EPIDURAL STIMULATION

A giant step for spinal cord injury research

The combination of spinal epidural stimulation and physical therapy is restoring walking function to people with spinal cord injury. With intensive rehabilitation, some participants are able to walk in their communities during stimulation and even regain control over previously paralyzed movement in the absence of stimulation.

Chet Moritz

Imagine a time when technology and rehabilitation have advanced to the point where people with spinal cord injury can rise from their wheelchairs and begin to walk again. For many centuries paralysis due to spinal cord injury was believed to be incurable after any recovery that may have occurred in the first 6 months after injury. But recently, through a combination of advanced technology delivering electrical stimulation directly to the spinal cord and intensive physical therapy, people with spinal cord injury are beginning to walk again.

Wagner and colleagues[1] demonstrate for the first time that patterned electrical stimulation of the spinal cord surface (termed epidural stimulation) enabled three people with spinal cord injury to walk across the laboratory with minimal assistance. Two of these participants were even able to walk in their communities using a wheeled walker for balance and safety.

The team accomplished this feat by developing a real-time system for triggering patterns of stimulation delivered to the spinal cord to enable coordinated movements of the hips, knees, and ankles and restore stepping movements of the legs. The participants retained control over the timing and height of each step, demonstrating that their brains were able to collaborate with the stimulator to restore over-ground walking. Perhaps most notably, after several months of stimulation, all three users regained control of previously paralyzed muscles even without the stimulator active, strong evidence that the brain and spinal cord had re-established natural connections.

A key technical innovation of this work is in triggering different patterns of spinal stimulation via an implanted device depending on the phases of gait. This patterned stimulation may have key benefits, as described in a companion paper by the same team in *Nature Neuroscience*[2]. Through an elegant combination of modeling and experimental studies, the team lays out a convincing argument that continuous epidural stimulation may actually interfere with the sense of proprioception—the body's sense of where the legs are located in space. Formento and colleagues[2] find that epidural stimulation pulses may collide with sensory signals coming from the legs, reducing or eliminating the user's sense of proprioception, which is known to be critical for coordinated movement. Interestingly, they find that this occurs in humans but not in smaller animals, such as rodents, used in previous studies. This is likely due to the longer conduction distances in humans compared to rodents. They test whether patterned electrical stimulation in humans can provide a potential solution to minimize this sensory interference and possibly even create artificial sensations by stimulating different spinal locations at a productive time during the step.

When these studies are combined with two recent reports[3,4] reporting restoration of walking over-ground in cases of complete paralysis, we should consider these results across three independent research groups as a breakthrough in the treatment of paralysis. Moving forward toward clinical applications, the differences in stimulation approaches employed by these three groups will need to be sorted out. For example, the Courtine group[1,2] demonstrated excellent results using patterned stimulation for participants with some level of preserved sensory and motor function, whereas the studies using continuous epidural stimulation[3,4] targeted individuals with motor-complete, and in some cases sensory-complete, spinal cord injuries, in which residual proprioception may be limited or absent. Studies with more individuals are clearly needed in order to determine the best approach for people with a range of spinal cord injuries.

One feature that all these studies share is the extensive and prolonged rehabilitation that appears critical to enable the benefits of epidural stimulation. Participants completed between 100 and 278 sessions of combined stimulation and rehabilitation across these three studies over a period of 5 to 21 months. This suggests that stimulation

People with spinal cord injury are beginning to walk again through a combination of electrical stimulation and rehabilitation, with some recovery even outlasting the stimulation.

alone is not a magic bullet, but rather an enabler of recovery that progresses through the combination of stimulation and intensive rehabilitation.

The concept of progressive recovery is bolstered by the exciting discovery that all three participants in the Courtine study regained some voluntary movement that persisted even when the stimulation was turned off. This reinforces previous observations of sustained improvements in natural movement following epidural[5] and even transcutaneous spinal stimulation[6,7].

All these recent studies should cause us to rethink how we view and treat spinal cord injury. Rather than a complete disconnection between the brain and the spinal cord, it now appears that many people can regain the ability to control their paralyzed limbs and even walk again through the innovative combination of spinal stimulation and rehabilitation practice[8]. The fact that control of movement is maintained even beyond stimulation, as shown by Courtine and colleagues, suggests that this stimulation combined with rehabilitation is actually helping to direct plasticity and healing of the nervous system around the injury[9].

This most recent pair of papers from the Courtine group clearly reinforces the bright future for the treatment of spinal cord injury. Through the hard work and many small steps of brave and dedicated participants in the laboratory, the field of spinal cord injury is poised to take a giant leap forward in the treatment of what was until very recently considered incurable paralysis. ❐

Chet Moritz

Depts. of Electrical and Computer Engineering, Rehabilitation Medicine, Physiology & Biophysics, University of Washington, Seattle, Washington, USA.
e-mail: ctmoritz@uw.edu

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Competing interests

The author declares no competing interests.