Synaptic Wiring in the Deep Dorsal Horn. Focus on “Local Circuit Connections Between Hamster Laminae III and IV Dorsal Horn Neurons”

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Neural circuits, structural and functional connections between neurons, are fundamental to nervous system function. Detailed understanding of the “built-in” connectivity is essential for insight into how a neural system works under normal and abnormal conditions. For many parts of the mammalian CNS, understanding of basic neural wiring remains limited. Despite its importance for somatosensory function, the local neural circuitry in the spinal dorsal horn has remained largely mysterious for over a century. An elegant study done recently by Schneider (2008) reports that an unusually high incidence of monosynaptic synaptic connections exists between neurons in spinal laminae III and IV.

The distribution of cells and fibers in the spinal gray matter exhibits a lamination pattern that Rexed (1952) used to divide the cat spinal cord into a series of layers. Rexed’s scheme has been extended to other species and is widely used for descriptive purposes. Laminae I to IV comprise the dorsal horn and are concerned with somatosensory afferent signaling. This zone serves as a junction between the primary afferent neurons and neurons of CNS. Both primary sensory fibers from peripheral tissues and descending projections from brain terminate throughout the dorsal horn. Terminals from different functional classes of primary afferents are segregated in different laminae. Lamina I and II (superficial dorsal horn, SDH) receive input largely from thinly myelinated (Aδ) and unmyelinated (C) fibers of specific thermoreceptors and various nociceptors, indicating a role in detecting tissue damage, temperature sense and light touch (Bessou and Perl 1969; Sugiura et al. 1986). Laminae III and IV (deep dorsal horn, DDH) receive their input from more heavily myelinated (A) fibers that signal vibration, touch, and pressure (Burgess and Perl 1973; Schneider 1992; Willis and Coggeshall 2004).

Currently there is rudimentary appreciation of the local neural circuits in the SDH (Lu and Perl 2003, 2005; Santos et al. 2007). Lu and Perl (2003, 2005) have recently reported explicit neural circuitry in the SDH in which particular combinations of neurons comprise modules arranged to modify and transmit sensory information arriving from Aδ and C primary afferent fibers. However, little is known about cell-cell connections in the DDH. Schneider has approached the question by using a technically challenging approach—simultaneous electrophysiological whole cell recordings.

Schneider’s study describes several important observations. First, the probability of finding monosynaptic connections between randomly selected neurons in the DDH is 30%, much higher than the reported 10% of linked cells using similar methods in the SDH (Lu and Perl 2003, 2005), the neocortex (Deuchars et al. 1994), and the hippocampus (Ali et al. 1998).

Schneider’s observation of a high incidence of connected neurons in DDH implies that the local circuits in this region are especially interactive. Neurons in the DDH display substantial diversity in their discharge properties (Schneider 1992, 2005). An effort has been made to correlate the synaptic connectivity and the firing patterns of the pre- and postsynaptic cells. However, neither linkage probability nor the type of synaptic connection was predicted by the firing properties of the neurons suggesting that the intrinsic circuits in the DDH receive input from mechanoreceptors belonging to multiple categories of neurons and in many combinations. In the SDH, however, distinct primary afferent fibers connect to specific recurring neuronal circuits, and thus form explicit labeled lines (Lu and Perl 2003, 2005). Therefore Schneider’s observations suggest fundamental differences in organization of local circuits between DDH and SDH. The processing of mechanosensory information within DDH neuronal circuits is conducted along multiple pathways, whereas the nociceptive and temperature information is processed by a few dedicated connections in the SDH.

Second, the synaptic connections between DDH neurons are predominantly unidirectional with a majority (69%) of these linkages being inhibitory. This observation is similar to Lu and Perl’s finding (2003) that >50% of connected cell pairs in rat SDH evidenced inhibitory linkages. A new study by Zheng, Lu, and Perl (2007) describes a similar proportion of inhibitory connections in mouse SDH. These observations suggest that inhibitory interneurons comprise a substantial proportion of intrinsic circuitry in both SDH and DDH. However, Safronov’s group recently reported that only 10% of cell pairs were linked by inhibitory connections, concluding that excitatory interneurons dominate in rat lamina II (Santos et al. 2007). This apparent disparity may be explicable in part to use of different recording procedures. Schneider and Perl’s groups used paired whole cell recordings and recorded PSPs in current-clamp mode, whereas Safronov’s group used cell-attached and whole cell recordings and recorded synaptic current under voltage-clamp conditions. Signal to noise conditions are usually better under current clamp than voltage clamp, suggesting that Safronov’s procedures may have underestimated weak connectivity.

Third, unlike SDH in which most inhibitory connections were mediated solely by GABA through activation of GABAA receptors (Lu and Perl 2003; Zheng et al. 2007), Schneider found that GABA and glycine are co-transmitters at inhibitory connections between DDH interneurons. This observation is consistent with evidence that glycinergic transmission is concentrated in the DDH (Cronin et al. 2004) and suggests that glycine connections play a significant part in local circuits receiving large fiber inputs from mechanoreceptors.

In summary, Schneider’s findings (2008) make significant contributions to understanding of the general organization of
local neural circuitry coding mechanosensory information in the DDH. They also demonstrate fundamental differences in the organization of local circuits in DDH and SDH.

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REFERENCES


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