A STUDY OF THE FUNCTIONAL RELATIONSHIP BETWEEN THE DORSAL COLUMN AND SPINOCERVICAL SYSTEM OF THE CAT

Connections between the Dorsal Column Nuclei and the Dorsal Part of the White Matter of the Spinal Cord

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by

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I N T R O D U C T I O N

THE DORSAL COLUMN SYSTEM

THE DORSAL COLUMNS

The dorsal columns in the cat are composed mainly of myelinated, primary, afferent fibres. Fibres from the caudal half of the cat's body course in the fasciculus gracilis; fibres from the rostral part of the body run in the fasciculus cuneatus.

Anatomical studies have shown that only 25% of the fibres which enter the dorsal columns in the lumbosacral region course to the nucleus gracilis (Glees & Soler 1951). This study involved transection of dorsal roots; these contain both proprioceptive and exteroceptive fibres. Electrophysiological experiments have shown that Group I muscle afferents from the hindlimb enter the dorsal columns, but leave in the lumbar segments of the cord to course in other parts of the spinal cord (Lloyd & McIntyre 1951, Oscarsson 1957). This suggests that many of the fibres which can be shown anatomically to leave the dorsal columns within a few segments of entry are proprioceptive. The projection of primary exteroceptive fibres to the most rostral levels of the dorsal columns has been shown by Brown (1968) and Petit & Burgess (1968).

Brown employed high cervical dorsal column stimulation; and lumbar dorsal column fibre, recording. He found evidence for dorsal column projection of Types T and G hair units, slowly adapting

receptors , rapidly adapting (RA) pad receptors, some other RA receptors (including RA slow receptors) and high threshold afferents. Petit & Burgess (1968) also used high cervical dorsal column stimulation but they recorded mainly from fibres in the sural nerve. They differed principally from Brown in that they found no projection of Type I touch corpuscles. Brown found no dorsal column projection of Type D hair units; Petit & Burgess found such projection to be rare.

Burgess & Clark (1969) investigated the projection of joint afferents, from the posterior articular nerve of the knee joint, and found that only a small percentage could be antidromically activated from the dorsal columns at C2. Brown (1968), recording at L2, commonly found joint afferent fibres. This suggests that joint afferents enter the dorsal columns and then leave to course in other parts of the cord.

Uddenberg (1968a, b) recorded from fibres in the dorsal columns which were activated by stimulation of forelimb nerves and by mechanical stimulation of the forelimb. He recorded from hair, slowly adapting (SA) claw, pad (SA), touch and vibration afferent fibres. There were also muscle afferents of low and high electrical threshold and afferents transynaptically activated from forelimb nerves. The latter were found to lie deep in the dorsal columns and were monosynaptically activated from both a muscle and a cutaneous nerve. Mechanical stimulation revealed an extensive receptor

convergence onto these units. The presence of forelimb muscle afferents of low and high electrical threshold is congruous with the passage in the dorsal columns of the cuneo-cerebellar tract (Oscarsson 1967), the dorsal funiculus spino-olivary cerebellar pathway (Oscarsson 1969) and the forelimb Group I muscle afferent projection to the cerebral cortex (Oscarsson & Rosén 1963).

Petit (1971) has recorded from cells in the nucleus gracilis which have similar receptive properties to the transynaptically activated fibres recorded in the dorsal columns by Uddenberg (1968b). This suggests that there is a hindlimb transynaptically activated path in the dorsal columns which is analogous to that found for the forelimb. The existence of such a path is confirmed by the finding of dorsal column fibres activated transynaptically fron a hindlimb nerve(Petit 1971).

THE DORSAL COLUMN NUCLEI

Considerable attention is paid in both the anatomical and physiological sections to rostro-caudal variations of properties within the dorsal column nuclei. This has been done because some of the results to be described also show rostro-caudal variation and these can thus be compared with what is already known of such variations within these nuclei.

ANATOMY

The dorsal column nuclei consist of the nucleus gracilis and the nucleus cuneatus and are the first relay nuclei for the primary afferent fibres of the dorsal columns. Anatomical evidence has shown that the transynaptically activated fibres in the dorsal columns do not project directly to the thalamus (Boivie 1971). The physiological studies of Petit (1971) suggest that these fibres project to the dorsal column nuclei.

The cytoarchitecture of the nucleus gracilis has been described by Hand (1966). He divides the nucleus gracilis into three parts. The rostral (reticular) part comprises the area from the obex to the most rostral part of the nucleus; the cells in it are small (10 x 10μ) and not clustered. The middle part starts at -2mm and finishes at -5 -6mm (the obex being 0): there is thus a transition zone between the rostral and middle regions. The cells in the middle zone are 20 x 30μ and are clustered. Caudal to the middle zone the cells are

larger (20 x 30μ) and are not in clusters. The presence of clusters in the middle part of the nucleus gracilis is limited to the dorsal part of the nucleus (Kuypers & Tuerk 1964). The cells in the clusters are round and have short, much branched dendrites. These dendrites intertwine but leave the centre of the cluster dendrite-free. The cells which do not lie in clusters are fusiform, multipolar or triangular.

The cytoarchitecture of the nucleus cuneatus has been described by Keller & Hand (1970). The caudal zone has cell clusters and includes all the nucleus from just rostral to the obex to the caudal border. Rostral to this lies the non-cluster (reticular) zone, in which smaller cells are dispersed. As with the nucleus gracilis, the cluster zone is limited to the dorsal part of the nucleus; ventrally the caudal zone resembles the rostral zone.

The primary afferent supply to the nuclei has been studied using dorsal root and dorsal column transection. Glees & Soler (1951) showed that fibres from the coccygeal, sacral and lumbar dorsal roots enter the nucleus gracilis from a dorsomedial direction; there is a smaller ventrolateral bundle comprising fibres from the thoracic dorsal roots. Their experiments with silver staining showed that there is little overlap in the terminal distributions of adjacent dorsal roots. They also showed that each afferent fibre branched two or three times and that these branches gave off collaterals; thus each afferent fibre contacts many cells. Kuypers & Tuerk (1964)

showed that the degeneration following transection of widely separated dorsal roots showed only minimal overlap in the cell cluster regions, but that elsewhere the overlap was more extensive.

Hand (1966) found a very small amount of degeneration in the contralateral nucleus gracilis after lumbar, dorsal root transection. Rustioni & Macchi (1968) found some degeneration in the rostral contralateral nucleus gracilis after coccygeal, sacral, lumbar and thoracic dorsal root transection. They found that, of the dorsal roots projecting to the nucleus gracilis, not all projected to the most rostral regions of the nucleus. However, Hand (1966) found no differential distribution, in the rostro-caudal plane, of the dorsal roots projecting to the nucleus gracilis. Keller & Hand (1970) found that the fibres terminating in the cuneate nucleus were differentially distributed in the rostro-caudal axis. The areas of degeneration shifted laterally within the nuclei as more rostral dorsal roots were transected. (Hand 1966, Keller & Hand 1970, Rustioni & Macchi 1968).

Another technique, used in investigations of the dorsal column afferent supply of the dorsal column nuclei, has been examination of the nuclei for signs of bouton degeneration, after transections of the dorsal columns. Walberg (1966) found that the boutons degenerating in the nucleus gracilis, after transections of the dorsal columns at C3, were medium (1.3 - 2.3μ) or large (greater than 2.3μ). He performed a count on the ventral half of the

nucleus and found that 18% of the boutons in contact with the dendrites, and 2% of the boutons in contact with the soma, were degenerating. Ekmqvist & Westman (1971) found that the boutons degenerating in the nucleus cuneatus, after transections of the dorsal columns, were also large. Both studies also investigated cortical afferents to the nuclei. Walberg bilaterally removed SI and Ekmqvist & Westman thermocoagulated the contralateral SI cortex. Both studies found that a very large majority of boutons were unaffected by either dorsal column or cortical lesions.

The cerebral cortex projection to the dorsal column nuclei has also been investigated with the silver staining technique (Walberg 1957, Kuypers & Tuerk 1964). Walberg found the degeneration to be mainly contralateral and to be distributed thoughout the nuclei, but to be greatest in the rostral and ventral regions. He stated that the areas of cortex projecting to the dorsal column nuclei were, in order of quantitative importance, the sensorimotor area, the occipital, the temporal, the medial and the basal areas of the cortex. He also described fine fibres degenerating in the medial lemniscus after cortical lesions. Kuypers & Tuerk (1964) removed the frontal cortex and subsequently found degenerating pyramidal tract fibres coursing dorsally, caudal to the pyramidal decussation, to reach the dorsal column nuclei. Terminal degeneration was found mainly in the deep parts of the nuclei, except rostrally

where degeneration was found throughout. There was only limited degeneration in the cell cluster regions.

After transections of the contralateral medial lemniscus, cells in the dorsal column nuclei are found to have undergone chromatolysis (Kuypers & Tuerk 1964). These retrograde changes are limited mainly to the round cells of the cell clusters. Busch (1961) traced degenerating fibres from the dorsal column nuclei into the contralateral medial lemniscus. At the level of the inferior olive the fibres were found to envelop the olivary nucleus, except at its dorsolateral border. At the level of the trapezoid body the lemniscus was broken into small bundles, but at the pontine level it became "lemniscal". Busch described three main sites at which fibres departed from the medial lemniscus, prior to its termination in the thalamus. In the rostral pons fibres, originating from the lateral cervical nucleus and from the caudal parts of the dorsal column nuclei, turned dorsally to run to the base of the inferior colliculus. In the rostral mid-brain single fibres, originating from all parts of the dorsal column nuclei, were seen to run latero-ventrally to a region between the brachium of the inferior colliculus and the lateral border of the substantia nigra. Thirdly, fibres originating from the rostral parts of the dorsal column nuclei were seen to run ventrally, ventral to the red nucleus, to reach the subthalamus, where they coursed along the dorsomedial border of the subthalamic nucleus. Busch agrees with Walberg on

the presence of descending fibres in the medial lemniscus: "finally, in the flat intermediate and lateral parts of the lemniscus scattered bundles of corticofugal fibres can be identified by their different fibre pattern." (Busch 1961).

The major site of terminal degeneration, after lesions of the dorsal column nuclei, is the contralateral nucleus ventropostero-lateralis (VPL) (Hand & Liu 1966, Boivie 1971). The nucleus gracilis projects to the lateral division of the VPL (VPLl), and the nucleus cuneatus projects to the medial division of the VPL (VPLm) (Boivie 1971). Hand & Liu were unable to demonstrate any difference in the sites of terminal degeneration, within VPL, of fibres originating from the three cytoarchitectural regions of the nucleus. However, they did find that fibres originating from the rostral part of the nucleus projected to other sites, in addition to the VPL; this was not so for fibres originating from the middle region of the nucleus. These additional sites were mainly contra-lateral and included the magnocellular region of the medial geniculate nucleus (MGmc), the posterior thalamic complex (PO), the red nucleus and the zona incerta (ZI). Boivie found terminal degeneration in the medial part of PO (POm), and in the ZI, but not in the MGmc, after lesions in the cuneate and gracile nuclei. There was no segregation of terminating gracile and cuneate fibres in the ZI or the POm. Boivie made no lesions which were restricted to the middle region of the nucleus gracilis, so that

direct comparison with the results of Hand & Liu is not possible. However, he did find terminal degeneration in the POm and the ZI after lesions in both the rostral and caudal parts of the nucleus gracilis ("caudal" lesions included part of the middle region). Within the VPL there was a "slight tendency for fibres originating just caudal to and rostral to the obex to terminate in the rostral two-thirds of the VPL only. The fibres from the caudal part of the gracile nucleus terminated in almost the whole VPLl".

PHYSIOLOGY

Slow Wave Studies

Therman (1941) used silver ball electrodes, on the surface of the cuneate nucleus, to record the potential changes which follow a shock applied to a cutaneous forelimb nerve. There was first a triphasic potential change, which indicated the arrival at the nucleus of the afferent volley. There was then a negative (N) wave, which had a duration of approximately 5 msec. Therman showed that the negative wave corresponded with the discharge of cuneo-thalamic relay cells by simultaneously recording from the killed ends of the contralateral medial lemniscus. The negative wave had two peaks; the second occurred approximately 2.5 msec after the first, and was equated by Therman with the activation of cuneate cells by the arrival, in the nucleus, of the discharges which comprise the dorsal column reflex. The dorsal column reflex has an analagous origin to the dorsal root reflex (Hursh 1940).

After the negative wave there was a long lasting positive (P) wave, which Therman thought was due to activity in the underlying reticular cells. This explanation is not now accepted (see below). A third slow potential (N') wave was observed by Towe & Zimmerman, following electrical stimulation of the skin (Towe & Zimmerman 1962). This second negative wave occurred just after the peak of the P wave. It was thought to be due to the discharge of cuneate cells caused by a corticofugal discharge.

The relative size of the N wave has been used as an indicator of the state of transmissibility of the dorsal column nuclei, although the discharge of interneurones presumably also contributes to it. With this index it has been shown that stimulation of the sensorimotor cortex causes inhibition of transmission through these nuclei (Dawson 1958, Scherrer & Hernández-Peón 1955). This has been confirmed by recording the summed responses in the medial lemniscus (Satterfield 1962).

An extensive analysis of the origin of the P wave was performed by Andersen, Eccles, Schmidt and co-workers (Andersen, Eccles, Schmidt & Yokota, 1964a and b; Andersen, Eccles, Oshima & Schmidt 1964). They showed that the P wave could be produced by a single shock applied to a peripheral cutaneous nerve and by repetitive stimulation of the contralateral sensorimotor cortex. They produced evidence that the P wave was a manifestation of a relative depolarization of the afferent terminals in the cuneate nucleus, and that this was

responsible, at least in part, for the depression of transmission through the cuneate nucleus which follows a conditioning shock applied to a peripheral cutaneous nerve. Transmission through the cuneate nucleus was tested by applying a shock to a cutaneous nerve and recording the evoked response from the killed ends of the medial lemniscus. A conditioning shock applied to another cutaneous nerve reduced the size of the test response with a time course similar to that of the P wave. When a shock was applied to the cuneate nucleus, two waves were recorded from the killed ends of the medial lemniscus. The first (A) wave was thought to be due to direct stimulation of the cuneo-thalamic relay cells and the second (B) to indirect activation of cuneo-thalamic relay cells, due to activation of presynaptic terminals within the nucleus. Both waves were depressed following a conditioning shock to a peripheral cutaneous nerve. Stimulation of the primary afferent terminals in the cuneate nucleus, at various times after a conditioning shock to a cutaneous nerve, provided evidence of increased excitability, with a time course similar to that of the P wave (Wall 1958). Finally, intra-axonal recording showed that there was a relative depolarisation of the afferents in the cuneate nucleus and that this depolarisation had a time course similar to that of the P wave. The schematic interpretation of these results, shown in Figure 11 of Andersen, Eccles, Schmidt & Yokota (1964c), is supported by the observation that the P wave reverses in polarity at depths greater than 1.0mm.

Andersen et al.(1964) also provided evidence of postsynaptic inhibition in the cuneate nucleus following a shock applied to a cutaneous nerve. With intracellular electrodes they recorded ipsps following cutaneous nerve stimulation. The A wave was also found to be depressed following a shock applied to a peripheral cutaneous nerve; this can be explained on the basis of postsynaptic inhibition of cuneo-thalamic relay cells.

The situation with regard to the inhibition produced by cortical stimulation is not as clear. Andersen et al. found evidence that cortical stimulation of SI and SII produced presynaptic inhibition of transmission through the cuneate nucleus. The evidence for cortically evoked postsynaptic inhibition is more equivocal. Andersen et al. only found A wave depression, after cortical conditioning, in some of their experiments. They recorded no ipsps after cortical stimulation and there was no failure of antidromic activation of cells following cortical stimulation.

It has recently been shown that mechanical stimulation of the skin produces N and P waves and that such stimulation also results in both pre- and post- synaptic inhibition in the dorsal column nuclei (Andersen, Etholm & Gordon 1970). In these experiments discernable P waves could be produced by mechanical pushers which moved only 1-2 hairs.

Unit Studies

The general somatotopic arrangement of the nuclei has been described by Johnson (1952) and Kruger, Siminoff & Mitkovsky (1961).

Both studies treated the gracile and cuneate nuclei as a single functional entity. They both found that the distal limb was represented dorsally in the nuclei and the proximal limb and trunk ventrally. The hindlimb and adjacent trunk were represented in the nucleus gracilis and the forelimb and rostral trunk in the nucleus cuneatus. The medial part of each limb was represented lateral, in the respective nucleus, to the lateral part. The main difference in the results from the two studies was that Kruger et al. found there to be no difference in the representation of the integument at different rostro-caudal levels, whereas Johnson found the ventral surface to be represented at more rostral levels than the dorsal surface.

Andersen et al.(1964c) categorized cuneate neurones as cuneo-thalamic (CTR) relay cells or as non-CTR cells. Their criterion for identification of CTR cells was a response at a constant latency of less than 2 msec to contralateral medial lemniscus stimulation. They found that CTR cells were usually only activated from one nerve. This usually occurred at shock strengths which were just suprathreshold. The number of discharges evoked usually fell if the shock strength was raised above 1.1 x thr. This phenomenon was attributed to activation of fibres which caused inhibition of the cell under study. Such inhibition could also be produced by stimulation of another peripheral nerve. No CTR cells were activated by cortical stimulation. Non-CTR cells were

assumed to be interneurones, although projection elsewhere than the contralateral medial lemniscus was not excluded. These cells were found to have properties different from the cells classified as CTR cells. Fifty six of the sixty nine supposed interneurones were activated from the contralateral sensorimotor cortex as well as from peripheral nerves. Twenty one of these cells were activated from all three peripheral nerves tested. In addition, it was found that, for these neurones, increasing the strength of the shock applied to the peripheral nerve did not reduce the number of discharges evoked. The depths of the cells were measured with respect to the surface of the nucleus. CTR cells were maximally distributed between 0.75 - 1.5 mm, whereas non-CTR cells tended to be deeper than 1.5 mm.

Extensive work on the properties of exteroceptive cells in the gracile nucleus of the cat has been carried out in this laboratory by Gordon and collaborators. Gordon & Jukes (1964a) recorded from 460 cells, which they were able to classify into the following types: hair (209), pad (7), hair and pad (19), claw (15), touch-pressure (70), hair and touch-pressure (8), vibration (22), refratory (22) and insensitive cells. The latter were not studied in detail. In addition, two joint activated cells were recorded, but no special study of joint activated cells was made. The receptive field sizes of touch-pressure cells were generally larger than those of hair cells, irrespective of the sites of the

fields on the body surface. The receptive fields, of both classes, were larger for cells subserving proximal skin areas than for those subserving distal areas; although the number of distal touch-pressure cells was small.

Gordon & Jukes also investigated the effects of mechanical and electrical stimulation of the skin surrounding the receptive field. The receptive field was defined as that area of skin whose stimulation would activate the cell under study. Inhibition was found for hair, pad, and claw cells from the area surrounding the receptive field. Subcutaneous cells were inhibited from the overlying skin. In all cases the mechanical stimulus necessary for production of the inhibition was of low intensity. For hair cells inhibition was produced by stimulation of hairs in a zone surrounding the receptive field; the percentage of hair cells which exhibited the property of "surround inhibition" varied according to which part of the nucleus was being considered. None of the nineteen touch-pressure cells tested were inhibited from the skin surrounding the excitatory receptive field. Facilitation from the skin surrounding the excitatory receptive field was observed for twenty-two cells and these included all eight touch-pressure cells which were tested in this way. Such facilitation was also found for hair, and hair and touch-pressure cells. Facilitation, of this type, had previously been shown by Gordon & Paine (1960) using nerve stimulation. Perl, Whitlock & Gentry (1962), in their study of the

nucleus gracilis, also described the phenomenon of "surround inhibition". In agreement with Gordon & Jukes, they demonstrated its occurrence for hair cells but not for touch cells.

Considerable attention has been paid to the relations between neuronal properties and position within the nucleus gracilis. It is proposed to consider such relations in four parts:

1. The relation between receptor type and position within the nucleus

Gordon & Jukes (1964a) found pad, claw, subcutaneous and vibration cells only in the middle region of the nucleus. (They divided the nucleus into three regions:- rostral, middle and caudal. These were 0-4, 4-7 and 7+ mm from the rostral border of the nucleus.) Hair, hair and touch-pressure, and hair and pad cells were found throughout the nucleus. Touch-pressure cells were found throughout the nucleus, except in the superficial part of the middle region. A similar distribution, with a preponderence of hair and vibration cells in the middle region and of touch cells in the rostral and caudal regions, was found by Perl et al.(1962). A rather different distribution was found by Winter (1965). He found hair cells mainly in the middle and caudal regions and joint cells mainly in the rostral region, but found no rostro-caudal variation for touch or deep cells. To complete the spectrum, Kruger et al.(1961) found no rostro-caudal variation for any of their cell types.

2. The relation between receptive field size and position within the nucleus

Gordon & Paine (1960) found that the mean receptive field size of cells in the rostral region was greater than the mean size for cells in the middle region; the mean size for caudal cells assumed an intermediate position. Perl et al.(1962) suggested that the reason for this correlation was that, as the middle region contained relatively more hair cells than the rostral region, and that as hair cells tended to have the smallest receptive fields, the mean receptive field size of cells in the middle region would be expected to be smaller than the mean size for rostral cells. This explanation was shown to be incorrect by Gordon & Jukes (1964a). They showed that the mean receptive field size of rostral hair cells was greater than that of middle hair cells. This difference was also shown for rostral and middle touch-pressure cells. That the difference for hair units was not due to uneven cell sampling can be seen by reference to Figure 2 of Gordon & Jukes (1964a). For the construction of this histogram, hair sensitive cells were divided into those whose receptive fields comprised part or all of the hindfoot and those whose receptive fields lay proximal to the hindfoot. Comparison of rostral and middle cells, within each category, showed that the mean receptive field size was smaller for the middle region cells than for the rostral region cells. In their study Gordon & Jukes (1964a) also found that, within the

middle region of the nucleus, the superficial hair sensitive cells had smaller receptive fields than the deeper hair cells; the sizes of deep hair cells were similar to those of the hair cells of the rostral region. Winter (1965), however, found no relation between receptive field size and recording position and found that the only valid association was between receptive field size and position of the receptive field on the body surface. Work on the nucleus gracilis of the rat has also demonstrated that cells in the middle region of the nucleus have a smaller mean receptive field size than cells in the rostral or caudal regions of the nucleus (McComas 1963).

3. The relation between surround inhibition and position within the nucleus.

Gordon & Jukes (1964a) found that 53% of hair sensitive cells in the rostral region of the nucleus could be inhibited from an area surrounding the excitatory receptive field. In the middle region of the nucleus 93% of hair sensitive cells exhibited this property.

4. The relation between cell projection and position within the nucleus.

Gordon & Seed (1961) investigated the projection of nucleus gracilis cells by attempting to activate them antidromically by stimulation of the contralateral medial lemniscus. Initially a pair of stimulating electrodes were used; in later experiments a

grid of six electrodes was inserted into the contralateral mid-brain. With the latter technique, Gordon & Seed found 60% of rostral cells, 93% of middle cells and 60% of caudal cells projected into the contralateral mid-brain. These projecting cells had similar receptive field properties to the non-projecting cells within the same nuclear region. An identical stimulating technique was used by Gordon & Jukes (1964a). Their criteria for identification of activation as antidromic was the production of a single impulse of constant threshold and latency to a lemniscal shock. In addition, the impulse had either to follow the first five shocks of a 2 x thr., 750 sec tetanus, or respond to the second of two 2 x thr. shocks at a shock interval of 0.6 msec or less. On two occasions the collision technique was used (Darian-Smith, Phillips & Ryan 1963). Gordon & Jukes found that 33% of rostral cells projected into the main body of the contralateral medial lemniscus. 31% of middle touch-pressure cells projected into the medial lemniscus, whereas 88% of the remaining cell types, in the middle region, were found to have such a projection. In a few later experiments a lemniscal stimulating grid was used in which the medial electrodes were longer than the lateral electrodes, so that, whilst the more lateral electrodes were in the main body of the lemniscus, the medial electrodes were in the ventromedial extension of the medial lemniscus described by Busch (1961). With this arrangement, 63% of rostral cells were found to project into the contralateral mid-brain. A collation of

the data of Gordon & Seed (1961) and Gordon & Jukes (1964a) (see Gordon & Jukes 1964a) showed that the projection of rostral cells into the contralateral brain stem and mid-brain was much more dispersed, especially in a medial and ventromedial direction, than the projection of middle region cells. Differences between rostral and middle cells were also observed for their antidromic latencies. There was a much greater latency scatter for rostral cells than for middle cells; although there was no difference for the minimal latencies in each group.

Thus it seems that the nucleus gracilis can be subdivided on functional as well as on cytoarchitectural grounds. The question of a cerebellar projection from the rostral region will be dealt with separately.

Gordon & Seed (1961), using the criteria of constant latency and high following frequency, found cells which they thought were antidromically activated from the cerebellar cortex. All eleven of these cells were found in the rostral region of the nucleus. Ten of the eleven were activated from the ipsilateral cerebellar cortex and one from the contralateral cerebellar cortex. One cell was thought to project to both the ipsilateral cerebellar cortex and the contralateral medial lemniscus. Gordon & Horrobin (1967) reinvestigated the question of a cerebellar projection of rostral cells, using the much more stringent criterion of "collision" for identification of activation as antidromic. In 7 experiments only

4 cells were antidromically activated from the cerebellar cortex. All four cells were within 1.2 mm of the rostral border of the nucleus. Eighteen rostral cells, all of which projected into the contralateral mid-brain, were transynaptically activated from the cerebellar cortex. In one experiment the DCCT was stimulated at C2; this failed to excite any of these cells, thus suggesting that they are not activated by collaterals of the DCCT. The cells which were synaptically activated from the cerebellar cortex were all slowly adapting. Cells in the rostral region, which were not activated from the cerebellar cortex, were rapidly adapting.

One of the major difficulties in studying the activity of cells of the dorsal column nuclei is the vascular pulsation of this part of the brain stem. Brown, Gordon & Kay (1971) have circumvented this difficulty by recording from axons in the medial lemniscus. This technique provides stable recording conditions, but does not provide information on the position of the cell body. However, the majority of the fibres were activated by stimulation of the dorsal columns at C3, which suggested that they were probably part of the dorsal column system rather than the cervico-thalamic system. The ratio of forelimb and upper trunk to hind limb and lower trunk was 10:1.74 of the fibres were activated by cutaneous stimuli, 15 by joint stimuli and 11 by deep stimuli. Almost half the cutaneous units studied in detail were activated by stimulation of a single receptor type and a large majority of these received

surround inhibition. The other cutaneous units showed a variable amount of receptor convergence and only a few received "surround inhibition".

