*J. Physiol.* (1967), **188**, *pp.* 403–423
*With 9 text-figures*
*Printed in Great Britain*



# THE LAMINAR ORGANIZATION OF DORSAL HORN AND EFFECTS OF DESCENDING IMPULSES

By P. D. WALL

*From the Department of Biology and Center for Communication Sciences, Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts, U.S.A.*

(*Received* 27 *July* 1966)

SUMMARY

1. An examination of the physiological properties of cells in cat lumbar dorsal horn shows that there are three horizontal laminae which correspond approximately to Rexed (1952) laminae 4, 5, and 6.

2. A summary diagram (Fig. 9) suggests the relation of the laminae to each other and to afferent and descending fibres. All three laminae respond to cutaneous stimulation but only lamina 6 responds to movement. By comparing responses of cells in decerebrate and spinal preparations, it is shown that the brain stem inhibits cutaneous responses and enhances movement responses. Pyramidal tract stimulation affects cells in laminae 4, 5, and 6.

3. Cells in lamina 4 have small cutaneous receptive fields and respond as though many different types of specific cutaneous afferents converge on them. Cells in lamina 5 respond as though many cells of lamina 4 converge on them. In the decerebrate animal the responses of lamina 5 cells habituate to repeated light pressure stimuli but the cells remain responsive to new stimuli in other parts of their receptive field. Impulses descending from the brain stem can switch the modality of lamina 6 cells from cutaneous to proprioceptive.

## INTRODUCTION

Extracellular single unit responses to peripheral stimuli can be recorded from the relatively large cells in Rexed's (1952) laminae 4, 5, and 6 in the dorsal horn (Fig. 1). This paper describes the physiological organization of those laminae and the effect of impulses descending from the brain stem and pyramidal tract.

Peripheral nerve fibres terminate in all three laminae (Sprague & Ha, 1964). There is evidence that cutaneous fibres are distributed in the more dorsal and proprioceptive in the more ventral regions of the dorsal horn. Wall, McCulloch, Lettvin & Pitts (1956) and Wall (1958) showed, by anti-

dromic stimulation, that the fastest fibres from the sural nerve ended in a layer dorsal to the terminations of fibres from the gastrocnemius. Coombs, Curtis & Landgren (1956) showed that the electric field generated by a volley of cutaneous origin lay dorsal to the field from a muscle nerve. Cells, responding monosynaptically to cutaneous afferents, have been located in the more dorsal laminae (Wall, 1960; Armett, Gray & Palmer, 1961). Wall (1965) showed that the dorsal border of this region of cutaneous cells coincided with the dorsal edge of lamina 4 described by Rexed (1952).

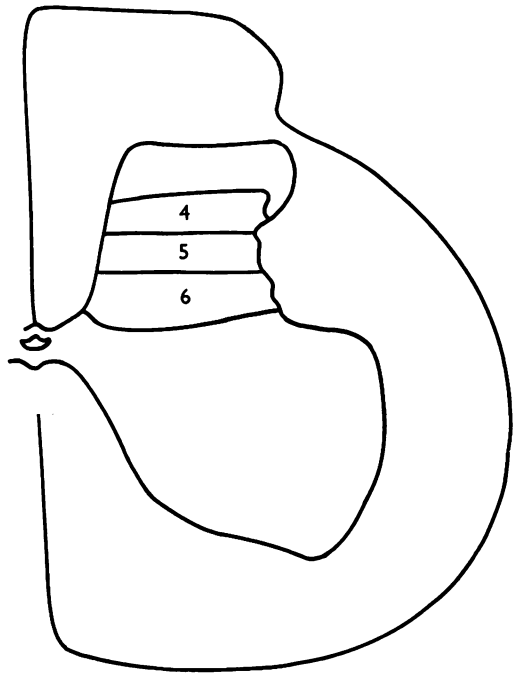


Fig. 1. Diagram showing the Rexed laminae 4, 6, and 5 in the L 7 segment of the cat cord (after Rexed, 1952). These laminae were recognized cytoarchitectonically on the basis of differences in shape and distribution of cell bodies.

Many fibres descend from the head and terminate in the dorsal horn (Kuypers, 1964), including rubro-, vestibulo- and reticulo-spinal fibres, the best studied being the cortico-spinal system. Descending tracts affect both the transmission of impulses from the periphery into ascending tracts and the transmission from the dorsal root to motoneurones over reflex pathways. Sherrington & Sowton (1915) showed that transection of the spinal cord in a decerebrate animal not only reduced stretch reflexes, but enhanced flexor reflexes. Holmqvist & Lundberg (1961) showed that this descending differential effect required only the dorso-lateral column for its transmission. In later work, Lundberg and his co-workers (Lundberg,

1964; Carpenter, Engberg & Lundberg, 1965) implied that the effect from the brain stem is exerted both presynaptically on incoming afferents and post-synaptically on dorsal horn cells. The cerebral cortex is known to affect the dorsal root potential evoked by cutaneous stimulation (Hagbarth & Kerr, 1954). This potential is generated by cells in laminae 2 and 3 (Wall, 1962). Since the pyramidal tract in the lumbar cord of the cat ends almost entirely in laminae 4, 5, and 6, it can only produce its effect on cells or dendrites in the dorsal horn.

The studies reported here were intended to investigate physiological correlates of the histological lamination. During the course of the experiments, two unexpected properties of cells were encountered, which may be important in explaining certain reflex and sensory phenomena.

## METHODS

The general methods of recording in the lumbar cord of the cat have been described previously (Wall, 1965). Glass micro-electrodes were used whose tip resistance was between 1 and 2 M. They were filled with either saturated KCl or NaCl. All electrode tracts were located by cutting off the electrodes and leaving them in position and by subsequent examination after clearing. The validity of this method, introduced in 1955 (Howland, Lettvin, McCulloch, Pitts & Wall, 1955), depends on a series of checks, two of which were always made. Immediately after the electrode was cut by fine notched iridectomy scissors, the cut ends were inspected under a dissecting microscope and were seen to be touching. This showed that no gross movement had been produced by the cutting. After the cord section containing the electrodes had been cleared, the actual depth of penetration of each electrode was compared with the distance which the micrometer had advanced from the first point of electrode contact with the surface of the cord to the depth at which the electrode was cut free. If these two measures failed to agree within $\pm 5\%$, data obtained from that electrode were rejected. This check showed that the clearing stages had not disturbed the electrode. A powerful reason for accepting the accuracy of this method is that consistent potential contour maps can be obtained from sets of parallel electrode tracks (Howland *et al.* 1955; Wall, 1962). This consistency guarantees that no independent movement of neighbouring electrodes has occurred. The location of single marginal cells (Wall, 1965) was measured in some tracks. Frozen sections were then cut from the block containing the micro-electrodes, stained with thionin, and the actual depth of the marginal cells was found to coincide with the depth from which the micro-electrode had recorded a marginal cell.

