



Sensory and Integrative Function in the Spinal Cord

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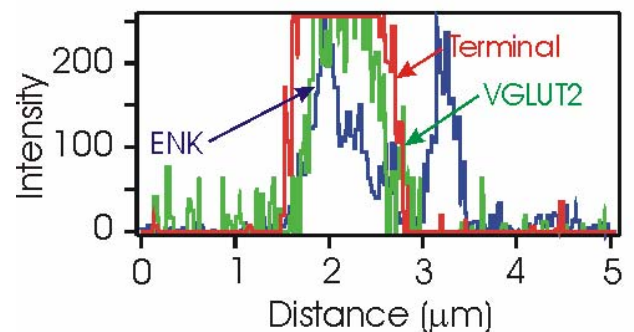
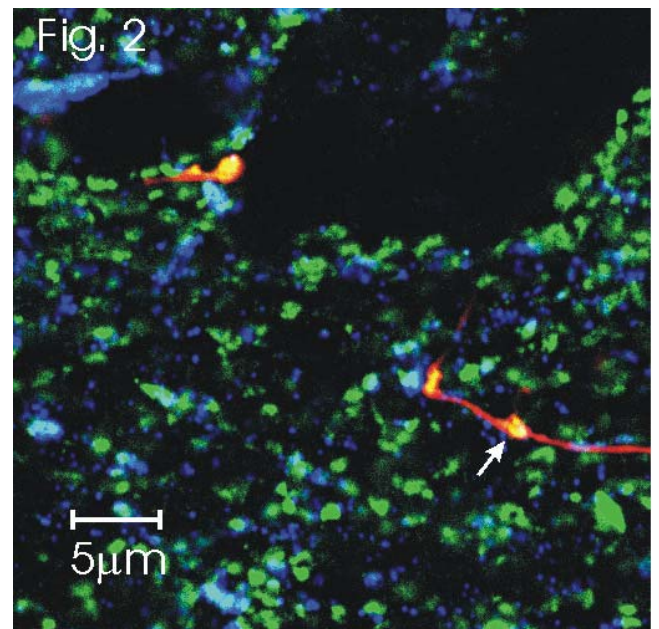
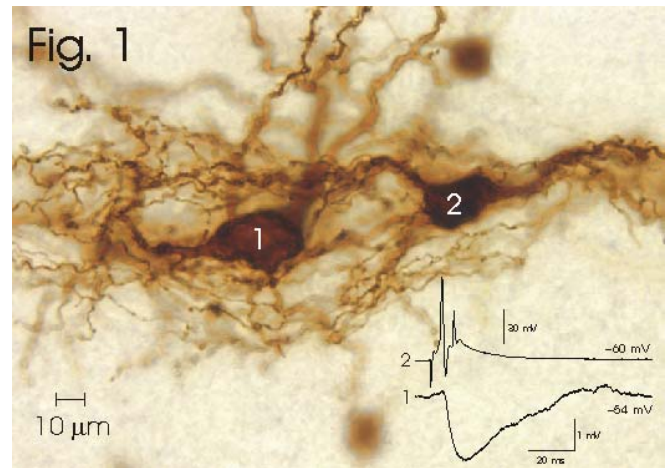
The dorsal horn of the spinal cord is a key structure that is vital for integrating sensory information from the body and mediating reflex behaviors. Our research focuses on two aspects of the dorsal horn. One set of studies explores the architecture of neural networks formed by interneurons in this region, which is crucial to an understanding of normal spinal function. The other investigates alterations in neuronal function that contribute to painful sensory sequelae of spinal cord and peripheral nerve injury.

To address these aims, our laboratory employs a combination of contemporary neurobiological techniques applied to *in vitro* slice preparations of mammalian spinal cord. Whole-cell patch clamp recordings, in conjunction with video microscopy, are used to examine physiological properties and synaptic connectivity of spinal interneurons and the basis for activity-related alterations in their signaling characteristics. Intracellular staining provides anatomical information about the connectivity of local circuit neurons established through electrophysiological means. With combined application of immunocytochemical techniques and laser scanning confocal microscopy we are also probing expression of neurochemical markers in spinal interneurons and relationships to synaptic function.

Our research has cast new light on how physiological properties of dorsal horn neurons normally influence integration of somatosensory information. We are presently engaged in studies that will help reveal the organization of complex circuits that interconnect these cells. This work will enhance our understanding of fundamental spinal cord neurobiology and ultimately foster new avenues for treatment of chronic pain.

Figure 1. Photomicrograph of two dorsal horn neurons stained intracellularly during simultaneous electrophysiological recordings. As show in the inset, an action potential in neuron 2 triggered by depolarizing current injected through the recording pipette activated a negative-going, inhibitory response in neuron 1, demonstrating synaptic communication between the cells. In experiments like these we are probing functional connectivity in neural circuits that process pain and other somatic sensations.

Figure 2. Scanning confocal microscopy of an axon belonging to a dorsal horn neuron studied similarly to the one shown in Fig. 1. The axon and synaptic terminals here are colored red. The green structures are excitatory, glutamate-releasing synapses stained with antibodies to the marker VGLUT2; the blue structures are inhibitory synapses containing the opioid peptide enkephalin, a naturally occurring analgesic. The arrow points to an axon terminal that appears to have both excitatory and inhibitory functions, as shown in the image analysis underneath. A goal of our research is to determine whether such neurons function in the spinal pain system and if their properties eventually can be exploited pharmacologically to alleviate chronic pain.



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