Recent evidence has indicated that the dorsal column nuclei are subject to more widespread peripheral control than was previously supposed. Jabbur & Benna (1968, 1970) found that transmission through the gracile and cuneate nuclei was inhibited by repetitive electrical stimulation of the other three paws and the face; the test stimulus being applied to the ipsilateral fore or hind paw. They demonstrated this effect on unit activity and on the focal response recorded from the killed ends of the medial lemniscus. Such widespread cutaneous stimulation was shown to produce a [illegible] wave and to cause increased excitability of primary afferent terminals. This suggests that the inhibitory mechanism of "widespread cutaneous inhibition (WCI)" is at least in part presynaptic. Jabbur & Benna did not investigate the nature of the receptor type which produced WCI. The phenomenon was shown to persist in the decerebrate state, but no further investigation of the pathway was made.

Similar observations were made in the rat by Davidson & Ryder (1969) and Davidson & Smith (1970). They showed that contralateral foreleg stimulation inhibited CTR cells but activated non-CTR cells. Afferents coursing in the dorsal columns were not responsible for this inhibition.

Tomasulo & Emmers (1970) found that tactile evoked responses could still be reproduced in the gracile nucleus after transection of the dorsal columns at C2. Responses could also be reproduced in the gracile nucleus by stimulation of the dorsal columns below the lesion at C3. They suggested that the pathway responsible for the latter responses might involve the spinocervical tract; the cells of origin of this tract being activated by collaterals of dorsal column fibres (Taub & Bishop 1965). Both responses were abolished by a lesion of the dorsolateral funiculus at C4. Earlier work by Giblin & Amassian (1966) on the latency of responses of cuneothalamic relay cells to stimulation of the adjacent dorsal columns had shown there to be a bimodal latency distribution. The modal separation was 0.25 - 0.90 msec, suggesting monosynaptic and disynaptic connections between dorsal column afferents and cuneothalamic relay cells. Tomasulo & Emmers found this bimodal distribution to be present in the nucleus gracilis, although their abstract does not indicate whether they were recording from relay cells. After transection of the dorsal columns at C2, stimulation of the dorsal columns rostral to the lesion produced only the early responses, and stimulation caudal to the lesion only the late ones. They suggested that activation of gracile nucleus cells by a pathway involving the spinocervical tract would explain the late responses.

Proprioceptive activation of cuneate cells has been studied

by Rosén (1969a,b). It was known from earlier work that stimulation of low threshold muscle afferents produced an early cortical potential (Oscarsson & Rosén 1963). The pathway responsible for the forelimb effects courses in the dorsal columns and relays in the dorsal column nuclei. The corresponding path from the hindlimb courses in the dorsolateral funiculus and relays in the nucleus Z (Landgren & Silfvenius 1971). Rosén used both focal and unit potential recording techniques to investigate the proprioceptive and exteroceptive activation of cells in the main and external cuneate nuclei. Cells were recorded in the main cuneate nucleus which were activated by a muscle afferent volley. Some of these cells were shown to project into the contralateral medial lemniscus. Most Group I activated cells were only activated from one muscle nerve. Twenty-five percent of Group I CTR cells and 52% of Group I non-CTR cells were also activated by low intensity stimulation of the superficial radial nerve. However, mechanical stimulation of the skin was not effective in activating these cells. Fifty-one percent of Group I CTR cells were inhibited by electrical stimulation of low threshold cutaneous afferents; 33% by stimulation of high threshold muscle afferents. Inhibition could also be produced by tetanic stimulation of Group I muscle afferents: this was much more common for cells of the external cuneate nucleus than for cells of the main cuneate nucleus. (Rosén & Sjölund 1969).

No focal potentials were recorded in the external cuneate

nucleus in response to stimulation of the contralateral medial lemniscus (Rosén 1969b). Such potentials were recorded in the main cuneate nucleus. They were found to be maximal dorsally, but were also recorded ventrally. Focal potentials, produced by Group I muscle afferent stimulation, were not found at the most rostral levels of the nucleus. They were greatest just caudal to the obex, and throughout the rest of the nucleus were much greater ventrally than dorsally. Focal potentials produced by stimulation of the superficial radial nerve were maximal dorsally.

The differential depth distribution, revealed by focal potential recording, was confirmed by studies of single cell activity. Group I CTR cells were found mainly at depths of 1.4 - 1.8 mm, whereas cutaneous relay cells were found mainly at depths of 0.5 - 1.5 mm. Rosén confirmed the findings of Andersen et al. (1964c) on the depths of interneurones. Both cutaneous and Group I muscle afferent activated interneurones tended to lie deeper than their respective relay cells.

Recent studies of the cuneo-cerebellar tract have revealed the presence of a projection from the rostral part of the main cuneate nucleus to the ipsilateral cerebellar cortex (Cooke, Larsson, Oscarsson & Sjölund 1971a,b). Cells in the external cuneate nucleus were found to be monosynaptically activated from Group I muscle afferents (CC-CCT) and almost all of these projected to the cerebellum. Recordings were made from 37 cells in the rostral part of the main

cuneate nucleus. 34 of these projected to the contralateral medial lemniscus and 29 to the ipsilateral cerebellar cortex (T-CBT). No projection was found for the remaining cells. The T-CBT cells were di- or polysynaptically activated by electrical stimulation of low threshold cutaneous afferents. Some were additionally activated from high threshold muscle afferents. Latency studies of the disynaptically activated cells indicated that the interneurones lay rostral to C1; they were presumed to lie in the cuneate nucleus. (50% of the cells which projected into the medial lemniscus were found to have monosynaptic connections with primary afferent fibres.) No inhibition of T-CBT cells was found. Investigations of the receptive fields of 20 T-CBT cells revealed that 50% were activated by hair movement and touch, and 50% only by touch.

Corticofugal Control

Corticofugal control of the dorsal column nuclei has been investigated using single cell recording techniques. The results of these studies differ from those in which the C wave was recorded in that they provide evidence for both excitatory and inhibitory influence on the nuclei. It is difficult to compare the results from the various studies because of the different procedures and terminologies used.

Levitt, Carreras, Liu & Chambers (1954) studied the corticofugal control of both the nucleus cuneatus and the nucleus gracilis. Most cells were either activated or inhibited following cortical

stimulation. Inhibition was usually observed as a diminution in resting activity; on some occasions inhibition of a peripherally evoked response was observed. Some cells which were activated by cortical stimulation subsequently underwent a period in which there was depression of the resting activity but not of an evoked discharge.

Gordon & Jukes (1964b) investigated the corticofugal control of the nucleus gracilis and their results were essentially in agreement with those of Levitt et al. Almost all cells were found to be influenced by corticofugal activity. Cells were either excited or inhibited; mixed effects were not seen. The term "excitation" was used to describe discharge of impulses. Inhibition was observed as either an interruption, or a reduced frequency, of the resting activity. The response of a cell to a cortical stimulus was found to depend on its receptive field properties and on its position within the nucleus. It was observed that cells in the rostral and deep middle parts of the nucleus were excited by cortical stimulation, whereas those in the superficial middle part of the nucleus were inhibited. This suggested that cells which received surround inhibition were inhibited from the cortex and cells which received peripheral facilitation were excited. This hypothesis was subsequently tested and verified (Gordon & Jukes 1964b). Gordon & Jukes also investigated the relation between corticofugal action and cell projection. All the cells which received corticofugal inhibition projected into the main body of the contralateral medial lemniscus.

projection was also demonstrated for some of the cells which were excited by cortical stimulation. The latter finding may indicate some difference between the nucleus gracilis and the nucleus cuneatus. Andersen et al. (1964c) found no cortical excitation of cuneo-thalamic relay cells. However, their criteria for projection may have underestimated the number of cuneo-thalamic relay cells so that some of the supposed interneurones may have projected into the medial lemniscus.

Towe & Jabbur and Jabbur & Towe (1961) investigated the effect of a conditioning cortical stimulus on the discharge produced by a cutaneous stimulus. The evoked discharge in most cells was either facilitated or depressed by the cortical stimulus. They found very few cells which were unaffected by the cortical stimulus. In the nucleus gracilis 67% were facilitated and 27% depressed, in the cuneate nucleus 30% were facilitated and 60% depressed. Inhibition of the resting activity was also observed for some of the depressed cells.

The studies described have indicated that most cells in the dorsal column nuclei are influenced by cortical stimulation and that this influence manifests itself either as excitation and facilitation, or as inhibition. The results of Winter (1965) do not agree with this conclusion. He found that only 53% of peripherally activated cells were influenced by cortical stimulation. 91% of the cortically influenced cells were inhibited. Inhibition was shown as

a depression of the response to a peripheral stimulus. 15% of these cells were facilitated, but not activated, by a cortical stimulus. 47% of these cells were activated by cortical stimulation. It can be seen from these figures that some cells showed mixed effects following cortical stimulation. Such mixed effects were seen for 45% of the cortically influenced cells; usually there was activation followed by inhibition. Winter found corticofugal effects to be more common in the rostral parts of the nucleus.

Rosén (1969b) investigated the corticofugal control of those cuneate cells which were activated by stimulation of Group I muscle afferent fibres. These proprioceptively activated cells were sub-divided into CTR and non-CTR cells. 7% of CTR and 75% of non-CTR cells were activated by cortical stimulation. 45% of CTR cells were inhibited by cortical stimulation. The corticofugal inhibition of transmission was also shown by depression of a Group I test response recorded from the killed ends of the medial lemnisci.

All investigators have found the corticofugal effects to be bilateral. Contralateral effects are more pronounced and have lower thresholds than ipsilateral effects. The various studies do not agree on the "best" cortical site for production of these effects. Winter (1965), and Jabbur & Towe (1961), found that the cortex immediately rostral to the cruciate sulcus was "best". Gordon & Jukes (1964), and Levitt et al. (1964), found the postcruciate area to have the lowest thresholds for corticofugal effects. These

four studies all found that excitation and inhibition were produced by stimulation of the same cortical sites. Rosén (1969) found that the best point for cortical excitation of non-CTR cells was the forelimb motor area, whereas the best point for inhibition and excitation of CTR cells was the lateral part of the posterociate gyrus. Since only a few CTR cells were excited it is difficult to know whether to interpret these findings as evidence of segregation of cortical excitatory and inhibitory areas, or as evidence of segregation of cortical projections to CTR and non-CTR cells. All studies of corticofugal control of the dorsal column nuclei have provided evidence of a somatotopic projection from the cortex to these nuclei.

The possible existence of a corticofugal projection from SII has also been investigated. Gordon & Jukes found no evidence for a projection from SII to the nucleus gracilis. Rosén (1969b), and Andersen et al. (1964c), both found evidence of a projection from this area to the nucleus cuneatus. However, Rosén only found evidence for such a projection in two out of five experiments; in both of these the corticofugal effects from SII were less pronounced than those produced by stimulation of the perisuciate area.

Many of the studies described also investigated the pathways responsible for the corticofugal control of the dorsal column nuclei. Levitt et al. found that transection of the medullary pyramids abolished excitatory but not inhibitory effects, whereas transection

of the caudal brain stem, sparing only the pyramids, abolished inhibitory but not excitatory effects. Jabbur & Towe (1961) found that all low threshold cortical effects were abolished by a bilateral lesion of the pyramids. Hunter (1965) found that stimulation of the bulbar pyramids paralleled the effects of cortical stimulation.

The identification of "best points", from experiments employing cortical stimulation, is difficult because of the problems of current and indirect trans-neuronal spread from the stimulating site. This problem is overcome in experiments in which the corticofugal projection is studied by recording from cells in the cortex and activating them antidromically by stimulation of the dorsal column nuclei. This technique has been used by Gordon & Miller (1965, 1969) in the cat and by McComas & Wilson (1968) in the rat. Gordon & Miller recorded cells which discharged a single impulse of short latency in response to a shock applied to the dorsal column nuclei. Some of these cells were conclusively proved to project to the dorsal column nuclei by the collision technique. The projection from the cortex was shown to be somatotopic and all the corticofugal cells were found to lie in area 3a of Hassler & Muhs-Clement (1964). A few corticofugal cells could be activated by stimulation of the periphery. No corticofugal cells were antidromically activated from the dorsolateral funiculus at C3. This indicates that the axons of corticofugal cells do not bifurcate to send a branch down the

corticospinal tract. McComas & Wilson found evidence for such bifurcation for three out of sixteen cells in their second series of experiments. However, in the rat, the corticospinal tract courses deep to the dorsal columns so that it is possible that the dorsal column nuclei stimulus may have activated underlying corticospinal fibres. Alternatively, there may be a species difference in this respect.

Anatomical studies, described earlier, indicate the presence of descending fibres in the medial lemniscus. Gordon & Jukes (1964b) found that stimulation of the medial lemniscus sometimes had transynaptic effects on the activity of cells in the nucleus gracilis. They subdivided these effects into three categories:

1. Transynaptic activation of the cell linked to antidromic excitation. This was seen for three cells and was thought to be due to activation of a recurrent excitatory pathway.
2. Transynaptic activation of the cell with a long and variable latency. This was seen fairly frequently, especially in the rostral and deep middle parts of the nuclei. The pathway was thought to be transcortical.
3. Transynaptic inhibition of the cell. This was found for 56% of the cells tested. It was found to occur in the absence of the contralateral frontal cortex and was thought to be due to the activation of a recurrent inhibitory pathway.

It is possible that the mechanism for 3 is not recurrent inhibition, but activation of descending fibres in the medial lemniscus.

THE S TROCORTICAL SYSTEM

MORIN'S PATHWAY

Morin described a new pathway by which cutaneous afferent impulses could activate cortical cells (Morin 1955). He showed that focal potentials could still be recorded in contralateral SI and SII, in response to hindlimb skin stimulation, after transection of the dorsal columns at C1. The pathway responsible was shown to course in the dorsolateral funiculus and to relay in the lateral cervical nucleus (Morin & Thomas 1955). A forelimb component was found by Catalano & Lamarche (1957). Mark & Steiner (1958) and Norrsell & Voorhoeve (1962) used peripheral nerve stimulation and found that the latency of the early cortical potentials, in response to hindlimb nerve stimulation, was increased by just over 2 msec after dorsolateral tract transection. Thus transmission from hindlimb nerves to cortex, through Morin's tract, was about 2 msec faster than through the dorsal column system. Norrsell & Colpow (1966) recorded focal potentials, in SI and SII, in response to stimulation of cutaneous, interosseous, joint and muscle nerves. Lesion experiments indicated that almost all responses persisted if either the dorsal columns or the dorsolateral funiculus was intact. The only exception was the response in SII produced by stimulation of low threshold afferents in the interosseous nerve. This was abolished after transection of the dorsal columns.

Lundberg & Oscarsson (1961) described a tactile tract in the dorsolateral funiculus, which was spatially separate from the dorsal spinocerebellar tract and whose fibres were monosynaptically activated from cutaneous afferent fibres. Lundberg & Norrsell (unpublished results 1961) showed that this tract ascended as far as the ipsilateral CI segment but no farther. This tract is now known as the spinocervical tract and is thought to be the spinal part of Morin's pathway.

Whitehorn, Morse & Towe (1969) investigated the role of the spinocervical tract in the production of the primary cortical response evoked by stimulation of the forepaw. They found no evidence for a significant contribution from the spinocervical tract to the early potentials recorded in SI and SII. They suggested that the cause of the disparity between their results and those of previous investigators was that previous investigators had made inadequate transections of the dorsal columns. Whitehorn et al. suggested that impulses, transmitted by a few remaining dorsal column fibres, underwent sufficient subsequent amplification to give rise to significant cortical potentials. There are a number of objections to this explanation. It does not account for the increase in latency of cortical potentials observed to occur after transection of the dorsolateral funiculus (Norrsell & Voorhoeve 1962, Mark & Steiner 1958). Secondly, it is unlikely that the postulated few remaining fibres would contain representatives from all the

peripheral nerves stimulated by Norrsell & Wolpow (1966). Yet, Norrsell & Wolpow found that with the exception noted above, the cortical potentials produced by stimulation of various peripheral nerves were present with either the dorsal columns or the dorsolateral columns intact. Thirdly, Andersson (1962) studied the receptive fields of a large number of cells in SII after various spinal cord transections. Such fields were found in large numbers in animals in which the dorsal columns had been transected. It is very unlikely that a few untransected dorsal column fibres could provide sufficient information to account for the presence of a large number of cortical cells with discrete peripheral fields. It would only be possible to reconcile the results of Andersson with the suggestions of Whitehorn et al. if it is supposed that spinocervical tract activation of cortical cells in SII does not contribute significantly to the early focal potentials in SII. This seems unlikely. Finally, work involving independent stimulation of dorsal column and dorsolateral fasciculi does not agree with the results of Whitehorn et al. It could be suggested that the production of postsynaptic potentials in thalamo-cortical relay cells by dorsolateral fasciculus stimulation is due to intermingling of dorsal column fibres in the supposed dorsolateral fasciculus. However, this would not explain why excitatory postsynaptic potentials in thalamo-cortical relay cells have different properties and shorter latencies when produced by dorsolateral fasciculus

stimulation than when produced by dorsal column fasciculus stimulation (Andersen, Andersson & Landgren 196(). Again, the reconciling explanation would be that cortical cells activated by these thalamo-cortical relay cells do not contribute to the early cortical potentials seen after skin stimulation.

In the majority of their experiments Whitehorn et al. achieved separate stimulation of the dorsal columns and the spinocervical tract by inserting a mica plate between the two tracts at C3 - C4. Any damage sustained during this procedure would be relatively more important for the spinocervical tract because of its much smaller number of fibres. Thus it is possible that the procedure of insertion of the mica plate caused complete functional disruption of the spinocervical tract with only trivial impairment of the dorsal columns. This would explain the presence of cortical potentials in response to dorsal column stimulation and the absence of such potentials with dorsolateral tract stimulation. Figure 2 of Whitehorn et al. illustrates the cortical potentials recorded at three sites in response to contralateral forepaw skin stimulation. Measurements made from these records indicate a definite reduction in the amplitudes of skin evoked potentials recorded at SI

[illegible] after insertion of the mica plate (the small amplitude of the SII response makes measurement rather difficult). Such an amplitude reduction is in agreement with the damage postulated to occur to the spinocervical tract by insertion of the mica plate.

Measurements made from Figure 4 of Whitehorn et al. indicate that the latency of cortical potentials was not increased after spinocervical tract transection. This does not contradict the studies indicating latency differences for cortical potentials when evoked by the two pathways, because latency measurements in these studies were made for the hindlimb pathway. The single cell studies of Andersson(1962) did indicate a latency difference but this was considerably smaller for forelimb than for hindlimb cells. Thus, with forelimb stimulation the latency difference between the two pathways may not be large enough to be appreciated by evoked potential recording techniques.

THE SPINOCERVICAL TRACT

Eccles, Eccles & Lundberg (1960) recorded from dorsal horn cells in low lumbar segments. One of these cells had monosynaptic connections with cutaneous nerves and projected into the ipsilateral dorsolateral funiculus. Such cells were probably cells of origin of the spinocervical tract. These cells were found mainly in the laminae 4 and 5 of Rexed. A similar position for spinocervical cells was found by Petz (1960). The cells recorded in their areas 1 and 2, by Holmodin & Lagglund (1960), were probably spinocervical cells. These authors, however, did not investigate the projections of the cells they investigated. Wall (1960) recorded cells in the "dorsal part of the dorsal horn". These cells had similar properties to fibres recorded in the dorsolateral funiculus of

segments L1 and L5 and thus they were probably spinocervical cells.

The afferent supply of spinocervical tract cells and fibres has been investigated in a large number of studies. Both nerve and mechanical stimulation have been used. Some studies have used stringent criteria for the identification of units as belonging to the spinocervical system. Lundberg & Oscarsson (1961, see also Lundberg 1961) recorded from axons in the dorsolateral funiculus at L1; they identified fibres as belonging to the "tactile tract" only if they were monosynaptically activated from below L5, and were not antidromically activated from the cerebellar cortex. These precautions were taken in order to eliminate inclusion of dorsal spinocerebellar tract fibres. Taub & Bishop (1965) recorded from fibres in the lumbar enlargement which were monosynaptically activated from the sural nerve. Almost all these fibres were found to project to the ipsilateral C4 segment. Further study of 24 fibres showed that 18 terminated in the region of the cord containing the lateral cervical nucleus. The remaining 6 fibres could be activated from rostral C1 but the conduction velocity of these fibres between C1 and C4 was only 50% of its value between C4 and the lumbar enlargement. Taub & Bishop suggested that these fibres were activated by current spread to the lateral cervical nucleus and that the conduction velocity over the C1 to C4 distance was lower because of terminal narrowing of the fibres. It is, however,

possible that these fibres were projecting elsewhere than the ipsilateral lateral cervical nucleus. The criteria of antidromic activation from C3 but not C1, or of activation from C3 and C1 with a 50% conduction velocity drop between these two sites, have been used in the studies of Brown (1968, 1970, 1971) and Brown & Franz (1969, 1970). Other studies have recorded from fibres in the lumbar enlargement without identifying their projection sites (Hall 1960, Taub 1964, Kendell & Hall 1965 and Kendell 1966). The results of Taub & Bishop would suggest that most of these fibres did indeed belong to the spinocervical system but, as noted above, some of these fibres may have projected to sites other than the ipsilateral lateral cervical nucleus. Recording caudal to L5 is not an infallible way of avoiding dorsal spinocerebellar tract fibres since Rusch (1961) found fibres running with the DSCT in the brain stem after lesions caudal to L5.

Recordings from dorsal horn cells in the low lumbar segments have also been made. Some of these studies have not investigated the projections of the cells studied (Hall 1960, 1967, Taub 1964, Price 1971). In other studies the projections of cells into the ipsilateral dorsolateral funiculus was investigated (Eccles, Eccles & Lundberg 1960, Fetz 1968, Hongo, Jankowska & Lundberg 1968). Fetz found that 43% of lamina 4 and 19% of lamina 5 cells projected into the ipsilateral dorsolateral funiculus. This suggests that caution should be observed in ascribing the dorsal horn cells of

Wall (1960, 1967) and Taub (1964) to the spinocervical system.

Many of these studies have described two populations of spinocervical units. One group consists of units which are activated by low threshold cutaneous stimulation. The units of the second group are also activated by low threshold cutaneous stimulation but they receive additional activation when stronger stimuli, such as heavy pressure and pinching, are applied. These two classes have been described both in the spinal (Wall 1960, Fetz 1968) and in the decerebrate animal (Taub 1964, Wall 1967, Lundberg & Oscarsson 1961, Lundberg 1964). Brown has made a more detailed investigation of the receptive fields of spinocervical units. He now describes three populations in the spinal state and four in the decerebrate state. The results of Brown will be discussed more fully when consideration is given to descending control of the spinocervical system.

Inhibition of spinocervical units has been described in a number of studies. Wall (1960) described units which were inhibited by heavy pressure and pinch of the skin but not by low threshold mechanical skin stimulation. Taub (1964) also described such inhibition, which was more common from the contralateral than from the ipsilateral limb; he found ankle squeezing to be the most effective stimulus. Taub also described inhibition produced by light brushing of the skin outside the excitatory receptive field. The distribution of the inhibitory receptive fields was variable

but was never of the "surround" type. Kenshalo et al. (1968) recorded losses in response to stimulation of hairs adjacent to, but not surrounding, the excitatory receptive field. They also recorded polysynaptic loops in response to pinching of the skin. Two types of inhibitory field have also been described by Brown.

Brown has studied spinocervical units in spinal and decerebrate preparations, and also in decerebrate preparations in which the dorsal half of the spinal cord could be cold blocked at low thoracic levels. He originally described three populations in the spinal state and five in the decerebrate state (Brown 1968). In more recent papers he classifies spinocervical units into four types (Brown 1970, 1971). All units were found to be excited by temperatures in the range of 40 - 50°C and many by temperatures in the range 4 - 25°C. Thermal stimuli were effective when applied to the same skin areas in which mechanical stimuli were effective. The four types of unit are given below.

Unit type	Decerebrate	Spinal
I	Tylotrich hairs	All hairs
II	Guard hairs and weakly by skin pressure	All hairs and skin pressure
III	All hairs and skin pressure	All hairs and skin pressure
IV	Not activated	Skin pressure

The skin pressure receptors were not type I or II touch corpuscles. This result disagrees with the findings of Iggo (1967).

Wall found that touch corpuscles (type I) were effective in exciting lamina 4 cells, some of which were presumably spinocervical cells. Brown found no evidence for projection, in the spinocervical tract, of cells activated from claw or pad receptors.

Studies of inhibition were mainly limited to unit types I and III. Inhibition was not found for type I units in either the spinal or the decerebrate state (Brown 1971). Virtually all type III units could be inhibited in the spinal state and 50% in the decerebrate state. The characteristics of the inhibitory fields described by Brown were essentially in agreement with the results of the previous investigations (see above). A particularly common effective inhibitory stimulus was squeezing the contralateral ankle.

Resting activity was present in the decerebrate state in units of types I - III. In the spinal state resting activity was also present in units of type IV and the frequency of resting activity in units of types I - III was increased. Evoked activity was also found to be increased in the spinal state. This was particularly so for Aδ and C fibre activation of type III units.

Wall (1967) also used a technique in which the spinal cord of decerebrate cats could be reversibly cold blocked at low thoracic levels. His studies on lamina 4 cells agree well with those of Brown on spinocervical axons. Thus, after cold block, cells were found to have increased resting activity and an increased evoked activity. Many cells which were initially activated only by low

threshold mechanical stimuli received additional activation from skin pressure and pinch after the cord had been blocked. The effects of cord block on lamina 5 cells were rather different. After block the mechanical threshold for activation of these cells was lowered and their receptive field sizes increased. Taub (1964) obtained "shrinking" of receptive fields of cells in laminae 4 and 5 when he stimulated various supraspinal sites. Brown (1971) found no effect of cord block on receptive field sizes.

Wall (1967) and Fetz (1968) have both studied the effects of stimulation of the medullary pyramids on the activity of lamina 4 and 5 cells. Fetz found 66% of lamina 4 cells were inhibited by such stimuli, whilst Wall could find no effect on lamina 4 cells. Both studies found that some lamina 5 cells were excited, some inhibited and some unaffected by pyramidal stimulation.

