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A brain spinal interface alleviating locomotor deficits after spinal cord injury

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SUMMARY

Various neurological disorders disrupt the communication between supraspinal centers and the spinal circuits that control lower limb movements.

Here, we introduce a brain spinal interface whereby cortical dynamics directly triggers electrical spinal cord neuromodulation protocols to adjust hindlimb movements in freely behaving non-human primates.

Two intact rhesus macaques received an epidural spinal electrode implant that was tailored to access flexor versus extensor muscle synergies for the left and right hindimbs.

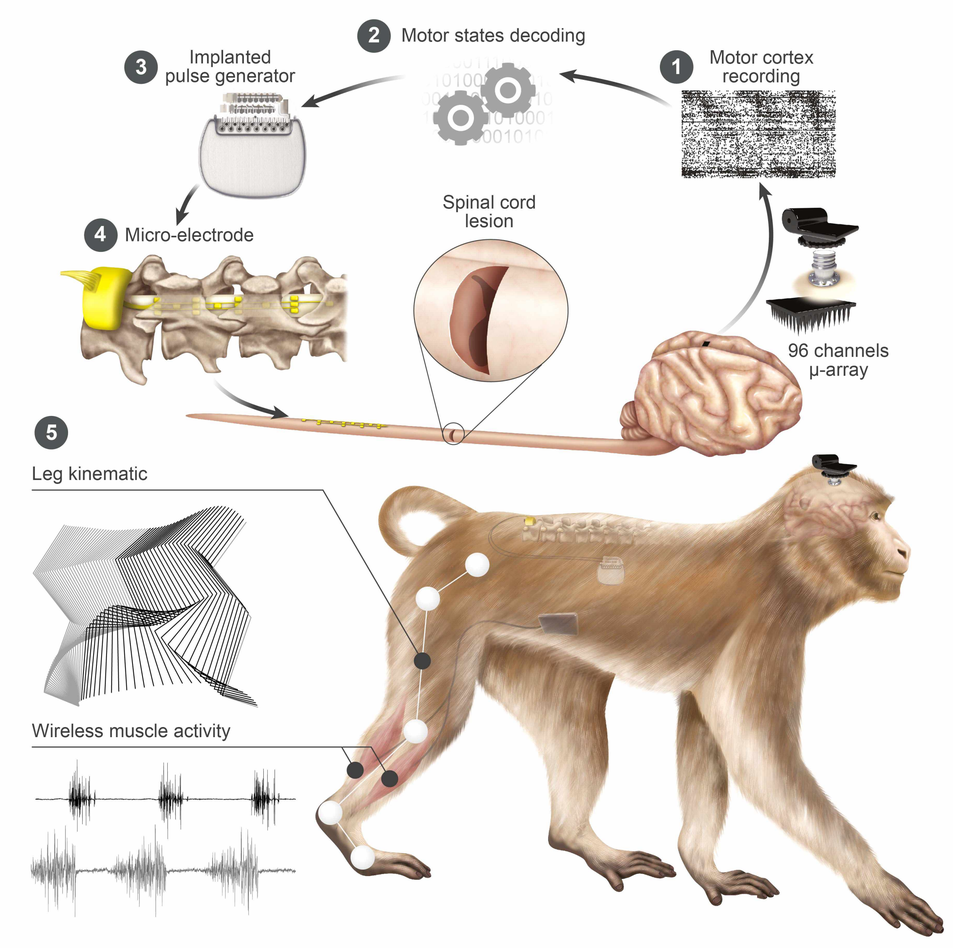
Motor intentions decoded from spiking activity of neurons located in the leg area of the motor cortex (M1) directly adjusted the location and timing of electrical spinal cord neuromodulation.

This brain spinal interface (BSI) allowed the monkeys to enhance the degree of flexion versus extension of their hindlimbs during continuous locomotion without disrupting the natural dynamics of gait.

After a unilateral lesion of the corticospinal tract, the BSI restored weight bearing plantar movements of the paralyzed hindlimb in the early stage after injury, and alleviated residual gait deficits in the late-stage of spontaneous recovery in both macaques.

