Distribution of activity in spinal pathways evoked by experimental dorsal column stimulation

HEINRICH BANTLI, PH.D., JAMES R. BLOEDEL, M.D., PH.D., DONLIN M. LONG, M.D., PH.D., AND Phudhiphorn Thienprasit, M.D.

Departments of Neurosurgery and Physiology, University of Minnesota Medical School, Minneapolis, Minnesota

Experiments were performed in rhesus monkeys to determine the distribution of activity evoked in spinal pathways by dorsal column stimulation. It was shown that many pathways in both the dorsal and ventral quadrants of the cord can be activated either directly or transsynaptically by stimulation with electrodes of the type implanted clinically. Moreover, the transsynaptically evoked responses recorded in each quadrant had somewhat different characteristics. Therefore, since the activation of each group of pathways may have differing effects in modifying the perception of noxious stimuli, the authors believe that changes in electrode position and stimulus parameters may be important in obtaining the therapeutic value of spinal cord stimulation for relief of pain.

KEYWORDS • spinal cord • dorsal column stimulation • pain • gate theory

THE purpose of this study is to examine the distribution of responses in the spinal cord evoked by commercially available dorsal column stimulators and to determine the effects of changing the parameters of stimulation on the various components of these responses. It will be shown that indeed dorsal column stimulation activates fibers in many spinal pathways located in both the dorsal and ventral portions of the spinal cord. Moreover, arguments will be presented suggesting that a more careful analysis of the role of electrode placement and stimulating parameters in the application of this therapeutic tool may be quite significant in directing its appropriate use.

Material and Methods

Experiments were performed on four large rhesus macaque monkeys anesthetized with a mixture of halothane and nitrous oxide, paralyzed with Flaxedil* and artificially respired. Heart rate, blood pressure, and body temperature were constantly monitored, and body temperature was maintained constant by means of a thermo-regulatory system. A laminectomy was performed from level T-4 through approximately T-10. A bipolar tinsel wire electrode and a three-

*Flaxedil (gallamine triethiodide) manufactured by Davis and Geck, American Cyanamid Company, Pearl River, New York 10965.
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Element bipolar stimulating electrode* were placed one behind the other over the dorsal columns. In some experiments, the stimulation was transdural, while in others the dura was removed. No differences were found in the recordings obtained under these two conditions. In one experiment, a monopolar stimulating electrode was placed subdurally over the dorsal columns. However, since the current spread from the monopolar stimulating electrode to the recording site was too large to allow adequate recording of the responses, this electrode was not employed in the studies. A second laminectomy was performed at approximately C-4. A glass micropipette filled with 4 M sodium chloride (resistance of 2 to 5 megohms) was used at this site for the recording and the localization of the field potentials evoked by stimulation with either of the two electrodes placed on the spinal cord. The evoked potentials were amplified with an AC coupled amplifier, displayed on a Tektronix 565 oscilloscope, and averaged with a Fabritek 1072 averaging computer.† All responses were summed at least 64 times prior to display.

Results

Responses to stimulation of the dorsal columns with either the tinsel bipolar electrode or the three-element bipolar electrode were first recorded from the surface of the dorsal columns. The responses in Fig. 1 were evoked by stimuli with amplitudes of four volts and frequencies ranging from 10 to 200 Hz. Stimulation with either type of electrode activated not only the rapidly conducting axons in the dorsal column as indicated by the initial negativity, but also a second population of axons which have a somewhat slower conduction velocity (indicated by the second negativity). This second component is very likely due to the direct rather than the transsynaptic activation of these elements, since this response followed stimuli applied at rates as high as 200 Hz and did not show any change in latency at these frequencies.² Although these experiments were not designed to define precisely which pathways were activated, it is clear that at least two distinct populations of axons in the dorsal part of the spinal cord were activated by the stimulus. The effect of stimuli applied at different strengths on these two components of the evoked response is shown in Fig. 2. As the stimulus intensity was increased, the amplitudes of both the first and second negativity became larger. Both components were present at stimulus strengths well within those commonly used therapeutically. It was also apparent from these records that the three-element bipolar electrode resulted in a much more significant activation of the more slowly conducting population at lower strengths.