These studies demonstrate that the properties of spinocervical units are influenced by descending control systems. The investigations of Brown indicate that in the decerebrate animal there is a tonically active inhibitory centre, and that this centre lies somewhere between the caudal part of the medulla and the mid-collicular level.

THE LATERAL CERVICAL NUCLEUS

ANATOMY

Attention was first paid to the lateral cervical nucleus in recent times by Rexed & Brodal (1951). They described the nucleus

as lying in the dorsal part of the lateral funiculus of the C1 and C2 segments of the spinal cord. In the rostral C1 segment the nucleus was seen to split into two or more bundles. These were connected to the adjacent dorsal horn by reticular cells. Farther caudally the nucleus was more compact and lay in a more lateral position within the dorsolateral funiculus. Brodal & Rexed (1953) described two populations of cells within the nucleus. Most cell-bodies were oval with dimensions of 24 - 30μ by 40 - 54μ. The larger dimension of these cells lay in the rostro-caudal axis of the spinal cord. Westman (1968a) and Truex, Taylor, Smythe & Gildenberg (1970) also described the majority of cells in the lateral cervical nucleus as being medium-large in size.

The dendrites of cells of the lateral cervical nucleus are large (Brodal & Rexed 1953, Ha & Liu 1966) and there is a tendency for them to be oriented in a longitudinal direction (Westman 1968a, Ha & Liu 1966). Spines are present on the soma and dendrites of both cell types (Westman 1968b). Boutons make contact with the spinous and non-spinous membrane of both soma and dendrites. The majority of boutons are about 1μ in size, though they range from 0.5 - 8μ. Boutons de passage have also been described in this nucleus (Westman 1968b).

The spinal afferent supply to the lateral cervical nucleus originates at all levels of the spinal cord and ocurses in the dorsolateral funiculus. There is no direct supply to this nucleus

from primary afferent fibres nor from fibres coursing in the dorsal columns (Brodal & Rexed 1953). The precise nature of the spinal afferent supply to the nucleus has been studied by a number of investigators. Brodal & Rexed observed that fibres entered the nucleus transversely from the lateral funiculus. The degenerating fibres seen in the nucleus, after spinal cord lesions, were much finer than the majority of fibres in the dorsolateral funiculus. This led Brodal & Rexed to suggest that the fine degenerating fibres might be collaterals of the coarser fibres seen in the dorsolateral funiculus.

Ha & Liu (1966) described the spinal afferent supply of the nucleus as coming mainly from the dorsolateral region of the lateral tract with a smaller contribution from the ventrolateral region. In their Golgi study they described coarse and fine fibres coursing lateral to the nucleus and fine fibres coursing medial to the nucleus. In order to specify more precisely the origins of the spinal afferent supply to the nucleus Ha & Liu attempted to make discrete lesions of the cells of Clarke's column, the cells of origin of the ventral spinocerebellar tract and cells in lamina 4 of the dorsal horn. They found that ablations in all three sites caused massive degeneration in the ipsilateral lateral cervical nucleus. Caution must be exercised in accepting these findings because of the probable concomitant damage to fibres in the dorsolateral funiculus (see Westman 1968a). Ha & Liu also transected

lateral tract fibres and observed collateral supply to the lateral cervical nucleus from fibres of both the dorsal and ventral spinocerebellar tracts.

Support for the hypothesis that the lateral cervical nucleus receives some afferent supply from collaterals of fibres coursing in the lateral tract is supplied from the work of Cajal, Busch and Westman. Thus, Busch (1961) states, "according to this author (i.e. Cajal), in Golgi-stained material, fine collaterals of the dorsal spinocerebellar tract as well as coarser fibres ascending in the lateral funiculus enter the nucleus to ramify profusely within the neuropil". Busch (1961) observed fibres passing from the lateral tract into the lateral cervical nucleus but did not explicitly state that they were collaterals of other ascending fibres. However, the presence of collaterals is implied in the summary of ch. 6: "This spinothalamic connexion, however, is indirect since it originates from the crossed lateral cervical nucleus, which receives its afferents from lower levels of the cord by way of the dorsal spinocerebellar tract." Westman (1968a), in agreement with Ha & Liu, observed that the major afferent supply to the lateral cervical nucleus came from lateral and dorsolateral regions of the spinal cord. Some of the afferent fibres were ascending fibres terminating in the nucleus, whilst others were collaterals of longitudinally oriented fibres. Both coarse and fine fibres were seen to enter the nucleus from the dorsolateral

funiculus; coarse fibres had much larger terminal fields than fine fibres.

In summary, it can be stated that there is considerable anatomical evidence that the lateral cervical nucleus is supplied partly by terminal ascending fibres and partly by collaterals of ascending fibres. However, there is no convincing evidence as to the nature or destination of the parent ascending fibres of these collaterals. Indeed, it is possible that they simply project to the most rostral parts of the lateral cervical nucleus.

Westman (1969) has studied the bouton degeneration which occurs after transections of the spinal afferent supply. Degenerating boutons were seen in contact with the medium-large cells but never with the small cells (i.e. cells with a diameter of less than 20μ). After an ipsilateral hemisection at C4, only an estimated 15% of boutons were found to degenerate. Westman suggested that untransected spinocervical tract fibres from segments C1 - 3 were unlikely to account for many of the undegenerated boutons, and that, in view of the evidence against descending fibres to the lateral cervical nucleus, the likely sources for these undegenerated boutons were interneurones (probably the small cells seen in the nucleus) and recurrent axon collaterals. The latter were seen in a Golgi study of the nucleus (Westman 1968a).

Rexed & Brodal (1953) observed chromatolysis of cells of the

lateral cervical nucleus after partial or total removal of the ipsilateral cerebellum. They therefore suggested that there was a major projection from the lateral cervical nucleus to the ipsilateral cerebellum. Morin & Thomas (1955) found no evidence of chromatolysis after cerebellectomy, and the original suggestion was withdrawn after further retrograde and orthograde degeneration experiments failed to confirm the proposition of the projection from the lateral cervical nucleus to the cerebellum (Grant, Boivie & Brodal 1968). Grant et al. suggested that the chromatolysis observed by Rexed & Brodal may have resulted from ischaemic damage to structures other than the cerebellum due to the rather extensive surgery employed. It is, however, worth noting that Busch (1961) observed a few degenerating fibres running with the dorsal spino-cerebellar tract, in the contralateral restiform body, after lesions involving the grey matter of the upper two cervical segments. A depiction of the lesion is shown in one case and this indicates that the lateral cervical nucleus was destroyed. There is now, however, no doubt that the majority of relay cells in the lateral cervical nucleus project to the contralateral thalamus (Morin & Thomas 1955, Busch 1961, Grant & Westman 1969, Boivie 1970).
In studies on kittens it was found that transection of the mid-brain caused loss of 89% of the cells in the contralateral lateral cervical nucleus (Grant & Westman 1969). The remaining cells could have been interneurones, cells projecting to sites other than the

contralateral mid-brain or cells with sustaining projections to other sites. The course of the projection from the lateral cervical nucleus was described by Busch (1961). Axons of LCN cells cross in the anterior white commissure of the cord and then course superficially in the anterior funiculus. Farther rostrally these fibres become displaced laterally to accommodate the medullary pyramids. At the olivary level the fibres are found lateral and ventral to the principal olivary nucleus. Farther rostrally the fibres of the cervico-thalamic tract come to lie in the dorsolateral part of the medial lemniscus. Busch observed fibres leaving the cervico-thalamic tract in the rostral pons and turning dorsally to course to the base of the inferior colliculus. The termination of the cervico-thalamic tract has been studied using silver impregnation techniques by Boivie (1970). Terminal degeneration was found throughout the VPLl but was greater dorsally than ventrally. There was terminal degeneration throughout the VPLm except in the medio-rostral region. There was considerably less degeneration in the MGmc and the POm; it was limited to the medial part of the MGmc and to the rostral two thirds of the POm. No terminal degeneration was found in the reticular nucleus. The fields of distribution of terminal degeneration were compilations from the results of many experiments. In any one cat large areas within these fields were devoid of terminal degeneration; this was not so for the projection from the dorsal column nuclei (Boivie 1971).

There is no anatomical evidence for a descending projection to the lateral cervical nucleus. Such a projection has been looked for, with the Nauta technique, after transections of medulla oblongata (Ha & Liu 1966), and after transections of the mid-brain (Grant & Westman 1969). In neither study was evidence found of terminal degeneration in the lateral cervical nucleus.

PHYSIOLOGY

Morin suggested that the cells of the LCN were activated by collaterals of DSCT fibres (Morin, Kitai, Portnoy & Demirijian 1963). This suggestion was tested by stimulation of the cerebellar cortex (Horrobin 1966). Only two cells were transynaptically activated from the cerebellar cortex in this study. This indicates that DSCT collateral supply is but a minor functional component in the activation of cells of the lateral cervical nucleus. The existence of a functionally distinct spinocervical tract which ascends as far as the LCN has already been described, and it appears that this is the main spinal afferent supply to the nucleus.

The existence of a somatotopic organisation within the nucleus is undecided. Wall & Taub (1962) found facial representation medially and hindlimb representation laterally whereas Horrobin (1966) found the hindlimb represented medially and the forelimb laterally. Catalano & Lamarche (1957) suggested that the forelimb relay was at more rostral levels within the nucleus than the hindlimb relay. The existence of a trigeminal component in the LCN was described by Wall

& Taub (1962) but was not found by other investigators.

The majority of cells of the lateral cervical nucleus are activated by light cutaneous stimuli, usually hair movement (Horrobin 1966, Oswaldo-Cruz & Kidd 1964, Morin et al. 1963, Wall & Taub 1962). Cells activated by such stimuli have continuous receptive fields on the ipsilateral body surface; the area of such fields increases as they shift proximally on the body surface. In addition to cells activated by light cutaneous stimuli, cells have been found which were responsive to skin pressure (Horrobin 1966, Morin et al. 1963), noxious cutaneous stimulation (Gordon & Jukes 1963, Horrobin 1966), deep stimuli (Oswaldo-Cruz & Kidd 1964) and joint movement (Morin et al. 1963). Cells with discontinuous receptive fields have also been described (Horrobin 1966, Oswaldo-Cruz & Kidd 1964). Some of these cells were activated by hair movement from non-adjacent areas of the body, others were activated from adjacent or non-adjacent areas by different stimuli.

Only in a few instances has mechanical skin stimulation been shown to produce inhibition of LCN cells. Inhibition, on these occasions, was usually produced by squeezing one or more heterologous paws. In none of these instances was inhibition of the surround type observed (Gordon & Jukes 1963, Oswaldo-Cruz & Kidd 1964, Horrobin 1966). With peripheral nerve stimulation there is profound inhibition of transmission through the lateral cervical nucleus in addition to any inhibition incurred at the dorsal horn relay site (Fedina, Gordon &

Lundberg 1969). This inhibition was produced by stimulation of muscle and cutaneous nerves in all three limbs tested. Lesion experiments showed that the majority of the fibres responsible crossed soon after entry into the spinal cord and ascended in the ventrolateral columns. Experiments involving single unit recording techniques demonstrated the presence of both presynaptic and post-synaptic inhibition within the nucleus.

The projection of cells of the LCN was studied by Gordon & Jukes (1963) and by Horrobin (1966). Both these studies found that these cells projected to the dorsal part of the contralateral medial lemniscus. No cells were found which projected to the cerebellum (Horrobin 1966). Stimulation of the contralateral medial lemniscus, at stimulus strengths below the threshold for antidromic activation of the relay cell under study, was sometimes observed to give long lasting inhibition. In addition some cells were found which were transynaptically activated by medial lemniscus stimulation. In view of the anatomical studies already described it is possible that these transynaptically activated cells were inhibitory interneurones which were activated from recurrent axon collaterals of projecting cells. No corticofugal effects have been observed on the cells of the lateral cervical nucleus (Gordon & Jukes 1963).

METHODS

ELECTROPHYSIOLOGICAL EXPERIMENTS

ANIMALS AND ANAESTHETICS

Cats, weighing 1.7 - 2.5 Kg and of both sexes, were used. In most cases they were anaesthetized with pentobarbital sodium (nembutal) intraparentally at 38 mg/Kg; maintenance doses were administered at a dilution of 1 in 5 or 1 in 3 as required to prevent the appearance of flexion reflexes. In five experiments the anaesthetic used was a-D(+) glucochloralose (chloralose) at 70 mg/Kg; the chloralose was filtered before use and administered intravenously at a temperature of 50 - 60°C. Induction in these cases was with fluothane and nitrous oxide. The animal was initially anaesthetized on "open circuit" from a B.O.C. MiniBoyle anaesthetic machine, with 2l/min O_2, 2l/min N_2O and 4% Fluothane (halothane) delivered by way of a funnel placed over the nose and mouth. When the animal was relaxed a tracheal cannula was inserted and the system used on a "closed circuit" so that the animal rebreathed a mixture of O_2 and fluothane (adjusted as required) from a bag. The circuit incorporated a CO_2 adsorbant. The modification of the B.O.C. machine for use on "closed circuit" was designed by Mrs A. Breeh. The conversion from volatile anaesthetic to chloralose was made immediately prior to moving the animal to the experimental stand.

SURGERY

The surgery was performed with the animal on a heated table. The temperature of the animal was monitored by a thermometer inserted into the rectum. The hair over the trachea and the upper ventral side of the left thigh was clipped. The cut hair was removed with a vacuum cleaner.

In the pentobarbital anaesthetised animals the venous and arterial cannulae were inserted before the tracheal cannula; in those animals operated on under volatile anaesthesia this sequence was reversed. The venous and arterial cannulae were of thin polythene tubing and were inserted into branches of the femoral artery and vein. They each ended distally in a two way tap. The tracheal cannula was Y shaped. After insertion and tying in of the cannulae the overlying skin was sutured.

At this stage the animal was turned so that it lay prone. The upper chest was supported on a sand bag so as to provide the required convexity in the neck region. The hair over the head and upper cervical region was clipped. The skin over the occiput and upper cervical region was incised in the midline and retracted. The neck musculature over the occiput and upper cervical regions was also incised along the midline with a scalpel and then retracted. Arterial bleeding was stopped by using arterial forceps (Spencer-Wells), the artery was subsequently tied off. Less severe bleeding was stopped by using a cautery blade heated to dull red heat or by using

Sterispon foam; the cautery was not used once bone was exposed. The remaining musculature was scraped from the occiput and atlas, and from the C3 - C6 vertebrae so as to obtain a clean bone surface in these regions. The atlanto-occipital membrane was then carefully cut. The anterior part of the atlas and the exposed part of the occiput were then removed using bone forceps, care being taken to leave the dura over the cerebellum and dorsal column nuclei intact. Bleeding from cut bone surfaces was stopped with bone wax. When sufficient exposure had been achieved the exposed areas were covered with paper tissue soaked in warm Ringer solution. A C3 - C6 laminectomy was then performed. One blade of a pair of bone cutters was carefully inserted into the articulation zone between C3 and C4 and a rostral cut made; this was done on both sides of the midline thus allowing a piece of C3 to be removed. This exposure was then increased rostrally, caudally and laterally using bone forceps; particular care was taken in the articulatory zones not to damage articulatory blood vessels. Bleeding from bone surfaces was stopped with bone wax. When sufficient exposure had been achieved this area was also covered with tissue which had been soaked in warm Ringer solution.

Hair was then removed with clippers from the T2 - T4 and lower lumbar regions. The vertebral spines of these regions were then exposed and one clamp fitted to an exposed thoracic spine and one to two adjacent lumbar spines. The animal was then transferred from the operating table to the experimental stand.

PREPARATIONS FOR RECORDING

The animal stand was of Lundberg-Källström design. The base was Formica covered and was fixed to the floor by concrete pillars. The clamps (see above) fitted on to two parallel steel bars, which were 12 cm apart. The head was held in place by a tapered steel bar in each external auditory meatus, a flat steel bar pressed down on the lower rim of each orbit and another bar pressed upward under the hard palate. These points of contact allow use of the Horsley-Clarke co-ordinates. The head was tilted ventrally at an angle of 25° - 28°.

The animal lay on an electric blanket which was thermostatically controlled from a rectal probe. The arterial cannula was attached to a blood pressure manometer. The blood pressure was normally in excess of 150 mm Hg. If it fell below 100 mm Hg, 10 - 20 ml of rheomacrodex was injected intravenously. On rare occasions a fall in blood pressure was combated with an intravenous injection of noradrenaline.

All experiments required the exposure of the dorsal column nuclei and the transection of the dorsal columns in the region C3 - C4 (Fig. 1). The dura over the exposed cervical cord was cut along the midline under a dissecting microscope (Zeiss) using fine forceps and spring scissors; the incision was extended laterally to allow full exposure of the dorsal columns and dorsolateral funiculi from C3 - C6. A suitably vessel-free part of the cord in the C3 - C4 region was then selected for transection of the dorsal columns. This was done

using fine forceps under a dissecting microscope. After the transection was completed the exposed cord was covered with warm paraffin. The dura over the caudal part of the cerebellum and over the upper part of the spinal cord was then incised in the same way. In order to expose the dorsal column nuclei fully the caudal part of the cerebellum was sucked away; bleeding was stopped by applying Sterispon and applying suction through a small piece of wet tissue paper. The exposed nuclei and upper cervical cord were then covered in warm Ringer solution.

When necessary muscle relaxation was induced with gallamine triethiodide (Flaxedil). This was injected in amounts sufficient to paralyse the diaphragm. The tracheal tube was then connected to a Starling respirator and the cat ventilated with air. Further Flaxedil was given in small repeated doses so that the anaesthetic level of the animal could be assessed. In some of these experiments a metal tube was inserted into each pleural cavity to create an artificial pneumothorax. The external end of each tube was fitted with a slightly inflated rubber balloon to prevent dehydration. The pneumothoraces were produced in an attempt to minimise the movement of the brain stem caused by the artificial ventilation.

The type of further preparation depended on which experiment was to be performed:

1. Experiments recording from units in the dorsal column nuclei (33)

   In a few experiments there was no lemniscal gild but otherwise the arrangement was as

shown in Figure 1a. In most experiments, however, a stimulating grid of six electrodes was inserted into the contralateral mid-brain at Horsley-Clarke co-ordinates A4.5 - A3.5 for the purpose of stimulating the axons of those cells which projected into the mid-brain. This grid was held in a Narashige micromanipulator. The micromanipulator was attached to the head holder prior to the experiment and the grid adjusted so that it was at right angles to the horizontal and vertical Horsley-Clarke planes. The micromanipulator was then adjusted so that the tips of the electrodes were at co-ordinate positions A3.5 - A4.5 and depth O; the readings on the micromanipulator were noted and the grid removed leaving the micromanipulator attached to the head holder. For insertion of the grid during the experiment the relevant area of the skull was exposed and cleared of muscle and fascia. A hole was drilled through the skull with a trephine and the area of exposure widened with bone forceps. Bleeding from bone was stopped with bone wax. This cortical exposure was on the side contralateral to the recording site; in most cases the recording site was on the right. The dura was then cut under a dissecting microscope using fine forceps and spring scissors. The grid was then replaced in the micromanipulator and the most medial electrode aligned with the midline of the skull; the grid was then moved 2.5 mm laterally and was slowly inserted so that the tips of the electrodes were at a depth of zero on the Horsley-Clarke co-ordinates. During the insertion the cortical

surface was carefully manipulated with blunt forceps to prevent the passage of electrodes through cortical blood vessels. The exposed cortical surface was then covered with a warm jelly made of a mixture of paraffin and vaseline. In most experiments the grid was inserted at A4.5 but in a few of the later experiments it was inserted at A3.5. The grid was then lowered to the depth at which thresholds for antidromic activation of dorsal column nuclei cells were minimal. It was assumed that antidromic activation at low threshcldz indicated that the tips of the electrodes were in the region of the medial lemniscus.

In three experiments the ipsilateral anterior lobe of the cerebellum was exposed to stimulate the axon terminals of direct spinocerebellar fibres. The bone over the occipital lobe of the cortex was cleared, removed by trephining, and the exposure extended with bone forceps. The dura was cut and the occipital cortex sucked out; bleeding was stopped with Steriscon sponge. This procedure exposed the dura on the anterior surface of the tentorium and allowed the venous sinus which runs along the edge of the tentorium to be tied off. The dura was then scraped from the anterior surface of the tentorium. A trephine was then used to expose the anterior lobe of the cerebellum and the area of exposure was increased with bone forceps. Bipolar silver stimulating electrodes were then placed on the exposed cerebellar cortex. They were moved from time to time during the experiment and the efficacy

of the stimulus was monitored at all times by monopolar recording, with a silver ball electrode, from the DLF caudal to the lesion of the dorsal columns. The indifferent electrode was placed in the adjacent neck musculature. This recorded a short latency potential following a shock applied to the cerebellar cortex and was assumed to be a discharge conducted antidromically along fibres of the DSCT. The exposed cerebellar surface was covered with the vaseline and paraffin mixture. This was easily removed with tissue paper to allow readjustment of stimulating electrode position.

In one unit recording experiment the brain stem was transected at a low pontine level. This involved removing a larger amount of cerebellum than usual. The transection of the brain stem was accomplished using a curved knife with a guarded tip.

In all the unit experiments the recording electrode was held in an arc which could be moved in all three planes. The arc was used with the tip of the electrode tilted 8° - 10° rostrally. The electrode was driven by a stepping motor with a range of 2 - 22μ per step drive (Eide & Källström 1968). The drive was triggered from the fly back of the oscilloscope sweep.

2. Experiments investigating the effects of DLF stimulation on the nuclear N wave (4^{+}).

The experimental arrangement is shown in Figure 1b. In these experiments the recording electrode was of lower resistance so that

it recorded mass rather than unit potentials. The electrode was inserted, just caudal to the obex, to a depth at which the P wave was beginning to reverse. A typical N wave was recorded in response to a shock applied to the dorsal columns rostral to the dorsal column lesion. The test response was conditioned by a series of 5 shocks at 500/sec applied to the ipsilateral DLF at C6. In two experiments the brain stem was transected immediately rostral to the dorsal column nuclei.

3. Experiments involving recording from the killed ends of the dorsal column fibres (3+).

The experimental arrangement for this modification of the Hall technique (Hall 1958) is shown in Figure 1c. The monopolar recording electrode was applied to the distal ends of the transected dorsal column fibres; the indifferent electrode was placed in the adjacent neck musculature. A test shock was applied to the cuneate nucleus by an electrode similar to that used for recording the N wave. This caused an antidromic volley to be conducted down the dorsal column fibres and was recorded by the silver ball recording electrode as a monophasic positive wave. The conditioning stimulus was a series of 5 shocks at 500/sec delivered to the ipsilateral DLF at C6. A calibration curve was obtained by using the test stimulus alone at shock strengths ranging from zero to those supra-maximal for the response. The effect of the conditioning was

+ In one case both of these experiments were performed on the same animal.

investigated for each of these test shock strengths. In all cases the variable measured was the area of the recorded monophasic wave (Eccles, Magni & Willis 1962).

ELECTRONICS

The output from the recording electrode was led to one grid of a double triode cathode follower valve. The other grid was earthed. The cathode follower output was led to an a.c. coupled preamplifier. The bandwidth of the preamplifier was set at 3Hz - 10KHz for unit recording experiments. For N wave recording experiments it was set at 0.3 Hz - 250 Hz or 0.3 Hz - 1 KHz, whilst for experiments recording the antidromically conducted monophasic response it was set at 30 Hz - 10 KHz. The preamplifier output was displayed on one beam of a Tektronix 502A oscilloscope.

The stimulus monitor signal was led to the other oscilloscope beam. This second beam also displayed the time marker from a crystal driven Dekatron counter. This counter also triggered the time base. Sweep repetition rates of 1, 2, 5, 10, 20 and 50/sec could be selected.

Signals from the Y plates of the oscilloscope were led directly to a 7 channel Ampex CP-300 magnetic tape recorder. Other recorded signals included speech (Reslo RDH microphone) and the trigger pulse. This allowed a later reconstruction of the experiment for analysis and photography.

The tape recorder introduced some signal distortion. Because of

this slow potentials were sometimes photographed directly, during the experiment, with a Shackman oscilloscope camera.

A Bannister & Kay (1965) transistorised stimulator was used. This produced current pulses of known and variable duration and amplitude. The pulses were timed by delay units triggered from the oscilloscope time base. Single, double or repetitive trains of shocks could be used. The three stimulator unit outputs were fed into distribution boxes for supply to the various stimulating sites.

STIMULATING ELECTRODES

1. Stimulation of the cerebellar cortex and of spinal cord tracts.

Spinal cord funiculi and the cerebellar cortex were stimulated by similar bipolar electrodes. A length of silver wire was placed in a bunsen flame and withdrawn after the formation of a ball at the end. Two such wires were mounted in a perspex tube, with the balls protruding by 4 cm.

2. Stimulation of the skin.

The skin could be electrically stimulated by pairs of steel needle electrodes. Each pair of needles was fixed to a perspex former with Araldite adhesive.

3. Dorsal column nuclei stimulation.

The dorsal column nuclei were stimulated with single "old" tungsten electrodes which had been previously used for unit recording and thereby had their resistances lowered. The other electrode was placed in the adjacent neck musculature.

4. Stimulation of the medial lemniscus.

The electrodes were made from fine steel beading needles. The eye ends of the needles were ground and tinned. Each electrode was then dipped in Araldite coating compound (925-1) and baked in the oven as recommended. The insulation was then tested; one coating was usually sufficient. The terminal 0.25 mm was then ground bare under a dissecting microscope. A piece of copper wire was soldered onto the tinned end of each electrode.

Six of these electrodes were then mounted on a perspex sheet engraved with a series of parallel grooves having their centres approximately 1.0 mm apart. The electrodes were then firmly fixed in place with Araldite resin and the perspex sheet itself similarly attached to a perspex holder which could be mounted in the micro-manipulator.

The copper wire from each electrode was soldered to a microplug. During the experiment these microplugs were inserted into the output sockets of one of the distribution boxes. The stimulating arrangements were such that current could pass in either direction between adjacent electrodes (i.e. all electrodes except those at each end of the transverse row could act as cathode or anode).

RECORDING ELECTRODES

1. Tungsten microelectrodes.

Tungsten microelectrodes, manufactured after the technique of Hubel (1957), were used for recording single unit responses and slow nuclear waves.

