A Computational Model of the Rat Spinal Cord: Multipolar Electrical Epidural Stimulation with Multi-Electrode Arrays

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EPIDURAL electrical stimulation (EES) of lumbosacral segments is a promising intervention to improve motor function after spinal cord injury (SCI). Recent experiments in rats with experimentsl SCI and in humans with severe spinal cord damage suggested that continuous EES applied over specific lumbosacral locations could facilitate distinct aspects of standing and walking. However, the mechanisms underlying site-specific facilitation of movement are poorly understood. Consequently, there is limited information available on the optimal strategy for the design and use of Multi-Electrode Arrays (MEAs) to achieve the highest possible degree of specificity in the recruitment of motor circuits and movement patterns with EES.

To address this question, we developed a realistic computational model of the rat lumbosacral spinal cord, which we comprehensively validated with electrophysiological and pharmacological experiments.

Our combined results revealed that EES, near-exclusively engages primary afferent fibers and laterally applied EES achieved side-specific modulation of induced limb movements.

However, EES applied with monopolar configuration has limited ability to recruit afferent fibers associated with specific muscular groups. For example, the selectivity of agonist/antagonist ankle muscles, the Medial Gastrocnemius (MG) and Tibialis Anterior (TA), was biased towards flexion. While the predictions of the computational model were confirmed in acute *in vivo* experiments, the effects of EES differed when delivered during continuous locomotion. Under these dynamic conditions, the modulation of segmental reflex systems promoted a high degree of selectivity in the functional effects of EES. To capitalize on this potential we exploited our advanced computer model do investigate the capacity of multipolar stimulation to facilitate specific aspects of leg movements in spinal rats.

We identified various configurations of balanced and unbalanced bipolar stimulations that significantly enhanced the capacity of EES to engage specific sensorimotor circuits. Moreover, we found that multipolar EES sites could be combined flexibly to promote bilateral or limb-specific movements of flexion and extension.

In particular, multisite monopolar stimulation is able to achieve very high limb specificity, recruiting limb specific muscle groups. However it lacks both of muscular and spatial (segmental) selectivity with an unbalance towards flexion muscle groups selectivity, and poor or negligible extensors groups selectivity. This phenomenon is due to the peculiar anatomical characteristics of the lumbosacral enlargement where roots afferents run longitudinally surrounding the cord. Multipolar stimulation instead, is able to achieve very high inter and intra-limb extensor selectivity. In terms of spatial selectivity a precise selection of lower and upper lumbar segments is possible, overcoming the difficulties found with classic monopolar EES. These results demonstrate the ability of multipolar EES to boost the controllability of spinal sensorimotor circuits during movement execution. For the first time, we applied a validated computational model to predict near-optimal configuration of the stimulation to facilitate specific types of movements with multipolar EES. These results establish a practical and mechanistic framework to steer the design of MEA configuration, and the development of multisite EES patterns, to facilitate recovery of motor functions after a range of neurological disorders.

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