The characteristics of the responses recorded on the surface of the dorsolateral fasciculus at the same recording distance from the stimulating electrode as that for DC recording were somewhat different (Fig. 3). The activation of rapidly conducting pathways once more evoked an early positive-negative potential change with a latency comparable to that of the first negativity observed in the responses recorded from the dorsal

*Bipolar tinsel wire electrode and stimulating electrode both available commercially from Medtronics, Inc., 3055 Old Highway 8, Minneapolis, Minnesota 55418.
†AC coupled amplifier made by Grass Instrument Company, Quincy, Massachusetts. Tektronix 565 oscilloscope made by Tektronix, Inc., 14150 S.W. Karl Braun Drive, Beaverton, Oregon. Fabritek 1072 averaging computer made by Fabri-Tek Instruments, Inc., 5225 Verona Road, Madison, Wisconsin.
Fig. 2. Recording of responses evoked in the dorsal columns by stimuli applied at different strengths with a tinsel bipolar (left column) and 3-element bipolar (right column) electrode. Stimulus voltages are indicated on the far left. Responses were summed 128 times. DC = dorsal column.

Fig. 3. Recording of responses evoked in the dorsolateral fasciculus by stimuli applied at different frequencies with a tinsel bipolar electrode. Notice the decrease in amplitude of the small, long-latency negativity as the stimulus frequency is increased. DC = dorsal column.

Therefore, the first component was probably due to the direct activation of axons in the dorsolateral fasciculus whose fibers have conduction velocities comparable to those in the dorsal columns. This argument is further supported by the observation that the duration of the short latency voltage change recorded over the dorsolateral fasciculus is less than that of the response recorded over the dorsal columns, a difference that cannot be ascribed to current spread. The effect of stimuli at higher frequencies on this response is quite different from that observed for transsynaptically evoked responses in the ventral quadrant.

As the electrode penetrated through the dorsal quadrant and was placed deep in the ventral quadrant, potential changes with long latencies could again be observed (Fig. 4, star). At this depth, an early negativity could also be observed which was probably generated by a volley in a group of rapidly conducting fibers activated directly by the stimulus. Since this potential change has a shorter time course and different latency than that recorded in the dorsal columns, it cannot be attributed to the spread of current from a compound action potential restricted to that pathway. The effect of stimuli applied with progressively increasing strengths is shown in Fig. 5, left column. Even at the lowest stimulus strength (4 V), one can observe potential changes with comparatively long latencies (marked with line b) in addition to the early negativity (line a). This long latency response (b) had different latencies and characteristics than the responses recorded from the surface of the dorsolateral fasciculus, suggesting that they were of different origin. In addition, it was probably evoked transsynaptically since its latency decreased at progressively greater stimulus strengths. The effect of stimuli applied at successively greater stimulus frequencies is shown in the right column of Fig. 5. Unlike the response evoked transsynaptically in the dorsolateral fasciculus, the response marked by the filled and empty circles increased in amplitude slightly as the stimulus strength increased to 100 Hz. When the stimulus was applied at very high rates (200 Hz), the amplitude of this negativity was reduced. One would not expect the direct activation of fibers by the stimulating electrode to cause this sequence of observations.
Discussion

Electrical stimulation of the dorsal columns has been employed for almost a decade for the relief of chronic pain. Despite this fact, very little is known about the mechanisms in the central nervous system which mediate this effect. Initially it was proposed that the activation of fibers in the dorsal column could affect interactions in the dorsal horn which were responsible for modifying the impulse activity evoked in the spinal cord by noxious stimuli. These interactions have been conceptualized as a gate responsible for reducing the central effects of peripheral afferents activated by noxious stimuli. The observation that dorsal column stimulation can be effective in producing pain relief has provided considerable support to this argument.

For this support to be valid, however, it must be assumed either that commercially available dorsal column stimulators activate only dorsal column fibers or that the activation of fibers in other pathways plays an insignificant role in modifying the perception of noxious stimuli. The first assumption may not be appropriate since the field generated by an electrode of the size utilized in therapeutic applications is likely to be quite large and therefore will result in the activation of fibers in several spinal pathways. The second assumption can also be challenged, since it has recently been reported that stimulation with an electrode placed over the ventral quadrant may also produce pain relief. Moreover, it is well known that many ascending and descending pathways that may be activated by a dorsal column stimulator affect the behavior of cells in the dorsal horn as well as in the ventral thalamic nuclei.