A 4 cm length of 0.15 mm diameter tungsten wire was mounted on a Luer No. 12 hypodermic needle. It was then electropolished to a fine tip in a saturated solution of potassium nitrite by passing a 4 - 5 volt a.c. current. This primary taper was achieved by dipping the electrode in and out of the solution about ten times. The terminal 1.0 mm was then immersed into the solution and a 1 - 2 volt a.c. current passed until electrolysis ceased. This produced a secondary tip. This was then examined under a microscope in order to make sure that it was sharp. The wire was then cleaned by immersion in distilled water and acetone. It was then allowed to dry.

Vinyl varnish was left to evaporate, at room temperature, for a few days until it had a suitable consistency.

The wire was then completely immersed, tip uppermost, in the varnish with a hydraulic double syringe device. Gentle blowing on it as it was withdrawn ensured that it was well coated. It was then left to dry for at least 24 hours. When such an electrode was used for the first time the resistance was usually too high for unit recording. The resistance was lowered, presumably by breaking some of the insulation at the tip, by passing a current of 15μA for some

seconds. This procedure was repeated, if necessary, until good cell responses were recorded.

The marking of recording positions during an experiment was achieved by passing a current of 10μA for 10 secs, the electrode being made negative.

2. Silver ball electrodes.

These were manufactured in the same way as described for silver ball stimulating electrodes.

HISTOLOGY

All spinal cord segments containing lesions and all mid-brains from experiments in which a lemniscal stimulating grid was used were prepared for histology. The majority of medullae from unit recording experiments were also prepared for histology. In a few cases this was not done and in these cases reconstruction of recording positions was achieved by noting the position of each track with respect to the bifurcation of the dorsal columns during the course of the experiment. In a few cases in which the medullae were sectioned, inability to find marking lesions meant that reconstruction of recording position was not possible.

At the end of experiments for which histology of the mid-brain or medulla was required the animal was perfused in situ. This perfusion was performed by inserting a cannula into the thoracic aorta, opening the sagittal venous sinus and allowing first 0.9% sodium chloride and then normal saline containing 5% formaldehyde to flow.

These were delivered to the cannula by a double "Blood Transfusion Set". At the end of all experiments the relevant parts of the spinal cord were covered with 5% formal saline and evaporation prevented by covering with tin foil.

The next day the relevant parts of the spinal cord were removed and fixed in formal saline. Cuts were made in the brain stem well rostral and caudal to the electrode tracks with a scalpel blade held in the arc at the same orientation as the recording electrode. Similarly parallel cuts, rostral and caudal to the grid position, were made in the mid-brain with a scalpel blade held in the Narashige micromanipulator. The animal was then decapitated and the head totally immersed in formal saline. After a few days the relevant segments were removed and left in formal saline for a further few days.

The spinal cord segments containing dorsal column transections were then processed in one of three ways:

1. Serial, 100µ frozen sections were cut and the sections stained with Weil's haematoxylin. In some cases photographs were taken of frozen sections before they were stained.
2. The segments were embedded in low viscosity nitrocellulose (LVN), 50µ serial sections cut and stained with Safranin and Weil's haematoxylin.
3. The segments were embedded in paraffin, 50µ serial sections were cut and stained with Weil's haematoxylin.

Spinal cord segments containing lesions of the VLF were embedded in LVN, 50μ sections were cut and stained with Cresyl violet.

Medullae and mid-brain segments were embedded in LVN and 50μ sections were cut. The sections were subsequently stained with Weil's haematoxylin or cresyl violet and luxol blue (Klüver's technique).

ANATOMICAL EXPERIMENTS*

Three animals were used in these experiments. In two of them the technique of successive degeneration was used (Sherrington & Laslett 1903). The dorsal columns of both sides were transected in the mid-cervical region and the animals then left for a period of over a year before a unilateral lesion of the dorsolateral tract was made. During the intervening period the degenerating fibres of the dorsal columns would have been readsorbed and thus no longer visible. In the third animal there was no dorsal column lesion preceding the transection of the dorsolateral tract. The animals were killed under deep anaesthesia by intravital perfusion of formaldehyde. The details of the lesion sites and the survival times are given below.

Cat No.	DC lesion site	DLF lesion site	DC-DLF lesion interval	DLF-death interval
OX1	Transection between C4-C5	Transection between T10-T11	401 days	6 days
OX2	Transection between C4-C5	C7	396 days	5 days
OX3	-	C5	-	6 days

The experimental material was subsequently investigated by Dr. Grant who has kindly supplied the results of this analysis and photomicrographs of the sections. Blocks of the spinal cord

*These experiments were performed jointly with Drs. Gordon and Grant.

containing the lesion were embedded in paraffin, sectioned and stained with thionin and Van Gieson's stain. Transverse sections of the medulla oblongata and upper part of the first cervical segment were cut on a freezing microtome. One set of sections was then stained with silver according to the method of Nauta, another according to the method of Fink and Heimer.

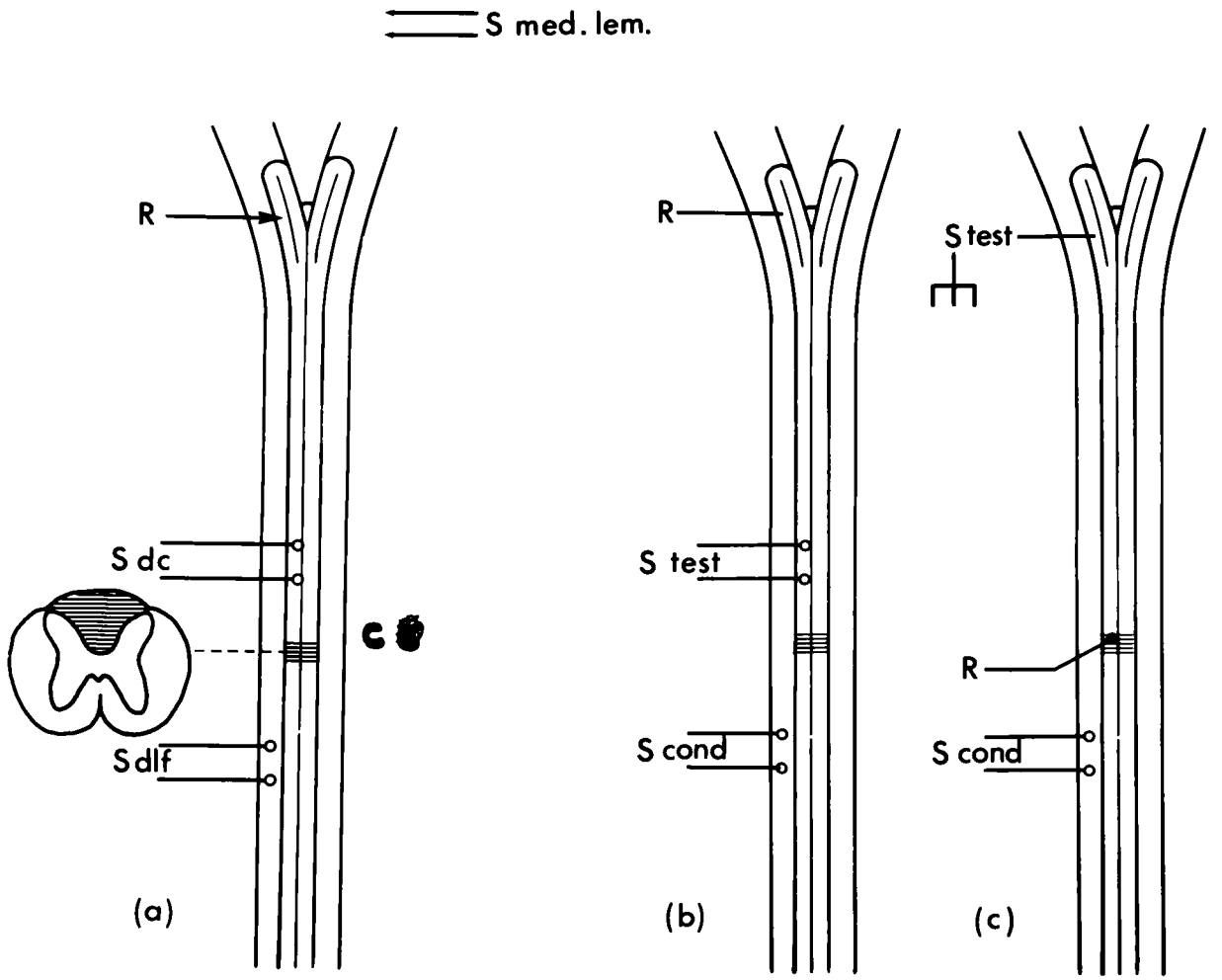

S med. lem.
R
S dc
S dlf
(a)
R
S test
S cond
(b)
S test
R
S cond
(c)

Fig. 1. Diagrammatic dorsal view showing the three types of electrophysiological experiment. In each, a total section of the dorsal columns is shown at C4 by cross-hatching.

(a) Unit recording experiments.
R, recording microelectrode in dorsal column nuclei. Three alternative pairs of stimulating electrodes are shown:- Sdlf (on DLF caudal to section), Sdc (on ipsilateral dorsal column rostral to section), and S med. lem. (in contralateral mid-brain).

(b) Conditioning the nuclear N wave.
R, coarse recording electrode in cuneate nucleus; S test, for test stimulation of the dorsal columns; S cond, for conditioning stimulation of the DLF.

(c) Testing excitability of dorsal column terminals in cuneate nucleus.
S test, test stimulating electrode in cuneate; R, recording electrode for antidromic wave elicited by S test; S cond, conditioning electrodes on DLF.

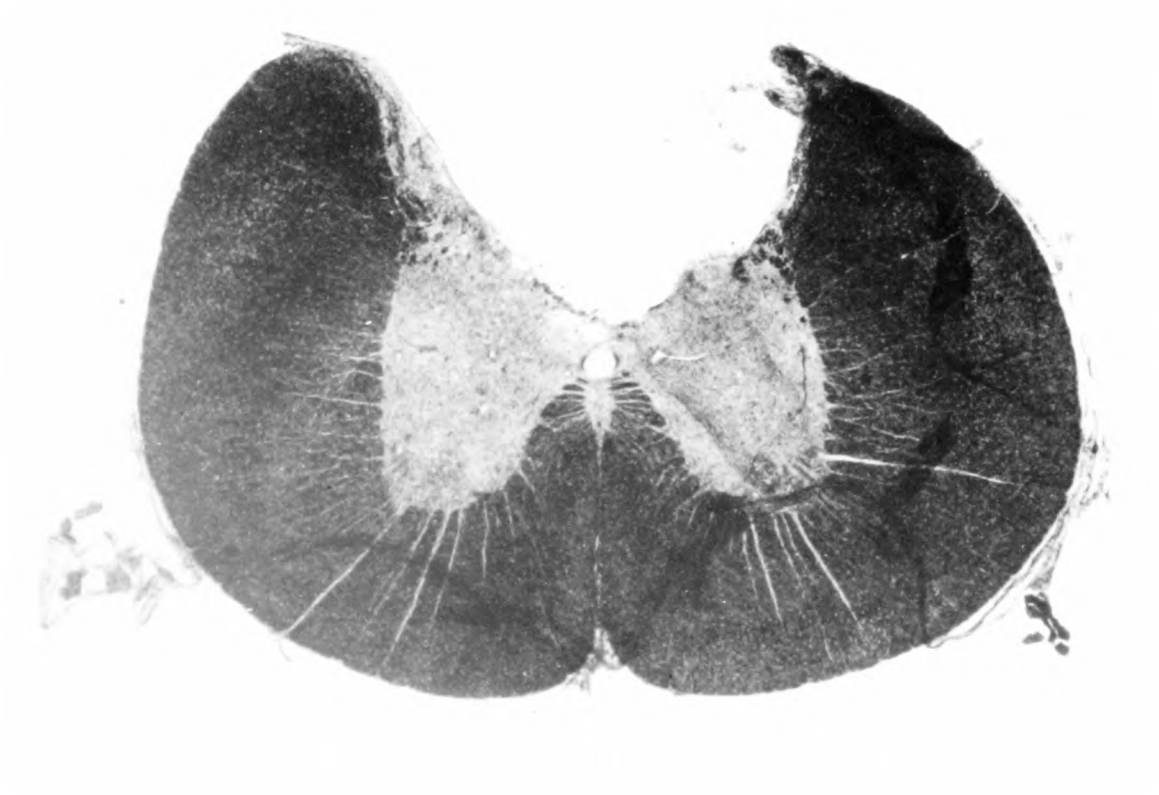


Fig. 2. Photomicrograph of an unstained, 100μ transverse section of the spinal cord at the level of transection of the dorsal columns.

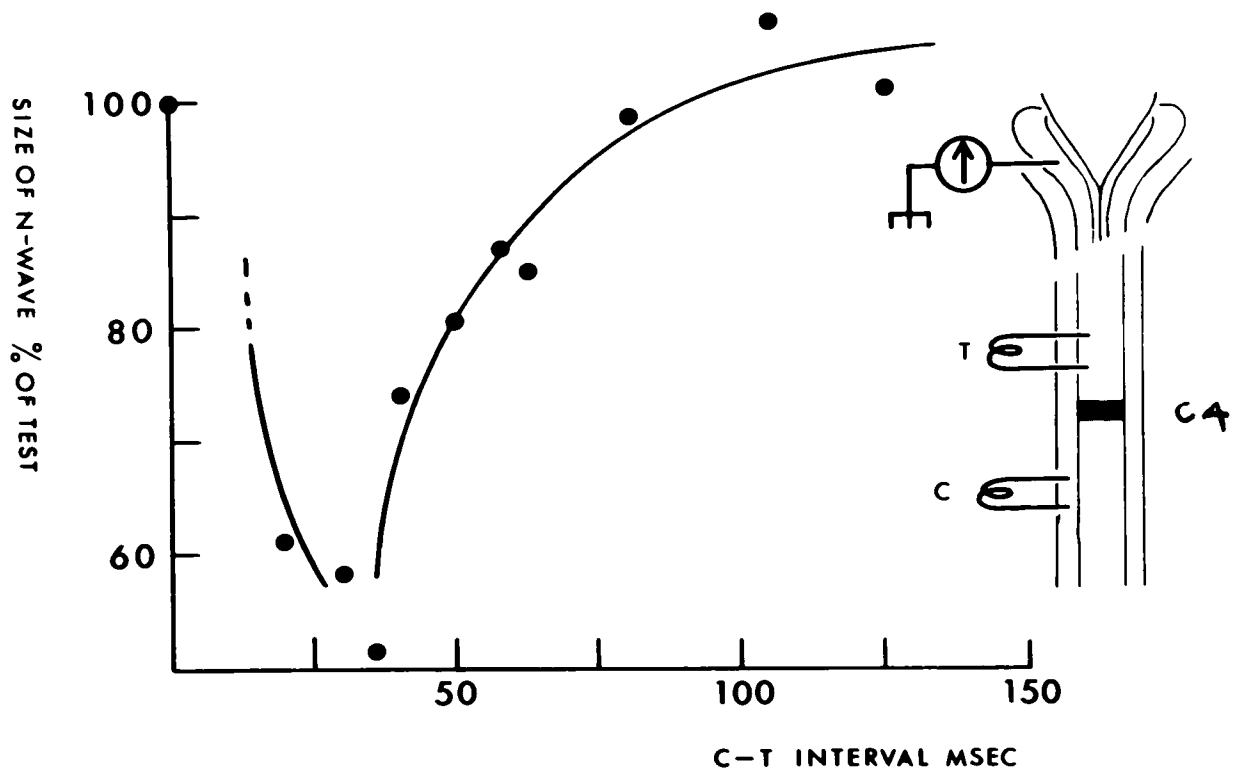

100
80
60
SIZE OF N-WAVE % OF TEST
50
100
150
C—T INTERVAL MSEC
T
C
C4

Fig. 3. The graph shows the time course of the effect of a series of 5 conditioning shocks at 500/sec applied to the ipsilateral DLF, caudal to the dorsal column transection, on the amplitude of the nuclear N wave. The N wave was produced by a single shock applied to the dorsal columns rostral to the dorsal column transection and was recorded at a depth of 1mm in the cuneate nucleus just caudal to the obex.

The accompanying diagram illustrates the experimental arrangement.

C-T INTERVAL 50 MSEC

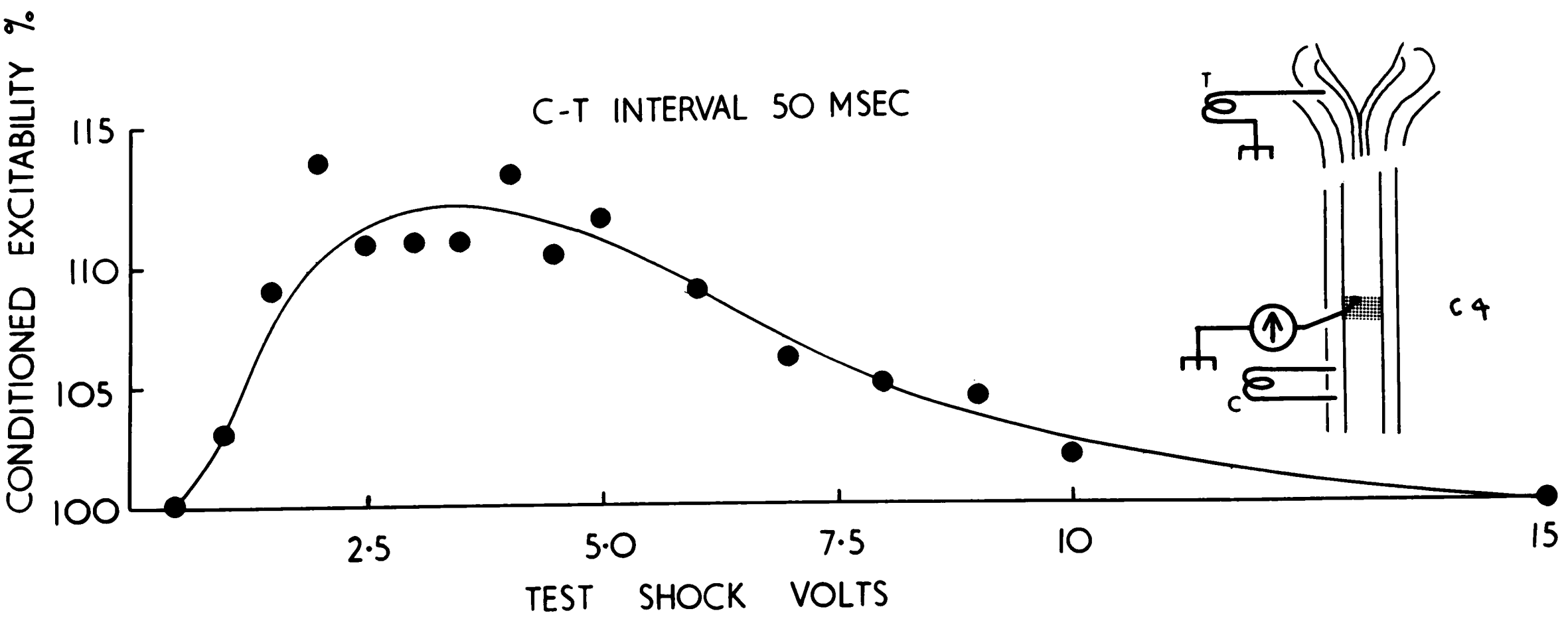


Fig. 4. The graph shows the increased excitability produced in terminals of dorsal column fibres in the cuneate nucleus by a series of 5 conditioning shocks at 500/sec applied to the ipsilateral DLF caudal to a transection of the dorsal columns. The excitability was tested by applying a shock to the cuneate nucleus through an electrode inserted into a depth of 1.0mm just caudal to the obex; the resulting antidromic volley was recorded from the killed ends of the dorsal column fibres at the rostral end of the dorsal column lesion. The effects of the conditioning tetanus were investigated at test shock strengths ranging from subthreshold to supramaximal for the antidromic volley.

The experimental arrangement is shown in the accompanying diagram.

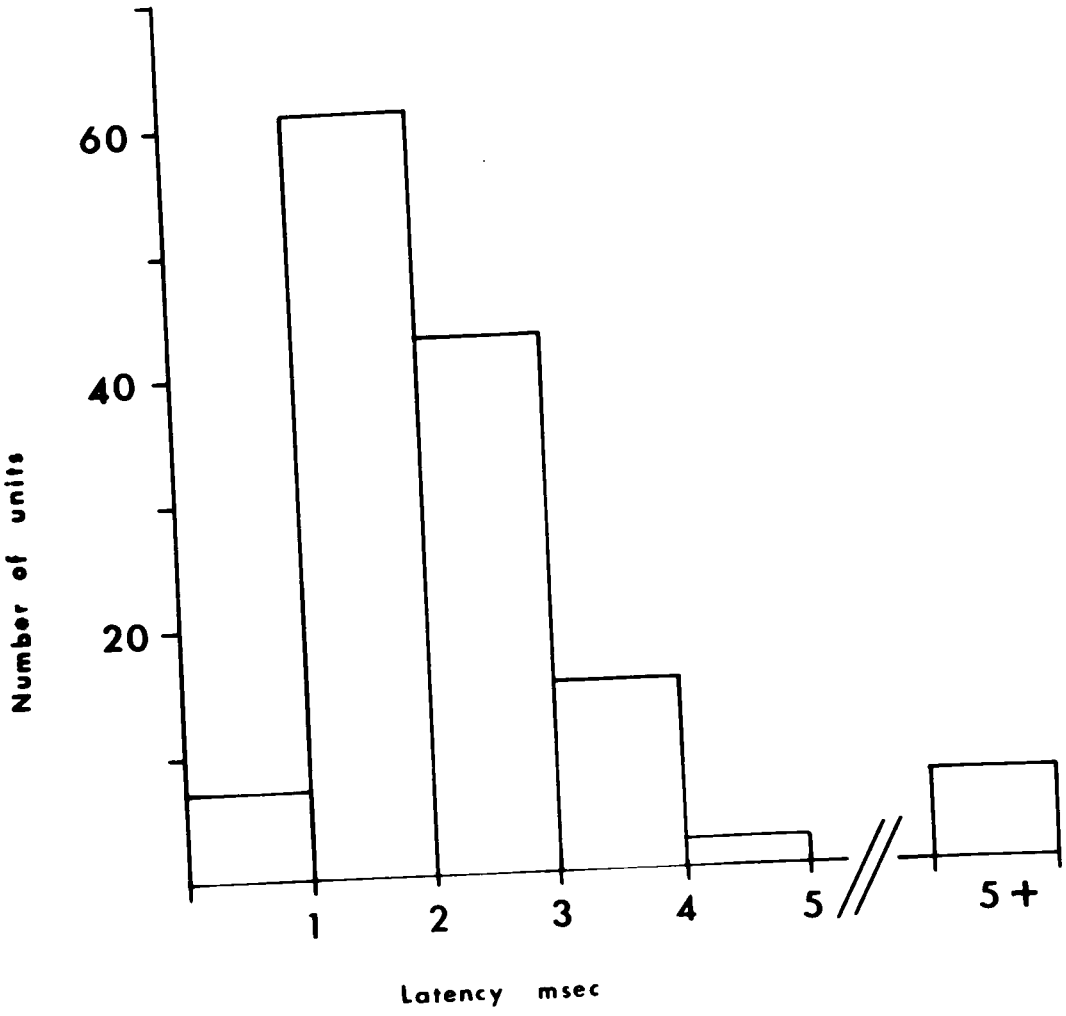
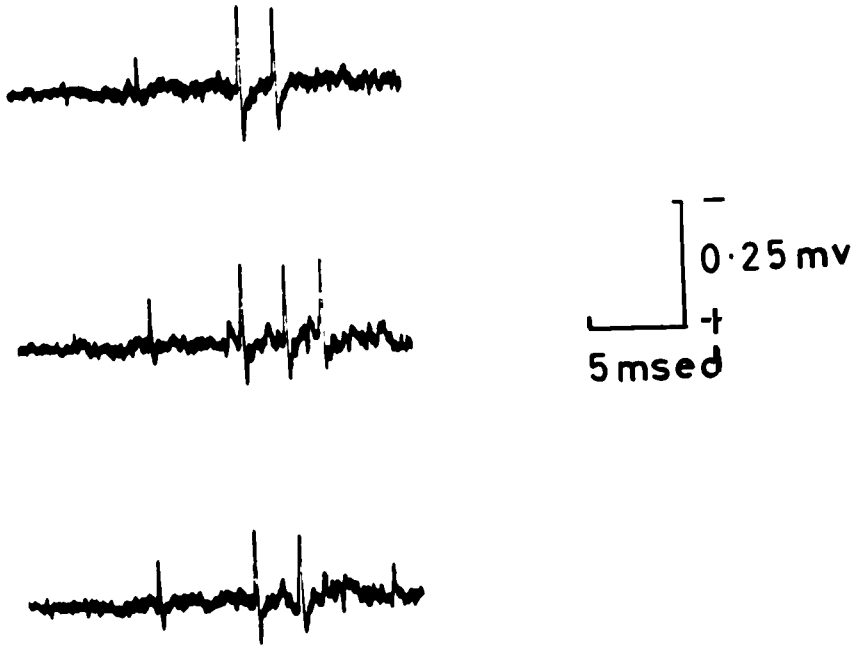

60
40
20
Number of units
1
2
3
4
5
5+
Latency msec

Fig. 5. Histogram showing the latencies of presynaptic units, recorded in the cuneate and gracile nuclei, in response to stimulation of the ipsilateral DLF caudal to a transection of the dorsal columns. All units included in this histogram were thought to be direct fibre connections between the dorsal column nuclei and the ipsilateral DLF. The conduction distance, in all cases, was approximately 50mm.



In this and all subsequent oscilloscope records negative deflection is upwards.

Fig. 6. Traces showing responses of a cell, recorded in the cuneate nucleus, to single-shock stimulation of the ipsilateral DLF caudal to a transection of the dorsal columns.

