## Spinal cord stimulation for walking restoration

Epidural Electrostimulation (EES) targeting the dorsal roots of lumbosacral segments restores walking in people with spinal cord injury (SCI). However, EES is delivered with multielectrode paddle leads that were originally designed to target the dorsal column of the spinal cord. Here, we hypothesized that an arrangement of electrodes targeting the ensemble of dorsal roots involved in leg and trunk movements would result in superior efficacy, restoring more diverse motor activities after the most severe SCI. To test this hypothesis, we established a computational framework that informed the optimal arrangement of electrodes on a new paddle lead and guided its neurosurgical positioning. We also developed software supporting the rapid configuration of activity-specific stimulation programs that reproduced the natural activation of motor neurons underlying each activity. We tested these neurotechnologies in three individuals with complete sensorimotor paralysis as part of an ongoing clinical trial ( www.clinicaltrials.gov identifier NCT02936453). Within a single day, activity-specific stimulation programs enabled these three individuals to stand, walk, cycle, swim and control trunk movements. Neurorehabilitation mediated sufficient improvement to restore these activities in community settings, opening a realistic path to support everyday mobility with EES in people with SCI <sup>1</sup>.

Wagner et al., introduced targeted spinal cord stimulation neurotechnologies that enabled voluntary control of walking in individuals who had sustained a spinal cord injury more than four years ago and presented with permanent motor deficits or complete paralysis despite extensive rehabilitation. Using an implanted pulse generator with real-time triggering capabilities, they delivered trains of spatially selective stimulation to the lumbosacral spinal cord with timing that coincided with the intended movement. Within one week, this spatiotemporal stimulation had re-established adaptive control of paralysed muscles during overground walking. Locomotor performance improved during rehabilitation. After a few months, participants regained voluntary control over previously paralysed muscles without stimulation and could walk or cycle in ecological settings during spatiotemporal stimulation. These results establish a technological framework for improving neurological recovery and supporting the activities of daily living after spinal cord injury <sup>2</sup>.

Long-term biointegration of man-made neural interfaces is influenced by the mechanical properties of the implant materials. Substantial experimental work currently aims at replacing conventional hard implant materials with soft alternatives that can favour a lower immune response. Here we assess the performance of a soft electrode array implanted in the spinal epidural space of a minipig model for a period of 6 months. The electrode array includes platinum-silicone electrode contacts and elastic thin-film gold interconnects embedded in silicone. textbfln-vivo electrode impedance and voltage transients were monitored over time. Following implantation, epidural stimulation produced muscle-specific evoked potentials and visible muscle contractions. Over time, postoperative and stimulation induced changes in electrode impedance were observed. Such trends provide a basis for future technological improvements aiming at ensuring the stability of soft implantable electrodes for neural interfacing <sup>3)</sup>.

Recovery of reaching and grasping ability is the priority for people with cervical spinal cord injury (SCI). Epidural Electrostimulation (EES) has shown promising results in improving motor control after SCI in various animal models and in humans. Notably, the application of stimulation bursts with spatiotemporal sequences that reproduce the natural activation of motoneurons restored skilled leg movements in rodent and nonhuman primate models of SCI. Here, we studied whether this conceptual framework could be transferred to the design of cervical EES protocols for the recovery of reaching and grasping in nonhuman primates. We recorded muscle activity during a reaching and grasping task in a macaque monkey and found that this task involves a stereotypical spatiotemporal map of motoneuron activation. We then characterized the specificity of a spinal implant for the delivery of EES to cervical spinal segments in the same animal. Finally, we combined these results to design a simple stimulation protocol that may reproduce natural motoneuron activation and thus facilitate upper limb movements after injury <sup>4)</sup>.

## 1)

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