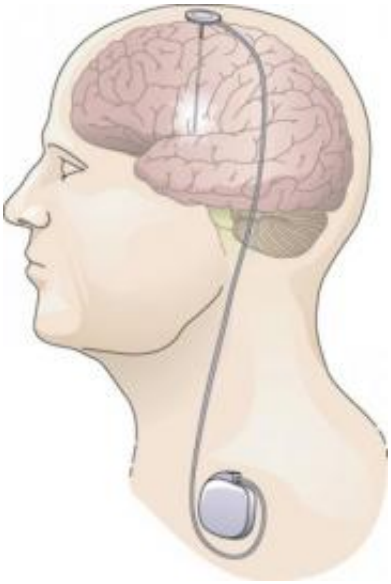

In deep brain stimulation for Parkinson's disease, fine wires are implanted within brain regions that are involved in motor control. Stimulation delivered via a pacemaker-like device quiets the abnormal brain signals that cause tremor, stiffness and other symptoms. Credit: National Institute of Neurological Disorders and Stroke

In a major study, investigators have compared how individuals with Parkinson's disease respond to deep brain stimulation (DBS) at two different sites in the brain. Contrary to current belief, patients who received DBS at either site in the brain experienced comparable benefits

for the motor symptoms of Parkinson's.

The results appear in the June 3, 2010 issue of the New England Journal of Medicine. This is the latest report from a study that has followed nearly 300 patients at 13 clinical sites for two years. The study was funded by the Department of Veterans Affairs (VA) and the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health. Additional support was provided by Minneapolis-based Medtronic, Inc., the makers of the DBS systems used in the study.

"These results establish that DBS delivered to these two brain areas linked to key motor control pathways can have equivalent effects on tremor, stiffness and other motor symptoms of Parkinson's disease," said Walter Koroshetz, M.D., deputy director at NINDS. "The important question now becomes how stimulation at each site affects some of the other important, non-motor symptoms and how to best individualize DBS therapy."

Motor control problems such as shaking, rigidity, slowed movement and poor balance are often the first and most troubling symptoms of Parkinson's disease. In later stages, patients tend to develop a variety of cognitive and mood problems, including depression, apathy, slowed thinking, confusion, impaired memory and trouble sleeping.

Medications such as L-dopa can control the motor symptoms of Parkinson's disease early in its course. The drugs alleviate some non-motor symptoms, but can worsen others. For patients with advanced disease, the drugs become less effective and more likely to cause side effects. DBS is a surgical intervention that can help restore the control of motor symptoms for these patients. It does not help the non-motor symptoms of Parkinson's, and may even aggravate them. Most patients continue to take carefully balanced medications after they start DBS.

When patients receive DBS for Parkinson's, a neurosurgeon precisely guides a very fine wire into one of two deep brain regions involved in motor control, the subthalamic nucleus (STN) or the globus pallidus interna (GPi). An implantable battery is used to send a finely tuned electrical current to stimulate the brain. Often, dramatic improvement of motor symptoms can be observed in the operating room when the wire is properly placed and the stimulator turned on. Stimulation on both sides of the brain, or bilaterally, is considered most effective.

There is a widely held view that of the two techniques, STN DBS is more effective at controlling motor symptoms but more likely to aggravate non-motor symptoms. The new study - the largest most comprehensive study ever done of patients receiving bilateral STN DBS or GPi DBS - challenges these ideas.

"We found that motor outcomes between the two groups were not significantly different. Meanwhile, there were very modest differences in mood and cognitive function between the two groups," said one of the study's lead investigators, Dr. Kenneth Follett, M.D., Ph.D., formerly affiliated with the Iowa City VA Medical Center and now chief of neurosurgery at the University of Nebraska Medical Center in Omaha. "Physicians and patients can have confidence in both types of DBS, and can make their choice based on the constellation of motor and non-motor symptoms that determine quality of life in Parkinson's disease."

As reported in 2009, the first part of the study compared bilateral DBS to best medical therapy, including medication adjustment and physical therapy. Bilateral DBS showed overall superiority to best medical therapy at improving motor symptoms and quality of life. In the second part of the study, 299 patients, including those who initially received best medical therapy, were randomly assigned to receive either bilateral STN DBS or GPi DBS.

Over a two-year period, the two groups experienced similar improvements in scores on the Unified Parkinson's Disease Rating Scale, which measures motor function. The two groups also reported similar improvements in quality of life.

On a variety of neuropsychological tests, there were no significant differences between the two groups. However, the STN DBS group experienced a greater decline on a test of visuomotor processing speed, which measures how quickly someone thinks and acts on information. Also, the STN DBS group had slight worsening on a standard assessment of depression, while the GPi DBS group had slight improvement on the same test. The importance of these two differences is not clear, and will be scrutinized in follow-up research, the investigators say.

In practice, after DBS surgery, the dosage of L-dopa and related medications is often reduced to prevent side effects such as dyskinesias, which are uncontrolled movements. In this study, medication use decreased more for the STN DBS group than for the GPi DBS group. That finding may influence the DBS target chosen for patients. For some patients, medications can cause unwanted side effects and a drop in medication may be favorable for them. For others a drop in medication could unmask symptoms related to cognition or mood that were previously under control.

About half of all patients in both DBS treatment groups had serious adverse events, the most common being surgical site infection. By the end of the two-year study period, 99 percent of all serious adverse events were resolved. Lower levels of electrical stimulation were needed for STN DBS, suggesting that over the long term, this procedure might be associated with lower costs and less need for replacing the pulse generator.

"From this study, we can conclude that of the two most common targets

for DBS, either one is a reasonable option for treating Parkinson's disease," said the study's co-lead investigator Dr. Frances Weaver, Ph.D., director of the Center for Management of Complex Clinical Care at Hines VA Hospital and professor of medicine at Loyola University, both in Chicago.

The investigators will continue to follow the same patients for several more years, looking at how the choice of DBS target affects patients' motor function and quality of life over the long term, as well as other factors such as the need to replace DBS electronics.

"VA was proud to partner with NINDS in the first comparative effectiveness study of the two types of DBS in a large, randomized trial," said Joel Kupersmith, M.D., VA Chief Research and Development Officer. "With the country's aging population, studies like this on treatments for Parkinson's offer real hope for individuals with a very debilitating and common disease of the elderly."

Provided by National Institutes of Health

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