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Letter to the Editor

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Pain following spinal cord injury

Chronic pain is one of the worst consequences of spinal cord injury (SCI). Consequently, exact characterization of such pain and understanding its underlying mechanisms is of utmost importance. We would, therefore, like to address two issues raised in the review 'Pain following spinal cord injury' by Siddall and Loeser (2001), which was published in volume 39 of *Spinal Cord*.[1] Those issues are the intensity of the chronic pain and its possible mechanism.

The authors review evidence for a possible correlation between the intensity of chronic pain and several factors including the nature of the spinal injury, the level of lesion, its degree of completeness etc. They conclude that psychosocial rather than physical factors are associated with the severity of pain following SCI.[1] Our conclusion, based on a series of studies we have conducted on SCI subjects suffering from chronic pain, are slightly different. We found that the intensity of chronic pain, measured using the McGill pain questionnaire (MPQ), in patients with complete spinal lesion, is significantly higher than that of patients with partial spinal lesion. Furthermore, this difference is restricted to the sensory dimension of pain sensation, and not to the emotional or cognitive dimension.[2] The sensory values of pain on the MPQ are considered to be indicators of the actual pain from which the patient is suffering unlike the other dimensions, which may reflect other psychological variables.[3,4] In addition to the more intense chronic pain observed in complete spinal cord injury patients, the area of the body to which chronic pain was projected was considerably larger in these patients compared to those with partial spinal cord damage. Furthermore, within group analysis showed that complete SCI subjects with pain areas larger than group mean suffer more intense pain than those complete SCI subjects with pain areas smaller than group mean.[2] Thus, it is a fair assumption that when and if chronic pain arises its intensity is correlated with the extent of spinal damage.

Although the exact mechanisms involved in the development of chronic pain following SCI are still unclear, Siddall and Loeser adopt the hypothesis by Beric *et al*[5] that Central Dysesthesia Syndrome arises if injury produces an 'imbalance' between spinothalamic and dorsal column function. Consistent with Beric *et al* we found a significant impairment of spinothalamic function with relative preservation of dorsal column function in incomplete SCI subjects with chronic pain below the lesion.[6] Temperature and pain perception was much more impaired than touch, graphesthesia and identification of speed of movement in body areas below the lesion. However, our control group of SCI subjects who did not suffer from chronic pain exhibited an almost identical imbalance between spinothalamic and dorsal column function. Furthermore, in chronic pain patients, we could not establish any relationship between the degree of this imbalance and the intensity of chronic pain.[6] Thus, the suggestion of Beric *et al* that chronic dysesthetic syndrome develops due to loss of spinothalamic system with limited damage to dorsal column function is not an adequate explanation for the appearance of this syndrome.

Somatosensory tests in which we compared painful and pain-free body regions (below lesion) in SCI subjects with chronic pain revealed that: (1) Thermal and pain sensibilities in painful regions were significantly impaired, whereas painfree regions exhibited normal sensibility to temperature and pain. (2) Chronic pain appeared only in those regions which were impaired in thermal and pain sensibilities. (3) Chronic pain could be found in areas without any impairment in dorsal column function. (4) Abnormal sensations, ie, allodynia, hyperpathia and increased wind-up pain could only be evoked in painful regions.[6] Thus, our findings show that damage to the anterolateral spinothalamic system, and not the dorsal column, is indeed a necessary but not a sufficient condition for the development of chronic pain.

We share the conclusion of Siddall and Loeser that damage to the nociceptive system will result in pathological pain states if plastic changes, resulting in both spontaneous and evoked hyperexcitability, take place in this system. Based on our findings, we believe that there is a strong genetic factor, which underlies the genesis of such hyperexcitability. Our results show that SCI patients with chronic pain suffer from spontaneous pain in all body regions in which spinothalamic function is impaired, but never in regions in which spinothalamic function is intact. In contrast, those SCI patients who do not suffer from chronic pain show spinothalamic damage, which is almost identical in magnitude to chronic pain patients but in no case shows evidence of neuropathic pain.[6] The idea that there is a genetic predisposition for the emergence of chronic pain has already been proposed to account for the fact that chronic pain does not always occur after peripheral nerve injury.[7–9] We believe that such an explanation is also tenable when damage of central nociceptive neurons occurs. Animal models of central pain have yielded strain differences in response to similar injuries in both monkeys and rats.[10,11] We also observed such differences in our laboratory, when following excitotoxic damage to the spinal cord only one strain of mice developed signs of chronic pain[12] (and unpublished data).

