Medical Xpress

Breakthrough neurotechnology for treating paralysis

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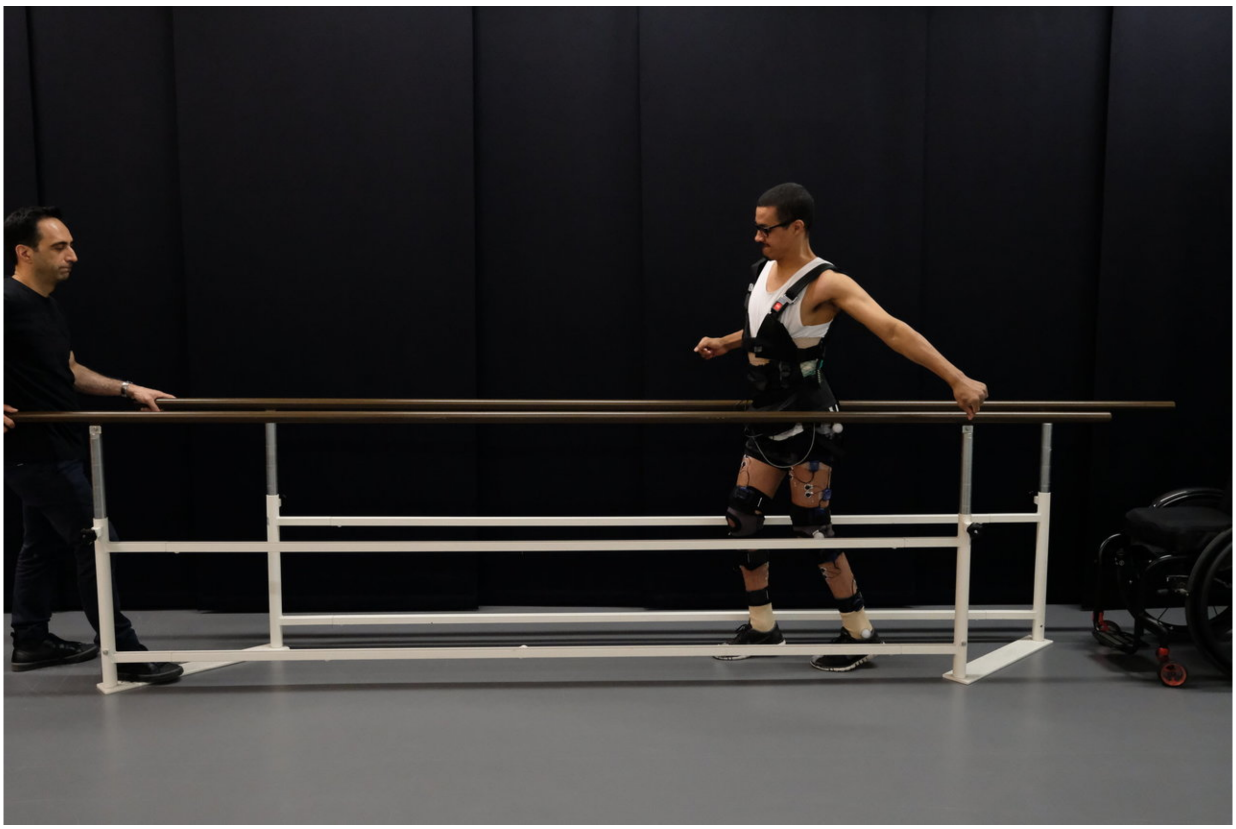

STIMO study participant David Mzee is now able to take a few steps of his own. He was totally paraplegic after a sports accident. Credit: EPFL / Jean-Baptiste Mignardot

Three patients with chronic paraplegia were able to walk thanks to precise electrical stimulation of their spinal cords via a wireless implant. In a double study published in *Nature* and *Nature Neuroscience*, Swiss scientists Grégoire Courtine (EPFL and CHUV/Unil) and Jocelyne Bloch (CHUV/Unil) show that after a few months of training, the patients were able to control previously paralyzed leg muscles, even in the absence of electrical stimulation.