Our findings conclusively demonstrate that stimulation of the dorsal surface of the spinal cord with commercially available stimulators used in the treatment of chronic pain activates fibers in many pathways, both directly and transsynaptically. These data show that the relief of pain produced by these devices cannot be taken as strong support for the "gate" theory of pain. Multiple components of the field potentials evoked by these stimuli were present at stimulus rates and intensities well within or below the range of parameters used in the clinical setting.

These data also imply that a more precise determination of the pathway which must be activated in order to produce pain relief may result in a more effective utilization of this therapeutic tool. For example, the transsynaptically evoked responses in the dorsolateral fasciculus and in the ventral quadrant of the spinal cord apparently behave differently when the frequency of stimulation

![Fig. 4](image1.png)

**Fig. 4.** Recordings of responses in the dorsal quadrant (DQ) and the ventral quadrant (VQ) made with a microelectrode following stimulation with a tinsel bipolar electrode. Frequency and voltage of the stimulus were 20 Hz and 4 V, respectively. The proposed transsynaptically evoked response is marked with a star. DC = dorsal column.

![Fig. 5](image2.png)

**Fig. 5.** Recordings of responses in the ventral quadrant (VQ) following stimulation with a bipolar tinsel electrode at different strengths (left column) and frequencies (right column). In the study shown on the left, the time of occurrence of the initial peak negativity is marked by line a. The time at which the second peak negativity occurred at the lowest stimulus strength (4 V) is indicated with line b. Recording on the right shows the effects of increasing the stimulus frequency on the responses indicated by the closed and open circles.

DC = dorsal column.
is increased. If the activation of either of these pathways is essential for the pain relief produced by these stimulating devices, it is likely that the optimal effects of stimulation may be obtained by changing the region of the spinal cord surface to which the stimulus is applied as well as by varying the stimulus parameters, particularly the frequency. This implication is supported by the recent observation that stimulation of the ventral quadrants of the spinal cord may be more effective in producing pain relief than stimuli applied on its dorsal surface. Moreover, dorsal column stimulation with monopolar electrodes, which we found to have the most diffuse field among the electrodes tested, has been very effective clinically in producing long-term pain relief, despite the probable wide-spread activation of several pain pathways.

This experimental protocol was not designed to determine which specific spinal pathways were activated by the stimulus. In all regions of the cord from which recordings were made, short-latency responses could be evoked by the stimulus. Although there are marked differences in the conduction velocities of spinal pathways, most of these short latency responses had relatively comparable latencies. This is probably caused by the stimulus activating both rapidly and slowly conducting fibers. Since the spectrum of conduction velocities is somewhat comparable among fibers in each region of the cord from which recordings were made,\footnote{1} one would expect latencies to be similar, particularly between the dorsal column and the dorsolateral fasciculus.\footnote{8} The differences in time course and latencies of the short latency responses recorded in each region of the cord, however, definitely imply that each results from compound action potentials in different populations of ascending and descending fibers.\footnote{7} Dorsal column stimulation probably activates both ascending and descending tracts, and some of the potential changes may reflect antidromic conduction in the latter. The activation of these descending pathways may also be partly responsible for the modification of sensory perception resulting from dorsal column stimulation.\footnote{1}

Differences between the distribution of responses evoked by the two types of stimulating electrodes that were evaluated did not seem to be significant. Despite slight differences in design, both are fairly large and would be expected to produce relatively large current fields. Therefore, any localization to be attained with these devices will probably be related to electrode placement and the stimulus strength. Thus, if selective stimulation proves valuable, increasing the flexibility of electrode placement over various quadrants of the cord may be desirable.

It is clear that to utilize this therapeutic tool most effectively, a better understanding of the consequences of dorsal column stimulation to the processing of information evoked by noxious stimuli is essential. At this time, success or failure of this device cannot support or deny specific theories of pain perception.

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Address reprint requests to: James R. Bloedel, M.D., Ph.D., Department of Neurosurgery, B-590 Mayo Memorial Building, University of Minnesota, Minneapolis, Minnesota.