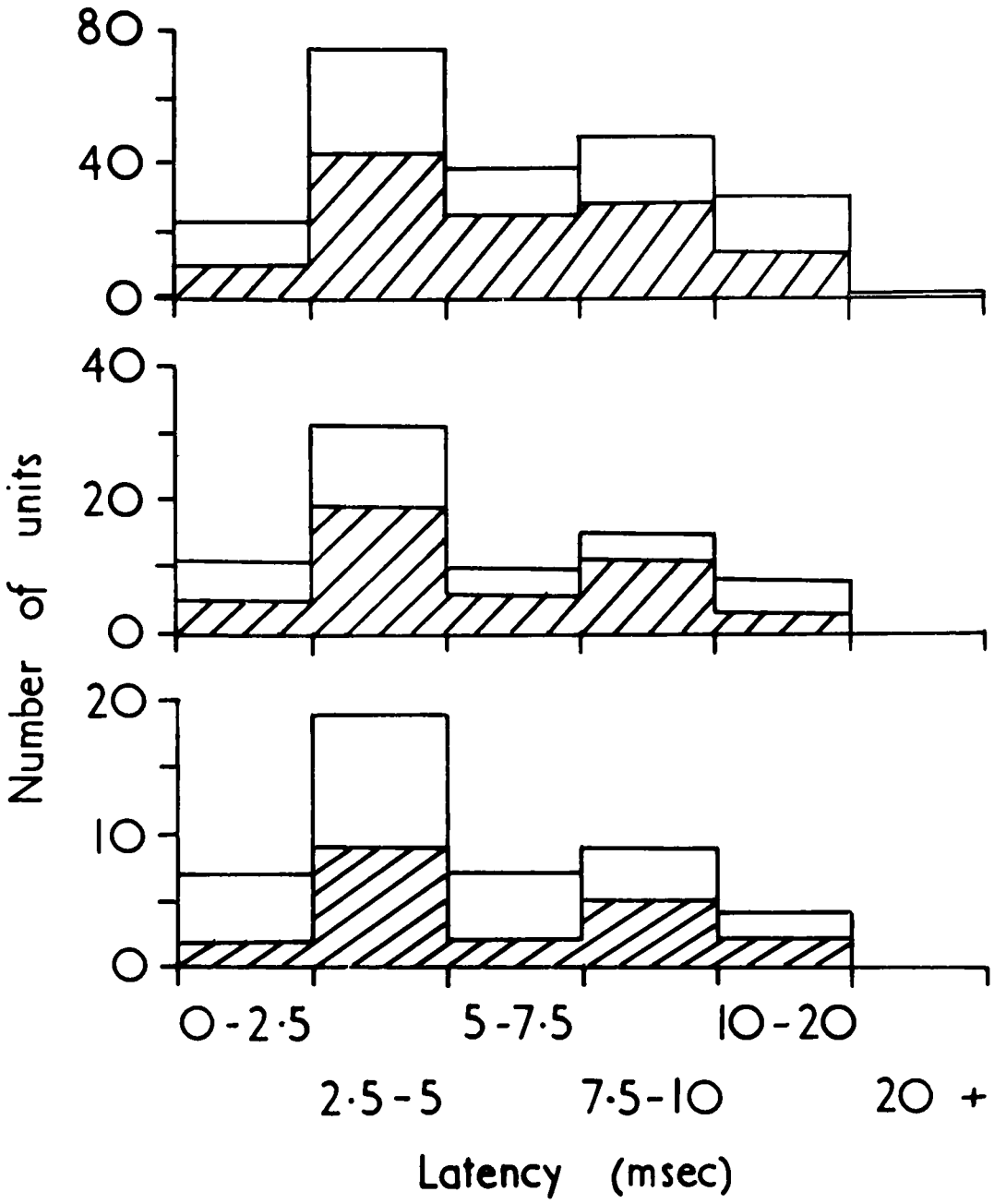

80
40
0
40
20
0
20
10
0
Number of units
0-2·5
2·5-5
5-7·5
7·5-10
10-20
20 +
Latency (msec)

Fig. 7. Histograms showing the latencies of units, recorded in the dorsal column nuclei, transynaptically activated by stimulation of the ipsilateral DLF. In cases where more than one shock was needed for activation of the unit the latency was measured with respect to the second shock. The hatched areas indicate repetitive responses.

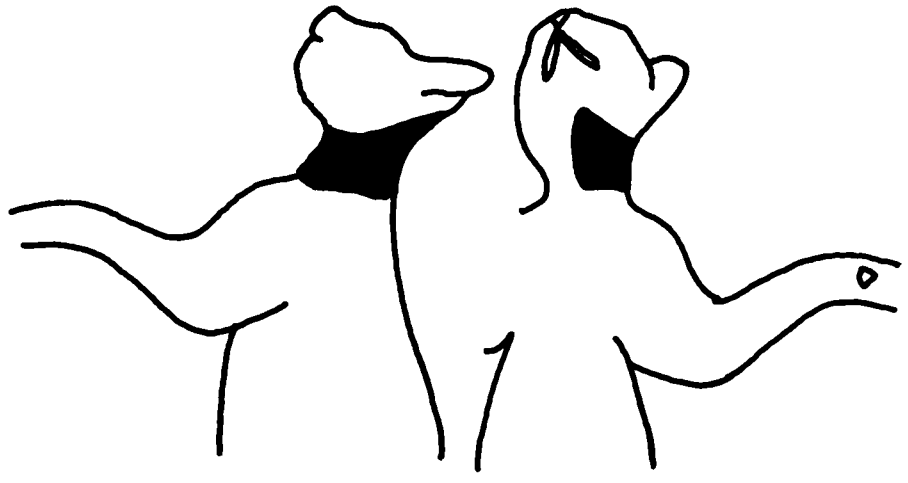
Upper:- This shows the latencies of all postsynaptic units.

Middle:- This shows the latencies of those units found to have excitatory receptive fields.

Lower:- This shows the latencies of those units found to project into the contralateral mid-brain.

The conduction distance, in all cases, was approximately 50mm.

C3



C4

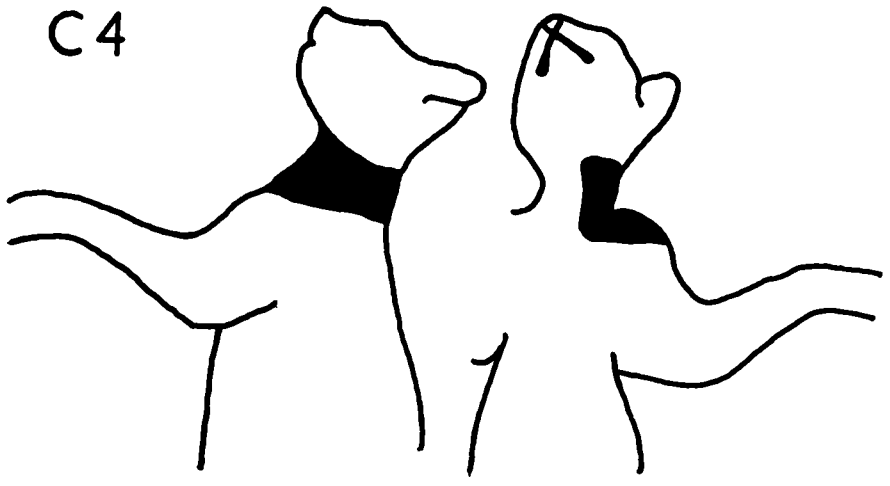


Fig. 8. Drawings taken from the paper of Hekmatpanah (1961) showing the C3 and C4 dermatomes of the cat.

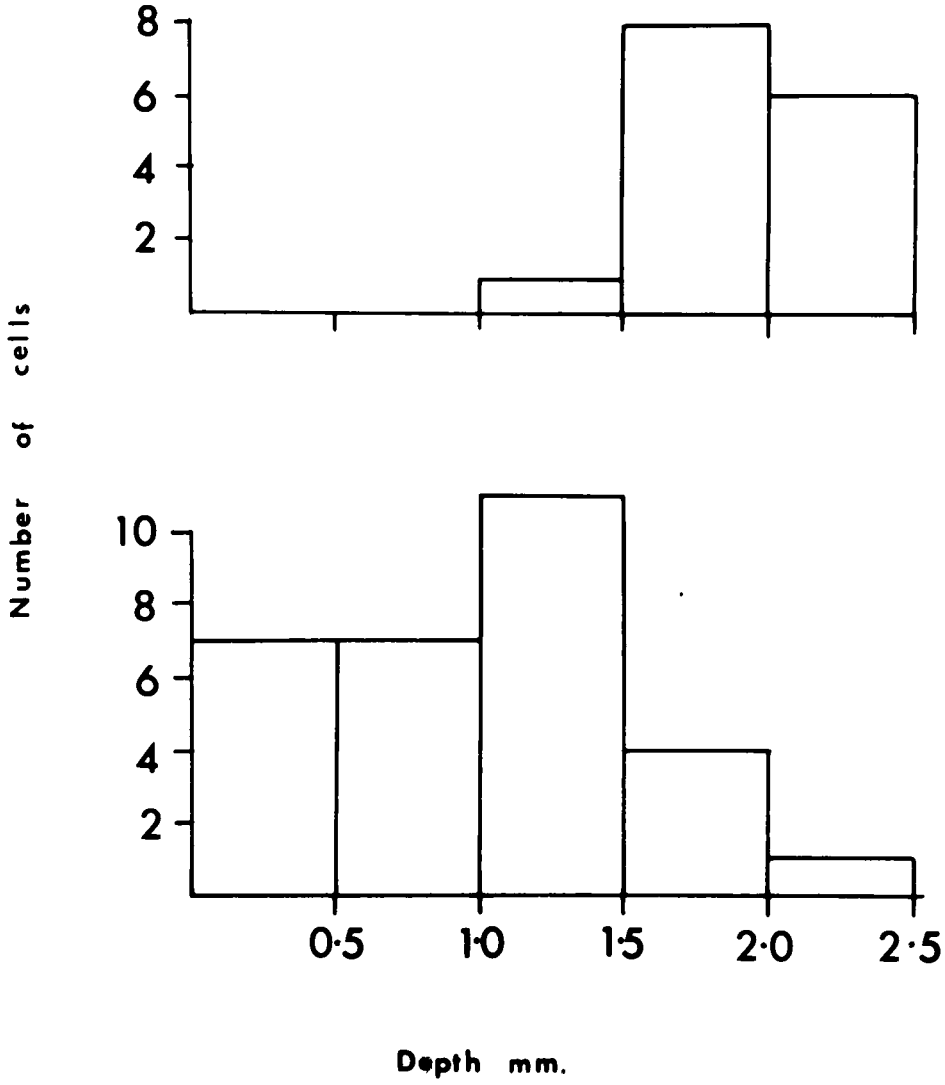

Number of cells
8
6
4
2
10
8
6
4
2
0·5
1·0
1·5
2·0
2·5
Depth mm.

Fig. 9. Upper: Histogram showing the depths, with respect to the surface of the medulla, of "noxious" cells.

Lower: Histogram showing the depths, with respect to the surface of the medulla, of "hair" and "hair and pad" cells.

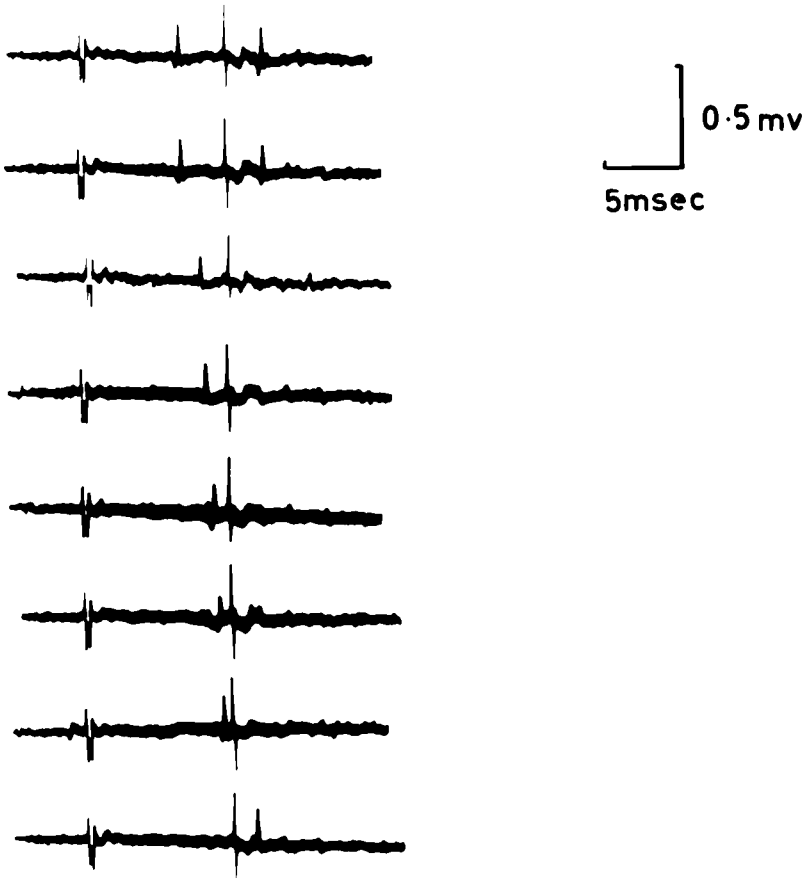

0·5 mv
5msec

Fig. 10. Traces showing "collision" for a cell projecting into the contralateral mid-brain. In each trace the shock to the ipsilateral DLF precedes the shock to the contralateral mid-brain. When the impulse produced by the DLF shock falls within the critical cancelling interval the impulse produced by the mid-brain shock fails to appear.

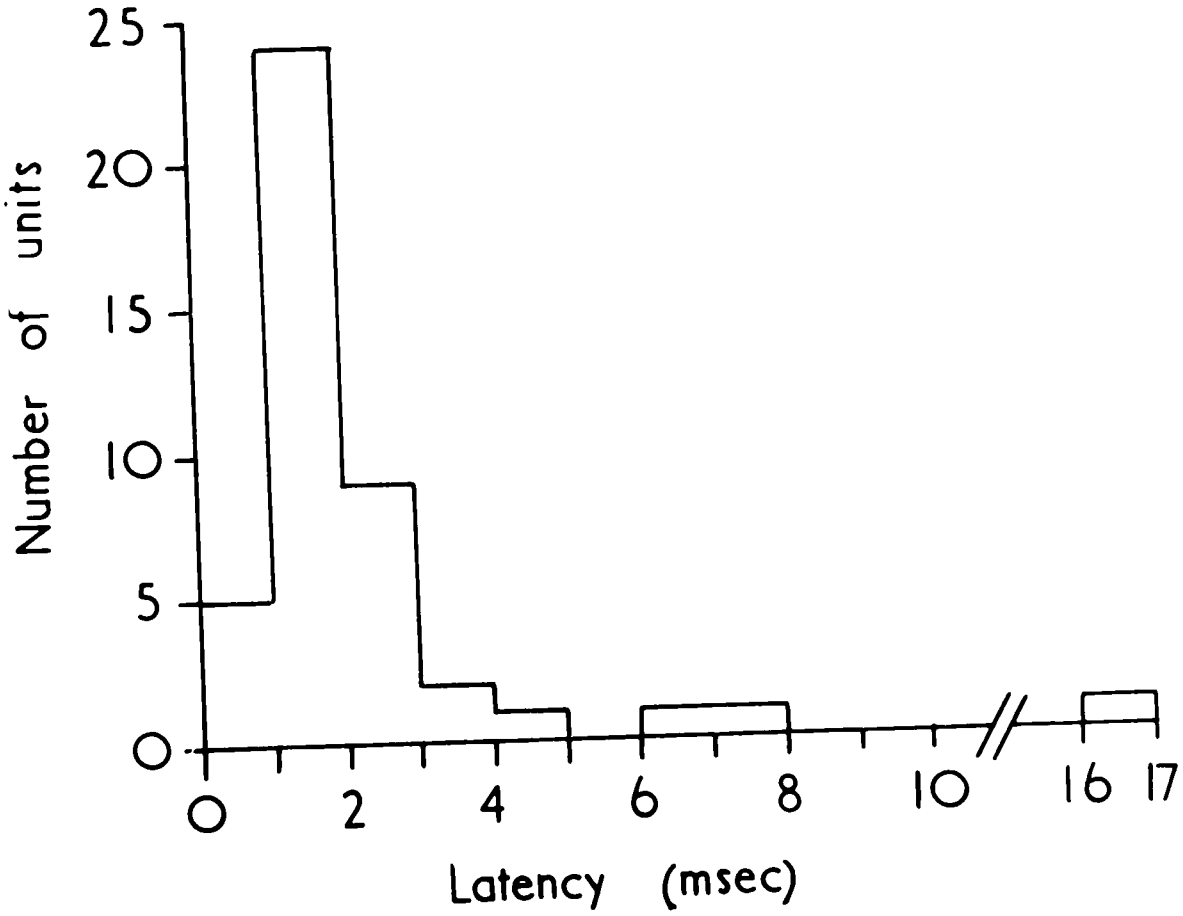

Number of units
25
20
15
10
5
0
0
2
4
6
8
10
16
17
Latency (msec)

Fig. 11. Histogram of the antidromic latencies of units shown to project into the contralateral mid-brain.

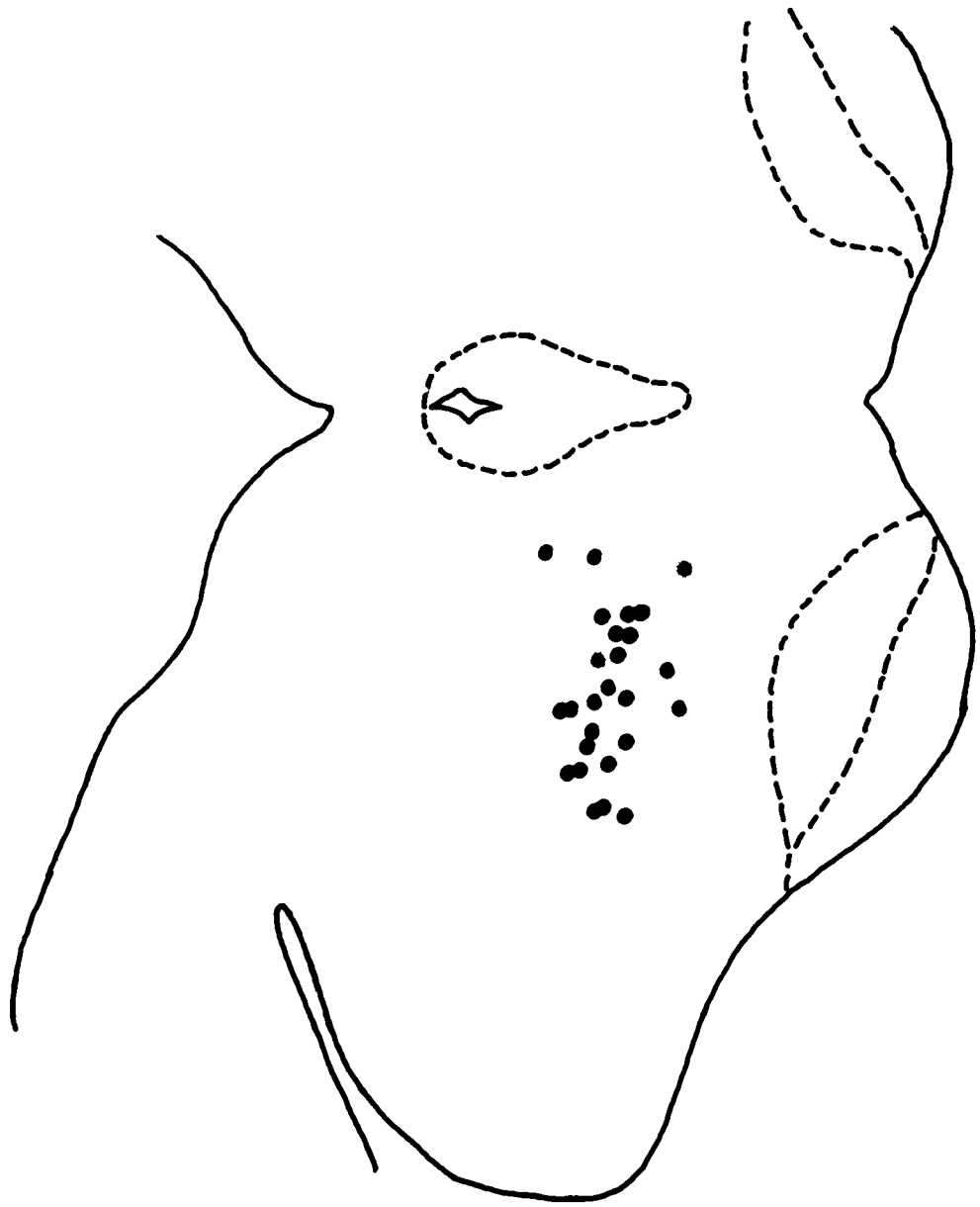


Fig. 12. Sites, at A4.5, from which axons of projecting dorsal column nuclei cells could be activated at minimum thresholds.

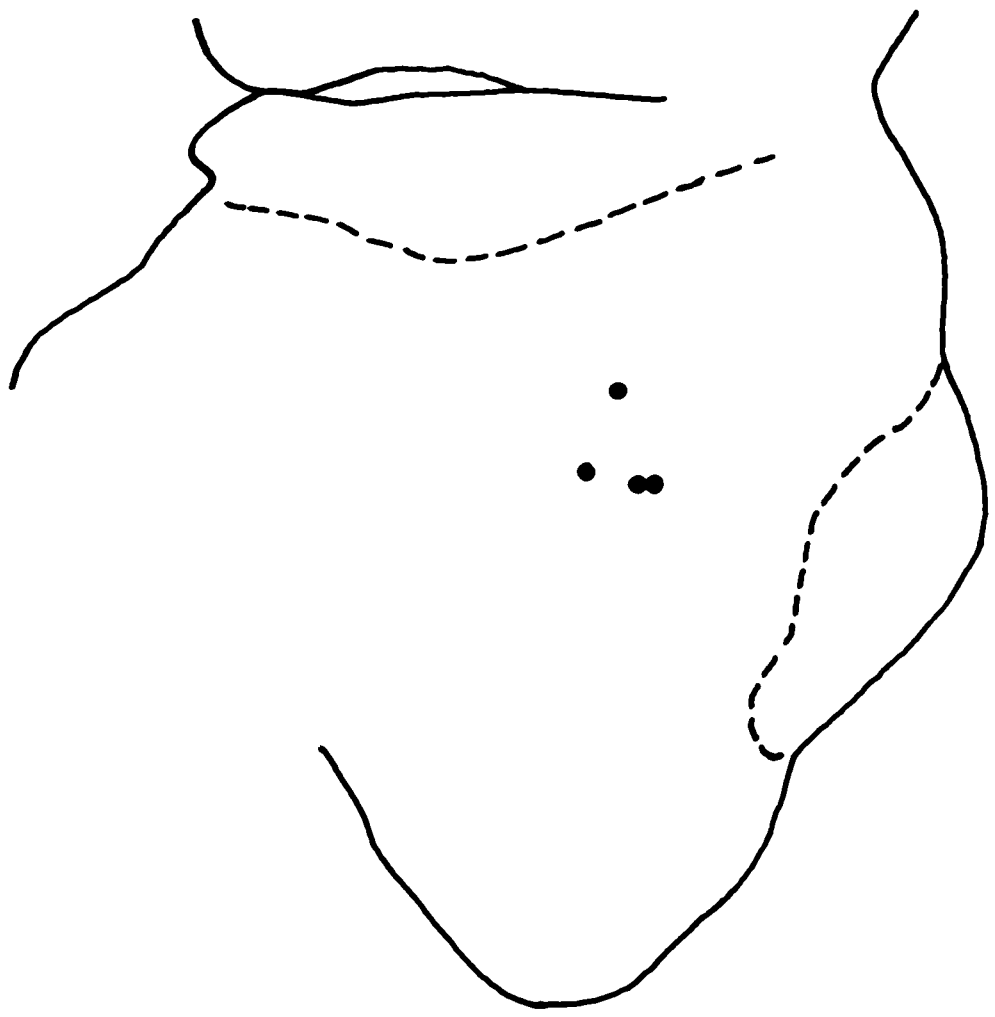


Fig. 13. Sites, at A6.0, from which axons of projecting dorsal column nuclei cells could be activated at minimum thresholds.