*Decerebration and pyramidal tract stimulation.* Cats were decerebrated under ether anaesthesia with the carotids temporarily occluded. A concentric stimulating electrode was placed in the pyramidal tract at the caudal end of the medulla. The electrode was a 20-gauge stainless-steel tube, insulated to the tip with a central insulated wire protruding 0·75 mm. beyond the tip. Square-wave stimuli of 0·1 msec were delivered at 100/sec. The electrode was placed in position in the absence of paralysis by gallamine. This allowed the tip to be located and the stimulus strength adjusted so that movement produced by the stimulus occurred only in the left hind leg. This method of stimulation ensured against stimulus spread to structures dorsal to the pyramidal tract.

*Reversible spinal block.* In order to study the performance of single cells in the presence or absence of descending influences, a temporary cold block of the spinal cord was introduced at T 13 and L 1. Three segments of cord T 12 and 13 and L 1 were exposed. Stimulating silver electrodes were placed on the dorsal columns at T 12. A small coccygeal root was cut peripherally and placed on recording electrodes. A brief stimulus applied to the dorsal

columns was adjusted until a maximal volley passed antidromically down the cord and out on to the root (Fig. 2). When a cold block of the cord was required, the oil surrounding the exposed segments was removed and two or three 1 ml. cubes of frozen mammalian Ringer solution were placed directly on the cord. During the next few minutes, the volley transmitted from T12 to the root slowed and finally completely disappeared. The block was produced

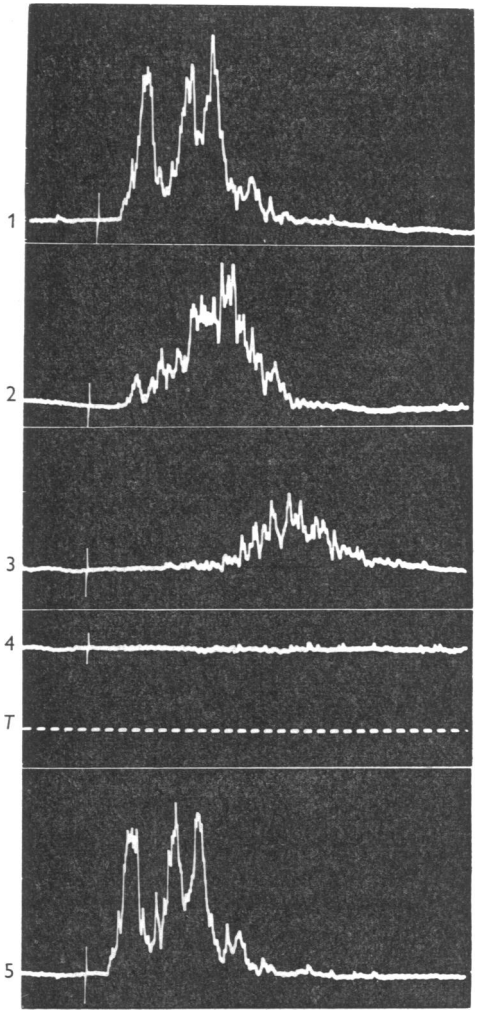


Fig. 2. Reversible spinal block: Recordings were made on the cut dorsal root, coccygeal 1. Stimulation was through electrodes placed on the dorsal columns at T12. The stimuli were 0·1 msec square waves at 5/sec with supramaximal intensity. Trace 1 shows the maximal antidromic response. Traces 2, 3, and 4 were photographed at 30 sec intervals after Ringer ice cubes had been placed on the dorsal surface of the cord at segments T13-L1. Time, *T*, is 1 msec. Trace 5 shows the recovery of conduction between T11 dorsal column and the coccygeal dorsal root, 10 min after the ice had been removed from the blocked segments.

and reversed successfully as many as 10 times in one animal. In order to confirm that a genuine block rather than a desynchronization had been achieved in the dorsal half of the cord, single units in dorsal roots were examined in some experiments.

*Peripheral stimuli*

Three categories of mechanical skin stimulation were used: brushing with a no. 2 camel hair brush; touching by resting a finger lightly on the skin: and pressing by picking up a fold of skin and exerting a gradually increasing pressure. The pressure stimulus was applied with a pair of forceps whose ends were 5 mm broad and were not toothed. The heaviest skin fold pressure did not produce pain or apparent damage if applied to the back of the experimenter's hand. Since many units were found in lamina 6 which respond to both movement and to cutaneous stimulation, the leg was held rigidly fixed while cutaneous stimuli were applied to a skin fold. Muscle and joint responses were evoked only by gentle passive movement of joints. The nature of the movement responses differentiated them clearly from responses to skin distortion. Since extreme flexion or extension of joints must always result in widespread skin stimulation in an intact leg, such stimuli were not used. Electrical skin stimulation with 0·1 msec square waves at 1/sec was carried out by placing two independent 30-gauge hypodermic needles intradermally in the receptive field of the unit under examination.

*Slow waves* were elicited by placing stimulating electrodes in the cutaneous receptive field of the cell which produced the highest amplitude spikes in the recording micro-electrode. The stimulus intensity was raised until it evoked a single spike discharge from the cell for about 50 % of the stimuli given at the rate of 1/sec. When the stimulus strength had been determined and the spikes observed, the amplifier filters were reset to pass from 0·6 to 100 c/s and the slow waves recorded.

*Latency of spike discharge* was determined with a peripheral stimulus of the same threshold intensity as that used to evoke the slow waves. The reason for using the threshold stimuli which gives a somewhat variable latency (Wall, 1959) was that higher intensity stimuli had the disadvantage of producing such large slow waves that it became difficult to observe the initiation point of the spike which arose from the fast rising phase of the slow wave. The average of thirty observations at each recording point was used for the data presented below.

## RESULTS

After a preliminary survey of all segments from L4 to S2, the experiments concentrated on the rostral half of L7 as a convenient place in which to collect data. This region receives its major input from the lateral toes and foot. Sixty-three successful mapping experiments were completed. A similar series of experiments on spinal rats revealed the same general laminar organization as reported below for cats.

