

SOURCES OF THE SPINORETICULAR AND SPINOTHALAMIC BRAIN SYSTEMS LABELED  
WITH HORSERADISH PEROXIDASE

V. A. Maiskii, T. G. Kebkalo,  
L. P. Savos'kina, and N. N. Oleshko

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The sources of the spinoreticular and spinothalamic fiber systems in the cat brain were studied by the axon transport of horseradish peroxidase (HP) method. In the upper segments of the spinal cord extensive regions of localization of HP-labeled neurons forming direct connections with the reticular formation and thalamus were found. In the lower segments these regions were confined to the medial part of the ventral horn and the intermediate zone of gray matter. Neurons of these regions send direct connections to the contralateral nuclei of the reticular formation and the ipsilateral and contralateral nuclei of the thalamus. The possible pathways of conduction of somatic and pain sensation are discussed.

KEY WORDS: labeled neuron; spinal cord; pathways of somatic and pain sensation.

The funicular trajectories and distribution of the endings of the spinoreticular and spinothalamic fiber systems in the brain of animals and man have been well studied in connection with research into somatic sensation and the physiological mechanisms of pain [2, 3, 9]. However, complete data are not yet available on the localization of neurons forming these supraspinal fiber systems, although the first results of a successful study of these neurons were published not long ago [6, 7, 10, 11].

Synaptic endings and injured axons can take up horseradish peroxidase (HP) and transport this enzyme toward the bodies of the parent cells. This retrograde axon transport of HP is nowadays used not only to determine the precise localization of the neurons acting as sources of various fiber systems of the brain, but also to determine their size, shape, and numerical relations [1, 5].

This paper gives the first description of HP-labeled neurons as sources of the spinoreticular and spinothalamic fiber systems along the whole length of the spinal cord.

#### EXPERIMENTAL METHOD

Experiments were carried out on cats weighing 2.5-3 kg. Unilateral microinjections, each of 0.5-1.5  $\mu$ l of a 30% aqueous solution of HP, were given to animals under pentobarbital anesthesia into the reticular formation of the medulla and pons (eight cats) and the medial nuclei of the thalamus (five cats). The direct use of certain types of HP was impossible because of their low activity. Highly active peroxidase (from Boehringer, West Germany, PZ  $\sim$  3), and also enzyme obtained by purification of a commercial type of HP (Reanal, Hungary, PZ  $\sim$  0.6) by ion-exchange chromatography, were used. Full details of the method of retrograde axon transport of HP were given by the writers previously [1].

#### EXPERIMENTAL RESULTS

The distribution of HP-labeled neurons after unilateral microinjections of the enzyme into the reticular formation of the pons and medulla is illustrated in Fig. 1a. Many labeled neurons were observed in the intermediate zone of gray matter in the cervical segments (C1-C7) and the density of their distribution fell sharply in the upper thoracic segments (T1-T6). Whenever microinjections were made into the substantia gelatinosa (Rexed's laminae I-II) or

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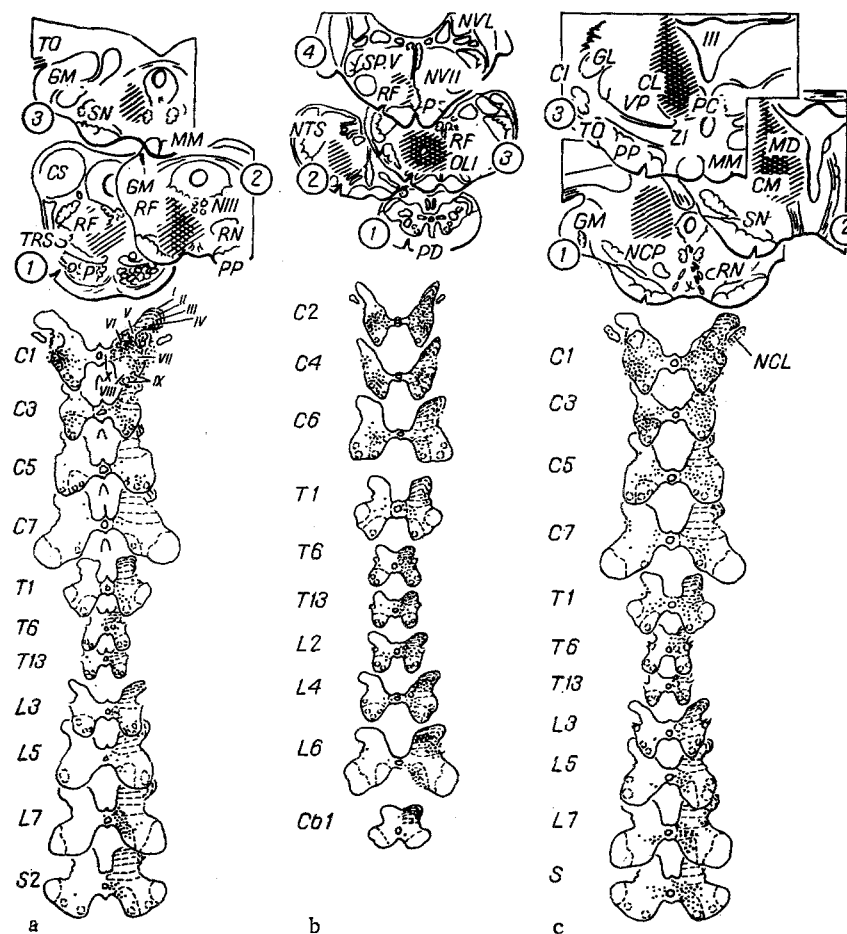


