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Review

# Cortical and subcortical plasticity in the brains of humans, primates, and rats after damage to sensory afferents in the dorsal columns of the spinal cord ☆

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**Abstract**

The failure of injured axons to regenerate following spinal cord injury deprives brain neurons of their normal sources of activation. These injuries also result in the reorganization of affected areas of the central nervous system that is thought to drive both the ensuing recovery of function and the formation of maladaptive neuronal circuitry. Better understanding of the physiological consequences of novel synaptic connections produced by injury and the mechanisms that control their formation are important to the development of new successful strategies for the treatment of patients with spinal cord injuries. Here we discuss the anatomical, physiological and behavioral changes that take place in response to injury-induced plasticity after damage to the dorsal column pathway in rats and monkeys. Complete section of the dorsal columns of the spinal cord at a high cervical level in monkeys and rats interrupts the ascending axon branches of low threshold mechanoreceptor afferents subserving the forelimb and the rest of the lower body. Such lesions render the corresponding part of the somatotopic representation of primary somatosensory cortex totally unresponsive to tactile stimuli. There are also behavioral consequences of the sensory loss, including an impaired use of the hand/forelimb in manipulating small objects. In monkeys, if some of the afferents from the hand remain intact after dorsal column lesions, these remaining afferents extensively reactivate portions of somatosensory cortex formerly representing the hand. This functional reorganization develops over a postoperative period of 1 month, during which hand use rapidly improves. These recoveries appear to be mediated, at least in part, by the sprouting of preserved afferents within the cuneate nucleus of the dorsal column–trigeminal complex. In rats, such functional collateral sprouting has been promoted by the post-lesion digestion of the perineuronal net in the cuneate nucleus. Thus, this and other therapeutic strategies have the potential of enhancing sensorimotor recoveries after spinal cord injuries in humans.


*Keywords:* Dorsal column; Spinal cord injury; Somatosensory cortex; Cuneate nucleus; Functional reorganization; Microelectrode mapping; Regeneration; Perineuronal nets; Chondroitin sulfate proteoglycans; Chondroitinase ABC

## Introduction

The dorsal (posterior) columns of the spinal cord consist mainly of sensory afferents that subserve the cutaneous sensations of touch, pressure, flutter, and vibration (Whitsel et al., 1972; see Fig. 1). Complete section of this pathway at a high level of the cervical spinal cord deactivates much of primary somatosensory cortex, and probably a number of other areas of somatosensory cortex as well. Such lesions abolish or greatly impair the ability to discriminate tactile textures, touch frequencies, and directions of moving tactile stimuli (see Mountcastle, 2005 for review). There are also impairments of motor control, most likely as a result of the loss of sensory

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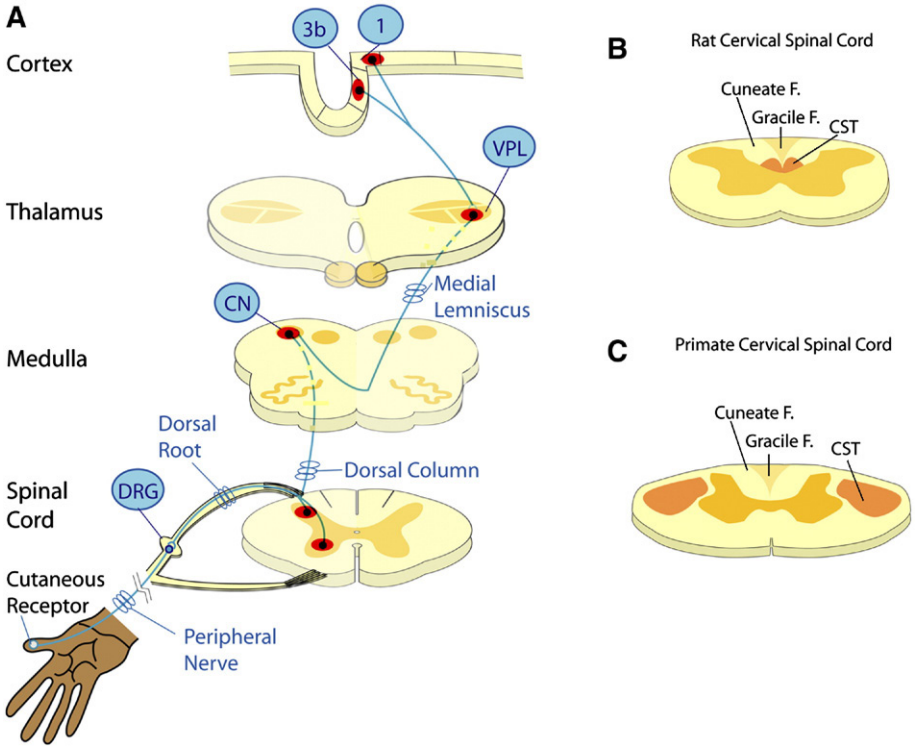


