

Beyond improving Parkinson's symptoms, does deep brain stimulation stall their progression?

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Parkinson's disease symptoms begin subtly and worsen as damage to certain brain cells continues. But an electrical stimulation device implanted deep in the brain and programmed remotely, along with medications, may provide some control of "motor symptoms" common to the disease, such as shaking, stiffness, and loss of muscle control.

What happens, however, if the drugs are stopped and the device is switched off after five years? Are the symptoms far worse than they were to start, as might be expected with a "progressive" degenerative disorder?

Surprisingly, no, says neurologist Michele Tagliati, M.D., director of the Movement Disorders Program at Cedars-Sinai Medical Center and one of the nation's leading experts in <u>deep brain stimulation</u> therapy. He and colleagues at Mount Sinai School of Medicine, where he served before joining Cedars-Sinai in September, evaluated several of their deep brain stimulation patients at one-year intervals: 21 patients at year one; 17 at year two; 14 at year three; 16 at year four; and nine at year five.

Part of their analysis – evaluating patients while their drugs temporarily were discontinued but brain stimulation continued – confirmed previous studies: Deep brain stimulation is an effective therapy for advanced Parkinson's disease up to five years from implantation, although there is a gradual reduction in benefit over time. This effectiveness decline



usually is attributed to the disease's unrelenting progression.

But the researchers also explored Parkinson's natural progression in these patients by temporarily discontinuing both their drugs and brain stimulation, then comparing motor function at these yearly intervals with pre-treatment scores.

"In these patients who were effectively treated with DBS stimulation, we found that motor symptoms remained remarkably stable over time. There was no significant progression. Now we need to do larger studies to find out why. It may be, as some have suggested, that deep brain stimulation stabilizes the motor progression of the disease, although other studies indicate that Parkinson's disease may just naturally stabilize after several years of progression," said Tagliati, pointing out that "nonmotor" symptoms, including depression, dementia and others, currently do not respond to deep brain stimulation and appear to continue to progress.

Tagliati, who leads an educational course on deep brain stimulator programming every year at the American Academy of Neurology meetings, has been studying the procedure for more than a decade, beginning several years before the device was approved as a therapy by the Food and Drug Administration. He and his counterpart at the University of California, Los Angeles, Jeff M. Bronstein, M.D., Ph.D., recently led a panel of international experts in developing a consensus on key issues related to the procedure for Parkinson's disease. Their document, with insight and guidance, was published in Archives of Neurology in October.

"Providing the most effective therapy requires teamwork and the experience and expertise that come from working in a specialized center. It involves placing the device in precisely the right location, programming and fine-tuning the device, properly adjusting



medications, studying many patients and outcomes, learning and teaching – all the activities found in an academic center," Tagliati says. "We're looking forward to pursuing innovative research strategies in the near future. Although we know DBS can help many patients with Parkinson's disease, there's much more we need to learn. We can see that stimulation works but we don't really know how it works."

Most patients suffering from Parkinson's disease first are treated with medication to improve levels of dopamine, a chemical lost when certain brain cells are damaged. But if drugs fail to provide adequate symptom control or if patients have unmanageable side effects, deep brain stimulation may be an option.

The device consists of electrical leads implanted in the brain and a stimulator located near the collarbone. The stimulator is programmed with a remote, handheld controller to block abnormal nerve signals that cause uncontrollable muscle activity.

This procedure does not replace drugs but it often allows their dosage to be reduced; the combination provides better muscle and movement control than drugs alone. Motor function improvements range from 27 percent to 72 percent within a year of deep brain stimulation surgery, according to earlier research.

The new study appears in the November issue of the *International Journal of Neuroscience*. Tagliati receives speaking honoraria and consulting fees from Medtronic Inc., manufacturer of the stimulation device.

More information: Citation: *International Journal of Neuroscience*, November 2010, "Lack of Motor Symptoms Progression in Parkinson's Disease Patients With Long-Term Bilateral Subthalamic Deep Brain Stimulation."



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