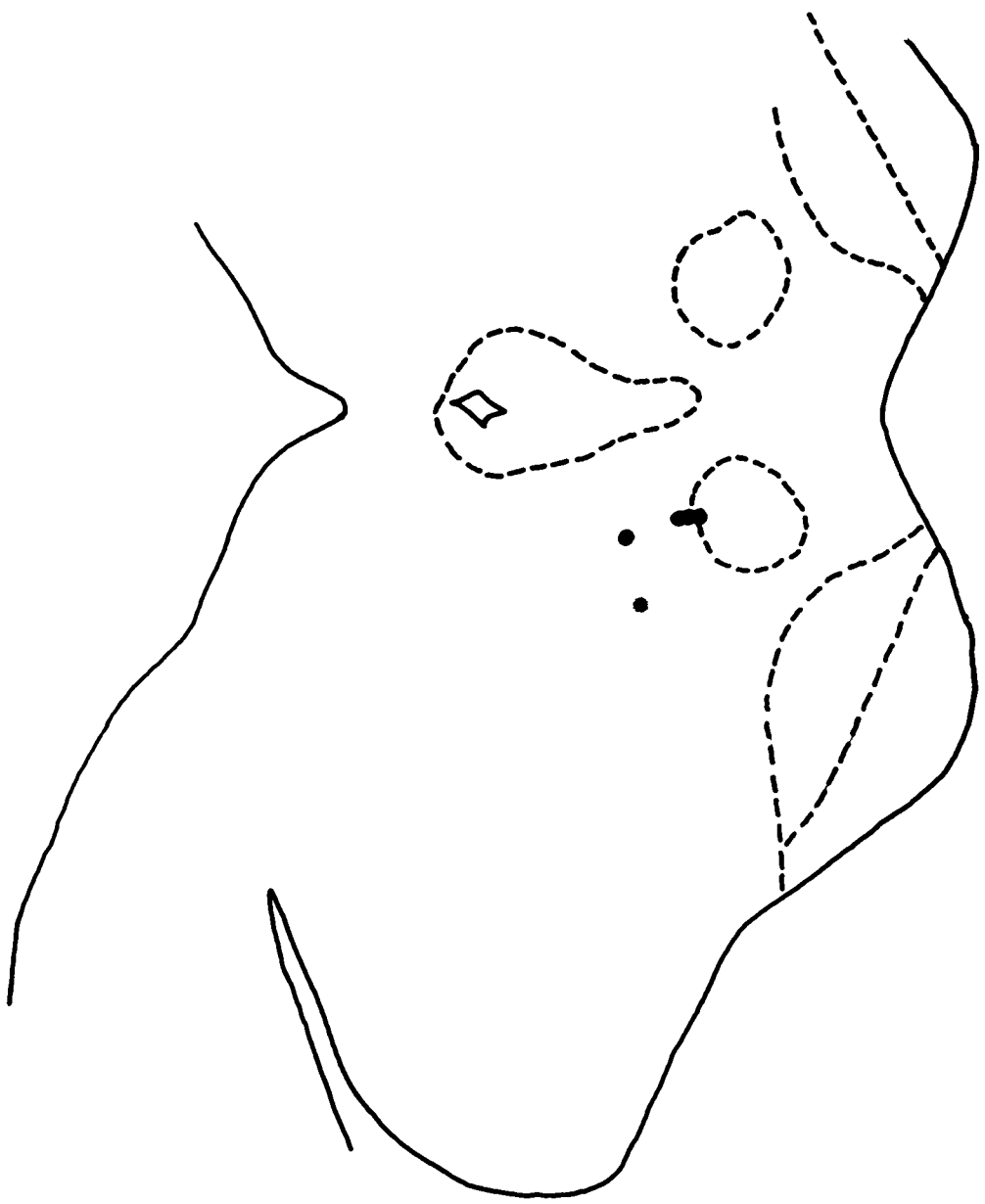
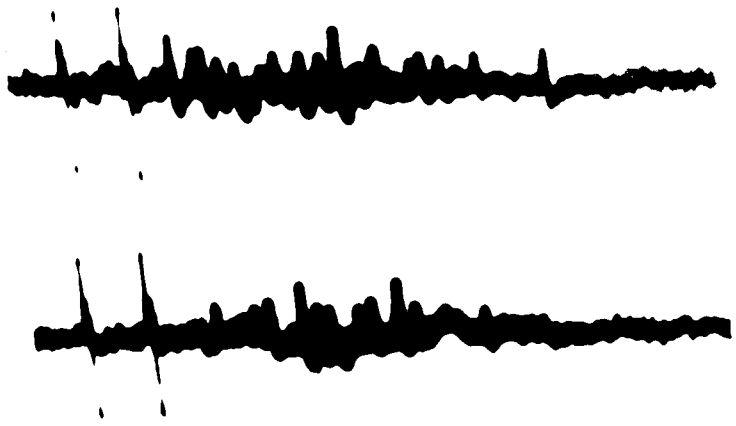
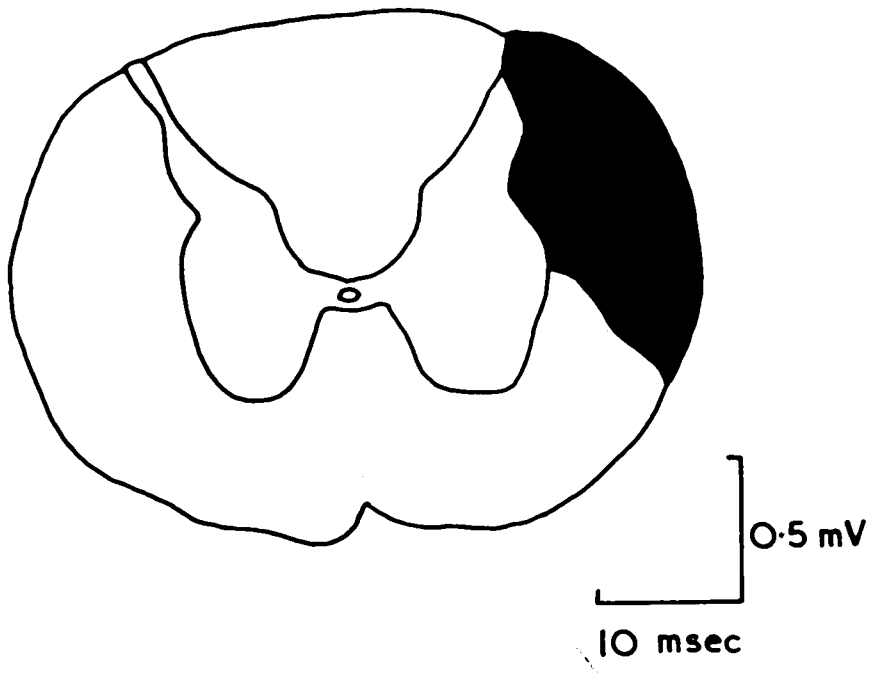


Fig. 14. Sites, at 14.5, from which dorsal column nuclei cells were activated transynaptically with minimum thresholds.

S S





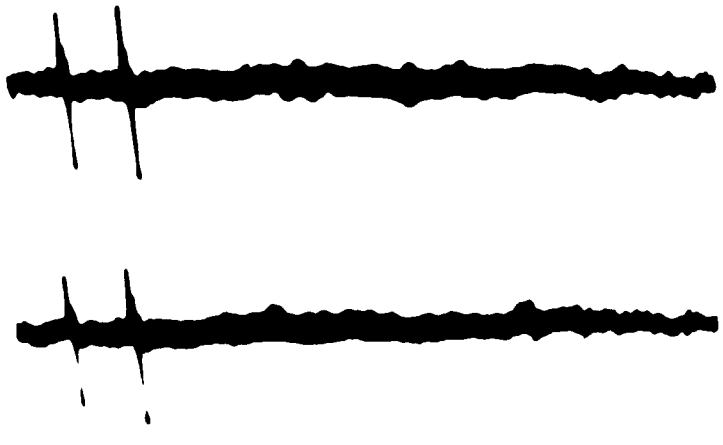


Fig. 15. The upper two traces show a small group of cells being activated by a twin shock applied to the DLF caudal to a transection of the dorsal columns. The lower two traces were obtained, without intervening movement of the recording electrode, after a transection of the ipsilateral DLF at C3. The same stimulus parameters were used in all traces. The extent of the transection is shown in the accompanying drawing.

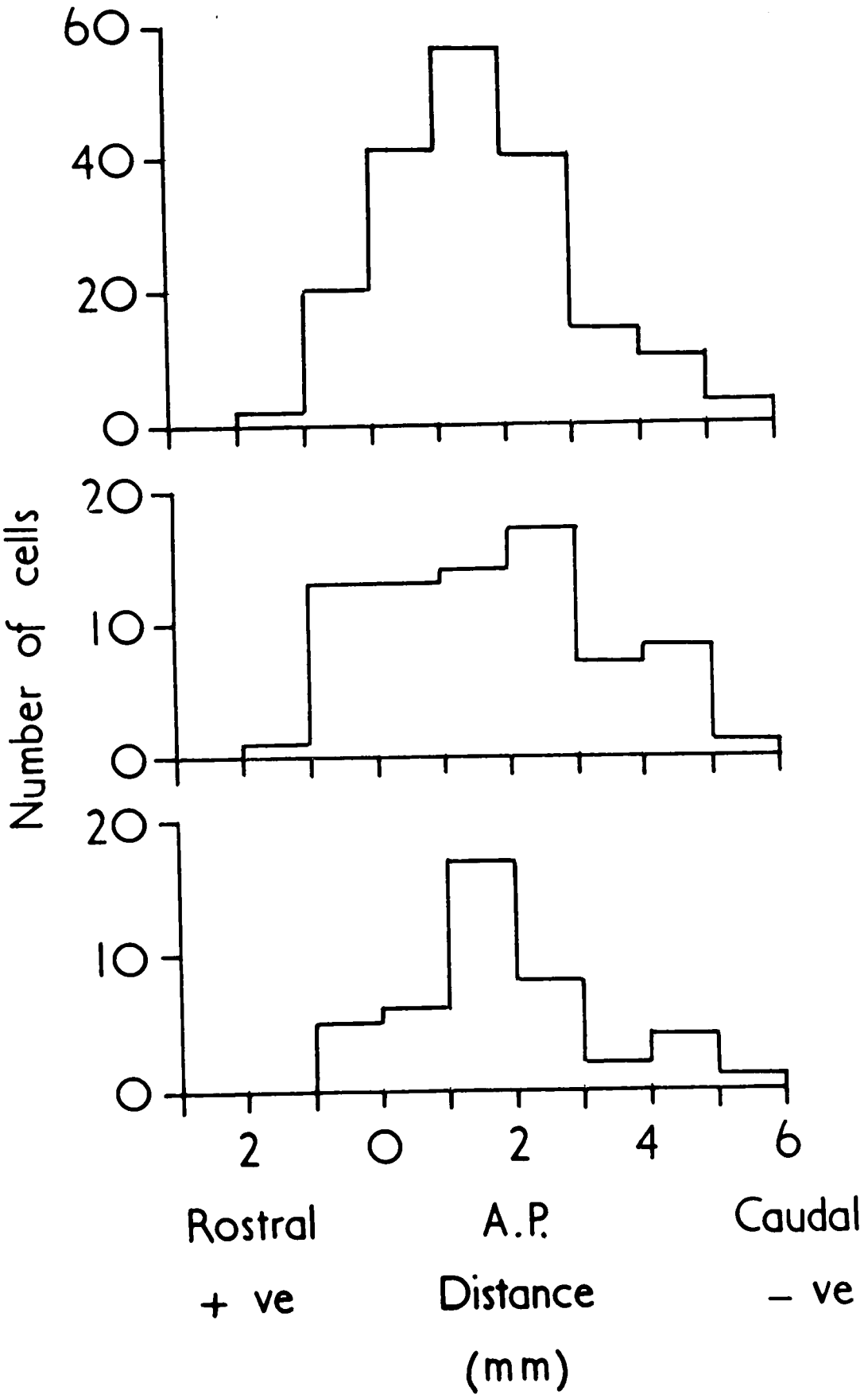

60
40
20
0
20
10
0
Number of cells
20
10
0
2
0
2
4
6
Rostral
+ ve
A.P.
Distance
(mm)
Caudal
– ve

Fig. 16. Upper:- Histogram showing the rostro-caudal positions of all cells transynaptically activated by stimulation of the DLF.

Middle:- Histogram showing the rostro-caudal positions of cells found to have excitatory receptive fields.

Lower:- Histogram showing the rostro-caudal positions of cells found to project into the contralateral mid-brain.

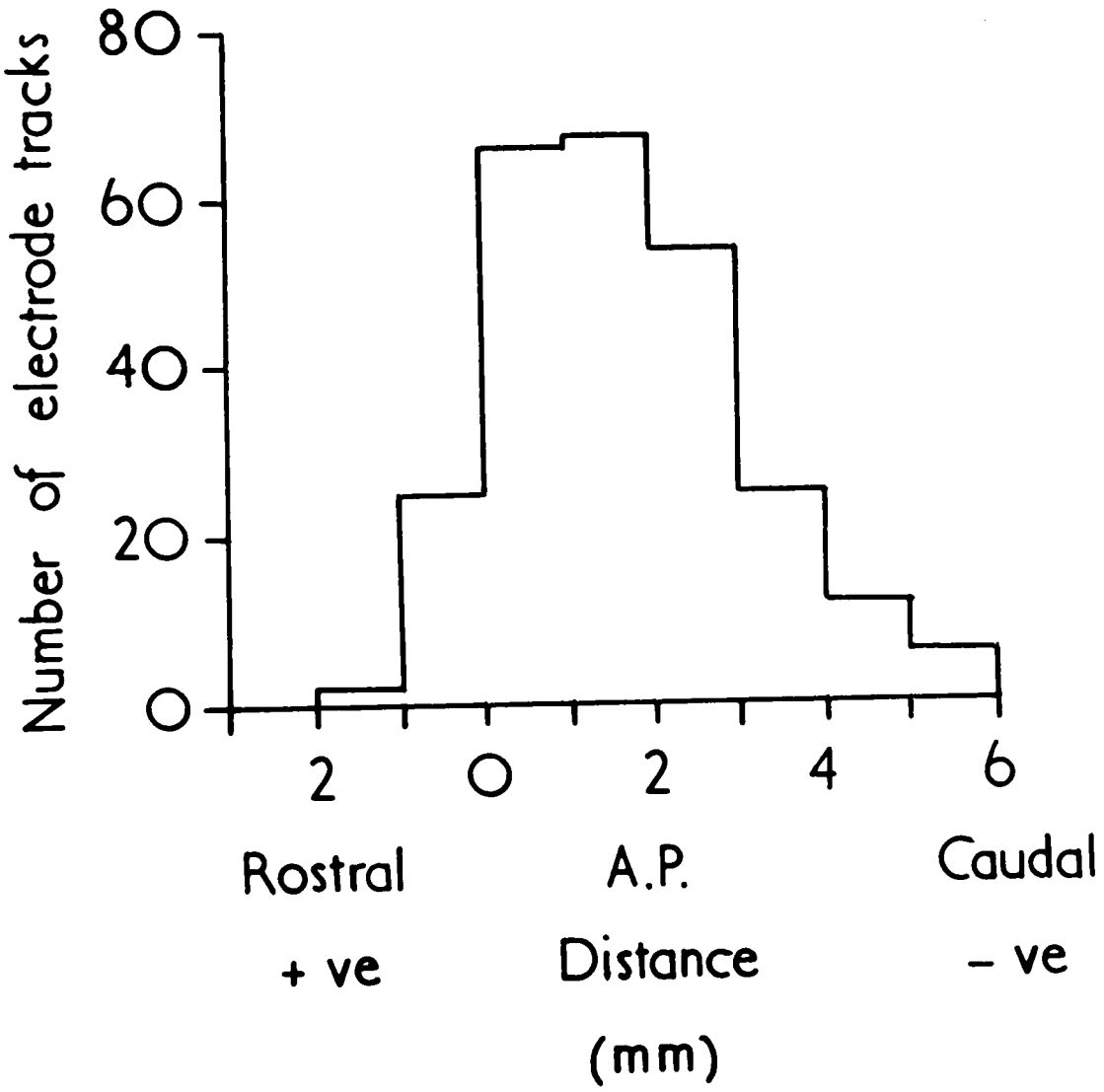

Number of electrode tracks
80
60
40
20
0
2
0
2
4
6
Rostral
+ ve
A.P.
Distance
(mm)
Caudal
– ve

Fig. 17. Histogram showing the rostro-caudal locations of electrode penetrations made in the dorsal column nuclei.

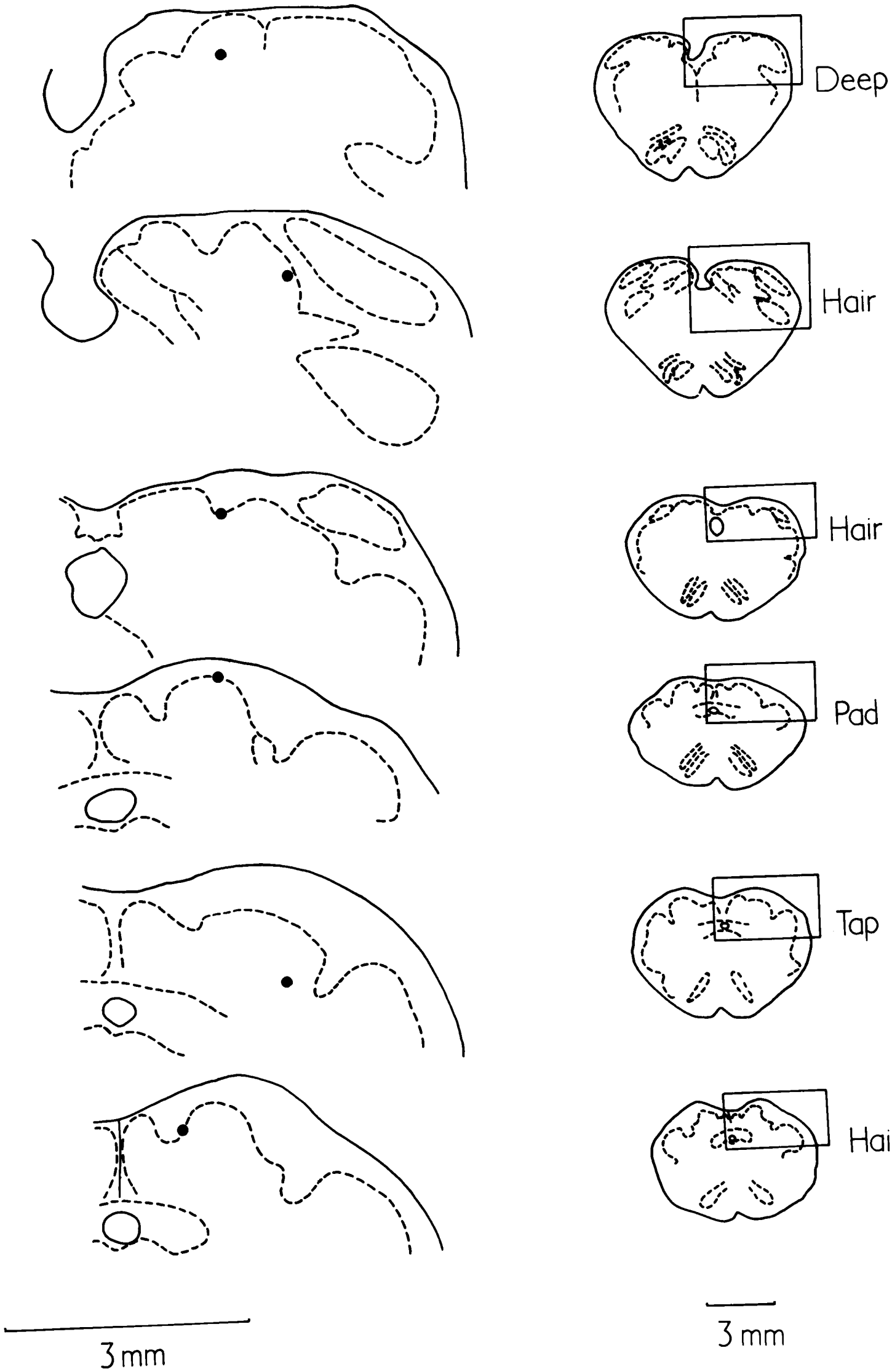

Deep
Hair
Hair
Pad
Tap
Hair
3 mm
3 mm

Fig. 13. Drawings of transverse medulla sections showing lesion sites marking the positions of cells responding transynaptically to stimulation of the DLF and found to project into the contralateral mid-brain. Each black spot marks the position of one cell. The receptive field type of each cell is indicated.

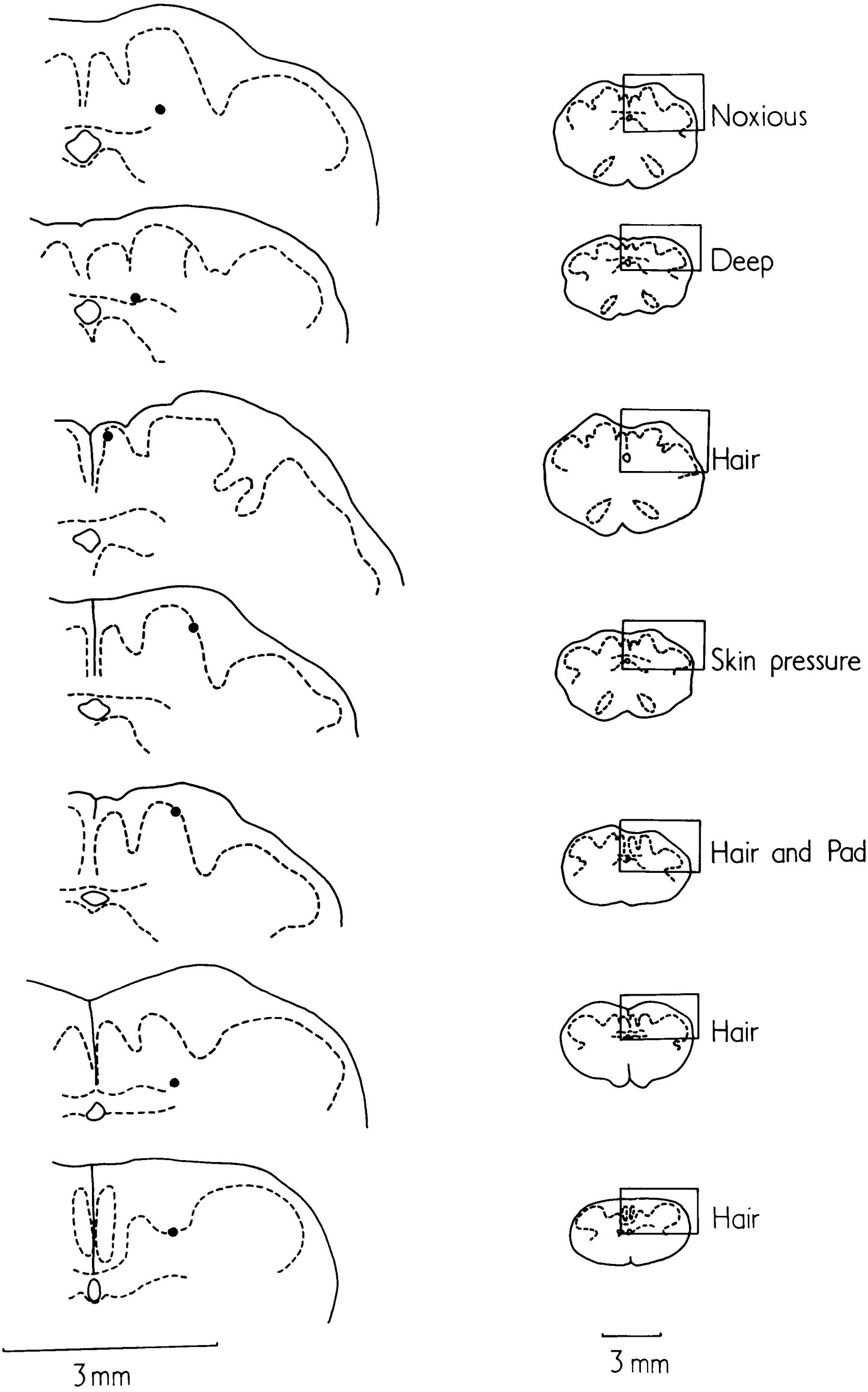
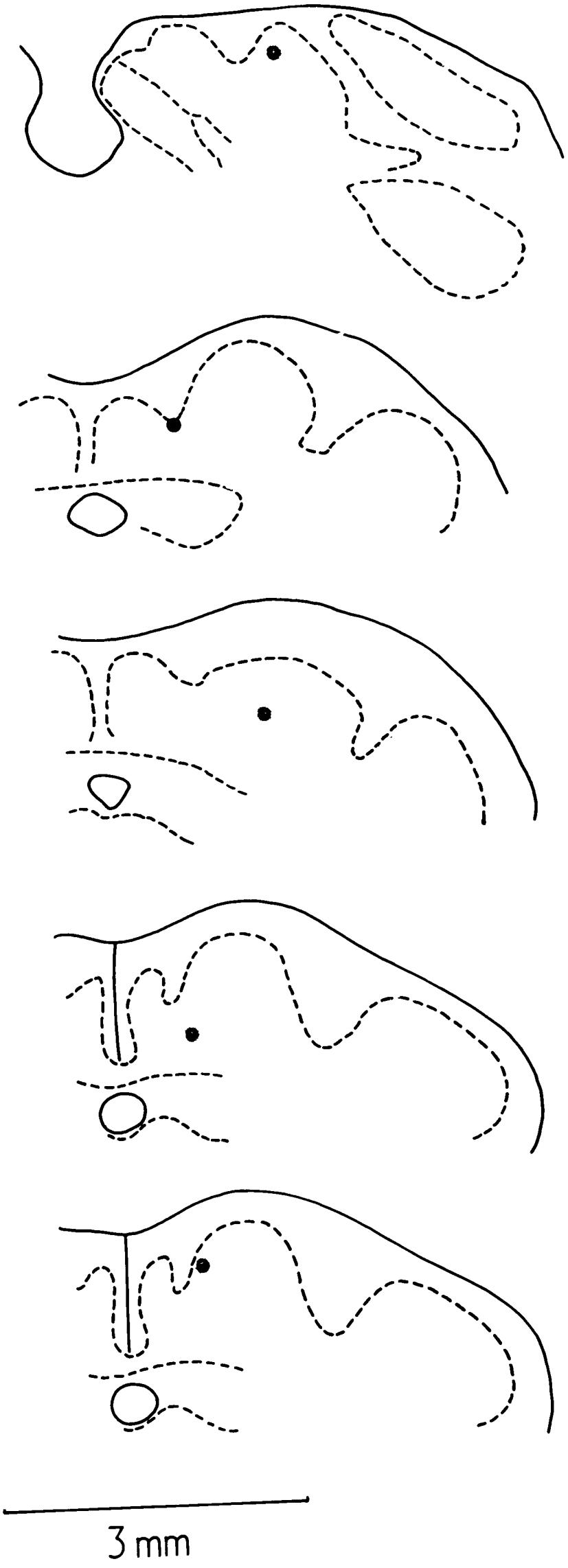

Noxious
Deep
Hair
Skin pressure
Hair and Pad
Hair
Hair
3 mm
3 mm

Fig. 19. Drawings of transverse medulla sections showing lesion sites marking the positions of cells responding transynaptically to stimulation of the DLF and found to project into the contralateral mid-brain. Each black spot marks the position of one cell. The receptive field type of each cell is indicated.


3 mm

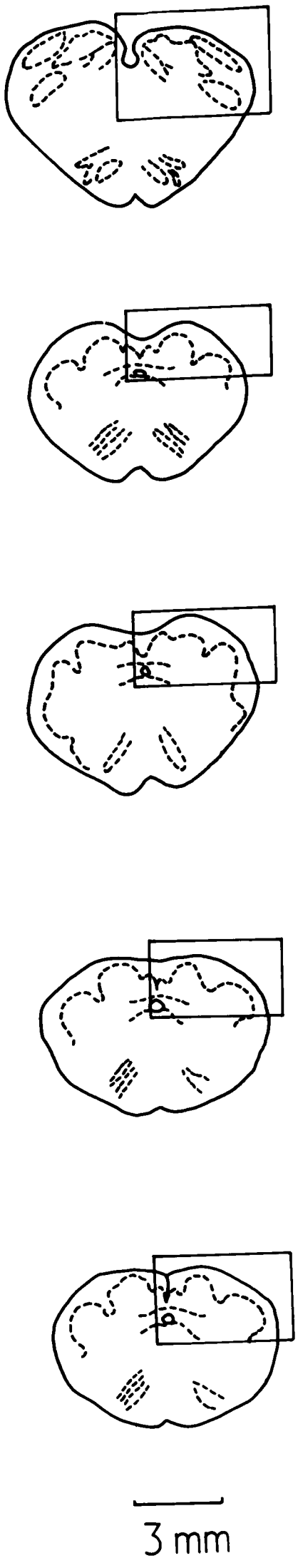

3 mm

Fig. 20. Drawings of transverse medulla sections showing lesion sites marking the positions of cells responding transynaptically to stimulation of the DLF and found to project into the contralateral mid-brain. Each black spot marks the position of one cell. Excitatory receptive fields were not found for any of these cells.

