brain
JULY 2004 BRIEFINGS

PATIENTS WITH THE MOVEMENT DISORDER PARKINSON'S DISEASE HAVE SEEN BENEFITS FROM DRUGS THAT TARGET BRAIN CHEMICALS. UNFORTUNATELY THE ADVANTAGES CAN DECLINE OVER TIME. RECENTLY, HOWEVER, SCIENTISTS DEVISED AND REFINED A DIFFERENT STRATEGY, TERMED DEEP BRAIN STIMULATION, WHICH NOW PROVIDES PATIENTS WITH AN ADDITIONAL OPTION. RESEARCH INDICATES THAT THIS ELECTRICITY-BASED TECHNIQUE CAN ALTER BRAIN ACTIVITY AND HELP MANY PATIENTS ACHIEVE GREATER CONTROL OVER THEIR MOVEMENTS. CONTINUED INVESTIGATIONS INTO HOW DEEP BRAIN STIMULATION CREATES ITS BENEFITS WILL ALLOW RESEARCHERS TO FURTHER IMPROVE THE TECHNIQUE FOR PARKINSON'S AND ALSO HELP THEM FIND WAYS TO USE IT FOR THE TREATMENT OF OTHER BRAIN AILMENTS.

## BRAIN STIMULATION AND PARKINSON'S

Electricity keeps Justin Timberlake's tunes blaring on the CD player, the milk chilled in the refrigerator, and the living room well lit. In recent years, the power of electricity has reached a whole new level.

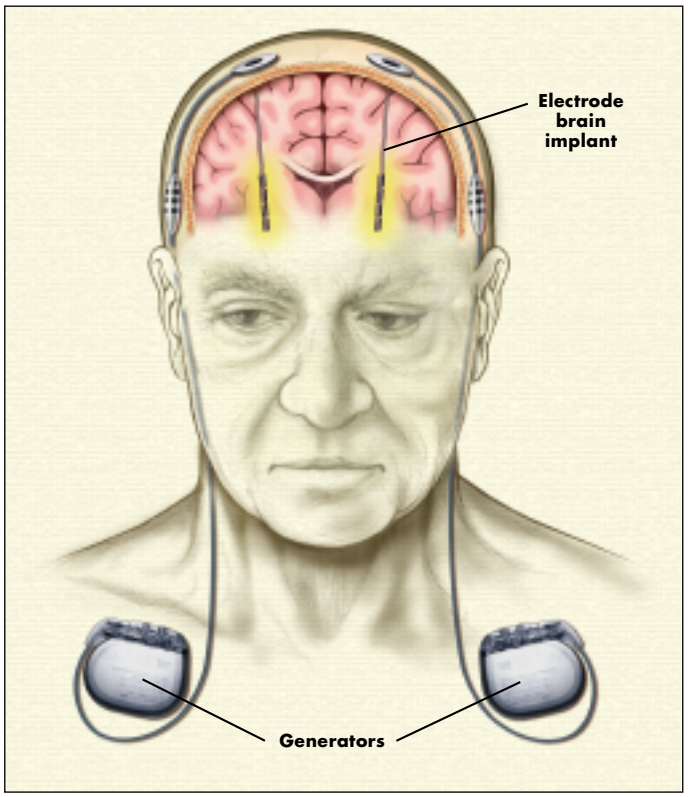
Scientists now have discovered an electricity-based technique that can aid the malfunctioning brain. Comprised of a brain implant that delivers electrical pulses, the strategy, termed deep brain stimulation, influences cell activity and alleviates the movement problems that mark the brain disorder Parkinson's disease (PD). The success of the technique is leading to:

- Improvements in the quality of life of many patients with PD.
- An increased effort to better understand the effects of electrical stimulation and further fine-tune treatment of PD.
- New ideas on how to use electrical stimulation to treat additional brain ailments.

PD afflicts some 1 million Americans. Symptoms include slowness of movement, muscle stiffness, and shaky tremors, which can harm a person's ability to walk, talk, write, and eat. Biologically, patients' brains hold depleted levels of dopamine. Since the 1960s, those with PD have seen considerable benefit from medications that help replenish levels of this chemical, but unfortunately the advantages can decline over time.

This led researchers to investigate the use of other techniques. Decades ago during an operation surgeons found by accident that the destruction of part of a brain area termed the thalamus, which aids movement control, suppressed tremors in a patient with PD. Surgical destruction of the area has since proved useful in additional patients, but deliberately destroying any part of the brain is a risky undertaking. In the mid-1990s researchers reported that there was a better option—electrical stimulation. Like the

▼ TO DATE, THOUSANDS OF PATIENTS WITH PARKINSON'S DISEASE HAVE BEEN TREATED WITH DEEP BRAIN STIMULATION. THE ELECTRICITY-BASED TECHNIQUE REQUIRES THE INSERTION OF ONE OR TWO PAGER-SIZED GENERATORS UNDER THE SKIN, USUALLY NEAR THE COLLAR BONE. THE GENERATOR EMITS TINY ELECTRICAL PULSES THAT PASS ALONG WIRES, ALSO UNDER THE SKIN, THROUGH ELECTRODES IMPLANTED IN SELECT AREAS OF THE BRAIN. SOME PATIENTS EXPERIENCE A TINGLING SENSATION, BUT TYPICALLY THE STIMULATION PULSES GO UNNOTICED.

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**FOR MORE INFORMATION**
please call Leah Ariniello, science writer, or Joseph Carey, senior director, communications & public affairs, at (202) 462-6688

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surgery, stimulation in the thalamus suppressed tremors in patients. Unlike the surgery, the stimulation response was reversible and easily adjusted to minimize unwanted effects.

More recently, animal research helped scientists identify other targets for stimulation that can alleviate additional symptoms of PD. Work in monkeys determined that the dopamine depletion in PD alters the cell activity in two movement-related brain areas, the subthalamic nucleus and the globus pallidus. Researchers reported that stimulation of either area improved movement in a large group of PD patients. Results indicate that it can reduce symptoms like slowness of movement, stiffness, and tremors. To date, doctors have treated thousands of PD patients with the "deep brain stimulation" technique.

Recent work indicates that the technique's benefits last. Patients treated with stimulation of the subthalamic nucleus and tested while off medication showed improvements in the movement-related signs of the disease for at least five years. Before surgery most patients depended on caregivers. At the five year mark, most performed their daily activities independently.

Currently researchers are conducting a large study to determine whether stimulation of the subthalamic nucleus more effectively reduces symptoms than stimulation of the globus pallidus and whether deep brain stimulation more effectively treats PD than available medications.

Researchers also want to decipher how deep brain stimulation creates its effects. Some ongoing work involving animals and computer models suggests that brain stimulation may alleviate the symptoms of PD by interrupting, altering, or masking irregular brain cell activity patterns produced by the depletion of dopamine. Insights into how the technique works could help researchers determine even better stimulation targets for PD.

These studies also could help scientists develop ways to use stimulation for other brain ailments. Already, small studies provide evidence that deep brain stimulation could potentially aid a range of disorders. For example, the technique diminished seizures in some patients with epilepsy, reduced compulsive behaviors in a patient with obsessive compulsive disorder, and decreased the number of tics that plagued a patient with Tourette syndrome. With continued research, scientists suspect that electricity will recharge the lives of an increasing number of people with brain ailments.

SOCIETY FOR NEUROSCIENCE
11 Dupont Circle, NW
Suite 500
Washington, DC 20036

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