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RESEARCH HIGHLIGHT

A digital bridge to reverse paralysis

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Injury to the spinal cord can disrupt the neural circuits necessary for locomotion. In a recent paper published in *Nature*, Lorach et al. demonstrate the feasibility of implementing a 'digital bridge' between the brain and spinal cord to improve locomotor function in an individual with chronic spinal cord injury.

Injury to the spinal cord causes disruption of the neural circuits that underlie locomotor activity and creates a hostile environment that is inhibitory to regeneration. While several strategies have aimed to ameliorate the inhibitory microenvironment of the injured spinal cord to facilitate axon regrowth and restore damaged circuits, these approaches have been met with significant challenges and to date there remains no effective treatment for spinal cord injury (SCI). Novel strategies that aim to stimulate spared circuitry or bypass the lesion epicentre have shown promise in improving locomotor function after SCI.

Previous work has demonstrated that epidural electrical stimulation of the dorsal root entry zones of the lumbosacral spinal cord during rehabilitation improves locomotor function in patients with both incomplete and complete SCI.[1–4] Epidural electrical stimulation of cervical spinal circuits has also enhanced voluntary upper limb motor control.[5,6] The development and incorporation of brain–machine interfaces into these neuromodulatory approaches has further aided in restoring natural movements. Indeed, brain–machine interface training of a neuroprosthetic device facilitated restoration of hand function in SCI patients.[7] Previously, a brain–spinal cord interface (BSI) connecting leg motor cortex activity with epidural electrical stimulation of the lumbar spinal cord improved locomotion following SCI in nonhuman primates.[8]

Building on this previous work, Lorach et al. have now demonstrated for the first time in an individual living with SCI that disruptions to locomotor circuitry can be partially restored through the use of a digital bridge (or BSI), which communicates the motor commands generated in the brain to target muscles (Fig. 1).[9] The participant described in the study sustained a C5/6 incomplete SCI 10 years prior to implantation of a BSI, and previously underwent an intensive neurorehabilitation program with targeted epidural electrical stimulation. While he had improved locomotor function after his initial training, his recovery plateaued and as such underwent implantation of the BSI.

The digital bridge employed in the patient was comprised of cortical and spinal implants. Placement of the cortical implant was based on a combination of anatomical and functional imaging data whereby cortical regions responding to the target lower limb movement were selected. Spinal leads were placed over the dorsal root entry zone of the lumbar spinal cord and further optimized using intra-operative electrophysiological recordings. Electrocorticographic signals were recorded during lower limb movement to extract the associated signal features and epidural electrical stimulation programs were configured to have control over activity of the target muscle. Calibration of the BSI involved the development of an algorithm to calculate the probability of intention to move a target muscle and predict the amplitude and direction of the movement. This information was subsequently translated to an analogue controller which modulated the stimulation command and fed to the pulse generator.

Use of the BSI improved voluntary control of walking and further facilitated activities requiring more complex coordination and locomotor abilities, translating to an improvement in several quality-of-life metrics. Moreover, the decoder features and stimulation programs remained stable over time and there was demonstrated reinforcement of cortical features suggesting lasting improvements in the patient's ability to modulate cortical activity with the BSI.

While this study describes a single patient's experience with a BSI, the results nonetheless support a promising strategy to improve locomotor function following SCI. Indeed, development of a BSI system ushers in a new era of neuromodulatory techniques that have the potential to transform the management of neurological disorders. As SCI is a heterogeneous injury, further studies testing BSI across the spectrum of injury severities, levels and chronicity will be critical. Specifically, the degree of recovery in complete SCI patients with application of a BSI remains to be explored. Understanding the contribution of spared circuitry to recovery will be an important step in selecting appropriate patients and predicting outcomes. Furthermore, additional investigation is needed before results can be generalized to restoring upper extremity function. In addition to direct effects on locomotor activity, maintenance of functional cortical connectivity through the use of a BSI may reduce maladaptive plastic changes after SCI.[10] As such, future investigation into the effects of BSI-assisted rehabilitation on attenuating spasticity and neuropathic pain is warranted.

