SPINAL CORD

Restoring walking

> “even when EES was switched off, the participants showed signs of recovery of neural function”

Many individuals with severe locomotor deficits or leg paralysis resulting from spinal cord injury (SCI) do not recover motor function, even with physical activity-based rehabilitation. Here, Wagner et al. show that application of epidural electrical stimulation (EES) together with rehabilitation allowed three people with SCI and severe locomotor problems to walk with limited assistance.

Previous studies had established that EES can activate proprioceptive circuits in the spinal cord, which then activate motor neurons, and that delivery of spatiotemporally regulated EES, when combined with locomotor training, can reorganize preserved spinal cord pathways and lead to an improvement in locomotion in animal models of paralysis.

Here, Wagner et al. implanted a 16-electrode array connected to a modified pulse generator into the spinal cords of three men with chronic cervical SCIs and severe deficits in or paralysis of the lower limbs that left them unable to walk over ground. The array was positioned to allow stimulation of the lumbosacral posterior roots, which innervate pools of motor neurons that project to muscles in the lower limbs.

Credit: Adam Drobiec/Stockimo/Alamy Stock Photo

The authors configured the electrode array to activate the different groups of motor neurons, by first generating motor neuron ‘activation maps’ in healthy individuals and then simulating how EES of the posterior roots could generate such maps in each individual with SCI. These configurations were refined for each participant in the study, by using muscle activity as a readout of the spatial selectivity for each electrode.

The study’s participants were unable to voluntarily generate isometric forces in most of the joints in their lower limbs. However, spatially selective EES via the configured array allowed each participant to generate this force in a given muscle but on its own led to little muscle contraction, indicating that EES increased the excitability of motor neuron pathways to facilitate muscle activation.

The execution of movements is influenced by cortical activity, and the authors detected activity in the contralateral sensorimotor cortex of participants while they attempted to produce isometric forces in the knee joints without EES. This activity increased in the presence of EES, suggesting that such stimulation also increases cortical excitability, which may promote movement.

The authors next configured sequences of EES to reflect the timings of sequential changes in muscle activities, and hence motor neuron activation pattern, during walking. Over the course of 5 days, they finely adjusted the parameters of the EES while participants stepped on a treadmill with body weight support, to increase the activity in muscles that had previously shown little activity. The authors found that patients could voluntarily walk with use of a gravity assist when the finely tuned EES sequences were provided, but not when the EES was turned off. Moreover, with this spatiotemporally tuned EES, the participants were able to change aspects of their gait, stop their movement and walk on a treadmill for a prolonged period without muscle fatigue.

The authors compared their spatiotemporal EES with a continuous EES approach, which has been used in two other recent studies by Gill et al. and Angeli et al. to enable walking in individuals with SCI and paralysis. Wagner et al. found that although continuous EES increased muscle activity, it did not improve performance in their study, with participants losing awareness of limb position. An accompanying study by Formento et al. reported that continuous EES interfered with proprioceptive information processing in humans, but that this issue is mitigated by using spatiotemporal EES.

The participants in the Wagner et al. study followed a locomotion rehabilitation program with EES for 5 months and all showed further improvements in walking, to the extent that during EES they could walk with walkers or cycle in their own community. Moreover, even when EES was switched off, the participants showed signs of recovery of neural function, suggesting that the combination of EES and rehabilitation had triggered neuroplastic changes.

Together, the study by Wagner et al. and the other reports represent a considerable advance in research for SCI.

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ORIGINAL ARTICLES Wagner, F. B. et al. Targeted neurotechnology restores walking in humans with spinal cord injury. *Nature* **563**, 65–71 (2018) | Formento, E. et al. Electrical spinal cord stimulation must preserve proprioception to enable locomotion in humans with spinal cord injury. *Nat. Neurosci.* **21**, 1728–1741 (2018)
FURTHER READING Gill, M. L. et al. Neuromodulation of lumbosacral spinal networks enables independent stepping after complete paraplegia. *Nat. Med.* **24**, 1677–1682 (2018) | Angeli, C. A. et al. Recovery of over-ground walking after chronic motor complete spinal cord injury. *N. Engl. J. Med.* **379**, 1244–1250 (2018)