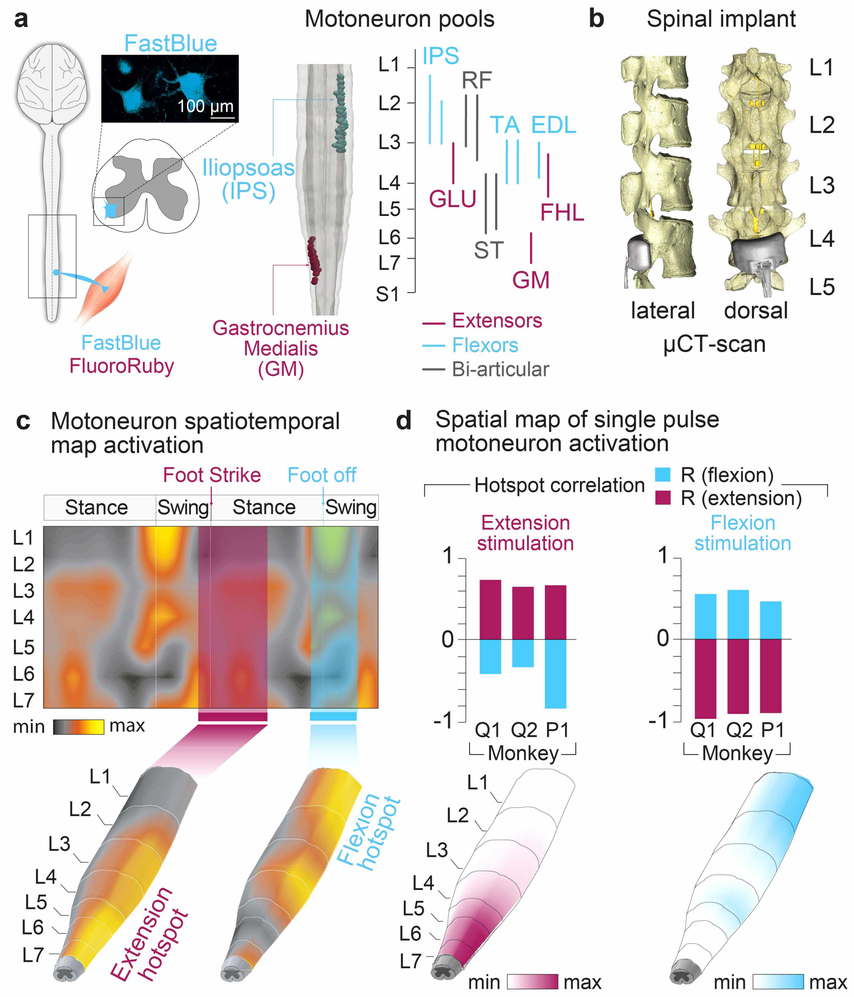
These technologies and concepts have the potential to translate into a brain spinal interface to improve leg motor control recovery after neurological deficits in humans.