While BSI systems are likely to have a profound impact on the management of SCI, any stimulation-based therapy requires a concurrent extensive rehabilitation plan. Prior to implantation of the BSI, the individual described in the study underwent a 5-month rehabilitation period with combined epidural electrical stimulation which was followed by BSI-supported neurorehabilitation. As such, it is imperative to determine the optimal rehabilitation strategy that is specific to the level of SCI and that targets the underlying disrupted circuitry. Furthermore, exploring synergistic effects of BSI-combined rehabilitation training with

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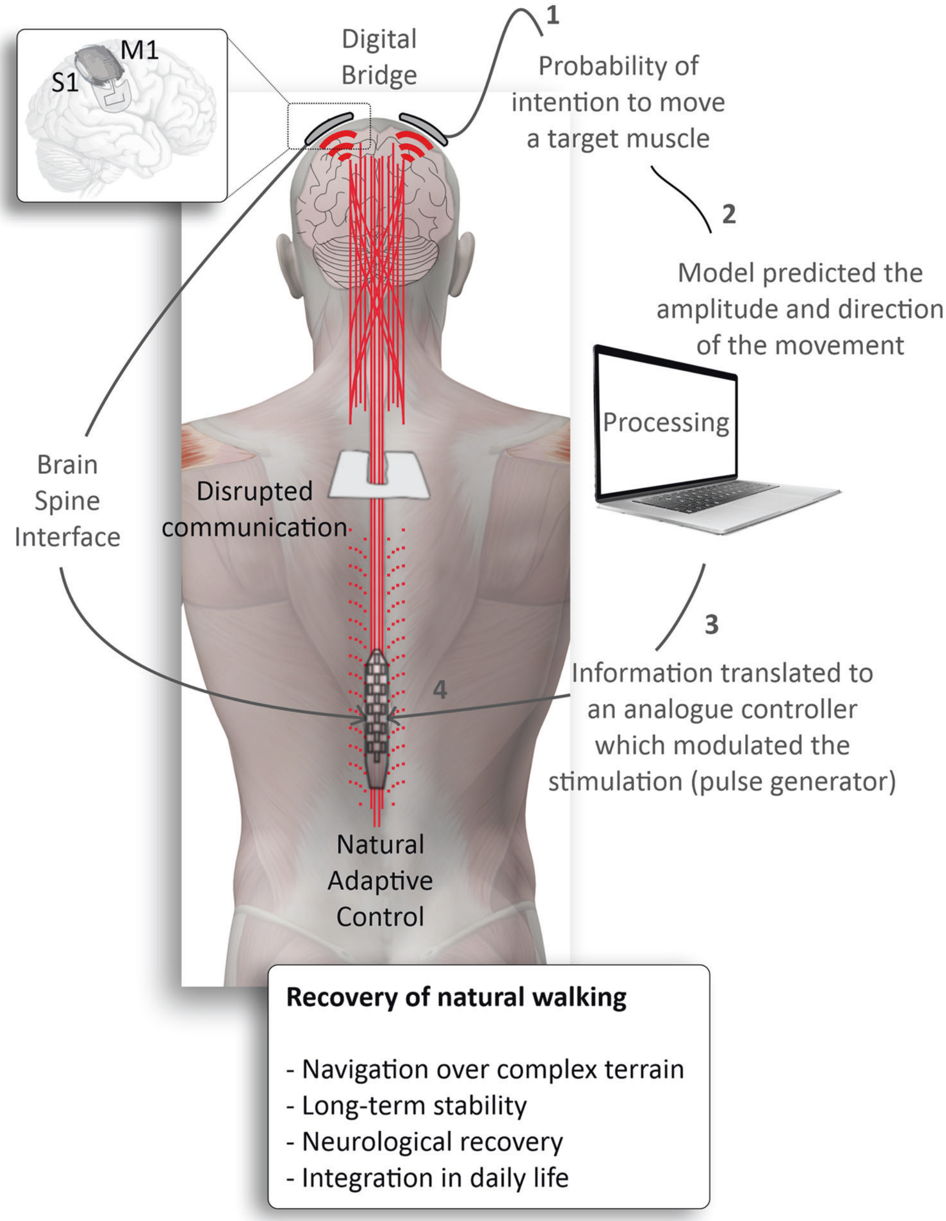

Fig. 1 Neural connections between the motor cortex and target muscles (red), are critical for appropriate control of movements. Disruption of this communication after SCI may be bridged by a digital interface, communicating the motor commands generated in the brain to the target muscles — also known as a brain–spine interface. Using this interface, a paralyzed individual could communicate motor intentions to the muscles in a naturalistic manner and regain the ability to walk — including over complex terrains.

other experimental treatment modalities for SCI that are on the horizon for clinical translation, such as pharmacotherapy, biological agents and cellular replacement strategies, may further augment functional recovery.

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ADDITIONAL INFORMATION

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