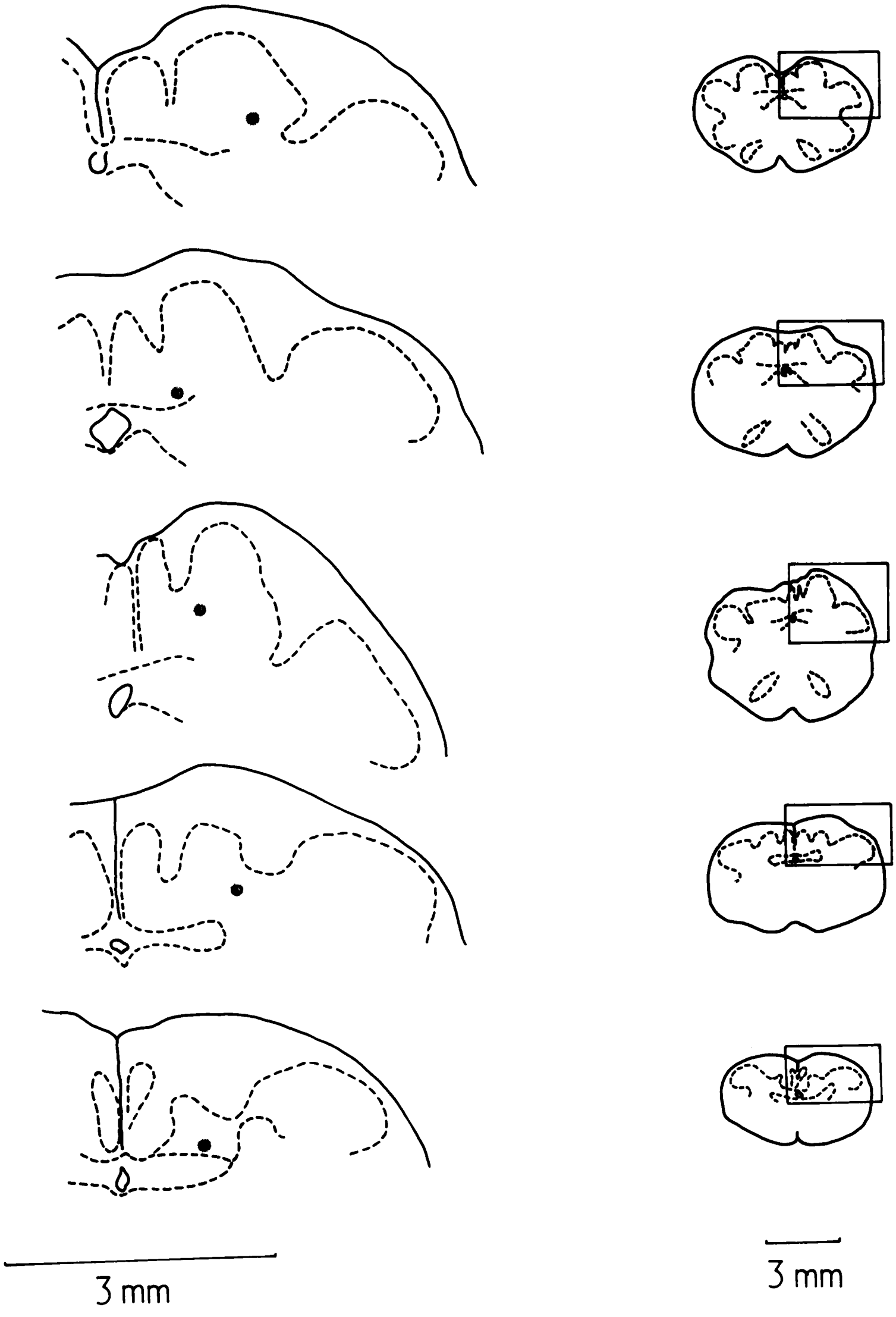
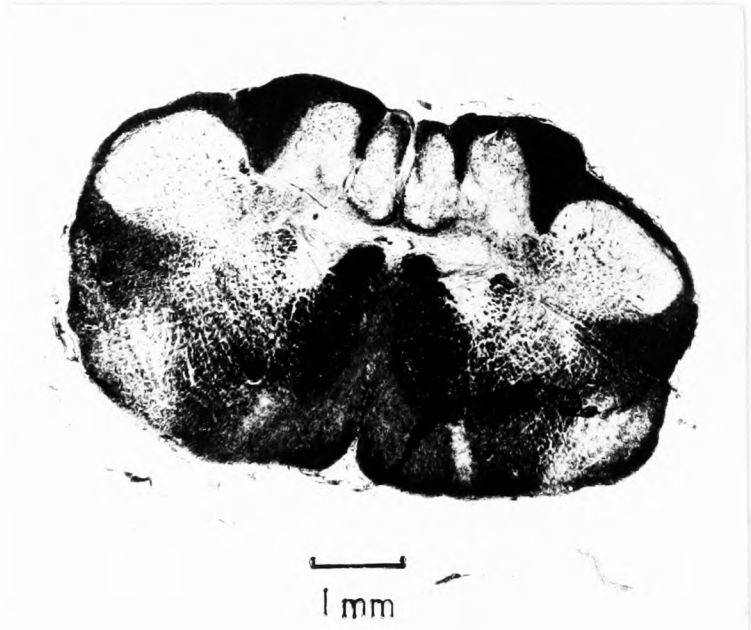

3 mm
3 mm

Fig. 21. Drawings of transverse medulla sections showing lesion sites marking the positions of cells responding transynaptically to stimulation of the DLF and found to project into the contralateral mid-brain. Each black spot marks the position of one cell. Excitatory receptive fields were not found for any of these cells.


1 mm

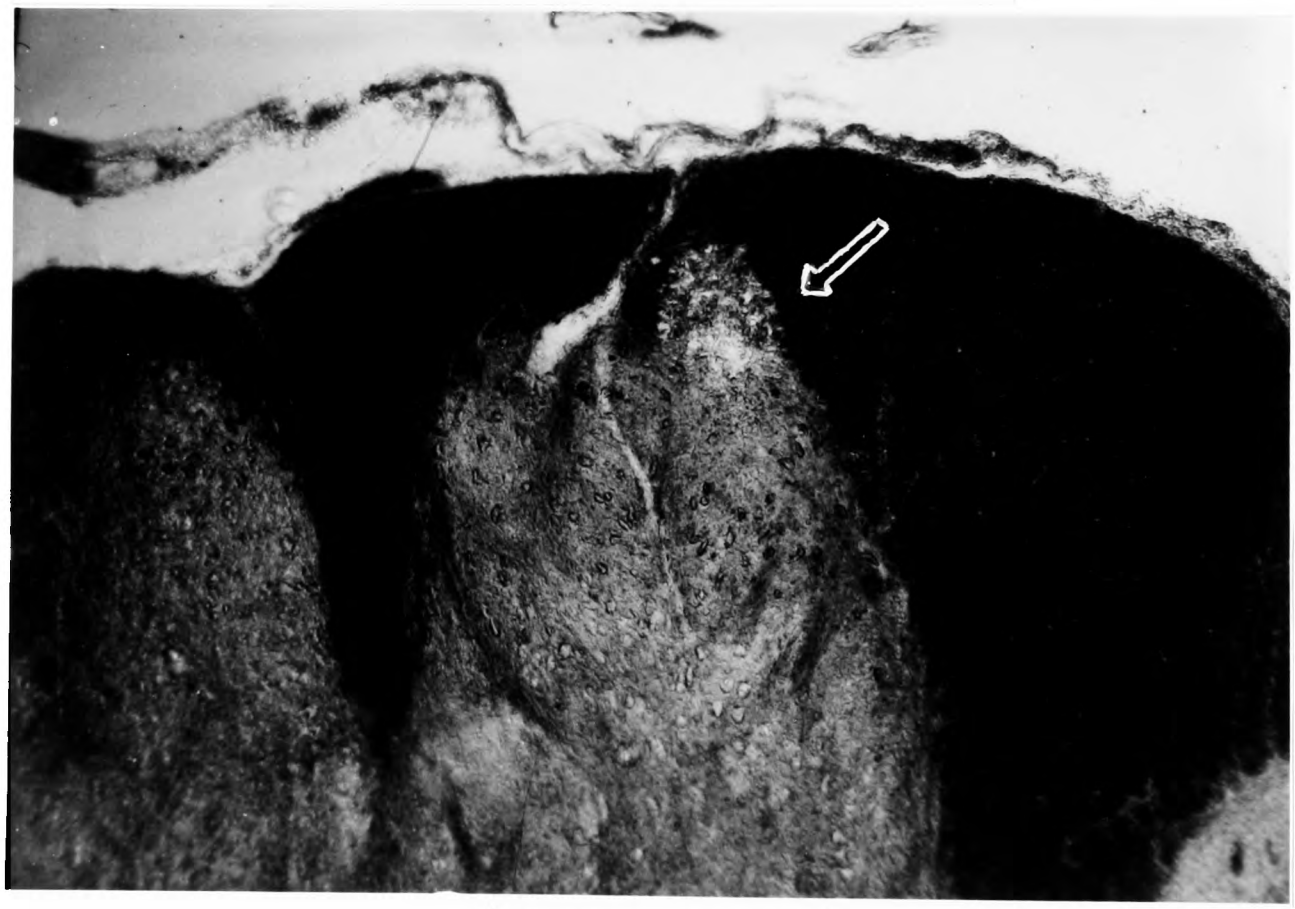

0·5 mm

Fig. 22. Photomicrographs of a transverse section of the medulla showing an electrolytic lesion marking the position of a cell transynaptically activated by stimulation of the DLF. Both photomicrographs are of the same section; the lesion site is indicated by an arrow in the higher magnification (lower) picture.

Stain - Weil's haematoxylin.

Section thickness - 50μ.

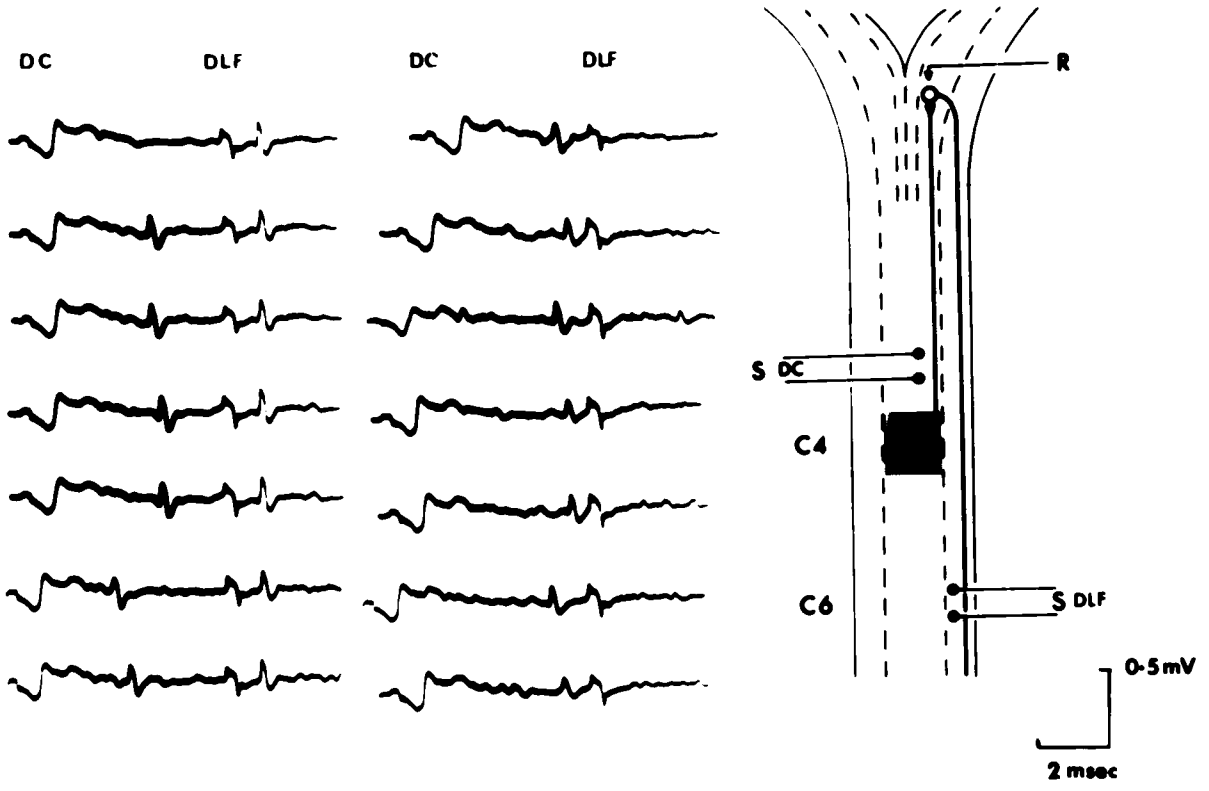

DC
DLF
DC
DLF
R
S DC
C4
C6
S DLF
0·5mV
2 msec

Fig. 23. Traces showing "collision" for a cell (cell 1) projecting into the ipsilateral DLF. In each trace the shock applied to the dorsal columns (DC) precedes the shock applied to the DLF. The impulse produced in response to the DLF shock fails to appear when the impulse produced by the shock to the dorsal columns falls within the critical cancelling interval. The beam intensity declined somewhat, in all sweeps, from left to right.

The accompanying diagram illustrates the experimental arrangement and the proposed neuronal connections. The conduction distance from the dorsal column nuclei to C6 was approximately 50cm.

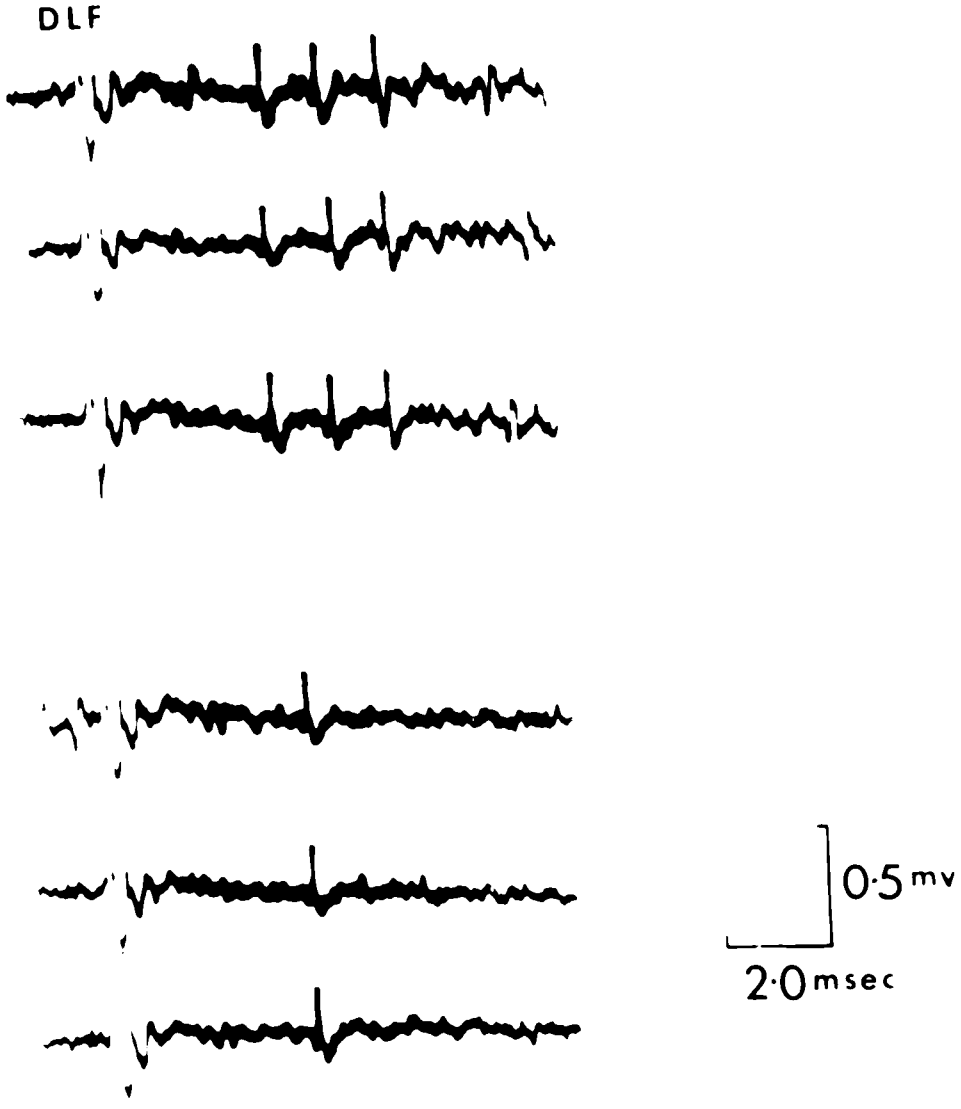

DLF
V
V
I
0·5 mv
2·0 msec

Fig. 24. Cell 3.

Upper three traces:- responses to a DLF stimulus at a repetition frequency of 2/sec.

Lower three traces:- response to a DLF stimulus at a repetition frequency of 50/sec.

For explanation see text (p. 98).

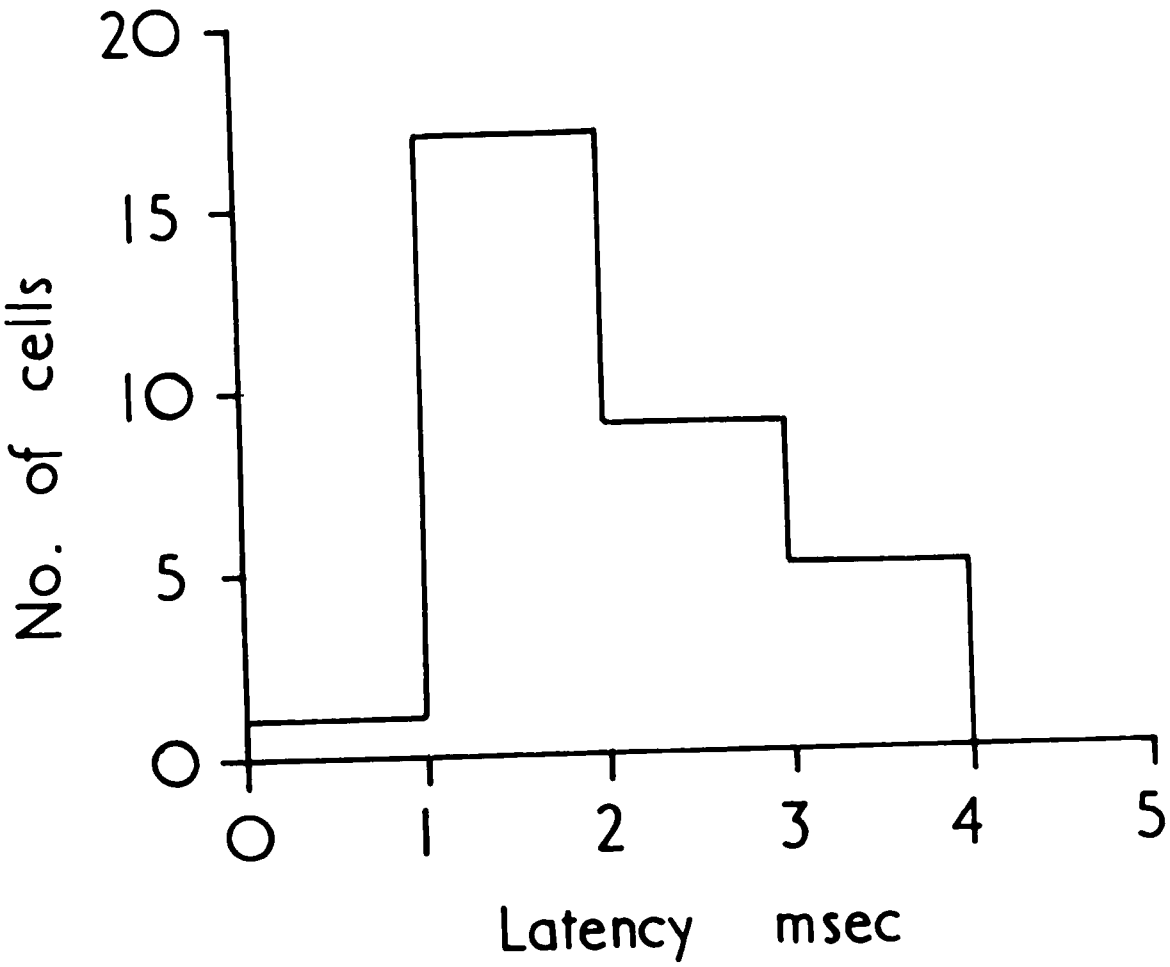

20
15
10
5
0
No. of cells
0
1
2
3
4
5
Latency msec

Fig. 25. Histogram showing the latencies of cells antidromically activated by stimulation of the ipsilateral DLF. The conduction distance was approximately 50mm in all cases.

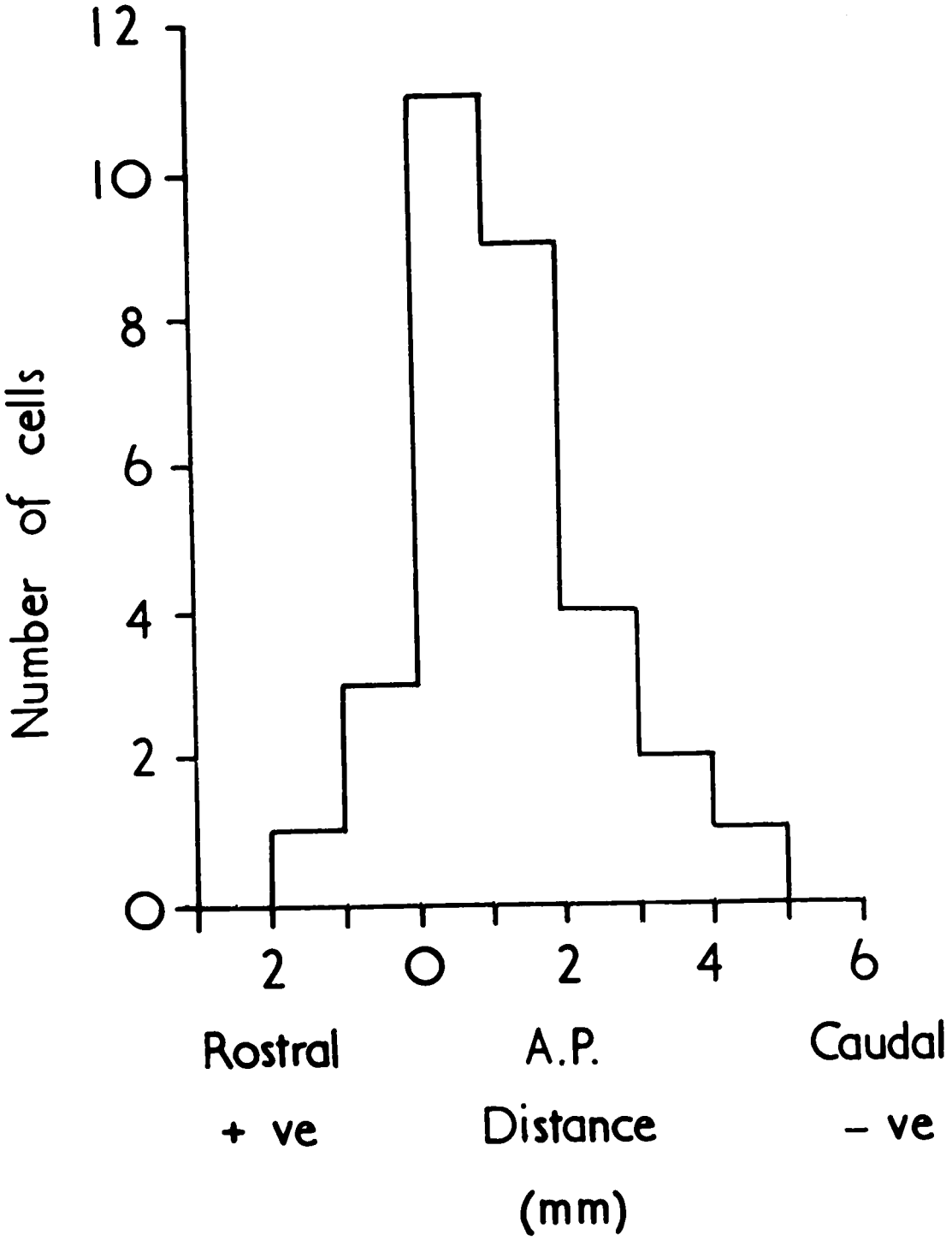
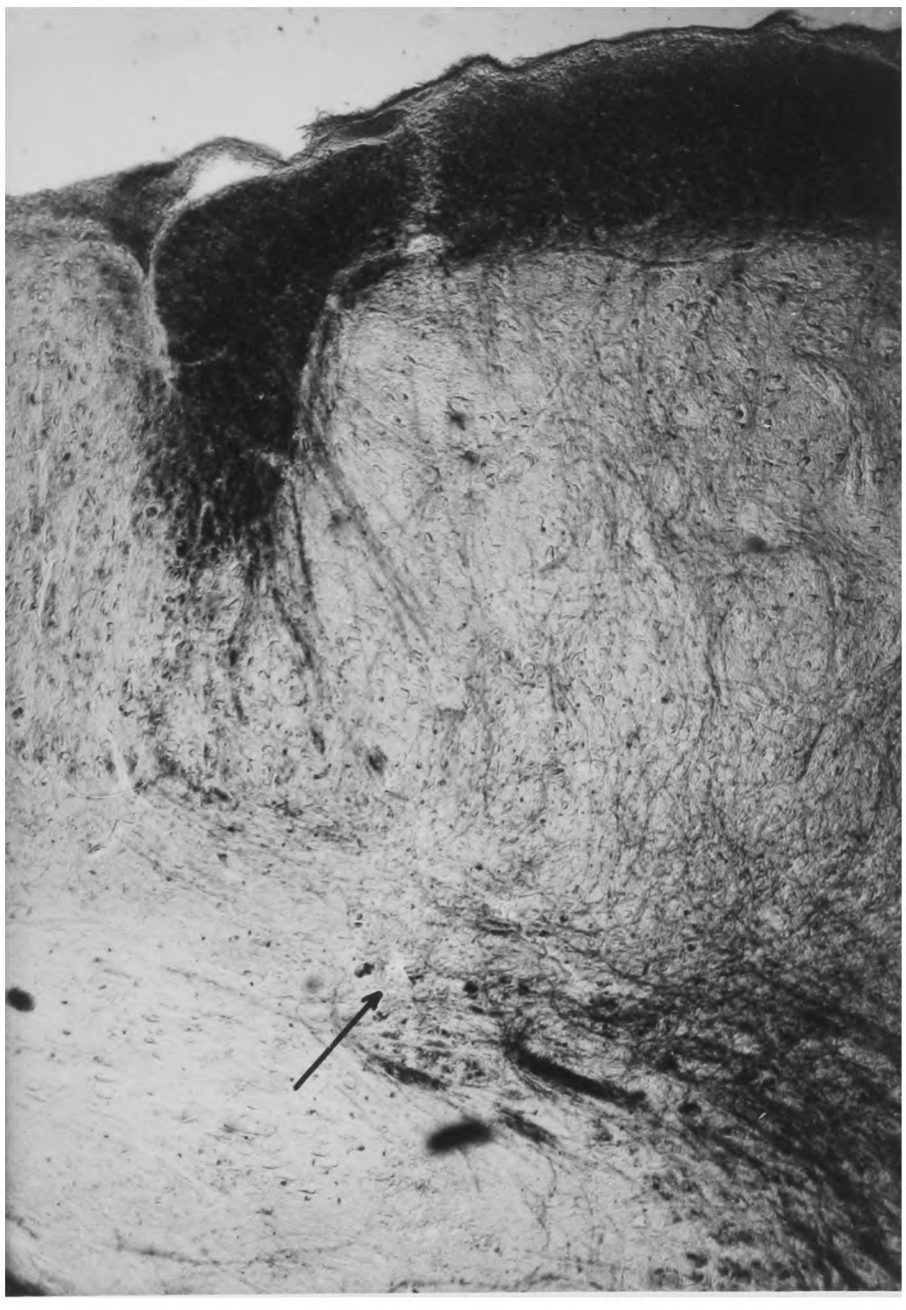

