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Unique spatiotemporal neuromodulation of the lumbosacral circuitry shapes locomotor success after spinal cord injury

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Abstract

© 2016, Mary Ann Liebert, Inc. 2016.Spinal cord epidural stimulation has resulted in the initiation of voluntary leg movements and improvement in postural, bladder, and sexual function. However, one of the limitations in reaching the full potential of epidural stimulation for therapeutic purposes in humans has been the identification of optimal stimulation configurations that can neuromodulate the spinal cord for stepping. In the present work, we investigated the mechanisms underlying the specificity of interaction between the rostral and caudal spinal cord circuitries in enabling locomotion in spinal rats (n = 10) by epidural spinal cord stimulation. By using unique spatiotemporal epidural stimulation parameters of the lumbar and sacral spinal cords, a robust stepping pattern in spinal rats was observed with only six training sessions and as early as 3 weeks post-injury. Electrophysiological evidence reveals that in addition to frequency of stimulation pulses at the stimulation sites, the relative timing between stimulation pulses applied at the lumbar (L2) and sacral (S1) segments of the spinal cord heavily impacted stepping performance. Best stepping was established at a higher stimulation frequency (40 Hz vs. 5, 10, 15, and 20Hz) and at specific relative time-intervals between the stimulation pulses (L2 pulse applied at 18-25 msec after the onset of the S1 pulse; S1 pulse applied 0-7 msec after the L2 pulse). Our data suggest that controlling pulse-to-pulse timing at multiple stimulation sources provides a novel strategy to optimize spinal stepping by fine-tuning the physiological state of the locomotor networks. These findings hold direct relevance to the clinician who will incorporate electrical stimulation strategies for optimizing control of locomotion after complete paralysis.

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Keywords

electromyography, epidural stimulation, locomotion, locomotor networks, neuromodulation, rat, spinal cord injury