CHAPTER 5

CHRONIC PAIN FOLLOWING SPINAL CORD INJURY

Radi Masri*1,2 and Asaf Keller2
1Department of Endodontics, Prosthodontics and Operative Dentistry, Baltimore College of Dental Surgery, University of Maryland Baltimore, Baltimore, Maryland, USA; 2Department of Anatomy and Neurobiology, Medical School, University of Maryland Baltimore, Baltimore, Maryland, USA
*Corresponding Author: Radi Masri—Email: radi.masri@gmail.com

Abstract: Most patients with insults to the spinal cord or central nervous system suffer from excruciating, unrelenting, chronic pain that is largely resistant to treatment. This condition affects a large percentage of spinal cord injury patients, and numerous patients with multiple sclerosis, stroke and other conditions. Despite the recent advances in basic science and clinical research the pathophysiological mechanisms of pain following spinal cord injury remain unknown. Here we describe a novel mechanism of loss of inhibition within the thalamus that may predispose for the development of this chronic pain and discuss a potential treatment that may restore inhibition and ameliorate pain.

INTRODUCTION

According to the National Spinal Cord Injury Statistical Center, the number of people in the United States who suffer from spinal cord injury is approximately 259,000,1 with some studies reporting an even higher incidence (1,275,000 individuals).2 It is estimated that the number of individuals suffering from SCI increases by approximately 12,000 new cases every year with many of these injuries occurring between the ages of 16 and 30.1 Injury to the spinal cord is devastating and leads to catastrophic consequences such as decreased ability to walk or move,3 loss of sexual function,4 diminished ability to control bladder or bowel function5 and the development of debilitating pain.6

Pain resulting from spinal cord injury is referred to as central pain which is “pain initiated or caused by a primary lesion or dysfunction in the central nervous system”.7
The pain is most often steady and unrelenting, and has been described “as if knives heated in Hell’s hottest corner were tearing me to pieces.” Central pain can be initiated by a variety of conditions and insults at any level of the spinal cord and the brain. The most common conditions are spinal cord injuries, multiple sclerosis (MS) and cerebrovascular lesions (stroke). The prevalence of pain in these conditions is alarmingly high: as many as 60-80% of spinal cord injury patients experience pain with at least 1/3 of the patients reporting severe pain. In MS patients almost 30% develop chronic neuropathic pain and in stroke patients the prevalence is as high as 10%. Because spinal cord injury is the most common etiology for central pain, this chapter is focused on pain resulting from spinal cord injury.

**PAIN CHARACTERISTICS FOLLOWING SPINAL CORD INJURY**

Several distinct types of pain can develop following spinal cord injury. One that can be observed in patients with spinal cord injury is musculoskeletal pain occurring due to muscle spasm, or due to overuse or abnormal use of structures such as the arms or the shoulders. The pain is often dull, aching and is relieved by physical therapy, exercise, non steroidal anti-inflammatory treatments (NSAIDs) and opioids. Another type of pain is visceral pain in the abdomen, which is dull, cramping and located in a region with intact innervation and is thought to occur due to normal peripheral inputs from sympathetic or vagus nerve. Both of these types of pain, musculoskeletal and visceral, have delayed onset after injury and are classified as nociceptive pains because they arise from stimulation or activity of peripheral nociceptive afferents.

However, the most debilitating pain and puzzling is the presence of sharp, shooting, and burning neuropathic pain. This pain is spontaneous in the majority of patients but can manifest both as an increased pain with noxious stimulation (hyperalgesia) and as pain in response to previously innocuous stimuli (allodynia). Neuropathic pain in patients with spinal cord injury can be classified into three categories based on the location of the painful region relative to the location of the spinal injury: (1) Below-level pain: The pain is diffuse and located in areas with interrupted sensory innervation below the level of spinal injury; (2) At-level pain at the border of normal and interrupted sensory innervation and distributed within a band of 2 to 4 segments surrounding the level of injury and (3) Above-level pain in regions with preserved sensory inputs above the level of injury. Neuropathic pain following spinal cord injury is largely resistant to conventional pharmacologic treatments and to this date the pathophysiological mechanisms involved in the development of central neuropathic pain remain a mystery and effective treatments are lacking. Therefore, the study of the mechanisms of central pain and the development of effective treatments and animal models that recapitulate the clinical characteristics of this condition are needed.

**ANIMAL MODELS OF SPINAL CORD INJURY PAIN**

Several animal models have been developed to study spinal cord injury pain (Table 1). In all of these models, the location, the extent and the means to produce injury vary. Some use controlled spinal contusions to mimic clinical traumatic injuries. Others have used ischemic lesions or a neurotoxic chemical injection into the