### *Lamina* 4

*General organization.* If a micro-electrode was lowered from the dorsal surface of cord into dorsal horn, a point was reached at which light brushing of the leg evoked single spikes with an amplitude of 50 $\mu$V. The location of these points defines a horizontal line across the horn which corresponds roughly to the border of laminae 2 and 3 (Wall, 1965). As the electrode was moved ventrally, the height of the evoked spikes increased up to several hundred $\mu$V and, in the spinal animal, 'spontaneous' activity was recorded. The points at which 'spontaneous' activity were

recorded made a second horizontal line across the cord which corresponds to the dorsal border of lamina 4 (Fig. 3) (also Wall, 1965). The 'spontaneous' activity was not due to injury because it remained stable for periods of recording over 1½ hr, was reversibly abolished by spinal cord block in the thoracic region, was abolished by dorsal root section, was abolished by anaesthesia, and because similar activity was recorded in the axons of those cells which run in the dorso-lateral column. Responses of

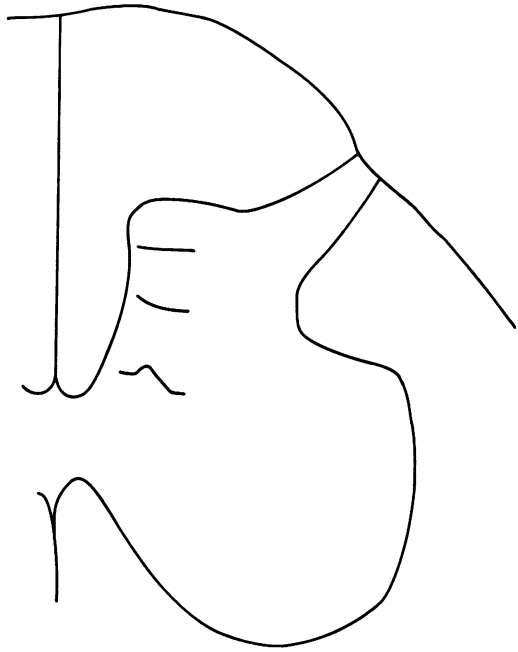

Fig. 3. Borders of laminae 4, 5, and 6. The outline of cord and horns was traced from a cleared section of rostral L 7. The section contained the seven micro-electrodes that had been used for recording. The depth of penetration at which changes of properties occurred was marked on each electrode track. These points were joined up and give the three lines shown in the dorsal horn. The upper line marks the locations from which evoked spikes were first recorded on brushing the skin (see also Fig. 5, Wall, 1965). The middle line shows the location of first recording of cells whose receptive fields were larger than those recorded more dorsally. In this region of dorsal horn, the receptive fields in lamina 4 were a fraction of one toe, while those in lamina 5 spread over two toes. The lower line joins the 7 points at which cells were first encountered which responded to joint movement.

cells in this lamina have been described previously (Wall, 1960; Taub, 1964; Mendell & Wall, 1965; Taub & Bishop, 1965). In rostral L7, cells in the most medial part of the lamina have their receptive fields on toes 2 and 3. More laterally, cells responding to the most lateral toe are found and, more laterally still, cells respond to stimuli on a strip of the lateral

foot. Sometimes the most lateral cells were found to respond to stimuli on the lateral ankle and lower lateral leg. Receptive fields on the toes were usually a fraction of the tip of one toe. More lateral cells responding to more proximal areas had larger receptive fields.

It was evident that many different types of specific cutaneous afferent fibres converged on to these cells and excited them. They responded to hair movement, touch and cooling with ethyl chloride. If touch corpuscles (Pinkus, 1904; Frankenhauser, 1949) could be seen on the skin surface within a cell's receptive field, the cells responded to localized pressure on the corpuscles as well as to the other types of stimulation such as hair movement. If the receptive field of a cell was tested with von Frey hairs, it was found to have a lower threshold at the centre than at the edge. Multiple small areas of low threshold were never found within the receptive field. If the intensity of pressure on the skin was steadily raised from light touch to heavy pinch, some cells continued to increase their firing rate in response to each increase of pressure. This type of cell has been shown to be excited by both A and C afferent fibres (Mendell, 1966). Some cells did not increase their firing rate as the pressure was intensified and are referred to as cells with a small dynamic range. All cells are in monosynaptic contact with the full spectrum of A fibres (Taub & Bishop, 1965). The closeness of their contact to excitatory C fibres is not known. No signs were ever detected that movement of joints or stretching of muscle affected the firing of cells in this lamina.

*Effect of blocking impulses descending from the brain stem.* In preliminary experiments, the region was examined first in the decerebrate animal and then a second time after the spinal cord had been transected at C1. Changes were observed between the properties of the cells in the decerebrate and in high spinal animals. These changes are presumably attributable to the effect of impulses descending into the lumbar cord from the brain stem. The same changes were observed when the cord was reversibly blocked by cooling at T13–L1. This latter preparation was then used in all subsequent experiments because it had the great advantage that single cells could be examined in both decerebrate and low spinal animals. A second advantage of the cold block was that it did not produce the marked blood pressure changes which are produced by transection at C1. The method of observation was to locate a single unit in lamina 4 and to describe the details of its receptive field and response characteristics. When this was completed, Ringer ice was placed on segments T13 and L1 until the cord was blocked, and then the properties of the unit were re-examined. After this examination, the cold block was removed and the unit again examined to check that it returned to its previous state.

In the decerebrate state, many units were not spontaneously active or

were active at a frequency of less than 5/sec. On blocking the cord, twenty-eight out of forty previously silent units became spontaneously active at a frequency of more than 5/sec. The majority, not only became more spontaneously active, but increased their firing rate to peripheral stimuli.

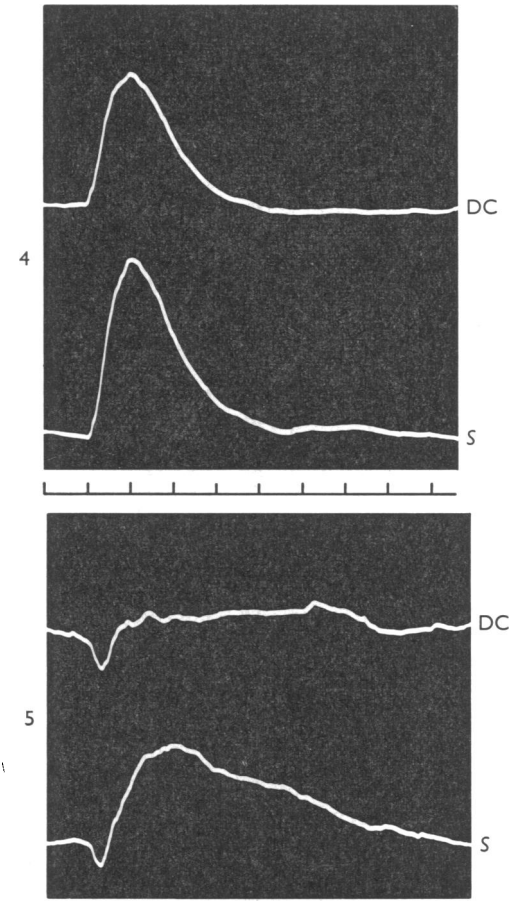


Fig. 4. Slow waves recorded in laminae 4 and 5 in the decerebrate and spinal animal. The recordings were made between a micro-electrode in dorsal horn and an indifferent electrode on back muscle. The stimuli were given through needles placed in skin of the receptive field of the nearest cell to the tip of the micro-electrode. The strength of the stimulus was just suprathreshold to produce firing in that cell. Filters were set to record between 100 and 0·6 c/s. Time marks at 5 msec; skin stimulus coincided with first time mark. 4 shows a recording made close to a cell in lamina 4 in the decerebrate animal (DC) and when the spinal cord was blocked (S). 5 shows similar recordings made near a cell in lamina 5 in the two stages. It will be seen that while there is a small increase of the response in lamina 4, there is a very large increase in lamina 5 when descending impulses from brain stem are blocked.