Fig. 1. Distribution of HP-labeled neurons (dots) in spinal cord segments after unilateral microinjections into reticular formation (a, b) and thalamus (c). 1-4) Different levels of frontal brain sections in rostral direction. Zones of injection of HP and of its diffusion indicated by double and single shading respectively; Roman numerals indicate Rexed's laminae. Pooled data from 12 (in a, b) or 50 (in c) serial sections are shown on each plan of the spinal cord. Brain sections cut in accordance with coordinates of stereotaxic atlas [8], from which corresponding names of structures are taken. Remainder of explanation in text.

motor nuclei, no neurons were found to accumulate the enzyme. Large labeled neurons measuring 50-80  $\mu$ , with numerous long dendrites, were found mainly in the central nucleus of the dorsal horn and the intermediate zone of the lower lumbar segments (L3-L7), and there were many small, long neurons (10-20  $\mu$  in diameter) on the contralateral side in lamina VI of the superior cervical segment and in lamina VIII of the lower lumbar segments of the spinal cord (Fig. 2a-c). When the zone of microinjection of HP included the nuclei of the dorsal columns, most labeled neurons were found on the ipsilateral side in the dorsal horn.

After microinjections into the thalamus (Fig. 1c) labeled neurons could be seen along the whole length of the spinal cord as far as the lower sacral (S2) and upper coccygeal (Cb1) segments. By contrast with microinjections into the reticular formation of the medulla and pons, in this case there were wider regions of distribution among the laminae on the ipsilateral side, including the lateral cervical nuclei also. In the lower lumbar segments most HP-labeled neurons were localized on the contralateral side in the medial part of lamina VI and in the dorsal part of lamina VIII. In both the cervical and the lumbar regions, neurons accumulating peroxidase varied in size (diameter 10-50  $\mu$ ) and shape (Fig. 2d).

The investigation showed that many small neurons in the medial parts of the ventral horn form a crossed system of fibers running toward the medial reticular formation of the medulla.

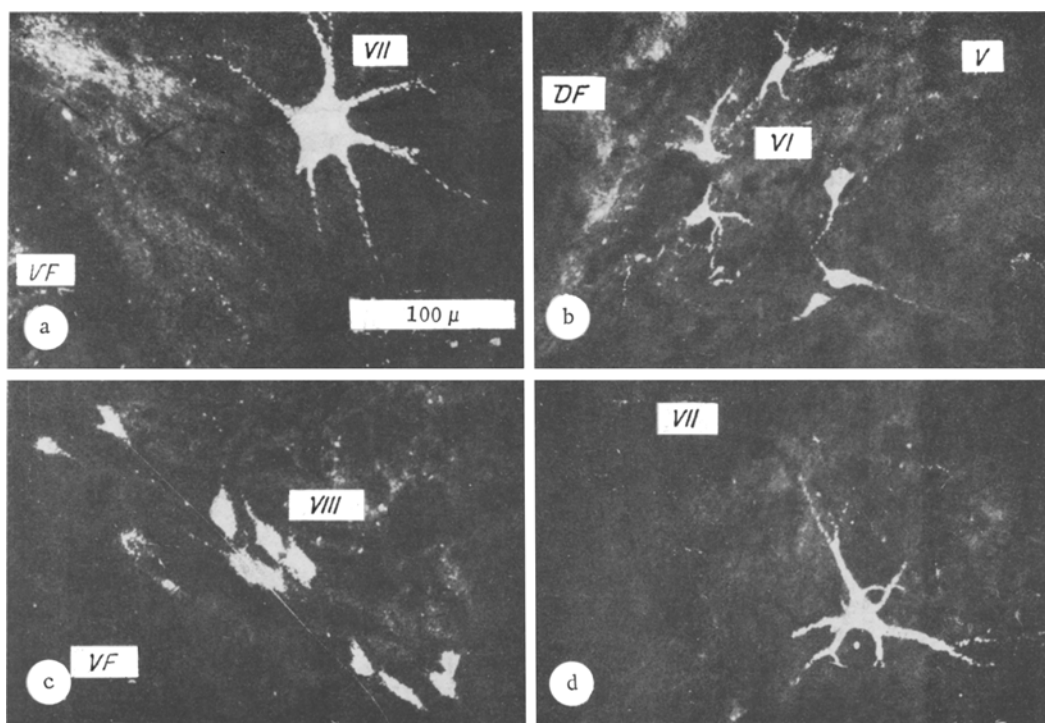


Fig. 2. Photomicrographs (dark field) of HP-labeled spinal neurons: a, b, c) in L7, C1, and L6 respectively after microinjections into reticular formation; d) in C5 after microinjections into thalamus. Magnification in a-d the same, scale shown in a. Remainder of explanation in text.

A few neurons in the lateral zones of the dorsal horn were also shown to form direct connections, whereas many neurons in adjacent regions form indirect connections with the contralateral thalamus. In the latter case, this was effected by the system of the lateral cervical nucleus and the crossed system of the medial lemniscus. In higher animals (monkeys) and in man they are duplicated by direct spinothalamic projections from the dorsal horn through a system of fibers running in the dorsolateral fasciculus [11]. However, both in the cat and in the monkey, neurons of laminae III-V of the dorsal horn form ascending fiber systems to nuclei of the dorsal columns. These nuclei give rise to an ascending system of fibers to the contralateral thalamus and a descending system of fibers to the spinal cord [4, 5]. Our microinjections of HP were limited to nuclei of the medial thalamus, where most spinothalamic fibers either run through or terminate [2]. During these microinjections HP did not spread into the indefinite region with which neurons of the substantia gelatinosa have direct connections.

The data on the sources of the spinoreticular and spinothalamic fiber systems of the brain thus agree partly with the results of electrophysiological and morphological investigations [6, 10, 11], but more extensive regions of localization of the neurons forming these ascending systems of somatic, temperature, and pain sensation were demonstrated.

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