Effect of dorsal-column stimulation on gelatinosa and marginal neurons of cat spinal cord

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Single neuronal units with physiological characteristics of superficial dorsal-horn neurons were recorded extracellularly in laminae 1, 2, and 3 of cat spinal cord. When focal electrical stimulation was applied to the ipsilateral dorsal column, most of the units were excited transsynaptically at various latencies consistent with an effect mediated by large myelinated axons. Units recorded in laminae 2 and 3 had earlier latencies of activation than units in lamina 1. Units with cutaneous receptive fields only for noxious stimuli were activated at significantly longer latencies than units responsive to innocuous stimuli. The time course of these effects was consistent with the concept that many cells in laminae 1 to 3 receive direct excitatory synaptic input from collaterals of dorsal-column fibers, and some lamina 1 cells receive excitatory synaptic input from lamina 2 neurons. Previous reports have emphasized the inhibitory action of dorsal-column stimulation on nociceptive responses of cells in laminae 4 and 5 of the dorsal-horn, particularly those of the spinocervical tract in cats and the spinothalamic tract in primates. The present study suggests that some of this inhibition might be sustained by a network of interneurons in or near the substantia gelatinosa and marginal layer. The therapeutic efficiency of dorsal-column stimulation for pain relief in humans may depend in part on the activation of neurons in the superficial layers of the dorsal horn.

KEY WORDS: analgesia, dorsal horn, electrical stimulation, pain, spinal cord, substantia gelatinosa, dorsal column, Rexed's laminae, cat.

NUMEROUS reports indicate that electrical stimulation of the dorsal columns of the spinal cord can relieve chronic pain. Despite more than 20 years of experience with cord stimulation in human patients, the physiological mechanism underlying success of this treatment is still not known. The concept that cord stimulation has a direct electrical blocking action on small-diameter primary afferent fibers is untenable for several reasons, not the least of which is the time course of the analgesic effect, which sometimes outlasts the period of stimulation. The analgesic effect does not appear to be mediated by endorphins. It is not reversed by naloxone, and direct measurements of cerebrospinal fluid (CSF) endorphins show no increase during stimulation. The most consistent physiological finding so far has been inhibition of neuronal responses deep in the dorsal horn of the spinal cord. Inhibition of the nociceptive responses of dorsal-horn neurons in laminae 4 and 5 by dorsal-column stimulation has been described in laboratory animals. To date there has been little or no information about the effect of dorsal-column stimulation on neurons in the superficial laminae, which include the substantia gelatinosa. Various lines of evidence implicate the substantia gelatinosa in mechanisms of analgesia.

The present study examines the effect of focal stimulation of the dorsal columns on single-unit activity in a population of neurons in the superficial layers of the dorsal horn, encompassing the substantia gelatinosa. The term “substantia gelatinosa” as used in this report refers to the pale region of the dorsal horn in myelin-stained sections or cleared cord specimens. As noted by Gobel, this region corresponds to Rexed's lamina 2 and probably also portions of lamina 1. Lamina 2 is subdivided into an outer portion (2o) subjacent to lamina 1 and a deeper inner portion (2i) bordering lamina 3.

Materials and Methods

Surgical Procedure

The care of animals during these experiments met the standards of the United States Public Health Service. Six adult cats weighing 2.0 to 4.0 kg each were anesthetized with ether and decerebrated. The trachea,
jugular vein, and carotid artery were cannulated. Ether was then discontinued. The animals were paralyzed with gallamine and mechanically ventilated to maintain the expiratory pCO2 level in a range between 3.0% and 4.0%. Blood pressure, electrocardiogram recordings, heart rate, body temperature, and temperature of the mineral oil covering the spinal cord were monitored throughout the experiments and kept within the normal range. Blood pressure was maintained above 80 mm Hg with intravenous infusions of 4% dextrose in saline.

The spinal cord was exposed by laminectomies at the lumbosacral enlargement and at the level of the T12–L1 segments. Prior to recording, the dorsal columns and Lissauer tracts were carefully transected at T-13 using high magnification and microsurgical instruments, with care taken to avoid surface vessels. The dorsolateral funiculi and ventral quadrants were left intact. The exposed cord segments were covered with warm mineral oil.

