# Novel spinal cord stimulator sparks hope for Parkinson's disease treatment

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A novel stimulation method, the first potential therapy to target the spinal cord instead of the brain, may offer an effective and less invasive approach for Parkinson's disease treatment, according to pre-clinical data published in the journal *Science* by researchers at Duke University Medical Center.

Researchers developed a prosthetic device that applies electrical stimulation to the dorsal column in the spinal cord, which is a main sensory pathway carrying tactile information from the body to the brain. The device was attached to the surface of the spinal cord in mice and rats with depleted levels of the chemical dopamine - mimicking the biologic characteristics of someone with Parkinson's disease along with the impaired motor skills seen in advanced stages of the disease.

When the device was turned on, the dopamine-depleted animals' slow, stiff movements were replaced with the active behaviors of healthy mice and rats. Improved movement was typically observed within 3.35 seconds after stimulation.

"We see an almost immediate and dramatic change in the animal's ability to function when the device stimulates the spinal cord," says senior study investigator Miguel Nicolelis, M.D., Ph.D., the Anne W. Deane Professor of Neuroscience at Duke. "Moreover, it is easy to use, significantly less invasive than other alternatives to medication, such as deep brain stimulation, and has the potential for widespread use in conjunction with medications typically used to treat Parkinson's

disease."

Researchers tested mice and rats with acute and chronic dopamine deficit using varying levels of electrical stimulation and in combination with different doses of dopamine replacement therapy, also known as 3,4-dihydroxy-L-phenylalanine or L-DOPA, to determine the most effective pairing.

When the device was used without additional medication, Parkinsonian animals were 26 times more active. When stimulation was coupled with medication, only two L-DOPA doses were needed to produce movement compared to five doses when the medication was used by itself.

"This work addresses an important need because people living with Parkinson's disease face a difficult reality - L-Dopa will eventually stop managing the symptoms," explains Romulo Fuentes, a postdoctoral fellow at Duke University and lead author of the study. "Patients are left with few options for treatment, including electrical stimulation of the brain, which is appropriate for only a subset of patients."

While deep brain stimulation (DBS) and other experimental treatments attack the disease at its origin - in the brain - Nicolelis and team took a different approach. The concept for the device began when researchers made a surprising connection with another neurological condition.

"It was a moment of sudden insight," explains Nicolelis. "We were analyzing the brain activity of mice with Parkinson's disease and suddenly it reminded me of some research I'd done in the epilepsy field a decade earlier. The ideas began to flow from there."

The rhythmic brain activity in the animals with Parkinson's disease resembled the mild, continuous, low-frequency seizures that are seen in those with epilepsy. One effective therapy for treating epilepsy involves

stimulating the peripheral nerves, which facilitate communication between the spinal cord and the body. Researchers took that concept and developed a modified approach for a Parkinson's disease model.

Nicolelis says that the low frequency seizures, or oscillations, seen in the animal model of Parkinson's disease have been observed in humans with the condition. Stimulating the dorsal column of the spinal cord reduces these oscillations, which researchers believe creates the ability to produce motor function.

In a healthy body, neurons fire at varying rates as information is transmitted between the brain and the body to initiate normal movement. This process breaks down in someone with Parkinson's disease.

"Our device works as an interface with the brain to produce a neural state permissive for locomotion, facilitating immediate and dramatic recovery of movement," says Per Petersson, co-author of the study. "Following stimulation, the neurons desynchronize, similar to the firing pattern that you would see when a healthy mouse is continuously moving."

Nicolelis says that if the device is proven safe and effective through further research, he imagines it mirroring similar spinal cord stimulator technology currently used to treat chronic pain. Small leads are implanted over the spinal cord and then connected to a portable generator, a small device capable of producing mild electrical currents. During the trial period, the generator is external, while for permanent treatment it would be implanted below the skin.

"If we can demonstrate that the device is safe and effective over the long term in primates and then humans, virtually every patient could be eligible for this treatment in the near future," Nicolelis said.

The Duke team is collaborating with neuroscientists at the Edmond and Lily Safra International Institute of Neuroscience in Natal, Brazil, to test the new procedure in primate models of Parkinson's disease prior to initiating clinical studies. Neuroscientists from the Brain and Mind Institute at the Swiss Institute of Technology (EPFL), in Lausanne, Switzerland, will also participate in this international research effort to translate these new findings into clinical practice.

Source: Duke University Medical Center