

Stimulating the brain

By David W. Roberts, M.D.

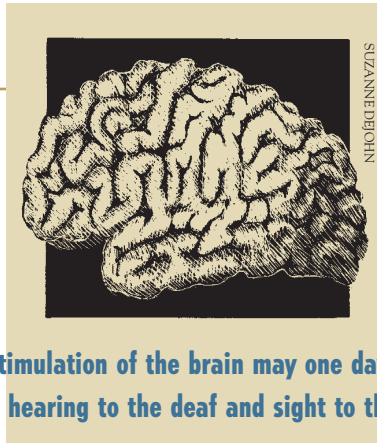
There used to be only two ways to control the tremor suffered by Parkinson's patients: drug therapy, which can lose its effectiveness over time, and ablative surgery, which involves removal of the affected part of the brain and is not reversible. Today, however, there is a great deal of interest in another approach—deep brain stimulation (DBS). Tiny pacemaker-like electrodes surgically implanted deep within the brain emit electrical signals that can alter the neuronal signals that are responsible for Parkinson's symptoms. The tremor disappears like magic but returns as soon as the DBS device is switched off.

DBS itself is relatively new, but it has evolved over the decades as a result of medical advances in several areas—including stereotactic surgery, neuroimaging, and our knowledge about the physiology of movement and of movement disorders.

Coordinates: The story begins 100 years ago. In the early 1900s, researchers in London developed a stereotactic frame—an apparatus that fits on the patient's head and has coordinates by which structures in the brain can be located—which allowed them to accurately direct delicate surgical instruments and probes deep into the brain. Back then, this was used only in animal investigation, but by the 1940s and 1950s, stereotactic surgery was being used to treat people with Parkinson's. Neurosurgeons had discovered that by making lesions in the thalamus (located in the midbrain region) and basal ganglia (near the thalamus), they could disrupt the abnormal circuits that triggered tremor and other symptoms.

Then, in the 1960s, the surgical treatment of Parkinson's was abruptly curtailed with the discovery of levodopa (also called l-dopa), a drug that could alleviate the characteristic tremor, rigidity, and slowness of movement associated with the disease.

Resurgence: By the late 1970s, stereotaxy was rediscovered as the limitations of l-dopa treatment—an increase in side effects and a decrease in effectiveness over time—were recognized. Concurrently, a revolution in imaging was creating new applications for stereotaxy. The scanning technologies of CT and MRI, which revealed previously undetectable pathology, were combined with stereotaxy to allow neurosurgeons to biopsy newly diagnosed brain tumors. The 1980s and 1990s brought a resurgence of interest in surgical intervention for Parkinson's. Surgeons realized anew the fact that destroying tiny areas of certain brain structures could correct the deep circuits that had run amok. Once again, they began performing procedures such as thal-



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amotomy (surgical destruction of small areas of the thalamus) and pallidotomy (surgical destruction of small areas of the globus pallidus, one of the components of the basal ganglia).

Meanwhile, electrical stimulation of the brain was emerging as a potentially powerful treatment.

For many decades, neurosurgeons had used the technique to map the parts of the brain that control motor function so they

could avoid disturbing critical areas when operating on a tumor or a seizure site. By the 1970s, electrical stimulation was being applied to the spinal cord and thalamus to treat chronic pain, and to the cerebellum to treat epilepsy. In the early 1990s, researchers in France and Austria discovered that electrically stimulating deep thalamic or basal ganglial circuits could alleviate Parkinson's symptoms.

In DBS, the neurosurgeon places a stimulating electrode within the brain. The electrode is connected to a battery-powered pulse generator that sends programmable electrical signals. DBS is completely reversible; the power can be turned up, down, or even off simply by holding a radio transmitter over the patient's chest.

Targets: It is also possible to treat both sides of the brain, and both sides of the body, more safely with DBS than with an irreversible surgical procedure. Physicians can also use deep-brain stimulation procedures to identify better targets for Parkinson's treatments, like the subthalamic nucleus (STN). Today, bilateral DBS of the STN is the most common procedure done for Parkinson's.

Electrical stimulation of the brain may one day be used to restore hearing to the deaf and sight to the blind; to alleviate certain refractory pain disorders; and to treat obsessive-compulsive disorders.

Equally important is the fact that this interface not only allows for electrical stimulation of the brain, but also can work in the other direction as well. Neuronal signals can already be processed to do things like move a cursor or an articulated arm on a robot. The implications are enormous. Imagine a paralyzed patient walking on electrically stimulated legs. And the possibilities go beyond motor function. What cognitive properties might one day be altered or enhanced?

Perhaps the most provocative aspect of the brain-machine interface is this closing of the loop: providing feedback after the interface has detected certain neuronal patterns or has driven an external action will make possible an eventual behavioral evolution that will surely take on a life of its own. As much as we now "ooh" and "aah" at seeing a tremor come and go when a switch is activated, we recognize that this is a very crude level of interface. Today it's a handful of electrical contacts. Tomorrow there may be tens of thousands. Independent of how quickly they evolve and of how we may view them, durable, sustainable, safe brain interfaces will become a reality. Soon, too, so will a host of related neuroethical issues. ■

"Bench to Bedside" explores the research underlying advances in clinical medicine. Roberts is a professor of surgery at DMS and chief of the Section of Neurosurgery at DHMC. Nationally recognized for his role in developing advanced neurosurgical instrumentation, he earned his M.D. from DMS in 1975 and did his residency in neurosurgery at DHMC.