**Stimulating and Recording Methods**

The goal was to determine whether the effect of dorsal-column stimulation on single units in laminae 1 to 3 was mediated by impulses traveling to the dorsal horn through collaterals of dorsal-column fibers or by impulses ascending the dorsal columns to the brain stem. To achieve this goal, stimulation was applied both above and below a complete transection of the dorsal columns while single-unit activity was recorded in the superficial portion of the lumbosacral dorsal horn. To be certain that the dorsal column transection was complete, numerous parallel penetrations of a recording microelectrode were used to explore the dorsal columns below the transection while stimulating the dorsal columns above the transection. No sign of antidromically evoked activity was ever seen during stimulation above the transection site.

The recording and stimulating arrangement is shown in Fig. 1. Stimulation above and below the level of dorsal-column transection was delivered through glass-coated tungsten microelectrodes. The tips of the stimulating electrodes were positioned 200 μm from the midline ipsilateral to the recording site and 50 μm below the pial surface. Stimulation consisted of 100-μsec square-wave pulses delivered through a stimulus isolation unit at 1 to 2 Hz. The stimulating current was gradually increased from 0 to 100 μA; if an effect was seen, its threshold was noted. Poststimulus-time histograms were computed with a NeuroLog NL 750 averager to assess in more detail the time course of dorsal-column effects on single units. Sweeps of the averager were triggered at 1 Hz by dorsal-column stimulus pulses.

In addition to these immediate time-locked responses, the receptive fields, ongoing neuronal activity, and other response properties of the single units were examined in more detail, as described below. Changes of ongoing activity and receptive fields were studied by applying repetitive stimulation to the dorsal column above or below the transection. Brief trains of 100-μsec square waves (1-second duration, 50 Hz) were delivered at currents just above the response threshold of the single unit, and changes of ongoing neuronal discharge rate, receptive field, or response to cutaneous stimuli were noted. Finally, responses to natural cutaneous stimuli were examined during continuous stimulation of the dorsal columns at various intensities and frequencies (10 to 100 μA, 1 to 200 Hz).

Single-unit recordings were made in the L-7 and S-1 cord segments through a 1- to 2-mm dural window opened over the ipsilateral dorsal column and dorsal root entry zone. The arachnoid was left intact to ensure optimal venous drainage from the cord. Mechanical stability was increased by unilateral or bilateral pneumothorax. Recordings were made in a series of closely spaced, parallel tracks directed ventrally and somewhat laterally across the dorsal horn to a depth of 1500 μm. The units were recorded using low-impedance (500 kOhm to 1 megOhm) platinum-surfaced tungsten microelectrodes insulated with glass, which had noise levels of less than 30 μV.

Units were first detected by their spontaneous activity or by responses produced by lightly stroking or pinching the skin of the hindlimb and tail. Isolation of single units was facilitated by slight depth adjustments of the microelectrode tip to maximize spike height, by adjustments of continuously variable filters in a range between 500 and 7500 Hz, and by constant observation of the unit's spike waveform on an oscilloscope. Spikes

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*D Averager manufactured by Digitimer Research Instrumentation and distributed in the United States by Medical Systems Corp., Great Neck, New York.*
Dorsal-column stimulation of gelatinosa and marginal neurons

Table 1

<table>
<thead>
<tr>
<th>Stimulus Location</th>
<th>Receptive Field Units*</th>
<th>Total Units</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT</td>
<td>BTP</td>
</tr>
<tr>
<td>lamina 1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>lamina 2o</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>lamina 2i</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>lamina 3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Lissauer tract</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>all locations</td>
<td>17</td>
<td>7</td>
</tr>
</tbody>
</table>

* BT = units responding to brush-touch only; BTP = units responding to brush-touch-pressure in graded fashion; P = units responding only to noxious pressure.

of appropriate height activated a NeuroLog NL 740 analog delay,† which permitted visualization of the entire spike waveform including the initial phase. Units reported in this paper had clearly isolated individual spike waveforms. No unit was included which showed any change of spike duration or shape during the observation period. Stimulus artifacts were greater than 2 mV peak to peak and were excluded by the window discriminator during testing. Typical single units recorded in laminae 1 to 3 or in the nearby Lissauer tract had relatively small spike heights of 60 to 250 μV and were recorded only within the pale histological boundaries of the substantia gelatinosa and marginal zone, or within 50 μm of these boundaries, as demonstrated by marking of recording sites with microlesions produced by a small direct current passed through the recording tip. In addition, fine glass micropipettes were inserted along recording tracks and cut short for use as markers to reconstruct and further verify the unit recording locations. Track markers were visualized in 1-mm thick cord sections cleared with methyl salicylate and drawn using a camera lucida. Sections 50 μm thick were cut and stained with solachrome cyanine to check the locations of microlesions.