Fig. 1. The dorsal column somatosensory pathway and comparative anatomy of rat and primate spinal cord. (A) Low threshold mechanoreceptor afferents transmit somatosensory information directly to secondary and motor neurons in the spinal cord and to thalamic relay neurons located in the either the cuneate (CN) or gracile nucleus. Axons from these neurons cross to the contralateral side of the medulla and ascend through the medial lemniscus where they synapse on cortically projecting neurons (areas 3b and 1) in the ventroposterior lateral nucleus (VPL) of the thalamus. Areas shown in red represent areas of potential reorganization following deaffrentation by injury. The result of this neuroplasticity can result in either improved functional outcome or in the formation of maladaptive pathways that produce phantom sensations or other detrimental outcomes. The development of treatments that promote the formation of new synaptic contract from intact portions of the pathway while preventing the formation of pathological circuits is the focus of current investigation. (B and C) The dorsal columns of rats contain both the ascending fine touch and vibratory somatosensory fibers and the descending corticospinal (CST) motor pathway. In primates, the corticospinal pathway is contained in the lateral columns. Because of this anatomical difference, injuries to the dorsal columns produce different central nervous system deficits in rats and primates. Cuneate Fasciculus-Cuneate F; Gracile Fasciculus-Gracile F.

feedback. Nevertheless, the ability to localize somatosensory stimuli survives, and locomotive behavior can appear to be quite normal. These and other functions remain after dorsal column sections likely because axon tracts ascending in the ventral and dorsolateral quadrants of the spinal cord, which provide sensory and proprioceptive feedback, are spared.

Confusion between functional recovery and compensation has complicated the characterization of sensory and motor deficits from dorsal column sections. The magnitudes of these deficits were not fully apparent until a series of carefully controlled studies on monkeys with dorsal column lesions were completed by Vierck and co-workers (e.g., Vierck, 1998). In contrast, earlier studies were often difficult to interpret because lesions were incomplete or included other parts of the spinal cord. As a result, Wall (1970) once argued that most sensory abilities were left intact after dorsal column lesions. Others concluded that the loss of sensory abilities was severe (Mountcastle and Darian-Smith, 1968; Nathan et al., 1986). Part of the reason for these differing conclusions was that the importance of a few remaining afferents in incompletely sectioned dorsal columns was not fully appreciated. For example, Schwartz and co-workers (1972), in a study of dorsal column section in monkeys, concluded that such lesions left the "discrimination of subtle tactile differences in textures, form, pattern and hardness unchanged or only slightly affected". However, the authors skeptically allowed the alternative interpretation that "very few residual fibers may mediate these complex discriminations". Here we review more recent findings in humans, monkeys, and rats showing that a few remaining dorsal column fibers may be very important in mediating recovery of functions. Furthermore, there is evidence that therapies that promote the survival, sprouting, or regeneration, of even a few such fibers are effective promoting recovery in animal models and may be of value to human spinal cord injuries.

## Dorsal column section in humans

The functions of the dorsal columns in humans are understood in part from the types of impairments that follow degenerative diseases that target the dorsal columns, such as neurosyphilis (tabes dorsalis), Friedreich's ataxia, and subacute combined degeneration (Harrison and Braunwald, 2001). Patients with these diseases show clinical deficits in two-point