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Safer Electrical Therapy for Parkinson's

Delivering electrical stimulation via the spinal cord could help ease symptoms of the disease.

By Lauren Gravitz

Delivering electrical stimulation to the spinal cord through tiny, platinum electrodes could ease the severe motor deficits of Parkinson's disease as effectively as a much more intrusive procedure currently in clinical use, according to a new study in rodents. If the findings are confirmed in humans, scientists say, the procedure could dramatically improve treatment for the disease by making electrical therapies safer and more broadly available.

Parkinson's is a neurodegenerative disorder that develops when the brain cells that produce, excrete, and reabsorb a neurotransmitter called dopamine mysteriously begin to die. Patients initially develop muscle tremors; in the later stages of the disease, their limbs go rigid, and their movements slow to a painful crawl. The disease can be treated by replacing dopamine with a drug called levodopa, or L-dopa, but the drug loses its effectiveness over time. When drugs fail, patients often turn to an invasive surgical treatment called deep brain stimulation, which uses an electric pacemaker to send pulses to very specific areas of the brain. Thousands of Parkinson's patients have received the brain implants to date.

Researchers at Duke University accidentally came upon the idea of stimulating the spinal cord as a possible treatment for Parkinson's. While examining rats engineered to exhibit symptoms characteristic of Parkinson's, they noticed that groups of neurons in two areas of the brain, the cortex and the basal ganglia, were firing synchronously. The rhythmic activity was reminiscent of the mild, continuous seizures seen in patients with epilepsy. "I had seen this a decade ago," says [Miguel Nicolelis](#), a professor of neurobiology and codirector of the Center for Neuroengineering at Duke University. At the time, Nicolelis and his collaborators were searching for ways to disrupt rhythmic seizures by stimulating peripheral nerves.

Nicolelis reasoned that a similar approach might work for Parkinson's. So he and his student Romulo Fuentes took their dopamine-depleted mice and rats and attached tiny platinum electrodes to the base of their spinal cords. "When we stimulated them with a small current, we got an effect that was identical--and even better--than what people get when they do this deep brain stimulation," Nicolelis says. The Parkinsonian animals' slow stiff movements were replaced with healthy mouse and rat behaviors.

When Nicolelis and Fuentes combined the electrical stimulation with L-dopa, the effects were even more startling. The electric pulses, combined with only 20 percent of the typical drug dose, resulted in a long-term effect that mimicked L-dopa therapy without appearing to replicate the drug resistance that normally builds up over time. The research was published yesterday in the journal [Science](#).

The implant itself is a much easier surgery than the one used for deep brain stimulation, with much lower risk of side effects. The device is relatively superficial, placed right under the vertebrae on the surface of the spinal cord. "It's a very easy, semi-invasive procedure," Nicolelis says. "In the future, we may be able to do this noninvasively, because there are ways you can actually pass currents through skin and through bone to get these fibers excited." Nicolelis plans to test the treatment in chimpanzees before initiating human trials. At least one spinal-cord stimulation therapy is already in clinical use to treat chronic pain.

While deep brain stimulation has changed the landscape for late-stage Parkinson's treatment, it's still a very complicated, expensive, and deeply invasive procedure, says [Patrick Aebischer](#), president of the Swiss Federal Institute of Technology, in Lausanne. "If you could do this in humans, it would be a fantastic step," he says, making electrical stimulation available to a much wider group of patients. A noninvasive device would be even more appealing: "If you could do this transcutaneously, you'd change the whole ball game," Aebischer says. "It opens up a very interesting new possibility for using electrophysiology to treat Parkinson's disease."

However, the research is in its early days. "We have to keep in mind that these are experimental data," says [Alim Benabid](#), a professor emeritus of biophysics at Joseph Fourier University, in Grenoble, France, who created the deep brain stimulation technique in the late 1980s. "It is too early to say whether this could replace levodopa treatment or the current deep brain stimulation." But Benabid is already looking at adding spinal-cord stimulation in his next set of trials, paired with another kind of deep brain stimulation (that of the subthalamic nucleus) in patients with "frozen gait" disorder, who have trouble walking.

Nicolelis isn't sure how the therapy works, but he believes that by targeting the spinal column--where huge bundles of fibers are responsible for carrying tactile information from the body to multiple targets in the brain--he and his colleagues are creating electrical current that influences dynamics of the whole neural circuit, rather than just a single spot in the brain. "Parkinson's is a disease of neuronal timing," he says. "My gut feeling is that this works because it desynchronizes these neurons in the motor cortex and the basal ganglia and other locations. This desynchronizes them, gets them out of phase--almost like it introduces a little bit of noise in the system."

In focusing on the spinal cord, Nicolelis says, "we're looking at a very interesting shift in the way you approach the disease. We're approaching it from a systemic point of view, looking at a whole circuit and gaining access to the whole circuit." The scientists are now looking to see whether starting spinal stimulation in combination with L-dopa early on could slow or even prevent the progression of disease.

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