Spontaneous and evoked discharge rates were recorded with a rate meter and plotted on a chart recorder. Cutaneous receptive fields were observed repeatedly at 5-minute intervals prior to any electrical testing. Receptive fields were mapped for response to gentle movement of hairs, touching of skin with a small blunt rod, and pinching skin folds with a broad-tipped (6-mm) forceps with a force that was moderately painful when applied to the investigator’s skin. Proprioceptive primary afferent fibers were frequently encountered and were recognized by their regular firing patterns and responses to gentle pressure on muscles or to slight movements of the tail or joints in the hindlimb. For each unit recorded, these responses were sought by gently moving all joints of the foot and leg, and the tail.

† Analog delay manufactured by Digitimer Research Instrumentation and distributed in the United States by Medical Systems Corp., Great Neck, New York.

Table 2

Fig. 2. Locations in the dorsal horn of 33 units which were examined for effects of dorsal-column stimulation are indicated by dots. The diagram corresponds to the portion of spinal cord delineated in the photograph. In the diagram the borders of lamina 1, 2o, and 2i are shown by solid lines, and the approximate borders of the Lissauer tract are indicated by dashed lines.

No unit included in the sample showed responses to these proprioceptive stimuli. The possibility that units with small receptive fields might be primary afferent fibers was excluded in all cases by the failure of the units to follow high-frequency electrical stimulation of the receptive field at fixed latency, and by the general complexity and variability of the receptive fields.

Results

Thirty-three single neuronal units were included in the experiment. Of these 33, nine were located in lamina 1 or within 50 μm of its dorsal border, six were in lamina 2o (the outer half of layer 2), 11 were in lamina 2i (the inner half), five were in lamina 3 within 50 μm of the ventral border of the substantia gelatinosa as seen in cleared cord sections, and two were in the Lissauer tract (Fig. 2). Responses to brushing hairs (“brush”), touching skin (“touch”), and pinching skin folds (“pressure”) bore some relation to the laminae in which the maximal spike heights of the units were recorded, as noted in Table 1. In all, 17 units had receptive fields for brush-touch only, seven showed fields for brush-touch with a greater response to pressure, and nine responded only to hard pressure. Units
responsive only to noxious stimuli (that is, pinching) were consistently located in lamina 1, lamina 2o, or in the lateral Lissauer tract adjacent to these laminae. Most of the units responsive only to innocuous stimuli (such as brushing hairs or touching) were located in laminae 2i or 3. Units with fields of the brush-touch-pressure type were found in laminae 1, 2o, 2i, and 3.

Receptive fields consisted of continuous excitatory zones ranging from small patches (0.5 to 1 sq cm) on one or more toes to very large fields (35 sq cm) including the toes, foot, and portions of the distal and proximal leg, or a portion of the tail in some instances (Fig. 3). In units responsive only to brush-touch, the field was often equally sensitive throughout, whereas in units responding only to pressure, or to brush-touch-pressure in a graded fashion, there was usually a central zone of maximal response to all three types of stimuli. This was typically surrounded by, or adjacent to, a larger area of diminished response or an area of response to only one type of stimulus. Rarely, faint inhibitory responses were seen outside these excitatory receptive fields, but the inhibitory responses were too inconsistent to be mapped. Unusual properties, such as sustained afterdischarge (1 to 30 seconds) following brief cutaneous brush or pinch stimuli, progressive habituation of response to brushing or pinching, or ameboid shifting of receptive field boundaries were common in these units.

Responses to stimulation of the dorsal columns below the transection site were examined in 29 units, of which 24 showed direct transsynaptic excitation. Excitation occurred at slightly varying latencies (> 4%) when dorsal-column pulses were applied at threshold level for a response, using very small currents (4 to 40 μA). Above threshold, stimulation often elicited multiple excitatory responses over a wider range of latencies between 1 and 12 msec. When signal averaging was

