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Neuroprosthetic technologies to improve functional recovery after neuromotor disorders

Functional restoration after spinal cord injury has been interpreted as the need to promote long-distance regeneration of severed fibers to their original targets. A radically new and more immediately applicable approach may instead capitalize on the capacity of neuronal circuits within the spinal cord to generate effective postural and locomotor tasks. To exploit this potential, however, the spinal circuitry must be reactivated and remodeled in the context of the post-injury neurophysiological state of the spinal cord. Here, I will introduce neuroprosthetic technologies combining intrathecal drug delivery, spinal electrode arrays and closed-loop control systems that are capable of reactivating spinal locomotor networks after a spinal cord injury. I will show the ability of multisite stimulation patterns to control locomotor foot trajectory of otherwise paralyzed rats in real-time and with a remarkable degree of precision. In combination with robot-assisted training, this electrochemical spinal neuroprosthesis restored supraspinal control over a range of leg movements in rats with a spinal cord injury leading to complete and permanent paralysis. We found that the recovery relied on the extensive and ubiquitous remodeling of neuronal pathways. Training encouraged the brain to elaborate de novo intraspinal detour circuits that relayed the supraspinal command to spinal locomotor circuits. These findings may inspire new thinking for the design of strategies to return motor function after spinal cord injury and other neuromotor disorders in humans.

Peer-reviewed Publications (selection)

1. Van den Brand R, Heutschi J, barraud Q, Digiovanna J, Bartholdi K, Huerlimann M, Friedli L, Vollenweider I, Martin Moraud E, Duis S, Dominici N, Micera S, Musienko PE, Courtine G (2012) Restoring voluntary control of locomotion after paralyzing spinal cord injury. **Science**. 336(6085): 1182-1185
2. Dominici N, Keller U, Vallery H, Friedli L, van den Brand R, Starkey ML, Musienko P, Riener R, Courtine G (2012) Novel robotic interface to evaluate, enable, and train locomotion and balance after neuromotor disorders. **Nature Medicine**. (18) 1142–1147.
3. Courtine G, van den Brand R, Musienko P (2011) Spinal cord injury: time to move. **Lancet** 377:1896-1898.
4. Courtine G, Rosenzweig ES, Jindrich DL, Brock JH, Ferguson AR, Strand SC, Nout YS, Roy RR, Miller DM, Beattie MS, Havton LA, Bresnahan JC, Edgerton VR, Tuszynski MH (2010) Extensive spontaneous plasticity of corticospinal projections after primate spinal cord injury. **Nature Neuroscience** 13:1505-1510.
5. Courtine G., Gerasimenko Y. P., van den Brand R., Yew A., Musienko P., Zhong H., Song B., Ao Y., Ichyama R., Lavrov I., Roy R. R., Sofroniew M.V., Edgerton V.R. (2009) Transformation of nonfunctional spinal circuits into functional and adaptive states after complete loss of supraspinal input **Nature Neuroscience**. 12(10):1333-1442.
7. Courtine G, Song B, Roy RR, Zhong H, Edgerton VR, Sofroniew MS (2008) Recovery of supraspinal control of stepping mediated by indirect propriospinal relay connections after severe spinal cord injury. **Nature Medicine**. 14: 69-74.
8. Courtine G, Bunge MB, Fawcett JW, Grossman RG, Kaas JH, Lemon R, Maier I, Martin J, Nudo RJ, Ramon-Cueto A, Rouiller EM, Schnell L, Wannier T, Schwab ME, Edgerton VR (2007) Can experiments in nonhuman primates expedite the translation of treatments for spinal cord injury in humans? **Nature Medicine** 13:561-566.