Many cells that had previously responded only to light stimuli and had not increased their rate when pressure was increased, showed a wide dynamic range when the cord was blocked. Surprisingly, no cell was observed whose receptive field expanded in spite of the obvious increase of excitability to peripheral stimuli. If electrodes were placed in the receptive field and a threshold stimulus was given to the skin, the number of spikes in the repetitive discharge increased and the slow wave recorded by the micro-electrode increased approximately 25% (Fig. 4).

*Pyramidal tract stimulation.* After the characteristics of a lamina 4 unit had been determined in the decerebrate state, the pyramidal tract stimulation (0·1 msec square waves, at 100/sec, with an intensity sufficient to produce movement only in the left hind leg) was turned on and the unit's characteristics again examined during continuous pyramidal tract stimulation. Using this method of stimulation, we could discover no cells in lamina 4 whose 'spontaneous' firing was affected by pyramidal-tract stimulation. Fetz (1966) has found that the responses to peripheral stimuli of twenty-six out of fifty cells in lamina 4 were inhibited by pyramidal tract stimulation at a strength close to movement threshold.

*Effect of anaesthesia.* If an anaesthetic dose of Nembutal (25 mg/kg) is injected intravenously into a decerebrate animal, there is a further decrease of spontaneous firing rates and of the length of repetitive discharge to peripheral electrical stimulation. The height of evoked slow waves and the dynamic range of response to pressure stimuli decreased. The response of the cells to peripheral C-fibre stimulation was entirely abolished. The cells still responded to brushing and the size of the receptive fields to brushing was not affected.

### *Lamina 5*

*General properties.* As micro-electrodes penetrated ventrally out of lamina 4, a number of changes occurred in the properties of local cells. In any one penetration, these changes all occurred at the same point and when these points in neighbouring electrode tracts were joined, a horizontal line could be drawn across the cord (Figs. 3 and 5). On crossing this line, the skin-pressure receptive fields of individual cells became much larger than those seen in lamina 4. Cells in the medial part of the lamina still received impulses from toes, while more laterally placed cells received inputs from more proximal and lateral parts of the foot and lower leg. In lamina 4, a toe cell's receptive field was always restricted to a fraction of one toe, while in lamina 5 cells received from more than one toe. More lateral cells had larger fields than the corresponding cells in lamina 4. Threshold in the centre of the receptive field was noticeably higher than in lamina 4. A marked gradient of threshold exists between the centre and periphery of receptive fields. In the centre, light brush or touch was suffi-

cient to fire the cell; at the edges pressure was necessary. The mediolateral somatotopic map of cells in lamina 4 of rostral L 7 runs as a strip from the second toe along the two lateral toes and the lateral side of foot and lower leg. The receptive fields of cells in lamina 5 remained within this strip but expanded along it. The latency between an electrical stimulus applied by intradermal needles in the middle of the receptive field and the response of cells in lamina 4 and 5 was measured. In sixty consecutive cells examined in this way, the average latency difference between the cells of layer 4 and layer 5 was 1·5 msec with a range from 0·9 to 2·0 msec. The average latency difference between cells in the same lamina was 0·2 msec with a range from 0·0 to 0·4 msec. Similarly, the local negative slow wave evoked

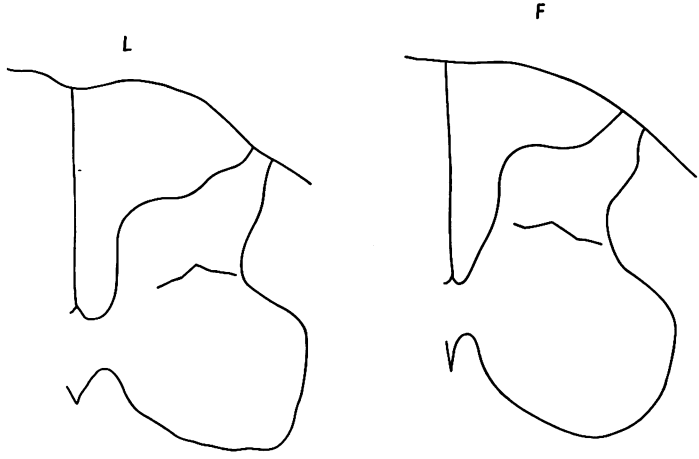


Fig. 5. Border of lamina 5: on the left, the latency of unit discharge to local electrical skin stimulation was measured. Points were recorded at which the latency increased by 1·5 msec over the latency of more dorsal cells. The line across the dorsal horn joins 6 points at which this latency increases was noted. On the right, from another animal, the line in the dorsal horn marks the position at which there was a change from cells with small receptive fields with a definite edge which characterize the lamina 4 cells to the larger more diffuse receptive fields which are seen in lamina 5 cells.

by such a stimulus also began approximately 2 msec later than the more dorsal slow wave. No differences were noticed between medially placed and lateral cells, apart from location of the receptive field. No signs were detected of any of these cells responding to gentle movement of joints or stretching of muscle. Examples of the receptive fields of three cells in lamina 5 are shown in Fig. 6.

*Effect of blocking impulses descending from the brain stem.* Twenty-five cells in lamina 5 were examined before, during, and after a block of descending impulses was established. Twenty-two cells showed a marked

increase of excitability and expansion of receptive fields to cutaneous stimulation when the cord was blocked. The threshold of the centre of the receptive field decreased. Many cells, which required touch or pressure of the skin to fire them in the decerebrate state, responded to light brushing in the centre of the receptive field in the temporary spinal animal. Three examples of this change are shown in Fig. 6. No effect was observed on two cells. One cell showed a decreased excitability and decreased receptive