![Fig. 3. Examples of cutaneous receptive fields (RFs) of units recorded in laminae 1, 2, and 3. Darkly shaded zones represent RFs for graded response to brushing, touching, and pressure. Lightly shaded zones are RFs for brushing and touching only. Vertically hatched areas represent RF components with response to hard pressure only. A: Ameboid RF of a unit recorded in lamina 1. Arrows indicate reversible spontaneous variation of RF boundaries in the absence of dorsal-column stimulation. B: Ameboid RF of a lamina 2o unit. Arrows indicate spontaneous RF variation without dorsal-column stimulation. C: Receptive field of a lamina 2i unit before and after dorsal-column stimulation (1-second train at 50 Hz). The RF showed stable borders before stimulation, and expanded after stimulation. D: Receptive field of a unit in lamina 3 recorded within 50 μm of the ventral border of lamina 2, and the response to dorsal-column stimulation (1-second train at 50 Hz) below the site of dorsal-column transection.](image-url)
Dorsal-column stimulation of gelatinosa and marginal neurons

used to compute poststimulation-time histograms, even at threshold it was common to see several discrete peaks of excitation, each representing a distinct transsynaptic response latency. If the stimulating current was increased slightly, additional peaks appeared in the poststimulation time histogram (Fig. 4), apparently due to recruitment of more dorsal-column axons by the stimulus pulses. All components of these responses were judged to be transsynaptic processes because their latencies varied more than 4% at threshold and they failed to reliably follow repetitive stimulus pulses at rates above 50 Hz.

Seven of nine lamina 1 units, including five with receptive fields only to noxious pressure, were activated transsynaptically by dorsal-column stimulation. Whereas units of laminae 2 and 3 were activated at various latencies including an earliest response at 1 to 3 msec, units of lamina 1 had initial response latencies greater than 4 msec (Fig. 5). When the initial response latencies for unit excitation by stimuli at or just above threshold were corrected to an arbitrary conduction distance of 75 mm, the mean latency of all lamina 1 units was 5.44 msec (range 4.2 to 6.0 msec). The mean latency to initial responses at threshold for laminae 2 and 3 units was 2.94 msec (range 1.0 to 6.6 msec). The difference of the means was significant by a t-test (p < 0.005). Thus, there was a difference of initial response latency according to laminar location of the units tested. There was also a difference in mean response latencies according to type of cutaneous receptive field.

Six of nine units having receptive fields only for noxious pressure showed a mean initial latency of 5.51 msec (range 4.2 to 6.6 msec). Four of seven units having receptive fields for brush, touch, and pressure showed a mean initial latency of 4.10 msec (range 1.8 to 5.8 msec). The mean initial latency of 14 units showing only brush-touch responses was 2.87 msec (range 0.9 to 5.1 msec). The difference between the mean values of the group responsive only to noxious pressure and the combined group of units responsive to brush-touch or brush-touch-pressure was significant by a t-test (p < 0.005).

Nine units were tested for responses to brief trains (1-second duration, 50 Hz) of dorsal-column stimulation delivered below the dorsal-column transection site at a level just above threshold for an excitatory postsynaptic response. In two units, the rate of ongoing discharge increased. In three units, the cutaneous receptive field expanded to a degree which exceeded spontaneous fluctuations of receptive field boundaries noted prior to stimulation (Fig. 6). In one other unit, the cutaneous receptive field expanded to a degree which did not exceed the spontaneous changes observed before stimulation. In the rest, there was no sign of prolonged facilitation or other alteration of response properties. Reliable unit responses to cutaneous stimuli from brush-touch or pressure could be demonstrated even during continuous stimulation of the dorsal columns at various frequencies (1 to 200 Hz) and intensities.

Twenty-five units were tested for responses to volleys ascending the dorsal columns. When 1-second trains of stimulation were delivered at 50 Hz and 100 μA, no excitatory or inhibitory effects were seen. During continuous stimulation at various frequencies (1 to 200 Hz), responses to peripheral brushing, touching, and pinching were unaltered from baseline. Small receptive field changes were seen (two expansions and one contraction) after trains of stimulation above the dorsal-column transection, but the changes were judged to be within the range of spontaneous variation seen in these units in the absence of electrical cord stimulation.

**Discussion**

In the present study, over 80% of neuronal single units recorded in the substantia gelatinosa and marginal

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**Fig. 4.** Poststimulus-time histograms showing the response of a lamina 2 unit to dorsal-column stimulation. Both histograms were computed from 128 sweeps of an averager with dorsal-column stimulation at time zero. Sporadic ongoing activity of the unit accounted for 0 to 3 spikes/bin. **Upper:** Stimulation at 8 mA produced excitatory responses at 1.7 and 1.9 msec (the earlier peak is an artifact). **Lower:** Increasing the stimulating current to 14 mA produced additional responses at 0.8, 1.0, 1.8, 2.0, and 2.5 msec.

