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Research Report

Anterograde labeling of ventrolateral funiculus pathways with spinal enlargement connections in the adult rat spinal cord

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ABSTRACT

The ventrolateral funiculus in the spinal cord has been identified as containing important ascending and descending pathways related to locomotion and interlimb coordination. The purpose of this descriptive study was to investigate the patterns of axon termination of long ascending and descending ventrolateral pathways within the cervical and lumbar enlargements of the adult rat spinal cord. To accomplish this, we made discrete unilateral injections of the tracer biotinylated dextran-amine (BDA) into the ventrolateral white matter at T9. Although some BDA-labeled axons with varicosities were found bilaterally at all cervical levels, particularly dense BDA labeling was observed in laminae VIII and IX ipsilaterally at the C6 and C8 levels. In the same animals, dense terminal labeling was found in the lumbar enlargement in medial lamina VII and ventromedial laminae VIII and IX contralaterally. This labeling was most apparent in the more rostral lumbar segments. These observations continue the characterization of inter-enlargement (long propriospinal) pathways, illustrating a substantial and largely reciprocal inter-enlargement network with large numbers of both ascending and descending ventrolateral commissural neurons. These pathways are anatomically well-suited to the task of interlimb coordination and to participate in the remarkable recovery of locomotor function seen in the rat following thoracic spinal cord injuries that spare as little as 20% of the total white matter cross sectional area.

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Abbreviations: VLF, ventrolateral funiculus; BDA, biotinylated dextran-amine; CPG, central pattern generator; CTB, cholera toxin beta-subunit

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1. Introduction

It is widely accepted that the central pattern generator (CPG) circuitry responsible for the alternating rhythmic bursting necessary for normal hindlimb locomotor activity in mammalian quadrupeds resides intrinsically within the spinal cord and is activated by reticulospinal pathways that reside largely within the ventrolateral funiculus (VLF; Jordan, 1991, 1998). In cats with chronic incomplete spinal cord lesions, bilateral disruption of pathways contained within the VLF abolishes all medullary locomotor region evoked locomotion (Eidelberg et al., 1980; Steeves and Jordan, 1980) leading to the suggestion that reticulospinal axons residing in the VLF comprise a critical locomotor command pathway. However, more recent studies suggest a redundancy among axons within the dorso- and ventrolateral white matter of the spinal cord capable of mediating overground locomotion (Sholomenko and Steeves, 1987; Vilensky et al., 1992; Brustein and Rossignol, 1998; Loy et al., 2002a,b; Schucht et al., 2002). The fact remains that preservation of a small percentage (20%) of white matter in the ventrolateral quadrant of the thoracic spinal cord following either laceration or contusive injuries is sufficient to permit not only the initiation of rhythmic stepping movements but also to provide for hindlimb weight support and hindlimb–forelimb coordination during open-field locomotion (Schucht et al., 2002; Basso et al., 2002) and alternating hindlimb kicking during swimming in the adult rat (Smith et al., 2006).

Rubrospinal, reticulospinal, vestibulospinal and long propriospinal axons have been shown to withstand damage sustained from contusion-type injuries much better than either corticospinal or short propriospinal axons (Hill et al., 2001; Basso et al., 2002; Conta and Stelzner, 2004). This innate differential sparing most likely results from several factors including the degree of axonal collateralization and their anatomical location within the spinal cord proper relative to the mechanical forces of the injury. Therefore, the meticulous task of determining the origin and termination of the minimal number of long descending and ascending axons contained within small amounts of white matter which are capable of subserving patterned movements becomes crucial to the development of therapeutic strategies aimed at restoration of locomotion following spinal cord injury (Behrmann et al., 1992; Basso et al., 2002, 1996; Schucht et al., 2002). Towards this goal, we recently used discrete unilateral injections of Fluorogold (FG) into ventral quadrant white matter at the thoracic (T9) segment paired with cervical and lumbar intraspinal (lamina VII) injections of Fluororuby (FR) to investigate inter-enlargement (long propriospinal) and reticulospinal pathways in the adult rat (Reed et al., 2006, 2008). We found substantial populations of both ascending and descending inter-enlargement axons that are commissural in nature, crossing the midline close to the cell bodies of origin (Reed et al., 2006). We also identified that approximately 30% of VLF-related reticulospinal neurons are commissural in nature and that the majority of neurons that were labeled from either lumbar or

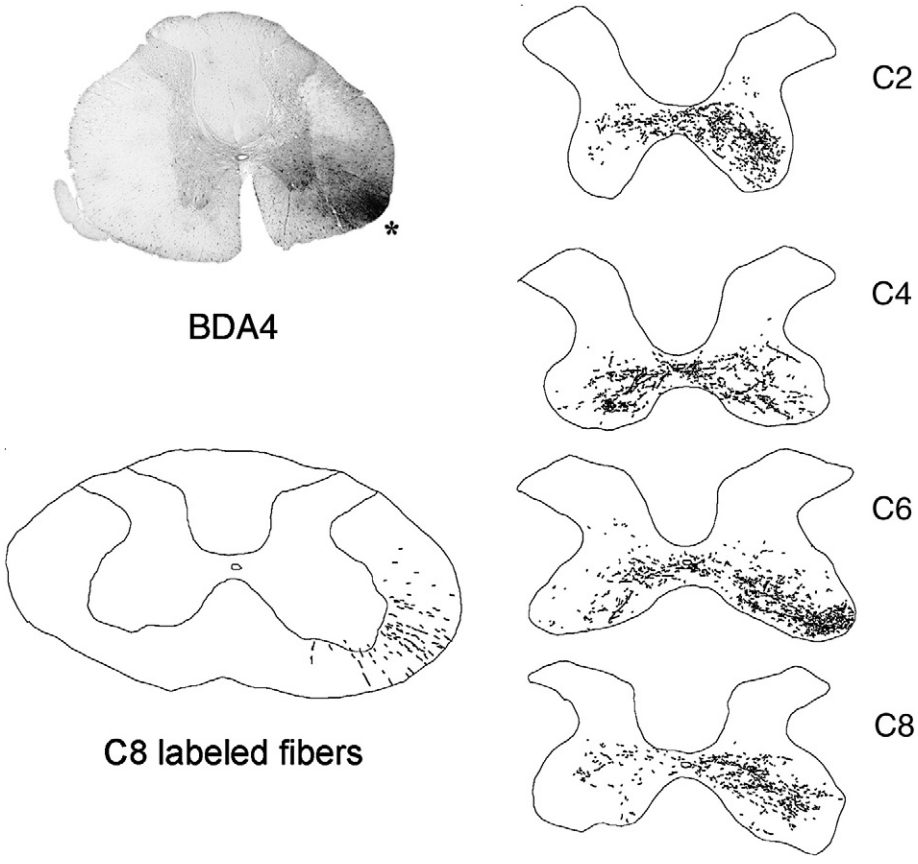

Fig. 1 – Shown are sections taken from the T9 VLF injection site (upper left, asterisk; 0.33 μl; BDA 4) and corresponding camera lucida drawings of BDA-labeled axons in the white matter at C8 and BDA-labeled axons with varicosities from five superimposed, 30 μm sections, 150 μm apart, taken from each of the cervical segmental levels examined (C2, C4, C6, C8).