Technological design of the Brain-Spinal Interface



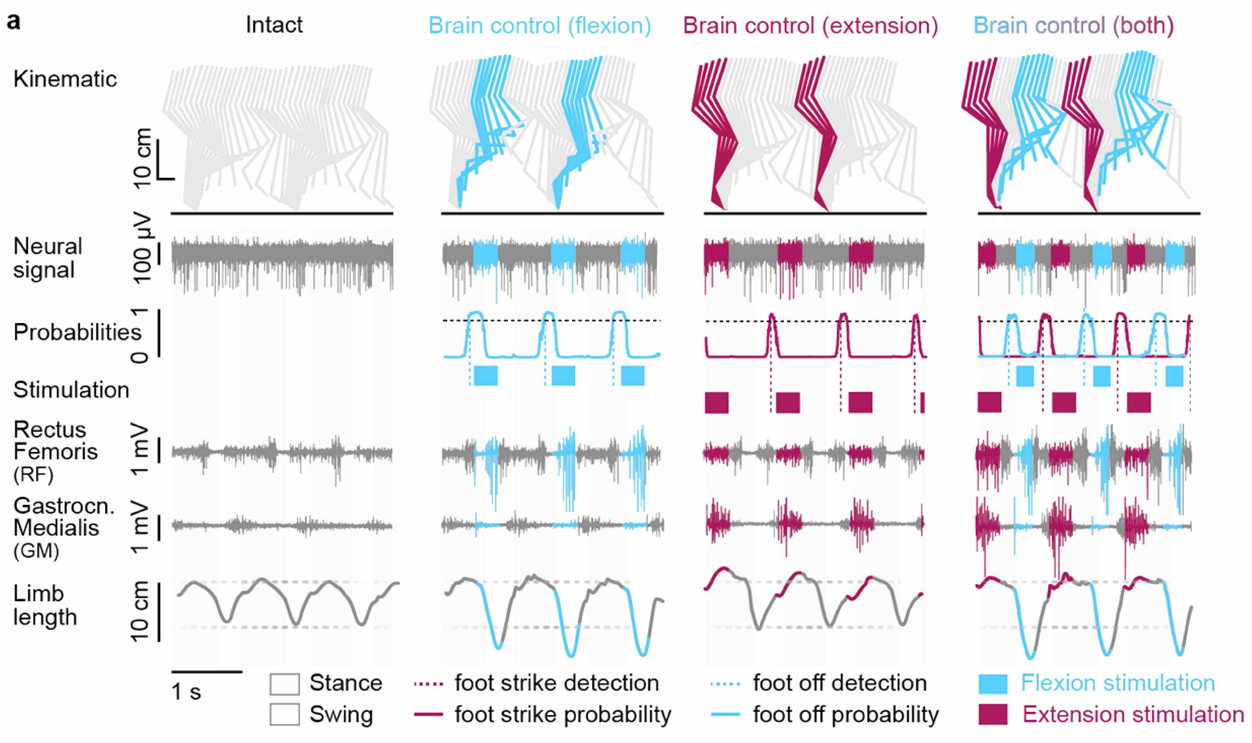
(1) Spiking activity was recorded wirelessly from a microelectrode array implanted in the leg motor cortex of freely moving monkeys. (2) A decoder running on the control computer identified motor states from these neural signals. (3) These motor states triggered electrical spinal cord stimulation protocols, via a pulse generator with real-time triggering capabilities. (4) The stimulator was connected to a spinal implant with electrodes that selectively targeted dorsal roots of the lumbar spinal cord. (5) Locomotor performance was quantified using kinematic and muscle activity recordings.