This study, called STIMO (STImulation Movement Overground), establishes a new therapeutic framework to improve recovery from spinal cord injury. All patients involved in the study recovered voluntary control of leg muscles that had been paralyzed for many years. Unlike the findings of two independent studies published recently in the United States on a similar concept, neurological function was shown to persist beyond training sessions, even when the electrical stimulation was turned off. The STIMO study, led by the Ecole Polytechnique Fédérale de Lausanne (EPFL) and the Lausanne University Hospital (CHUV) in Switzerland, is published in the 1 November 2018 issues of *Nature* and *Nature Neuroscience*.

"Our findings are based on a deep understanding of the underlying mechanisms, which we gained through years of research on animal models. We were thus able to mimic in real time how the brain naturally activates the spinal cord," says EPFL neuroscientist Grégoire Courtine.

"All the patients could walk using body weight support within one week. I knew immediately that we were on the right path," adds CHUV neurosurgeon Jocelyne Bloch, who surgically placed the implants in the patients.

Back: Grégoire Courtine, EPFL professorFrom l. to r.: Sebastian Tobler, Gert-Jan Oskam, David Mzee, the three participants of the STIMO study Credit: EPFL / Hillary Sanctuary

"The exact timing and location of the electrical stimulation are crucial to a patient's ability to produce an intended movement. It is also this spatiotemporal coincidence that triggers the growth of new nerve connections," says Courtine.

This study achieves an unprecedented level of precision in electrically stimulating spinal cords. "The targeted stimulation must be as precise as a Swiss watch. In our method, we implant an array of electrodes over the spinal cord, which allows us to target individual muscle groups in the legs," explains Bloch. "Selected configurations of electrodes are activating specific regions of the spinal cord, mimicking the signals that the brain would deliver to produce walking."

The challenge for the patients was to learn how to coordinate the neural intention to walk with the targeted electrical stimulation. But that did not take long. "All three study participants were able to walk with bodyweight support after only one week of calibration, and voluntary muscle control improved tremendously within five months of training," says Courtine. "The human nervous system responded even more profoundly to the treatment than we expected."

Helping the brain help itself

The new rehabilitation protocols based on this targeted neurotechnology lead to improved neurological function by actively training natural overground walking capabilities in the lab for extensive periods of time, as opposed to passive training like exoskeleton-assisted stepping.

During rehabilitation sessions, the three participants were able to walk hands-free over more than one kilometer with the help of targeted electrical stimulation and an intelligent bodyweight support system. Moreover, they exhibited no leg-muscle fatigue, and so there was no deterioration in stepping quality. These longer, high-intensity training sessions proved crucial for triggering activity-dependent plasticity—the nervous system's intrinsic ability to reorganize nerve fibers—which leads to improved motor function even when the electrical stimulation is turned off.

Previous studies using more empirical approaches, such as continuous electrical stimulation protocols, have shown that a select few paraplegics can take steps with the help of walking aids and electrical stimulation, but only over short distances and under continuous stimulation. As soon as the stimulation is turned off, the patients immediately return to their previous state of paralysis and are no longer able to activate leg movements.

Next steps

The startup GTX medical, co-founded by Courtine and Bloch, will use these findings to develop tailored neurotechnology to turn this rehabilitation paradigm into a treatment available at hospitals and clinics everywhere. "We are building next-generation neurotechnology that will also be tested very early post-injury, when the potential for recovery is high and the neuromuscular system has not yet undergone the atrophy that follows chronic paralysis. Our goal is to develop a widely accessible treatment," adds Courtine.

More information: Fabien B. Wagner et al, Targeted neurotechnology restores walking in humans with spinal cord injury, *Nature* (2018). DOI: 10.1038/s41586-018-0649-2

Leonie Asboth et al. Cortico–reticulo–spinal circuit reorganization enables functional recovery after severe spinal cord contusion, *Nature Neuroscience* (2018). DOI: 10.1038/s41593-018-0093-5

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