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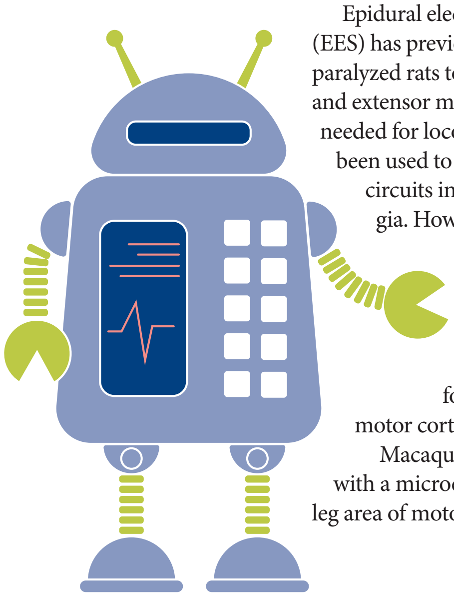
SYSTEMS NEUROSCIENCE

Opening the gait

> application of the brain–spine interface restored weight-bearing locomotion to the impaired limb

Damage to the spinal cord can result in permanent limb paralysis below the site of injury. Although it is currently not possible to achieve functional recovery of movement by repair of spinal cord tissue, an alternative approach is to use a 'brain–spine interface' to bypass the injury site and deliver brain-derived signals to the spinal neurons that drive movement. Here, Capogrosso *et al.* design a wireless brain–spine interface in macaque monkeys that combines locomotion-related activity patterns in motor cortex and spinal cord to restore gait after spinal injury.

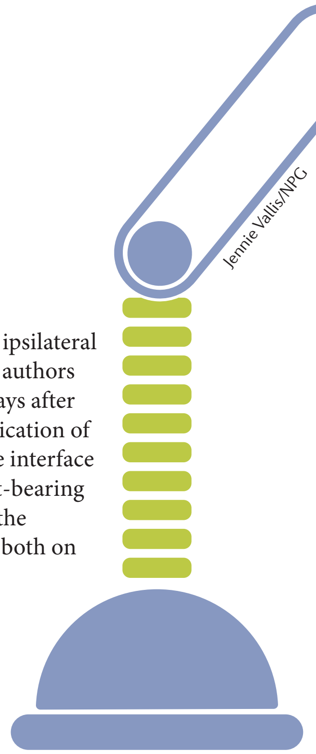
Epidural electrical stimulation (EES) has previously been used in paralyzed rats to activate the flexor and extensor muscle groups that are needed for locomotion, and has also been used to activate spinal motor circuits in people with paraplegia. However, voluntary movement requires input from the brain, and the authors sought to develop a system that could transform input from the motor cortex into an EES signal.



Macaques were implanted with a microelectrode array in the leg area of motor cortex and with electrodes in the leg muscles that are involved in locomotion. The readout of these electrodes allowed the authors to build a picture of how patterns of activity in motor cortex related to activation of extensor and flexor muscles during locomotion. They found that spiking activity in the motor cortex was cyclic and phase-locked with the contralateral leg movements. In addition, when muscle activity patterns during locomotion were projected onto spatiotemporal maps of spinal motor neuronal activation, the extension and flexion phases were revealed to be accompanied by successive activation of specific spinal cord regions, which the authors termed 'hotspots'.

To develop a brain–spine interface capable of driving volitional locomotion the authors integrated signals decoded from the motor cortex with gait-generating patterns of activity in the spinal cord. These activity patterns were delivered wirelessly and in real time to an EES system that sent pulses of activation to the locomotor hotspots.

To test the ability of this system to restore gait two monkeys were subjected to unilateral spinal injury in the thoracic region, which resulted in impaired locomotor function of the ipsilateral hind limb. The authors found that, 6 days after the lesion, application of the brain–spine interface restored weight-bearing locomotion to the impaired limb, both on a treadmill and over ground. Performance was reduced slightly over the next few days, possibly owing to cortical reorganization, but was followed by a further improvement in gait quality and quantity.



Overall, these data demonstrate the use of a brain–spine interface to produce functional recovery of gait in a primate model of spinal cord injury and indicate that this approach could hold promise for humans with paralysis resulting from spinal cord damage. A feasibility clinical trial is evaluating the spine-part of the interface.

Sian Lewis

ORIGINAL ARTICLE Capogrosso, M. *et al.* A brain–spine interface alleviating gait deficits after spinal cord injury in primates. *Nature* **539**, 284–288 (2016)