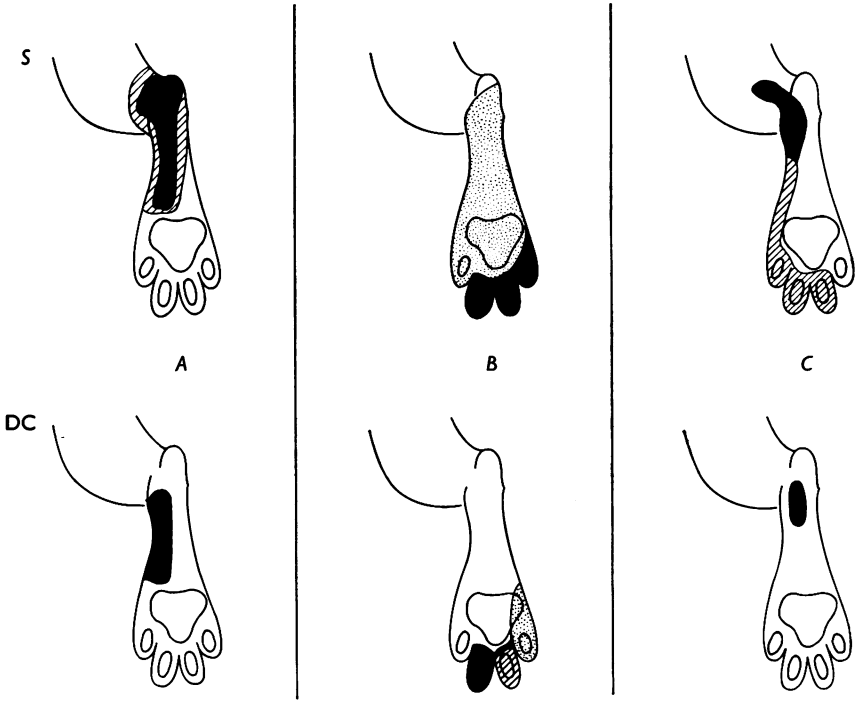


Fig. 6. Receptive fields of three cells in lamina 5. *S*, above, shows the receptive fields in the spinal animal; below, DC, shows the receptive fields of the same cells in the decerebrate state. Black indicates the region in which the cell responded to brushing; hatching, the region that required touch; and stippling, the area where pressure on a skin fold was required to fire the cell. It will be seen that in each case, the field greatly expanded when the spinal cord was blocked.

field in the spinal state. We have shown, in Fig. 5, the effect of blocking the cord at T12–L1 on the evoked slow wave in lamina 4. The lower pair of traces in that illustration show the effect in lamina 5. The technique used was the same. Stimulating electrodes were placed in the middle of the cutaneous receptive field of the nearest cell to the recording micro-electrode and the stimulus was adjusted to be close to threshold for the response of that cell. When the cord was blocked, there was always considerable increase in the height of the evoked slow local wave.

*Pyramidal-tract stimulation.* Nineteen cells were examined in the decerebrate animal before, during, and after continuous pyramidal-tract stimulation. The stimulus was given at 100/sec in 0·1 msec square waves, with the strength of the stimulus and location of the electrode adjusted to give movement only in the left hind leg. Of the nineteen cells, six were excited, twelve were inhibited, and one unaffected. The cells that were excited responded continuously to the continuing pyramidal stimulation and had a decrease of threshold to stimuli within their receptive fields, and an increase in size of receptive field. The cells that were inhibited showed an abolition or decrease of their on-going firing, a decrease of response to cutaneous stimuli, and a shrinkage of receptive field. The cells that were excited by pyramidal tract stimulation still failed to respond to movement of joints. It must be stressed that extreme flexion or extension of joints and quick movements were not tested because such stimuli spread mechanically and stimulate skin receptors that were clearly able to produce responses in these cells.

*Effect of anaesthesia.* Nembutal (25 mg/kg I.V.) in a decerebrate animal produced a profound depression of the responses of the cells in this lamina. Both the spontaneous activity and evoked activity disappeared from many cells. The effect is so striking that, if the region is searched with a microelectrode while pressure stimuli are delivered to foot skin, the area is silent. It is evident that the cells of this lamina are even more severely depressed by anaesthesia than the cells of lamina 4.

*Histology.* While re-examining the morphological differences between the laminae as described by Rexed, we noticed a further difference between laminae 4 and 5. Horizontal sections were cut 25 $\mu$ thick from formalin-fixed, paraffin-embedded, L7 cord segments. The sections were stained with thionin. The outlines of cell bodies and their orientation were compared in the region of lamina 4 and 5. It was noticed in two of the three specimens examined that the cell bodies in lamina 4 were randomly oriented, while those in lamina 5 had a striking tendency to be mediolaterally oriented across the cord (Fig. 7). Rexed (1952) had noticed this to be the case in sacral and upper lumbar cord. It also becomes apparent in lower lumbar cord if horizontal sections are examined.

*Novelty detection cells.* Many lamina 5 cells showed an unusual type of habituation which we shall call 'novelty detection', in which the response of a cell faded if intermittent stimuli were applied to one region of the receptive field, but immediately reappeared if the stimulus point was shifted to another region. This phenomenon was seen only in the decerebrate animal and was abolished by blocking impulses descending from the brain stem. If a light brush stimulus was applied intermittently every few seconds to one region of the cell's cutaneous receptive field, the response

of the cell gradually faded. It required at least 1 min of rest before the cell would again respond to the stimulus. If the stimulus was moved to a new point in the cell's receptive field during the period of habituation to the original stimulus, a response to the new stimulus appeared. The best way to demonstrate this phenomenon was by intermittent light brushing of

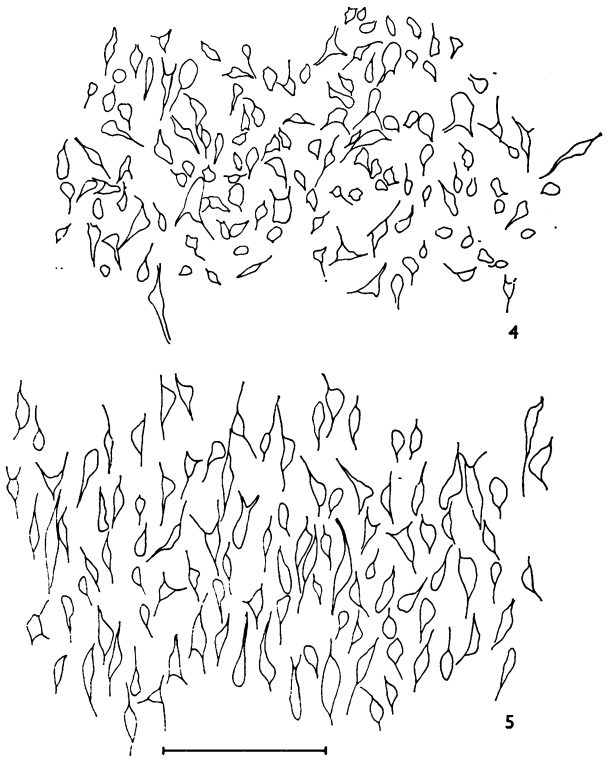


Fig. 7. Outlines of cell bodies seen in horizontal sections in laminae 4 and 5. The cells were observed in thionine-stained, formalin-fixed, paraffin-embedded horizontal sections of L 7. Cell bodies which contained Nissl granules were selected and drawn by camera lucida. In the drawings, the lateral side of the cord is at the top. It will be seen that the cell bodies in lamina 5 tend to be spindle-shaped and to lie across the cord in the mediolateral direction. Scale: 100 $\mu$.

part of the receptive field. It could also be demonstrated by electrical stimulation. Needles were placed in the skin with the cell's receptive field separated by as wide a distance as possible. A 0·1 msec square wave stimulus slightly above threshold was then given at a frequency of 1/sec. The length of the repetitive discharge shortened with each stimulus and often the response disappeared completely. If the polarity of the stimulus was reversed so that the needle in the distant part of the receptive field became

the cathode, the response of the cell immediately returned and again faded with each succeeding stimulus. If the strength of the peripheral stimulus was increased so that prolonged repetitive firing of the cell occurred, the response did not fade.

