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Dorsal column lesion reduces mechanical allodynia in the induction, but not the maintenance, phase in spinal hemisected rats

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Abstract

The dorsal column–medial lemniscal (DC–ML) system is known to be a route of ascending input signals for mechanical allodynia following peripheral nerve injury. We examined whether the pain signals after spinal hemisection were transmitted via the DC–ML system in the induction and maintenance phases of the neuropathic pain. Under enflurane anesthesia, rats were subjected to spinal hemisection at T13 level and bilateral DC lesion was made at T8 level 1 day or 3 weeks after the hemisection. The DC lesion 1 day after the hemisection significantly reduced the mechanical, but not cold, allodynia, whereas the DC lesion 3 weeks after the hemisection did not change both mechanical and cold allodynia. These results suggest that the signals for mechanical allodynia following spinal hemisection should be transmitted via the DC–ML system in the induction, but not maintenance, phase.

Keywords: Dorsal column–medial lemniscal system; Central neuropathic pain; Mechanical allodynia; Spinal hemisection; Cold allodynia; Spinal cord injury

Spinal cord hemisection elicits chronic central neuropathic pain such as mechanical (touch-evoked) and thermal allodynia resembling that associated with peripheral nerve injury [2,4,9]. To date, the ascending pathway and pathogenesis of the central neuropathic pain remain still unclear.

Recently, several reports indicated that the dorsal column–medial lemniscal (DC–ML) system was a possible route of input signals for mechanical allodynia following peripheral nerve injury. Interruption of the DC–ML system 2 weeks following peripheral nerve injury reduced the signs of mechanical, but not thermal, allodynia [6,18,19]. In addition, peripheral nerve injury increased neuronal activity [5,22] and substance P levels [22] in the ipsilateral gracile nucleus. However, the neurochemical and neuroanatomical changes caused by spinal cord injury (SCI) are quite different from those caused by the peripheral nerve injury, in spite of their similar pain responses [7,17]. It is also uncertain whether the DC–ML system mediates the signals for neuropathic pain in the SCI, or not.

In the present study, we examined whether the signals for neuropathic pain such as mechanical and cold allodynia following spinal hemisection were transmitted via the DC–ML system in the induction and maintenance phases.

Preliminary data have been presented in an abstract form [11].

Experimental procedures were carried out in accordance with the guideline set by Korea University College of Medicine Animal Research Policy Committee. Fifty-eight male Sprague–Dawley rats (body weight: 150–200 g) were used. Animals were kept in a 12-h light:12-h dark cycle with light on 07:00 a.m.

Under enflurane anesthesia (mixture of 4% enflurane and 95% O_2), a laminectomy was performed, and the spinal cord was hemisected and resected at the level of T13 with a #11 blade. Interruption of the bilateral DC pathway at the level of T8 was performed 1 day or 3 weeks after the hemisection. Under the dissecting microscope, the DC pathway was transected by microscissors up to 1 mm depth. The extent of DC lesion was verified histologically after behavioral tests.

Animals were divided into four groups: (1) Hemisection-DC 1d group (n = 14), bilateral DC lesion 1 day after spinal

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hemisection; (2) Hemisection-sDC 1d group ($n = 7$), sham DC lesion 1 day after spinal hemisection; (3) Hemisection-DC 3w group ($n = 25$), bilateral DC lesion 3 weeks after spinal hemisection; (4) Hemisection-sDC 3w group ($n = 12$), sham DC lesion 3 weeks after spinal hemisection.

Mechanical allodynia was assessed by measuring the frequency of hindpaw withdrawal response to normally innocuous mechanical stimulus, using a von Frey hair (VF) with a bending force of 2 g (19.6 mN). Each rat was placed under a transparent plastic dome on the metal mesh floor and the VF hair applied to the plantar surface of the hindpaw. The VF hair was applied 10 times (once every 3–4 s) to each hindpaw. The frequency of hindpaw withdrawal was expressed as a percent.

To assess cold sensitivity of the foot, brisk foot withdrawal in response to the application of a drop of acetone was measured. The animal was placed under a transparent plastic chamber on the metal mesh floor and acetone was applied to the plantar surface of the hindpaw. To do this, an acetone drop was formed using a piece of small polyethylene tubing, which was connected to a syringe. The acetone was applied five times (once every 5 min) to each hindpaw. The paw withdrawal response with supraspinal signs, such as shaking, licking and vocalization, to acetone application was interpreted as the sign of cold allodynia. The frequency of paw withdrawal was expressed as a percent: number of frequencies of paw withdrawal/number of total trials × 100. Behavioral tests were conducted blindly.