Selective spinal cord stimulation protocols



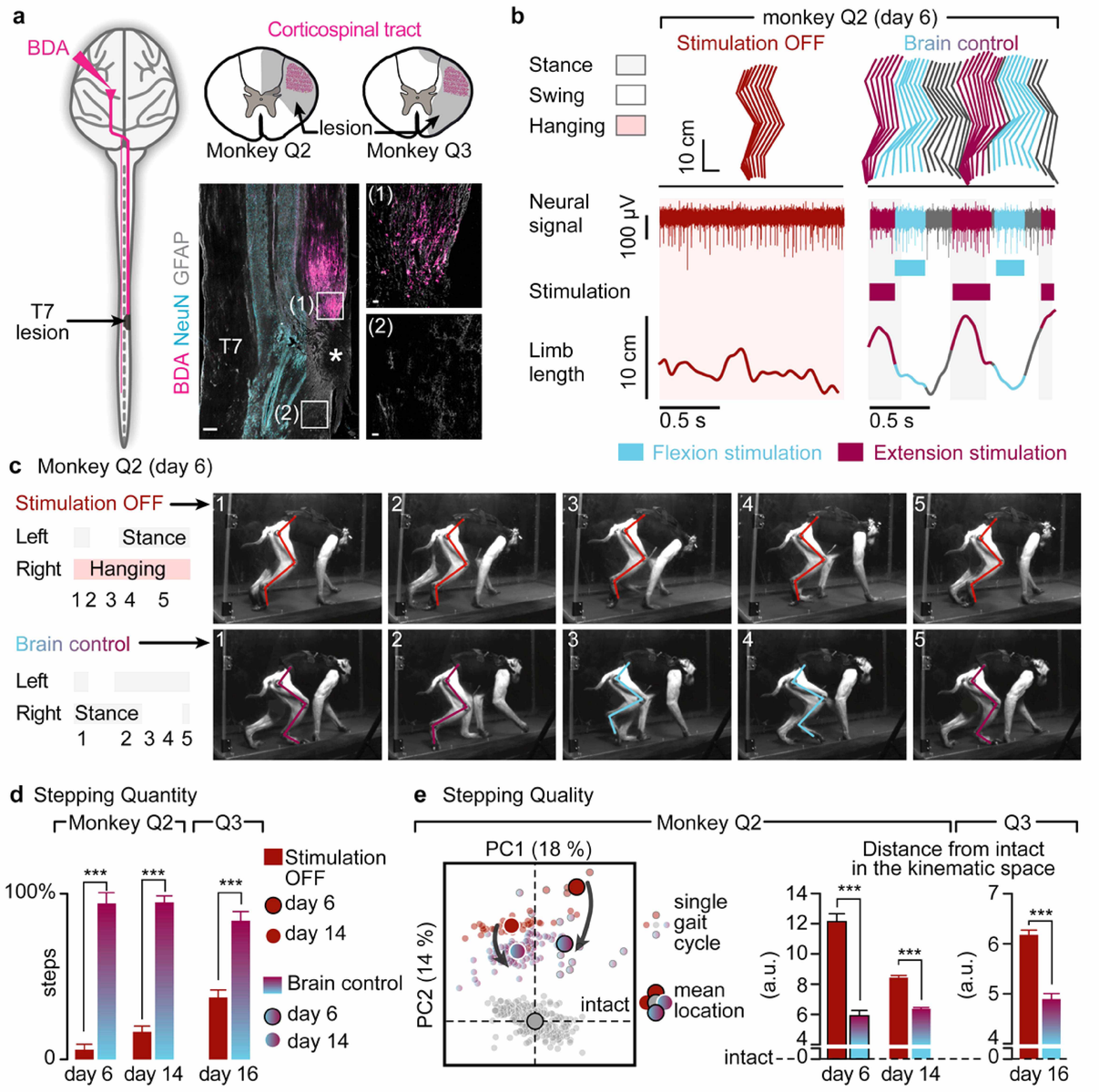
(a) Motoneurons labeled by retrograde tracers injected into leg muscles and their rostrocaudal distribution along the spinal cord. (b) High–resolution µ-CT scans of the spinal implant. (c) Spatiotemporal map of motoneuron activation (spinal map) during locomotion of an intact monkey and the average maps around foot off and foot strike showing 2 hotspots. (d) Spinal maps resulting from single pulses delivered through the electrodes targeting the extension and flexion hotspots, and their correlation with the spatial maps obtained in (c).

Brain-controlled stimulation modulates leg flexion and extension in intact monkeys



(a) Intact monkey walking on a treadmill without stimulation and with brain-controlled stimulation of the flexion hotspot, extension hotspot, or both. Top to bottom: stick diagrams showing leg movement; single-channel neural recording; foot off and foot strike probabilities; flexion vs extension stimulation (resp. cyan, magenta); EMG recordings; limb length. (b) Step height and activity of the ankle extensor as a function of stimulation frequency or amplitude. (c) Mean step height and ankle extensor activity with and without stimulation (monkey Q1: n = 125 steps; monkey Q2: n = 119 steps). (d) Decoder confusion matrices during stimulation.

Brain-controlled stimulation alleviates gait deficits after spinal cord injury



(a) 2 monkeys received a unilateral corticospinal tract lesion (grey), interrupting fibers from the motor cortex (BDA, pink). Scale bars: 500µm and 50µm. (b-c) The lesion provoked a paralysis of the ipsilateral leg. Brain-controlled stimulation restored leg movement (Q2, 6 days post-lesion). (d) Percentage of steps without paralysis in the absence of stimulation (Q2: n = 6 for day 6, n = 39 for day 14; Q3: n = 68) and during stimulation (Q2: n = 12 for day 6, n = 93 for day 14; Q3: n = 31). (e) PCA applied on 26 gait parameters calculated from all steps without paralysis in Q2. Bar plots: mean Euclidean distance between pre-lesion and post-lesion steps in kinematic space.