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Investigating the Neural Circuits of Spinal Cord Stimulation

Abstract

Neuromodulation approaches such as spinal cord stimulation (SCS) provide important alternative strategies for treating pain conditions when other therapies have failed. Despite widespread clinical implementation, the mechanisms underlying the analgesic actions of SCS remain poorly understood. We have identified a novel form of long-term synaptic depression of high-threshold C-fiber evoked excitatory synaptic currents induced by a SCS-like conditioning protocol (Aβ electrical stimulation, Aβ-ES) in superficial dorsal horn (SDH) neurons. It is unknown whether this synaptic depression leads to a sustained change in the activity of SDH neurons. The overall objective of the present application is to dissect the neuronal network mediating the analgesic effects of Aβ-ES. I hypothesize that Aβ-ES achieves analgesia by modulating SDH nociceptive networks, inducing a prolonged decrease in noxious-evoked activity of excitatory interneurons and an increase in activity of inhibitory interneurons. The proposed experiments take advantage of state-of-the-art imaging of genetically encoded calcium indicators expressed specifically in inhibitory or excitatory neuronal populations to delineate the effect of Aβ-ES on activity of these populations in real time over the entire SDH. I will pursue two Specific Aims.

1. Determine the extent to which a conditioning train of Aβ-ES increases the activity of inhibitory interneurons in the SDH evoked by high-threshold stimulation.
2. Determine the extent to which a conditioning train of Aβ-ES depresses the activity of excitatory interneurons in the SDH evoked by high-threshold stimulation.