**Fig. 5.** Poststimulus-time histogram showing the time course of activation of a lamina 1 unit by dorsal column volleys. The unit responded only at a latency of 5 to 7 msec. It was not spontaneously active. The histogram was computed from 128 sweeps of an averager, triggered by dorsal-column stimulation at time zero, at 1 Hz.
The difference was great enough to be consistent with an effect mediated by large myelinated axons. Latencies of lamina 1 cells were significantly longer. The earliest response latencies of laminae 2 and 3 responded at shorter average latencies than did lamina 1 units. The receptive fields of laminae 1 to 3 were transsynaptic, as indicated by a slightly varying latency of response (>4%) and by failure to reliably follow dorsal-column stimulation. In their investigations, using high-impedance glass micropipettes in unanesthetized cats without decerebration, have reported predominantly excitatory receptive fields for substantia gelatinosa neurons which are quite different. Cervero, et al.,6-10 reported predominantly inhibitory receptive fields in laminae 1 and 2 cells of cats anesthetized with chloralose, a finding not yet confirmed by other groups. Price, et al.,11 reported predominantly excitatory receptive fields for neurons in laminae 1 and 2 when they used low-impedance metal microelectrodes. Bennett, et al.,7 in their investigations using high-impedance glass micropipettes together with intracellular labeling with dye in barbiturateranesthetized animals, noted that stalked cells of lamina 20 had excitatory receptive fields; some showed prolonged discharges to brief cutaneous stimuli. In their work in which electrical nerve stimulation rather than natural stimulation was employed to locate the units initially, Perl, et al.,31-44 found that the superficial neurons were responsive to noxious stimuli in anesthetized animals. Fields, et al.,15 recording in lamina 1 of cat spinal cord with glass micropipettes of moderately high impedance, noted that there were relatively few cells with large-amplitude (>200 μV) spikes, and that these were interspersed with numerous smaller units whose

Fig. 6. Drawings of a hindlimb showing the cutaneous receptive field (RF) of a single unit recorded in lamina 20. Dark shading indicates area responsive to brushing, touching, and pressure in graded fashion. Vertically hatched area represents an RF responsive only to noxious pressure. A: Extent of ameboid variation of the RF observed prior to dorsal-column stimulation. B: Expansion of the RF after a 1-second train of stimulation to the ipsilateral dorsal column, delivered below the site of dorsal-column transection.

D. Dubuisson
Dorsal-column stimulation of gelatinosa and marginal neurons

spikes were buried in noise. In lamina 2, this type of electrode did not record any neuronal activity. These authors speculated that the high-amplitude spikes represented large “marginal cells” of layer 1.

It is evident that different recording techniques sample different populations of neurons in the substantia gelatinosa region. Differences in animal preparation, such as decerebration or general anesthesia, undoubtedly bring out certain features of the receptive fields while hiding others. In a previous investigation the author has observed profound and long-lasting receptive field changes in a majority of substantia gelatinosa neurons during induction of general anesthesia with barbiturate or chloralose in previously unanesthetized decerebrate cats. The changes included shrinkage, diminished response to cutaneous stimuli, disappearance of sustained afterdischarges, and appearance of inhibitory zones. These factors undoubtedly account for much of the controversy and apparent discrepancy in the literature regarding substantia gelatinosa neurons. In the present study, the use of unanesthetized decerebrate cats, the low-impedance extracellular recording technique, and the search for units by means of relatively natural cutaneous stimuli favored identification of units with small spike heights, spontaneous ongoing activity, and excitatory receptive fields.

Several studies have shown that stimulation of the dorsal columns may diminish the responses of cord neurons in laminae 4 and 5 to noxious stimuli. Inhibition of spinocervical tract neurons by dorsal-column stimulation has been reported in unanesthetized decerebrate cats. Some of the inhibition was shown to be mediated by impulses ascending the dorsal columns and relaying in the brainstem. This effect was abolished by sectioning the dorsal columns between the site of stimulation and the recording site. The activation of units in the substantia gelatinosa and marginal layer by dorsal-column stimulation is therefore conspicuously different from the predominantly inhibitory response seen in neurons of deeper laminae. Antidromic activation from dorsal-column stimulation was never encountered in the units. It is therefore unlikely that any of the units projected axons in the dorsal columns as part of the dorsal-column postsynaptic system, even though some dorsal-column postsynaptic cells can be found near the border of laminae 2 and 3.