### *Lamina* 6

*General properties.* As micro-electrodes descended through lamina 5, a point was suddenly reached when cells were encountered which responded to gentle movements of joints (Fig. 3). The horizontal line joining these points ran across the lower part of dorsal horn and corresponded roughly with the dorsal border of Rexed lamina 6. Since these cells obviously responded to movements of joints, it was particularly important to examine the skin with great care to avoid movement of joints during skin stimulation. The relevant joints were splinted and skin stimuli applied to raised folds of skin. When this was done, it was found that almost all of the cells responded to skin stimulation. The thresholds were about the same as those observed for the cells of lamina 5. The latency of response of single units to just suprathreshold cutaneous electrical stimuli was approximately 2 msec longer than for lamina 5 cells, and therefore 3·5 msec longer than for lamina 4 cells (forty cells: average 1·9 msec: range 1·4–2·6 msec). The required electrical stimulus threshold for evoking responses was about the same as for lamina 5 cells. The receptive fields were slightly larger than those of the more dorsal cells. Heavy pressure stimuli to skin folds were avoided because of the danger that underlying muscle might be stimulated by a spread of the pressure. An assurance that these cells genuinely responded to both cutaneous and movement stimuli and that they were not being affected by the mechanical spread of one type of stimulus to nearby structures was provided by the experiments to be reported below in which the sensitivity to the two types of stimuli could be varied independently. Responses to joint novement rarely occurred over the full range of joint movement. Some cells responded only during movement. More commonly, a joint angle could be found at which the cell would begin to respond with some relatively steady firing frequency. Further bending of the joint would increase the firing rate. When a joint angle was fixed, the firing rate would settle down to a steady frequency. The cells discussed here all lay between lamina 5 and the most ventral extension of dorsal columns. In this region, almost all cells had mixed cutaneous and movement receptive fields; none responded to movement of any joints other than those of the ipsilateral lower leg and foot. Cutaneous excitatory receptive fields did not spread proximal to the knee. No signs were noticed within the lamina of ordered groups of cells responding to either flexion or extension. Many cells responded to movement of both toes and ankle.

*Effect of blocking impulses descending from the brain stem.* Twenty-three cells were examined before, during, and after block of cord at T13–L1. In twenty-two there was a marked increase of their excitability to cutaneous stimuli and an increase of the receptive fields during spinal block.

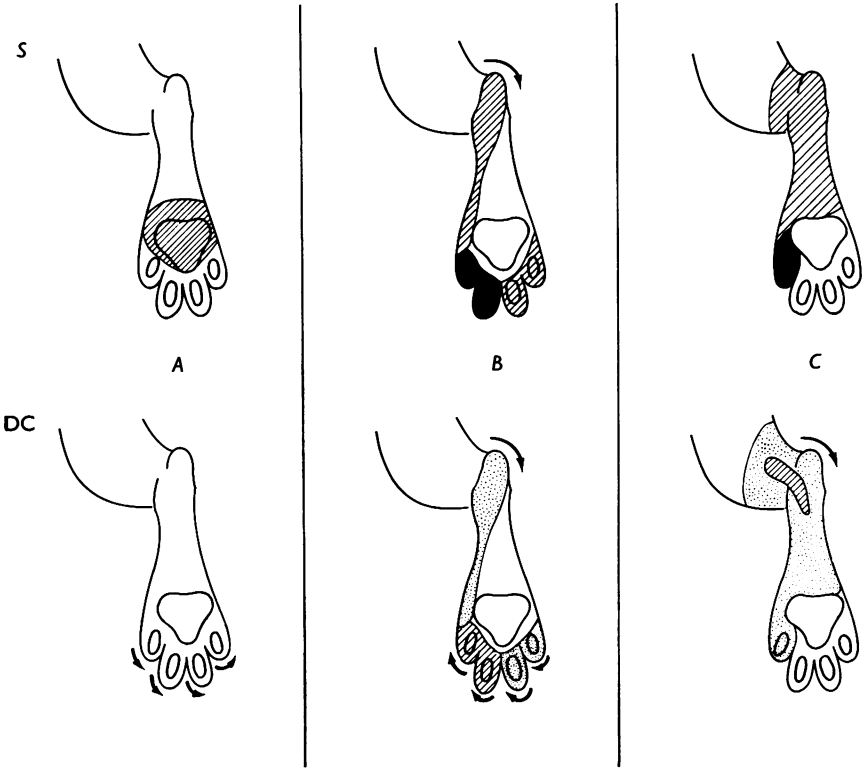


Fig. 8. Receptive fields of three cells in lamina 6. *S*, above, shows the receptive fields in the spinal animal; below, DC shows the receptive fields of the same cells in the decrebrate animal. Black indicates the region in which brushing produced firing of the cell; hatching, the region that required touch; and stippling, the region that required pressure. Arrows about joints show the direction of movement which produced responses in the cell. It will be seen that, in the spinal animal, the cells were dominated by the cutaneous stimuli, while, in contrast, in the decerebrate state, the effect of cutaneous stimuli decreased and the effect of movement increased.

One was inhibited. In sixteen of the twenty-three, there was a concomitant decrease of their sensitivity to movement of joints. In the remaining seven, the movement response seemed unaffected. Three of the cells are shown in Fig. 8. The extreme type of cell responded only to joint movement in the decerebrate animal and only to cutaneous stimuli in the spinal animal. Much more commonly, there was a relative shift of the domination of the cell by the two types of stimuli. The impulses descending from the brain

stem evidently inhibited the input of cutaneous origin so that receptive fields were small and thresholds high. At the same time, the descending inpulses enhanced the effectiveness of the joint and muscle input to most of the cells so that they responded at a smaller angle of joint flexion.

*Pyramidal-tract stimulation.* Nineteen cells were examined during pyramidal-tract stimulation of the type used to influence lamina 5 cells. Eleven were excited, seven were inhibited, and one was unaffected. The excitation and inhibition seemed to apply equally to both the effects of cutaneous and movement stimuli. The angle of a joint at which firing of the

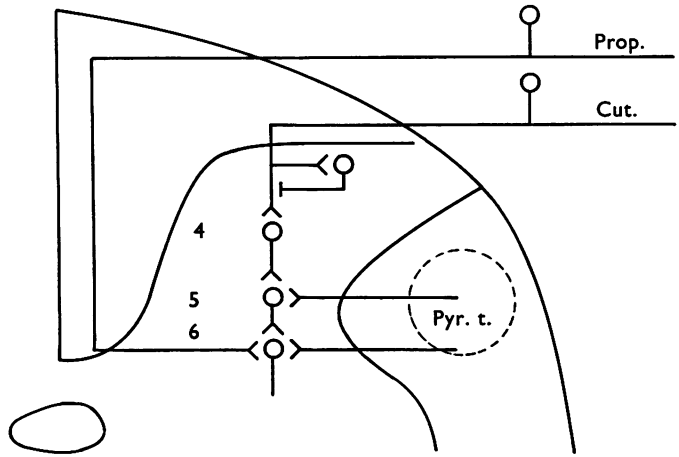


Fig. 9. Summary diagram of one interpretation of the results. The cutaneous afferents are shown ending on cells of lamina 4 with a presynaptic control exerted on them by small dorsal cells. Lamina 5 cells are shown affected by lamina 4 cells. Incoming fibres that respond to passive movement of the limb, PROP, are shown ending on lamina 6 cells which also receive from lamina 5. All laminae are affected directly or indirectly by descending impulses from the brain stem and by the pyramidal tract.

cell began was changed by pyramidal stimulation. Many of the cells that were inhibited by pyramidal stimulation responded with a vigorous burst of firing that lasted several seconds when the stimulus was turned off. Both the thresholds to cutaneous pressure stimuli and the size of receptive fields were affected. The number of cells examined was too small to decide whether the pyramidal stimulation was having a preferential effect on cells involved in flexion or extension.