To exclude the rats showing DC lesion-induced motor deficiency, motor function was evaluated using the BBB Locomotor Rating Scale [3] before and after DC lesion. One rat showing DC lesion-induced motor deficiency was excluded in this experiment. The extent of DC lesion was also verified histologically after the behavioral tests. Spinal cord sections were mounted and stained with Luxor Fast Blue and Cresyl Violet to check out intact and disrupted sites. Histological findings demonstrated that dorsal corticospinal tract and the gray matter were not disrupted (data not shown).

All values were expressed as mean ± S.E.M. Between-groups comparisons of the score obtained on a given experimental day were conducted with Mann–Whitney U-test. $P < 0.05$ was considered as statistically significant.

Locomotor function was evaluated in both hindlimbs using the BBB scale [3] by open field test (data not shown).

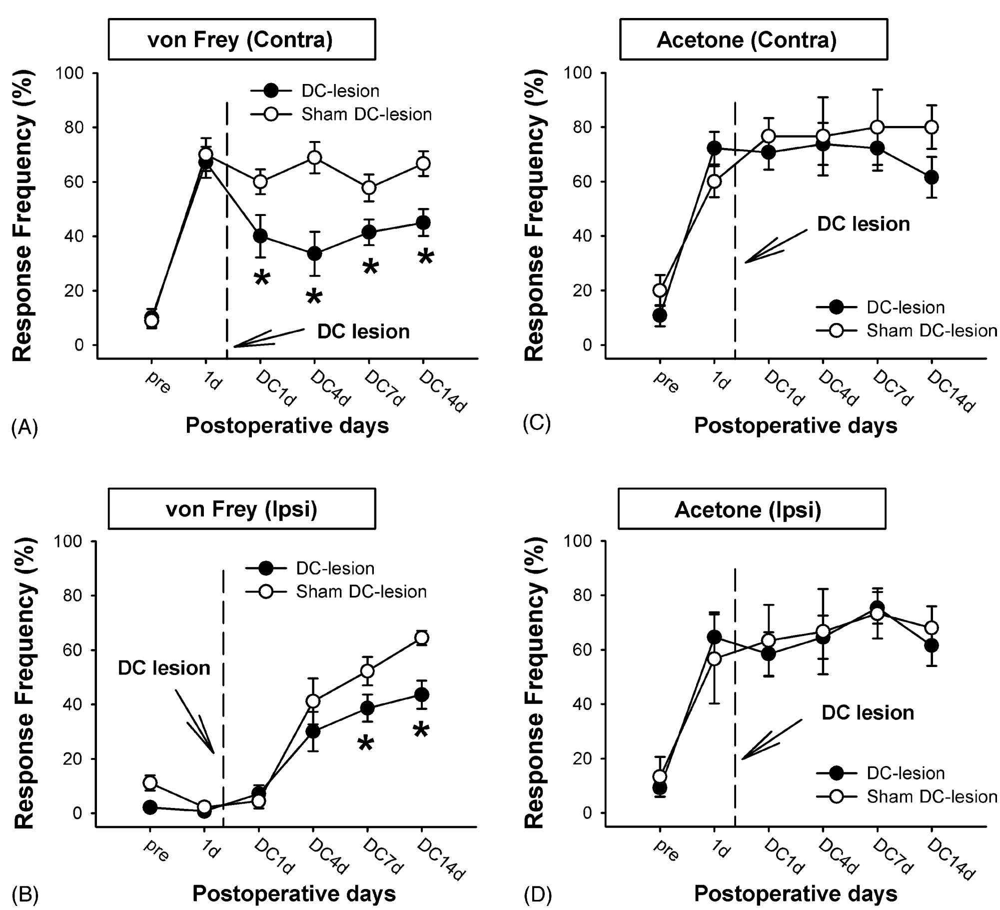

Fig. 1. Effects of bilateral DC lesion (T8) 1 day after spinal hemisection (T13) on mechanical and cold allodynia in the bilateral hindpaws. The withdrawal frequencies of von Frey stimulation to the ipsilateral (A) and contralateral (B) hindpaws, and acetone application to the ipsilateral (C) and contralateral (D) hindpaws are expressed as mean ± S.E.M. The results of the between-group comparison by Mann–Whitney U-test are indicated by asterisks. Significant difference between sham and DC-lesion (* $P < 0.05$).