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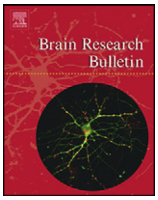

Review

Propriospinal pathways in the dorsal horn (laminae I–IV) of the rat lumbar spinal cord

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ABSTRACT

The spinal dorsal horn is regarded as a unit that executes the function of sensory information processing without any significant communication with other regions of the spinal gray matter. Within the spinal dorsal horn, however, the different rostro-caudal and medio-lateral subdivisions intensively communicate with each other through propriospinal pathways. This review gives an overview about these propriospinal systems, and emphasizes that the medial and lateral parts of the spinal dorsal horn show the following distinct features in their propriospinal interconnectivities: (a) A 100–300 μm long section of the medial aspects of laminae I–IV projects to and receives afferent fibers from a three segment long compartment of the spinal dorsal gray matter, whereas the same length of the lateral aspects of laminae I–IV projects to and receives afferent fibers from the entire rostro-caudal extent of the lumbar spinal cord. (b) The medial aspects of laminae I–IV project extensively to the lateral areas of the dorsal horn. In contrast to this, the lateral areas of laminae I–IV, with the exception of a few fibers at the segmental level, do not project back to the medial territories. (c) There is a substantial direct commissural connection between the lateral aspects of laminae I–IV on the two sides of the lumbar spinal cord. The medial part of laminae I–IV, however, establishes only a minor commissural propriospinal connection with the gray matter on the opposite side.

Contents

Abbreviations: BDA, biotinylated dextran amine; CGRP, calcitonin gene-related peptide; GABA, gamma-amino butyric acid; GAD, glutamic acid decarboxylase; GLYT, glycine transporter; PHA-L, phaseolus leucoagglutinin.

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1. Introduction

A number of hypothetical neural circuits underlying sensory information processing in the dorsal horn of the spinal cord were constructed by various authors in the last few decades (Szentágothai, 1964a,b; Réthelyi and Szentágothai, 1969, 1973; Price, 1984; Réthelyi, 1984; Ruda et al., 1986). These models substantially differ from each other in many respects but all of them are based on two common principles. The dorsal horn (laminae I–IV) is regarded as a unit that executes the function of sensory information processing without any significant communication with other regions of the spinal gray matter. In addition to this, the models suggest that the different subdivisions along the medio-lateral extent of laminae I–IV can be regarded as identical structures. However, a large body of experimental evidence has been accumulated in recent years that do not agree with these principles. On the one hand, it has extensively been demonstrated that the medial and lateral subdivisions of the superficial dorsal horn show many distinct features concerning cytoarchitectonic organization (Bice and Beal, 1997a), primary afferent inputs (Light and Perl, 1979; Perl, 1980; Fuji et al., 1983; Sugiura et al., 1988; Chung et al., 1989; Cruz et al., 1993), synaptic and neurochemical properties of interneurons (Gibson et al., 1981, 1984; Ren and Ruda, 1994; Tachibana et al., 1994), densities of terminals arising from various brain stem nuclei (Marlier et al., 1991; Antal et al., 1996) as well as numbers of neurons with axons projecting to supraspinal brain centers (Willis et al., 1979; Menétrey et al., 1983, 1992; Granum, 1986; Apkarian and Hodge, 1989; Bice and Beal, 1997b). On the other hand, a steadily growing body of physiological evidence indicates that the activities of various regions of the ipsi- and contralateral spinal gray matter exert a substantial influence on the nociceptive information processing machineries of the superficial dorsal horn through propriospinal connections. It has been reported that propriospinal neurons originating from various areas of the spinal gray matter modulate background activity and noxious heat-evoked responses of neurons in the superficial dorsal horn (Sandkühler et al., 1993). Experimentally induced unilateral hindpaw inflammation produces bilateral changes in the expression of immediate early genes (Williams et al., 1990; Herdegen et al., 1991a,b; Ren and Ruda, 1996), substance P, CGRP and GAD immunoreactivities (Sluka et al., 1992; Mapp et al., 1993), NADPH-diaphorase activity (Solodkin et al., 1992) as well as in dorsal horn postsynaptic currents (Colvin et al., 1996). After mechanical or thermal noxious stimulation of the hind limb and tail of decerebrated spinal rats, short-latency excitatory or inhibitory inputs were recorded in neurons of the contralateral spinal dorsal horn, suggesting the existence of a segmental contralateral control over dorsal horn cell activity (Fitzgerald, 1982, 1983). It has also been reported that unilateral constriction of peripheral nerves on the lower limb evokes bilateral electrophysiological and behavioral changes (Attal et al., 1990; Colvin et al., 1996), bilateral cell death (Sugimoto et al., 1989), and bilateral increases in spinal cord dynorphin levels (Wagner et al., 1993) in the lumbar spinal dorsal horn. Increased bilateral mRNA expression of preprotachykinin and calcitonin gene-related peptide in dorsal root ganglia has also been observed in the initial period of adjuvant monoarthritis in the rat (Donaldson et al., 1992).

Concerning the anatomical substantiation of the propriospinal interconnectivity of the superficial dorsal horn, however, until recently we had to rely exclusively on the classical degeneration and Golgi-impregnation studies of Szentágothai (1951, 1964a,b), Scheibel and Scheibel (1968) and Réthelyi and Szentágothai (1973). Based on his degeneration studies, Szentágothai (1951) reported that degenerated "boutons-terminaux" were seen in the dorsal horn following lesions of the intermediate gray matter. In addition to this propriospinal projection from the intermediate gray matter to the dorsal horn, Golgi-impregnation and degeneration studies revealed also a considerable number of dorsal commissural fibers that originate and terminate in the dorsal horn (Szentágothai, 1964a,b; Scheibel and Scheibel, 1968; Réthelyi and Szentágothai, 1973).

In the last decade a considerable progress has been achieved on this field. There have been attempts to make an accurate account concerning the propriospinal relations of the spinal dorsal gray matter by employing the highly sensitive anterograde and retrograde neural tracers *Phaseolus vulgaris* leucoagglutinin (Gerfen and Sawchenko, 1984) and biotinylated dextran amine (Rajakumar et al., 1993) in combination with immunocytochemical methods to investigate the neurochemical properties, the potential excitatory and inhibitory nature of the various propriospinal systems (Petkó and Antal, 2000; Petkó et al., 2004; Petkó, unpublished observations). These studies provided a substantial amount of new data about the arborization pattern, synaptic relations, and neurochemical properties of propriospinal pathways in the spinal dorsal horn. This review would like to give a short summary of this new knowledge.

2. Propriospinal pathways of the spinal dorsal horn

2.1. Short rostro-caudally oriented propriospinal connections in the medial aspect of laminae I–IV of the rat spinal dorsal horn

2.1.1. Distribution of propriospinal neurons and their axon terminals

Following injections of PHA-L into a 100–300 μm wide area of the medial part of laminae I–IV, labeled axon terminals were revealed in a 2.0–2.5 mm long section of the spinal dorsal horn ipsilateral to the injection site. The stained terminals showed a specific laminar distribution. The majority of the labeled terminals were found in a region of the medial aspect of the superficial dorsal horn that corresponded to the rostro-caudal elongation of the area in which the injection was located. Most of the terminals at this location were revealed in laminae IIi, III and IV. Terminals within the confines of laminae I–IIo were found exclusively at the level or close to the level of the injection site. In addition, labeled terminals were