*Effect of anaesthesia.* Intravenous Nembutal (25 mg/kg) severely depressed the response of cells in this lamina to cutaneous and movement stimuli. Extreme extension or flexion of joints or heavy pressure on the skin was often necessary to evoke responses. Brief taps to skin sometimes evoked a brief burst of firing. Such stimuli obviously spread mechanically

to distant structures, and we found little useful information from such stimuli.

*Novelty detection cells.* As in lamina 5, the cells in lamina 6 showed the novelty detection response to light intermittent brushing stimuli but showed a maintained response to heavy pressure stimuli. The response to small movements of the joint also faded if the movement was repeated at intervals of a few seconds. When a cell responded to movement of two joints, the fading of response to intermittent movement of one joint did not affect the brisk first response to movement of the other joint. It is interesting to note that in these decerebrate cats habituation was observed both of the flexion reflex to light stimuli and of the leg flexion set off by threshold intensity pyramidal tract stimulation.

## DISCUSSION

*Lamination.* It is evident that the results demonstrate that a laminar separation of physiological properties exists in the dorsal horn and that these laminae correspond approximately to three of the laminae of Rexed (1952). The physiological demonstration of lamination required the use of suitable methods. Extracellular recording was necessary because intracellular electrodes frequently penetrate axons (Hunt & Kuno, 1959; Wall, 1959) and record from relatively few units. It was necessary to locate all electrodes and not to pool results from many animals because the relation of internal structures to external landmarks varies from animal to animal. Unanaesthetized preparations had to be used because anaesthesia produces too profound a depression of responses to natural stimuli to allow the observation of many cells on each electrode penetration. Electrical stimulation of peripheral nerves was not used because it submerges the initial unit responses in the steeply rising phase of the evoked slow wave, and because it produces a gross expansion of receptive fields in contrast to the small receptive fields observed in lamina 4 when cutaneous pressure stimuli are used (Wall, 1960). Finally, since it had been shown that unit spikes may be recorded at a considerable distance from the cell body (Wall, 1965) the location of the maximal height of particular units was recorded. These points coincided with the location of the cell body. The experiments were designed specifically to discover if laminae existed. The method of marking the location of the first unit which showed properties different from more dorsal cells produced three roughly horizontal demarcation lines across the dorsal horn. This line gives an artificial accuracy to the lamination because units were encountered in lamina 5 which had the properties of lamina 4, and in lamina 6 which had the properties of lamina 5 cells. One must also warn that the method of recording selects

the largest cells preferentially, and we have no information on the smaller ones. The laminae shown here should be regarded as zones of concentration rather than absolutely separate laminae of distinct specialization.

*Lamina* 5. The simplest explanation of the properties of cells in this lamina is that they are fired by the cells of lamina 4. There is a latency difference of 1·5 msec between the responses in the two laminae to threshold stimuli. Armett *et al.* (1961) described short and long latency units which seem to correspond in location and properties to the cells of laminae 4 and 5. They showed that their short latency units were connected monosynaptically to the afferent A fibres while the long latency units were not connected monosynaptically to afferent A fibres. The latency jump cannot be attributed to conduction delay in peripheral fibres. The spindle shape of many of the cell bodies in this lamina would suggest that their dendrites may be arranged in line with the direction of the cell body which is mediolateral across the cord. These dendrites would be well placed to collect information from a mediolaterally directed strip of lamina 4 cells lying immediately dorsal to each lamina 5 cell. The receptive fields of the lamina 5 cells would then be made up of an overlapping mosaic of the smaller receptive fields of the lamina 4 cells. The shape and location of the lamina 5 receptive fields fits very well with this suggested connexion from lamina 4 cells.

*Novelty detection cells.* When a response to repeated stimulation is observed to fade, the first suggestion for the origin of this phenomenon would be that it is a property of peripheral receptor-fibre units. We can reject this hypothesis with some certainty. No such changes have been observed in peripheral cutaneous A fibres subjected to slowly repeated, low-intensity stimuli. Furthermore, the phenomenon is entirely abolished by spinal-cord block, a procedure that is not known to change the adaptation properties of peripheral receptors in mammals. The cells in lamina 4 showed absolutely no sign of adaptation to repeated stimuli. Peripheral A volleys produce a regularly repeated repetitive discharge in these cells (Wall, 1959). If lamina 4 cells are bombarded by C volleys (Mendell & Wall, 1965), the response increases with the arrival of each succeeding barrage.

Since the essence of novelty detection is that the cell responds briskly to a new pattern of input, it is clear that the cell as a whole cannot be inhibited by the previous repeated volleys. One must assume therefore that while one convergent pathway to the cells is turned off as a result of repeated activity, other convergent pathways, that have not taken part in the first pattern of afferent stimulation, retain their ability to conduct impulses and fire off the cell. Since habituation did not occur in either peripheral fibres or lamina 4 cells, the location of the mechanism for novelty detection must be a selective control mechanism established over

the contact between cells of laminae 4 and 5. First, this mechanism could be a presynaptic control of the axonal arborization of lamina 4 axons ending on lamina 5 cells dendrites. Secondly, it could be a mechanism associated with dendrites of lamina 5 cells which selectively turned off those dendrites that had been receiving activity. Thirdly, the novelty detection could be established by some adaptation or transmitter exhaustion in terminals of lamina 4 cell axons which had been active. This possibility seems unlikely because the phenomenon is abolished by spinal block which would not be expected to change fundamental membrane properties. We conclude, therefore, that the most likely explanation, one that requires the invention of no new phenomenon, is that novelty detection originates in the establishment of a presynaptic block restricted to previously active pathways connecting cells in laminae 4 and 5.

The fact that novelty detection disappears when the cord is blocked does not necessarily mean that rostral structures must be consulted by lumbar neurones in order to decide whether the pattern of afferent bombardment is novel. Impulses descending from the brain stem in the decerebrate cat may raise the activity of local cutaneous inhibitory mechanisms in the spinal cord to a level at which they can exert their selective action. It is evident that the novelty detection mechanism depends on weak inhibitory processes because strong peripheral stimuli overcome the habituation. A further reason for believing that a cord mechanism may produce the phenomenon without specific reference to brain stem structures is that an identical phenomenon to that seen in the decerebrate cat can be observed in lamina 5 cells of the spinal rat.

