

Sacral dorsal column stimulation induced locomotor-like activity is enhanced via tubocurarine and output-based positive feedback

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Stimulation of primary afferent fibers can activate the spinal locomotor central pattern generator (CPG) and modify ongoing activity. We have demonstrated that electrical stimulation of the sacral (S2-S4) dorsal columns initiates bouts of locomotor-like activity (LLA) recorded at the lumbar ventral roots. Here we present data which further characterizes the pathway(s) involved and implements feedback-controlled sacral dorsal column (sDC) stimulation as a means to reinforce ongoing motor patterns. Experiments were undertaken in the isolated neonatal rat spinal cord with stimulation trains of 2 Hz pulses used to activate the CPG.

We previously described adrenoceptor involvement in sDC stimulation-evoked LLA as α -adrenoceptor antagonists abolish the induced LLA (3/3). Using a split bath preparation (separated at L4 or L6), we now report that adrenoceptor antagonist actions are restricted to the caudal bath, attenuating alternating activity 67% of the time (8/12). Application of the same antagonists to the rostral bath had no effect (5/5). In addition, we previously reported sDC stimulation evoked LLA is attenuated by cholinergic receptor antagonists (atropine, DHbE, and mecamlamine) in the rostral bath. We now report that the nicotinic receptor antagonist, tubocurarine (5-10 μ M), enhances the duration of stimulus-evoked LLA (3/4). We will test the hypothesis that tubocurarine reduces presynaptic inhibition in activated primary afferents.

We next examined the effect of sDC stimulation on 5HT/NMDA induced LLA. Single pulses produced resetting phase advances of the locomotor pattern and revealed that sDC stimulation caused an overall enhancement of the CPG output (3/3). We then devised a simple closed-loop feedback system that autonomously triggered stimulation of the sDC following threshold-based motor burst detection. Weak, irregular LLA was neurochemically induced; after implementing closed-loop stimuli, we observed less variable motor patterns in all ventral roots with phase relations consistent with LLA (2/2).

Overall, we plan to merge pharmacological insight of the neural circuitry generating sDC stimulation-induced LLA with closed-loop manipulation of the motor pattern to optimize locomotor rhythmogenesis. Results obtained may translate into novel rehabilitative therapies for those with spinal cord injury.

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