The processing of nociceptive information in the spinal dorsal horn may undergo significant plastic changes following peripheral nerve injury or inflammation to perhaps lead to the development of chronic pain. We have used the well-established loose ligation of the rat sciatic nerve model of neuropathic pain, and reported that injury-induced, activity-dependent long-lasting synaptic plasticity in the spinal dorsal horn might be at least one important contributor to the development of chronic pain. In the brain, long-lasting synaptic plasticity may enable learning and memory. In the spinal dorsal horn, however, it may lead to an undesirable change in synaptic function that transforms the essential but rapidly terminated sensation of acute pain into unnecessary and unproductive persistent pain. The development of long-lasting synaptic plasticity in the spinal dorsal horn may help explain how a low-intensity, innocuous peripheral stimulus may be transformed into a high-intensity, painful central sensation.

The goal of our present work is to identify at least some of the neuroactive substances whose action is modified by injury to lead to the development of long-lasting synaptic plasticity in the spinal dorsal horn (and by extension to chronic pain). Most recently we have focused on cyclic AMP response element binding protein (CREB), a nuclear regulatory protein, and brain-derived neurotrophic factor (BDNF), a trophic factor essential for neuronal growth and differentiation. In the hippocampus, activation of CREB may up-regulate BDNF transcription to promote the strengthening and remodeling of synaptic connections and critically contribute to long-lasting synaptic plasticity. Our most recent findings support the notion that both CREB and BDNF may similarly promote long-lasting synaptic plasticity in the spinal dorsal horn.

We are hopeful that successful completion of our studies will enhance our understanding of how sensory information processing in the spinal cord is modified after injury to lead to the development of chronic pain. An enhanced understanding of the role of potential contributors to spinal plasticity should promote the development of novel, mechanistically based, and successful analgesic treatments to prevent or abolish chronic pain and minimize or eliminate patient suffering.

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