Genetic factors might also underlie the emergence of a state of hyperresponsiveness seen in subjects with chronic pain following SCI. In our study, allodynia, hyperpathia and wind-up pain were present almost exclusively in SCI subjects suffering from chronic pain as opposed to painfree SCI subjects, and only in their painful body regions.[6] Such a combination of spontaneous pain and hyperresponsiveness is seen also following peripheral nerve injuries[13–15] and brain lesions.[16] Nevertheless, although both are usually attributed to hyperexcitability of central

neurons, in some cases following spinal lesions, as the authors mention in their review, a recorded hyperexcitability produces no signs of either evoked pain or spontaneous pain behaviour. Certainly, further research in human subjects and animal models is needed to explore the exact conditions in which debilitating chronic pain and pathological sensations develop in some but not in all subjects following SCI.

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References

1 Siddall PJ, Loeser JD. Pain following spinal cord injury. *Spinal Cord* 2001; **39:** 63–73.
2 Defrin R, Ohry A, Blumen N, Urca G. Acute pain threshold in subjects with chronic pain following spinal cord injury. *Pain* 1999; **83:** 275–282.
3 Valleux S, Melzack R. Pain in psychiatric patients. *Exp Neurol* 1976; **52:** 535–543.
4 Reading AE, Everitt BS, Sledmere CM. The McGill pain questionnaire: a replication of its constriction. *Br J Clin Psychol* 1982; **21:** 339–349.
5 Beric' A, Dimitrijevic' MR, Lindblom U. Central disesthesia syndrome in spinal cord injury patients. *Pain* 1988; **34:** 109–116.
6 Defrin R, Ohry A, Blumen N, Urca G. Characterization of chronic pain and somatosensory function in spinal cord injury subjects. *Pain* 2001; **89:** 253–263.
7 Devor M, Seltzer Z. Pathophysiology of damaged nerves in relation to chronic pain. In: Wall PD and Melzack R (eds). *Textbook of pain*. Churchill Livingstone: Edinburgh 1999, pp. 129–164.
8 Devor M, Raber P. Heritability of symptoms in an experimental model of neuropathic pain. *Pain* 1990; **42:** 51–67.
9 Shir Y, Raber P, Devor M, Seltzer Z. Mechano- and thermo-sensitivity in rats genetically prone to developing neuropathic pain. *Neuroreport* 1991; **2:** 313–316.
10 Levitt M, Levitt JH. The deafferentation syndrome in monkeys: dysesthesias of spinal origin. *Pain* 1981; **10:** 129–147.
11 Wiesenfeld-Hallin Z, *et al*. Genetic factors influence the development of mechanical hypersensitivity, motor deficits and morphological damage after transient spinal cord ischemia in the rat. *Pain* 1993; **55:** 235–241.
12 Defrin R, Urca G. Kainate induced spinal cord lesion: an animal model of central neuropathic pain of spinal origin. *Pain* 1993; **6** (Suppl): S28–S29.
13 Campbell JN, Raja SN, Meyer RA. Myelinated afferents signals the hyperalgesia associated with nerve injury. *Pain* 1988; **32:** 89–94.
14 Gracely RH, Lynch SA, Bennett GJ. Painful neuropathy: altered central processing maintained dynamically by peripheral input. *Pain* 1992; **51:** 175–194.
15 Bennett GJ. Neuropathic pain. In: Wall PD and Melzack R (eds). *Textbook of pain*. Churchill Livingstone: Edinburgh 1994, pp 201–224.
16 Boivie J. Central pain. In: *Textbook of pain*. Churchill Livingstone: Edinburgh 1994, pp. 871–901.