Most of the neurons of the substantia gelatinosa region are thought to exert local effects within the dorsal horn by way of short axons in the superficial dorsal horn and in the Lissauer tract. In the gate-control theory of pain, the substantia gelatinosa was postulated to be the site of a sensory gating mechanism whereby afferent activity in large myelinated fibers (or dorsal columns) might produce a blockade of responses in dorsal-horn neurons of the spinoholamtic tract and other ascending somatosensory pathways. The finding that a majority of substantia gelatinosa neurons are excited by dorsal-column stimulation while deeper cells of the dorsal horn are inhibited is consistent with the idea that a population of cells in the superficial layers of the dorsal horn might function as a local inhibitory network modulating sensory inputs to the cord. Wall reported that focal stimulation of the Lissauer tract, which contains axons of substantia gelatinosa cells, inhibited responses of some neurons of laminae 4 and 5 to noxious stimuli. In decerebrate cats with spinal cord transection or unanesthetized decerebrate cats most lamina 1 and 2 neurons can be activated transsynaptically by focal stimulation of a descending axonal system in the dorsolateral funiculus. The latency of transsynaptic excitation is consistent with an effect mediated by medullary raphe-spinal axons, and the time course of excitation mirrors the period of inhibition seen in deeper dorsal-horn cells. Medullary raphe stimulation excites or facilitates activity in some neurons of laminae 1 to 3. An excitatory effect of medullary raphe stimulation was seen in half of a group of lamina 2 neurons labeled intracellularly in barbiturate-anesthetized animals. Although the focal dorsal-column stimulation delivered through a microelectrode in the present study was too close to the midline and the current intensities were far too small to excite axons in the dorsolateral funiculus (for biophysical data see the paper by Ranck), the same might not always be true of dorsal-column stimulation delivered through gross electrodes in human patients. Cord stimulation in humans may provide effective pain relief when applied to white matter tracts other than the dorsal columns; excitation of dorsolateral funiculus axons might be an additional substrate of the analgesic effect.

There are two mechanisms by which substantia gelatinosa neurons might contact and inhibit deeper cells of the dorsal horn. Studies using the Golgi method show that some laminae 4 and 5 neurons have long dendrites which extend into the substantia gelatinosa or along its ventral border. Some cells of laminae 1 to 3 send axons into deeper laminae. A recent study employing intracellular marking identified a type of cell in lamina 2 which sent its axon into deeper laminae. If some substantia gelatinosa neurons are inhibitory interneurons, the sustained inhibition of sensory transmission which outlasts dorsal-column stimulation might be related to the prolonged afterdischarges and variable ongoing activity seen in superficial dorsal-horn cells (in the absence of general anesthetics). Moreover, these neurons synapse on each other within the substantia gelatinosa, so that self-sustaining activity in a local neuronal network is possible. Neurons of laminae 1 to 3 contain a variety of neurally active peptides, transmitters, and chemical substances of uncertain function, including enkephalin, neurtensin, cholecystokinin-like peptide, and gamma aminobutyric acid. The activation of these cells by synaptic inputs from dorsal-column collaterals as well as from the dorsolateral funiculus and Lissauer tract might release one or more chemical substances, leading to in-
hition of transmission in terminals of small-diameter primary afferent fibers, or inhibition of responses in larger-projection neurons. These inhibitory effects would be prolonged by the tendency of substantia gelatinosa cells to show sustained afterdischarges. Such a mechanism might explain the analgesic effect of dorsal-column stimulation in humans and the tendency of the effect to outlast stimulation.

Acknowledgments

The author thanks Professor Patrick D. Wall of University College, London, in whose laboratory the experiments were carried out. Valuable technical support was provided by A. Ainsworth, D. Conway, and J. T. Patel.

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264

J. Neurosurg. / Volume 70 / February, 1989
Dorsal-column stimulation of gelatinosa and marginal neurons


Manuscript received April 22, 1988.
This work was supported by the Medical Research Council of Canada and the National Institutes of Health.
Dr. Dubuisson is the recipient of Teacher Investigator Development Award NS00853 from the National Institutes of Health.
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