

Neuropathic Pain and Lumbar Disc Herniation

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Received: August 08, 2017; **Published:** September 07, 2017

Neuropathic pain represents a major neurologic complication associated with neuronal injury. It occurs when any injury, disease, or dysfunction involves the peripheral or central nervous system. A wide spectrum of mechanisms including mechanical injury, inflammation, focal ischemia, neurotoxicity, viral infection, metabolic abnormalities, and dysfunction of several neurotransmitters has been described as the causative factors. Common clinical examples include pain resulting from diabetic neuropathy, post herpetic neuralgia, neuralgia associated with late – stage cancer, partial nerve injury, multiple sclerosis, amputation and pain due to lumbar disc herniation (LDH).

The occurrence of the latest one, also known as sciatalgia, sciatica, painful radiculopathy, or leg pain, is a common and disabling feature for these patients. Because neuropathic pain is often immutable and maladaptive in nature, it can reduce the patient's ability to work, walk, or sleep, as with other forms of painful disabilities. Nerve root mechanical compression and neuroinflammation are the two main discussed theories for the pathogenesis of neuropathic pain during LDH.

Animal studies have also shown that nerve fibers manifested ectopic irritability at or near the injury site. This might be either owing to the abnormal distribution of sodium channels or owing to an abnormal response to endogenous pain evoked by the release of cytokines and inflammatory mediators [1]. Although this sensitization might work as a compensatory mechanism for the functional deficits of the nervous system, the result would be a global sensitization of the nervous system (or central sensitization), which is responsible for the chronicity of the pain and hyperalgesia.

When no compensatory intervention exists, both central and peripheral mechanisms will be involved. Initially, the injured axon is the pain producing site. Later on, neurons of the dorsal root ganglion, and even post synaptic neurons of the dorsal horn of the spinal cord and higher order neurons up to the cortex will be recruited to emit pain signals [2,3].

As a result, neuropathic pain is believed to be a progressive disease of the nervous system. Such processes contribute to the slow progression of the disease, which is also known as the pain memory. So, the main goal of therapeutic modalities for the neuropathic pain is to hinder the development and the progression of the pain memory with preventive methods.

Human brain imaging studies suggest that neuropathic pain has a strong emotional component that is mediated by medial prefrontal cortex (mPFC) activity; in rodents, the mPFC is involved in emotional and cognitive aspects of behavior, including the extinction of behavior fear conditioning [4]. Together, these findings suggest that the cortex may modulate the memory trace of pain.

The efficacy of several drugs on neuropathic pain has been tested in animal studies. These include morphine [5], antidepressants [6-8], clonidine, dexamethasone [9], anticonvulsants [10], ketoprofen [11], magnesium sulfate [12] and cannabinoids [13]. All of them have different side effects in gastrointestinal, cardiovascular, respiratory and electrolytes abnormalities. Based on the accepted spinal mechanisms of pain, glutamate the most prevalent excitatory neurotransmitters, binds to two classes of ionotropic receptors termed NMDA

(N-methyl-D-aspartate) and non – NMDA. When the spinal cord is in its normal state in the absence of tissue damage, there is a voltage – dependent Mg^{2+} block of the NMDA receptor ion channel. When noiceptive afferent fibers are excited by a noxious stimulus glutamate is released from the central terminals exciting postsynaptic neurons [14-20].

D-cycloserine (DCS) is a partial agonist of the NMDA receptors and can prevent neuropathic pain theoretically. In animal Studies, repeated oral administration of DCS reduced mechanical sensitivity of the injured limb with mPFC changes in a dose-dependent manner. In addition, reexposure to DCS further enhanced antinociceptive behavior.

The decision to treat remained neuropathic pain after lumbar discectomies should be taken before the operation. New drugs such as DCS can be effective to decrease remaining leg pain by the end of 24 hours in post-discectomy patients based on new studies.

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Volume 7 Issue 6 September 2017

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