The term 'novelty detection' is used here in order to differentiate the effect from generalized spinal cord reflex habituations and because the cells are most reminiscent of the 'novelty cells' described as responding only to novel visual stimuli in the frog tectum (Lettvin, Maturana, Pitts & McCulloch, 1961).

*Switching.* Lamina 6 cells are switched in modality by impulses originating in the brain stem from being dominated by cutaneous inputs to responding primarily to proprioreceptive inputs. This differential control of convergence was a surprising finding. It does, however, fit with the observation of Sherrington & Sowton (1915) that proprioreceptive reflexes predominate in the decrebrate cat while cutaneous reflexes are more apparent in the spinal animal. Lundberg & Oscarsson (1961) reported two cells that were affected by both muscle and skin. These two cells were switched by descending impulses in the opposite direction to those reported here. Switching cannot be explained by a simple inhibition of the cutaneous input because there is a concomitant facilitation of the proprioceptive effect. There is anatomical and physiological evidence that proprio-

ceptive afferents end directly on lamina 6 cells (Eccles, 1964; Sprague & Ha, 1964). The proprioceptive facilitation could be either pre- or post-synaptic. If it were post-synaptic, one would expect a facilitation of other inputs to the cell. In fact, the cutaneous response of the lamina 6 cells was even more inhibited than the response of the lamina 5 cells. It would therefore seem likely that the control of both the inputs is exerted pre-synaptically since there is a simultaneous inhibition of one with a facilitation of the other.

The author is greatly indebted to Miss Diane Major for the histological preparations. This work was supported in part by The Teagle Foundation, Inc., the National Institutes of Health (Grant 5 RO1 NB-04897-03), the U.S. Air Force (Aerospace Medical Division) under Contract AF33(615)-3885, and Bell Telephone Laboratories, Inc.

## REFERENCES

ARMETT, C. J., GRAY, J. A. B. & PALMER, J. F. (1961). A group of neurones in the dorsal horn associated with cutaneous mechanoreceptors. *J. Physiol.* **156**, 611–622.

CARPENTER, D., ENGBERG, J. & LUNDBERG, A. (1965). Differential supraspinal control of inhibitory and excitatory actions from FRA to ascending spinal pathways. *Acta physiol. scand.* **63**, 103–110,

COOMBS, J. S., CURTIS, D. R. & LANDGREN, S. (1956). Spinal cord potentials generated by impulses in muscle and cutaneous afferent fibres. *J. Neurophysiol.* **19**, 452–467.

ECCLES, J. C. (1964). The excitatory responses of spinal neurones. *Prog. brain Res.* **12**, 1–34.

FETZ, E. E. (1966). Pyramidal tract effects on spinal cord interneurons. Ph.D. thesis, Massachusetts Institute of Technology, Cambridge, Mass.

FRANKENHAUSER, B. (1949). Impulses from a cutaneous receptor with slow adaptation and low mechanical threshold. *Acta physiol. scand.* **18**, 69–74.

HAGBARTH, K. E. & KERR, D. L. B. (1954). Central influences of spinal afferent conduction. *J. Neurophysiol.* **17**, 295–307.

HOLMQVIST, B. & LUNDBERG, A. (1961). Differential supraspinal control of synaptic actions evoked by volleys in the flexion reflex afferents. *Acta physiol. scand.* **54**, Suppl. 186, 1–51.

HOWLAND, B., LETTVIN, J. Y., MCCULLOCH, W. S., PITTS, W. H. & WALL, P. D. (1955). Reflex inhibition by dorsal root interaction. *J. Neurophysiol.* **18**, 1–17.

HUNT, C. C. & KUNO, M. (1959). Properties of spinal interneurones. *J. Physiol.* **147**, 346–363.

KUYPERS, H. G. J. M. (1964). The descending pathways to the spinal cord. *Prog. brain Res.* **11**, 178–202.

LETTVIN, J. Y., MATURANA, H. R., PITTS, W. H. & MCCULLOCH, W. S. (1961). Two remarks on the visual system of the frog. *Sensory Communication*, ed. ROSENBLITH, W. R., pp. 757–776. Cambridge, Mass.: The M.I.T. Press.

LUNDBERG, A. (1964). Ascending spinal hindlimb pathways—the cat. *Prog. brain Res.* **12**, 135–163.

LUNDBERG, A. & OSCARSSON, O. (1961). Three ascending spinal pathways in the dorsal part of the lateral funiculus. *Acta physiol. scand.* **51**, 1–16.

MENDELL, L. M. (1965. Responses of single dorsal cord cells to peripheral cutaneous fibres. *Expl neurol.* **16**, 316–332.

MENDELL, L. M. & WALL, P. D. (1965). Responses of single dorsal cord cells to peripheral cutaneous unmyelinated fibres. *Nature, Lond.* **206**, 97–99.

PINKUS, F. (1904). Uber Haltsinnes Organe Heben Menschlichen Haar Haarscheiben. *Arch mikrislk. Anat. EntwMech.* **65**, 121–179.

REXED, B. (1952). The cytoarchitectonic organization of the spinal cord of the cat. *J. cell. comp. Neurol.* **96**, 415–495.

SHERRINGTON, C. S. & SOWTON, S. C. M. (1915). Observations on reflex responses to single break shocks. *J. Physiol.* **49**, 331–343.

SPRAGUE, J. M. & HA, H. (1964). The terminal fields of dorsal root fibres in the lumbosacral spinal cord of cat (and site of excitatory inhibitory terminals in monosynaptic pathways). *Prog. brain Res.* **11**, 120–154.

TAUB, A. (1964). Local, segmental and supraspinal interaction with a dorsolateral spinal cutaneous afferent system. *Expl Neurol.* **10**, 357–374.

TAUB, A. & BISHOP, P. O. (1965). The spinocervical tract: dorsal column linkage, conduction velocity, primary afferent spectrum. *Expl Neurol.* **13**, 1–21.

WALL, P. D. (1958). Excitability changes in afferent fibre terminations and their relation to slow potentials. *J. Physiol.* **142**, 1–21.

WALL, P. D. (1959). Repetitive discharge of neurons. *J. Neurophysiol.* **22**, 305–320.

WALL, P. D. (1960). Cord cells responding to touch, damage, and temperature of skin. *J. Neurophysiol.* **23**, 197–210.

WALL, P. D. (1962). The origin of a spinal-cord slow potential. *J. Physiol.* **164**, 508–526.

WALL, P. D. (1965). Impulses originating in the region of dendrites. *J. Physiol.* **180**, 116–133.

WALL, P. D., MCCULLOCH, W. S., LETTVIN, J. Y. & PITTS, W. H. (1956). The terminal arborisation of the cats's pyramidal tract. *Yale J. biol. Med.* **28**, 457–464.