PATTERN GENERATING NETWORKS IN THE HUMAN LUMBAR SPINAL CORD: ELECTROPHYSIOLOGY AND COMPUTER MODELING

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Abstract: Epidural spinal cord stimulation can produce rhythmic motor output to the lower limbs of motor complete spinal cord injury people. The electromyographically recorded activity consists of a series of modulated stimulus time-related compound muscle action potentials (CMAPs). Here, we investigate phase dependent modification of the CMAP latencies and present a computer model that mechanistically describes putative locomotor pattern generating circuitries of the human lumbar spinal cord. Thereby we gained insight into the organization of the human spinal pattern generating networks, revealed common control characteristics with the central pattern generators for locomotion described in animal experimental work and highlighted specifities of the studied model.

Keywords: Locomotor pattern generators, human lumbar spinal cord, spinal cord injury, epidural spinal cord stimulation

Introduction

The existence of locomotor pattern generating neural networks in the human lumbar spinal cord is meanwhile well accepted. Yet, little is known about their organization. Epidural stimulation over the lumbar spinal cord can produce rhythmic activities in the paralyzed lower limbs \cite{1, 2}, comprised of stimulus-triggered compound muscle action potentials (CMAPs), the posterior root-muscle (PRM) reflexes \cite{3, 4}. Their modulation gives insight into the operation of the neural circuits in the lumbar spinal cord. Here, we present electrophysiological analyses of CMAP modulation during rhythmic EMG activity in motor complete spinal cord injured subjects during epidural spinal cord stimulation as well as a computer model incorporating the findings of the electrophysiological study.

Methods

Electromyographic recordings of quadriceps, hamstrings, tibialis anterior and triceps surae, bilaterally in response to epidural stimulation at 2 Hz–42 Hz were analyzed in 10 individuals with motor complete postrumatic SCI. Thirty-nine segments (duration: 10 s) of rhythmic activities in motor complete spinal cord injured subjects during epidural spinal cord stimulation as well as a computer model incorporating the findings of the electrophysiological study.

Results

In all 10-s segments, rhythmic activities of all muscle groups had the same cycle frequency. In-between muscles, rhythmic activity occurred largely synchronous or alternating, in other words bursts were either co-active or reciprocal between any two muscle groups. PRM reflexes constituting bursts during the extension phases had monosynaptic latencies. These responses were predominantly suppressed during flexion and were replaced by delayed, oligosynaptic PRM reflexes in quadriceps, tibialis anterior and triceps surae (for an example see figure 2).
The modeled pattern generating networks could be activated by pulsed stimulation. Their frequency-dependent activation was strongly related to the time constant of persistent Na channels. Rhythmic activity was produced by bursting and non-bursting neurons of the pattern generating half-centers. Stimulus-coupled responses as the only components comprising the rhythmic activity can be explained when the interneuronal network is only exerting subthreshold modifications of the motoneurons’ membrane potential when activated by pulsed epidural stimulation, thus only modifying their excitability. In the extension half-center, direct afferent connections play a dominant role in exciting motoneurons as suggested by constant CMAP latencies. The existence of a mono- and a separate oligosynaptic pathway with presynaptic inhibition of the afferent fibers of the flexor half-center synapsing on the motoneurons and disinhibition of an oligosynaptic pathway explains the substitution of the short latency CMAPs by prolonged ones. Inhibition acting on the motoneurons through postsynaptic potentials would influence both pathways and would not explain their independent regulation. Again, the timed input from the afferents, here over the mono- or oligosynaptic path, are causative for the action potential generation in the motoneurons, hence producing stimulus time-related CMAPs.

Discussion

The pulsed nature of the stimulation, providing a causal relation between input and output, along with the computer simulation of the processing network revealed components of the organization of the locomotor pattern generating networks in humans. Together, the electrophysiological data and the computer model suggest a half-center organization of the human locomotor pattern generating networks in the lumbar spinal cord with asymmetric control of flexors and extensors with common rhythm generating circuits.

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Bibliography