Number of cells
12
10
8
6
4
2
0
2
0
2
4
6
Rostral
+ ve
A.P.
Distance
(mm)
Caudal
– ve

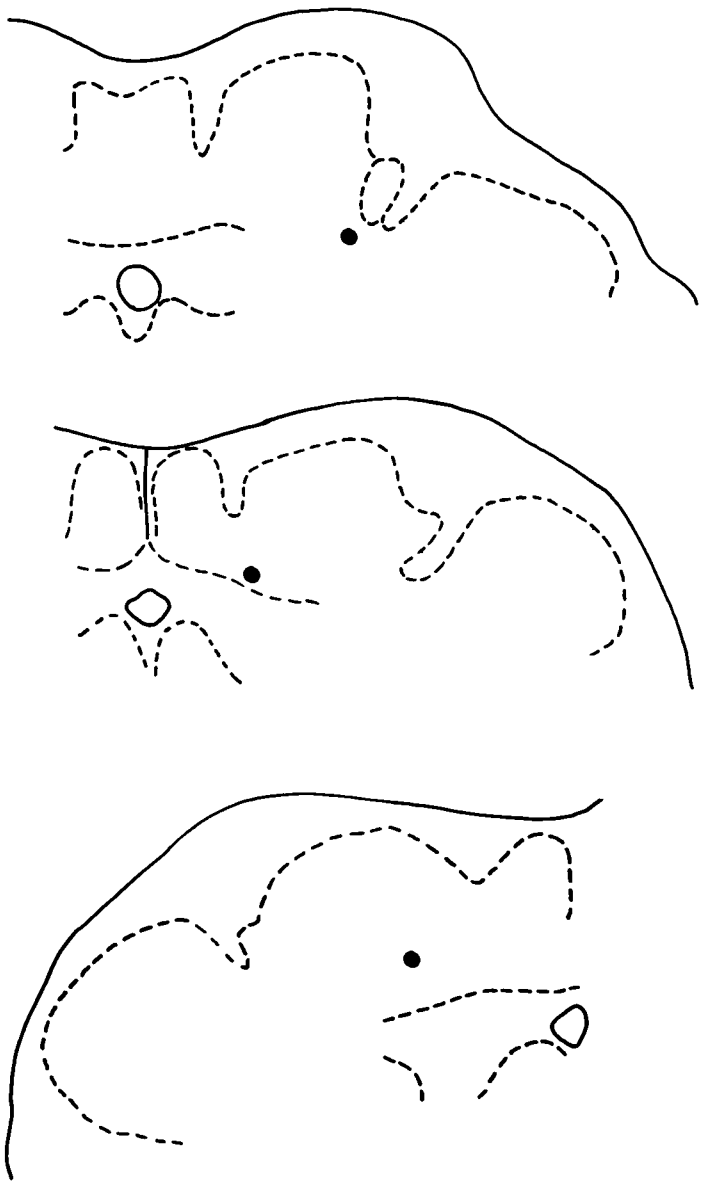
Fig. 26. Histogram showing the rostro-caudal locations of cells which project into the ipsilateral DLN.

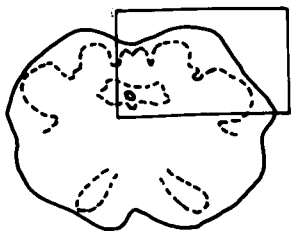


0·5 mm

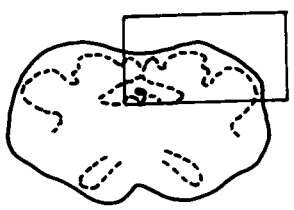
Fig. 27. Photomicrograph of a transverse section of the medulla showing an electrolytic lesion marking the position of a cell projecting into the ipsilateral DLF (cell 2). The lesion is indicated by the arrow.

Stain - Weil's haematoxylin.
Section thickness - 50μ.

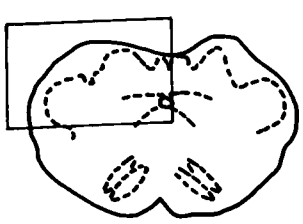




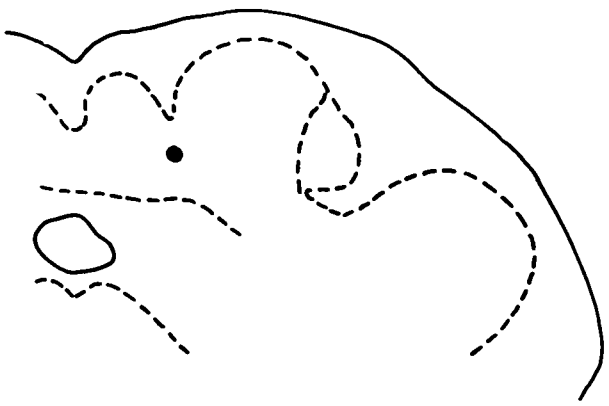
Cell 1

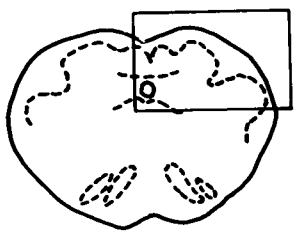


Cell 2



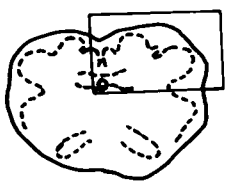
Cell 3



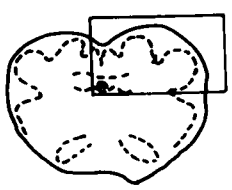


Cell 4









3 mm

3 mm

Fig. 28. Drawings of transverse medulla sections showing lesion sites marking the positions of cells found to project into the ipsilateral DLF. Each black spot marks the position of one cell.

OX1

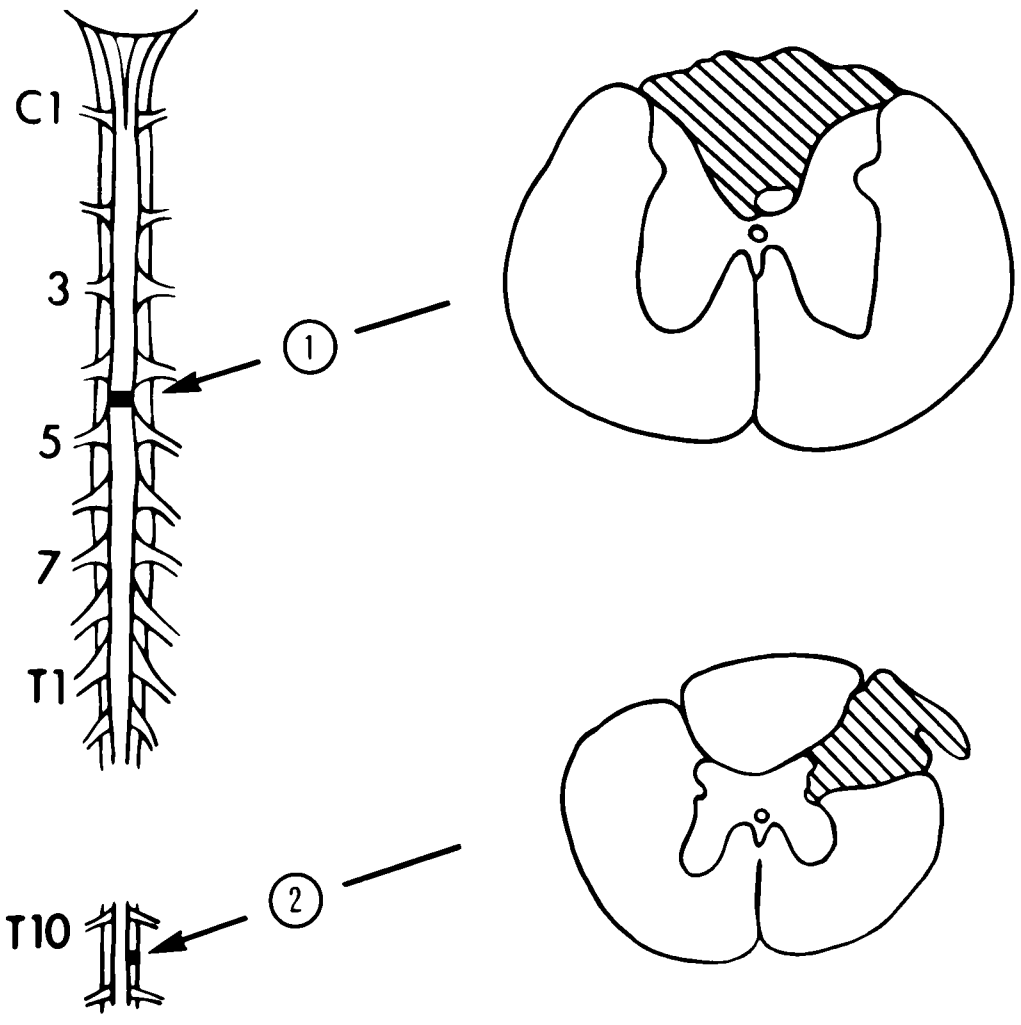


Fig. 29. Diagrams showing the sites and extent of lesions of the dorsal columns (1) and the dorsolateral funiculus (2) in the anatomical experiment DX1.

OX2

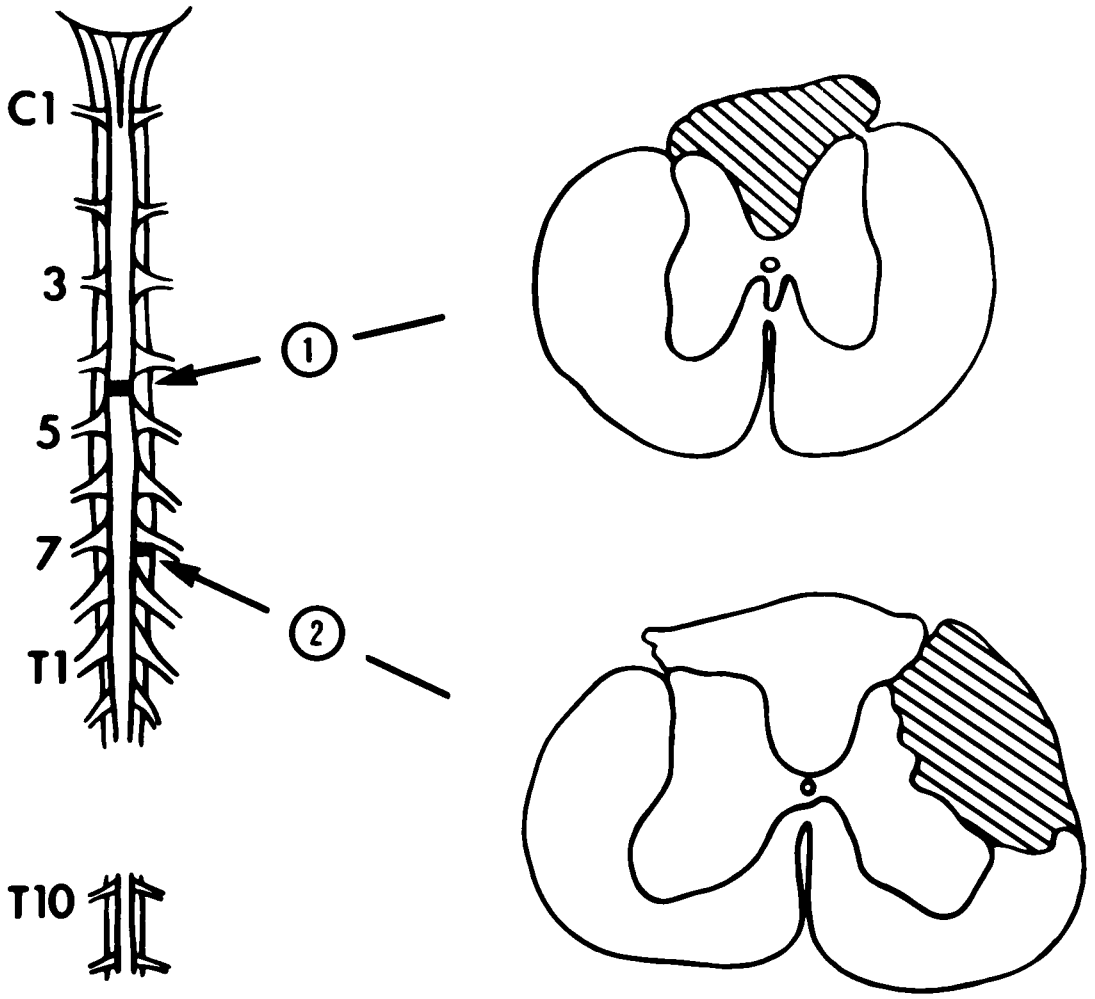
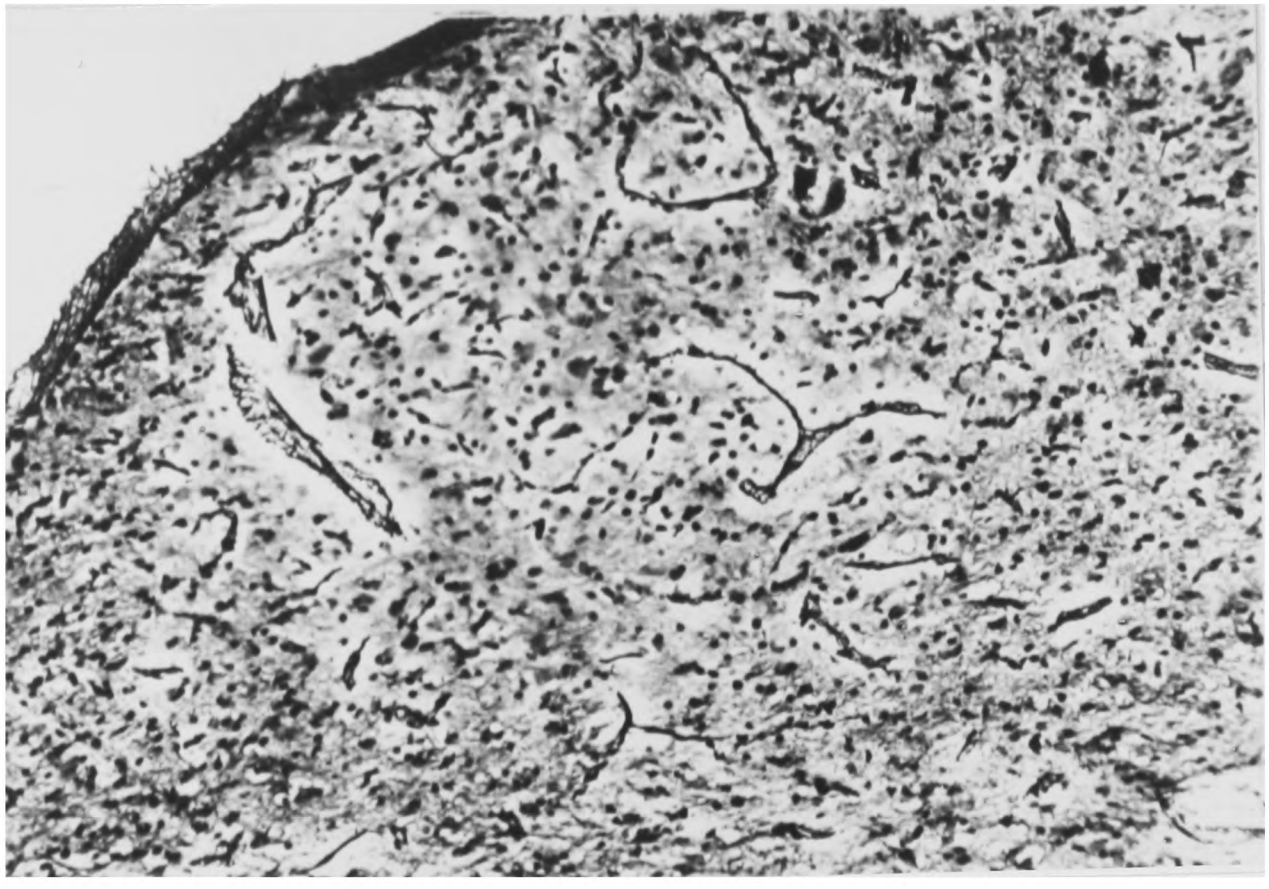


Fig. 30. Diagrams showing the sites and extent of lesions of the dorsal columns (1) and the dorsolateral funiculus (2) in the anatomical experiment OX2.



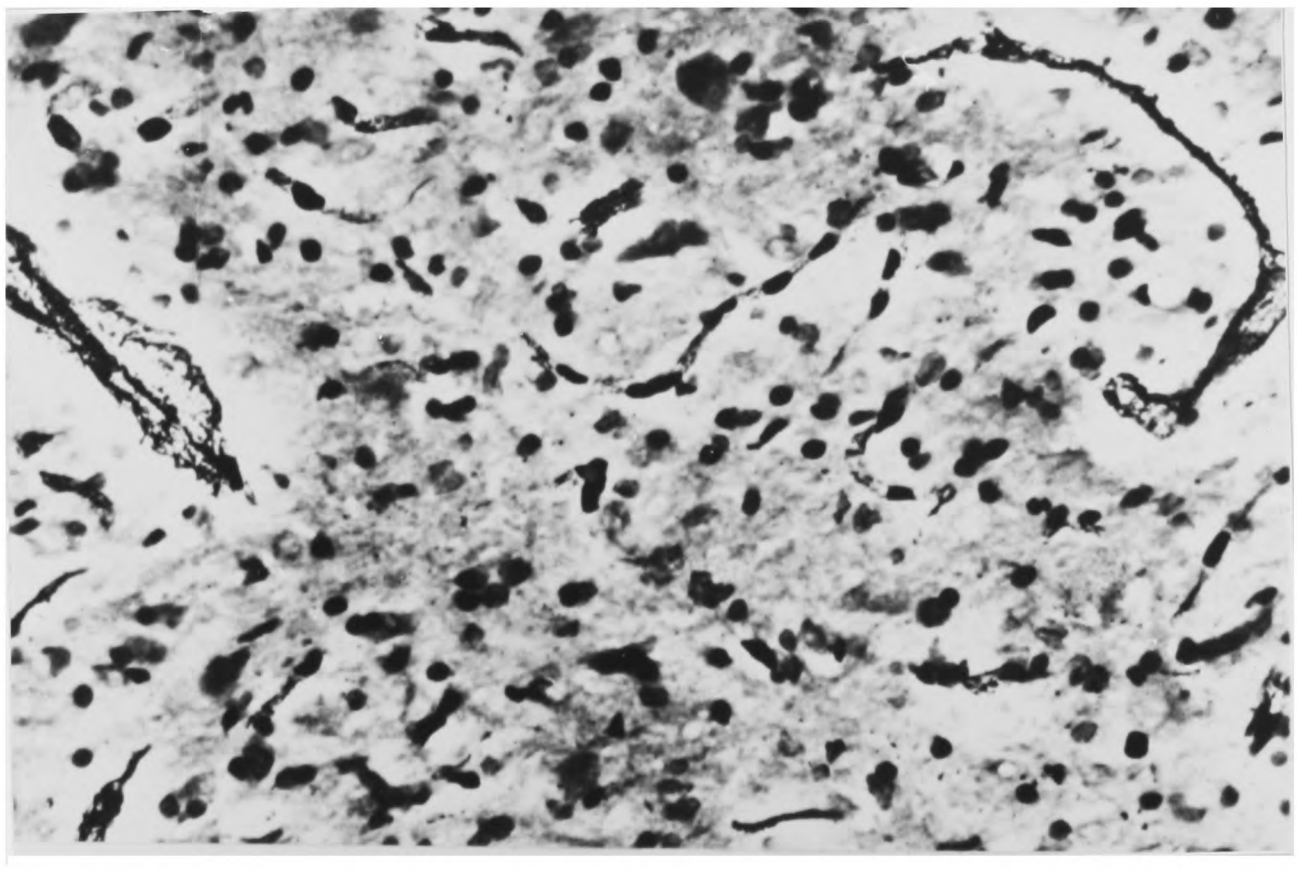
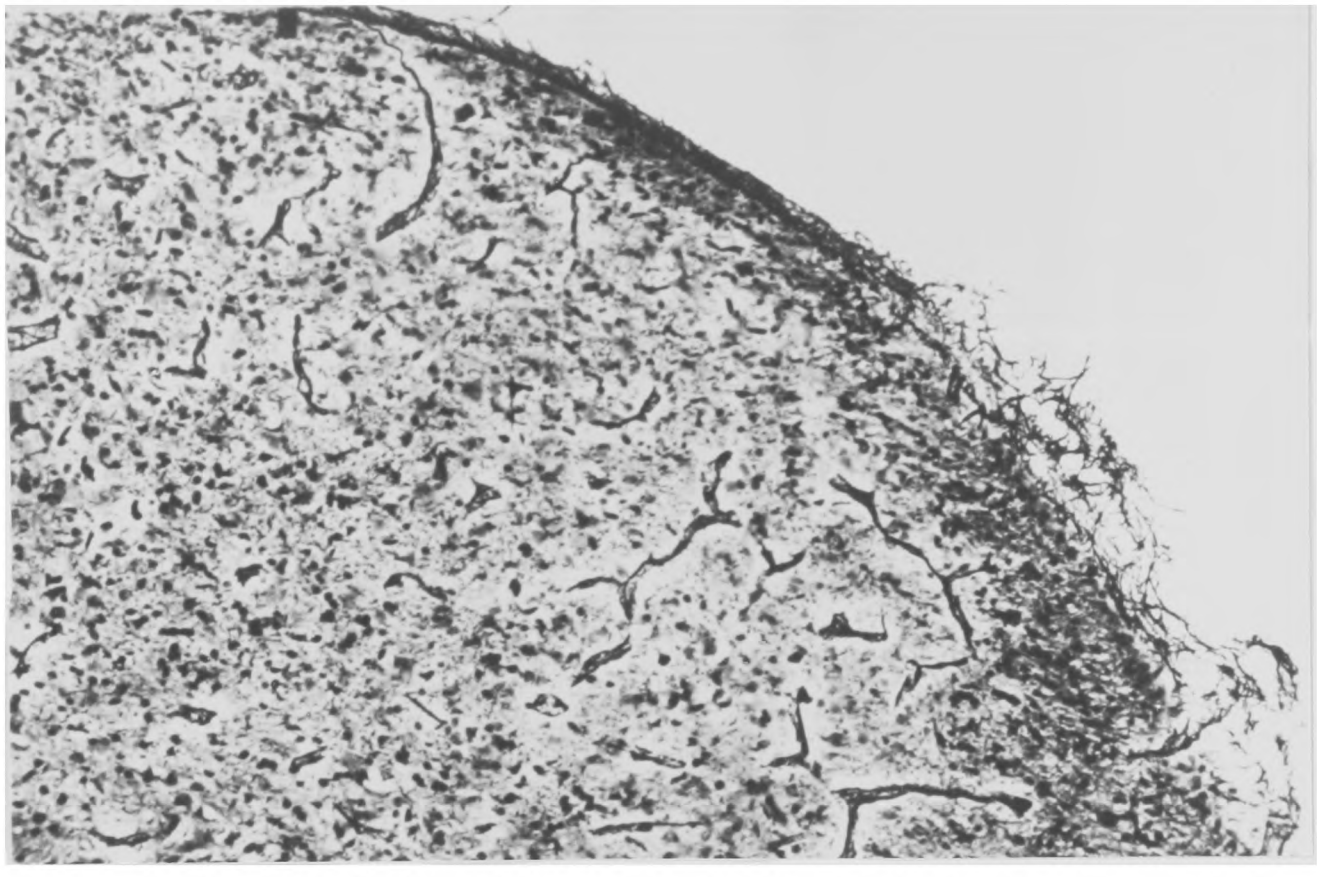


Fig. 31. Photomicrographs of part of a section of the medulla, from experiment CX2, showing the nucleus gracilis on the side opposite to that on which the DLF was transected.

Upper:- Magnification 125x.

Lower:- Magnification 310x.

Stain - the silver method of Fink-Heimer.



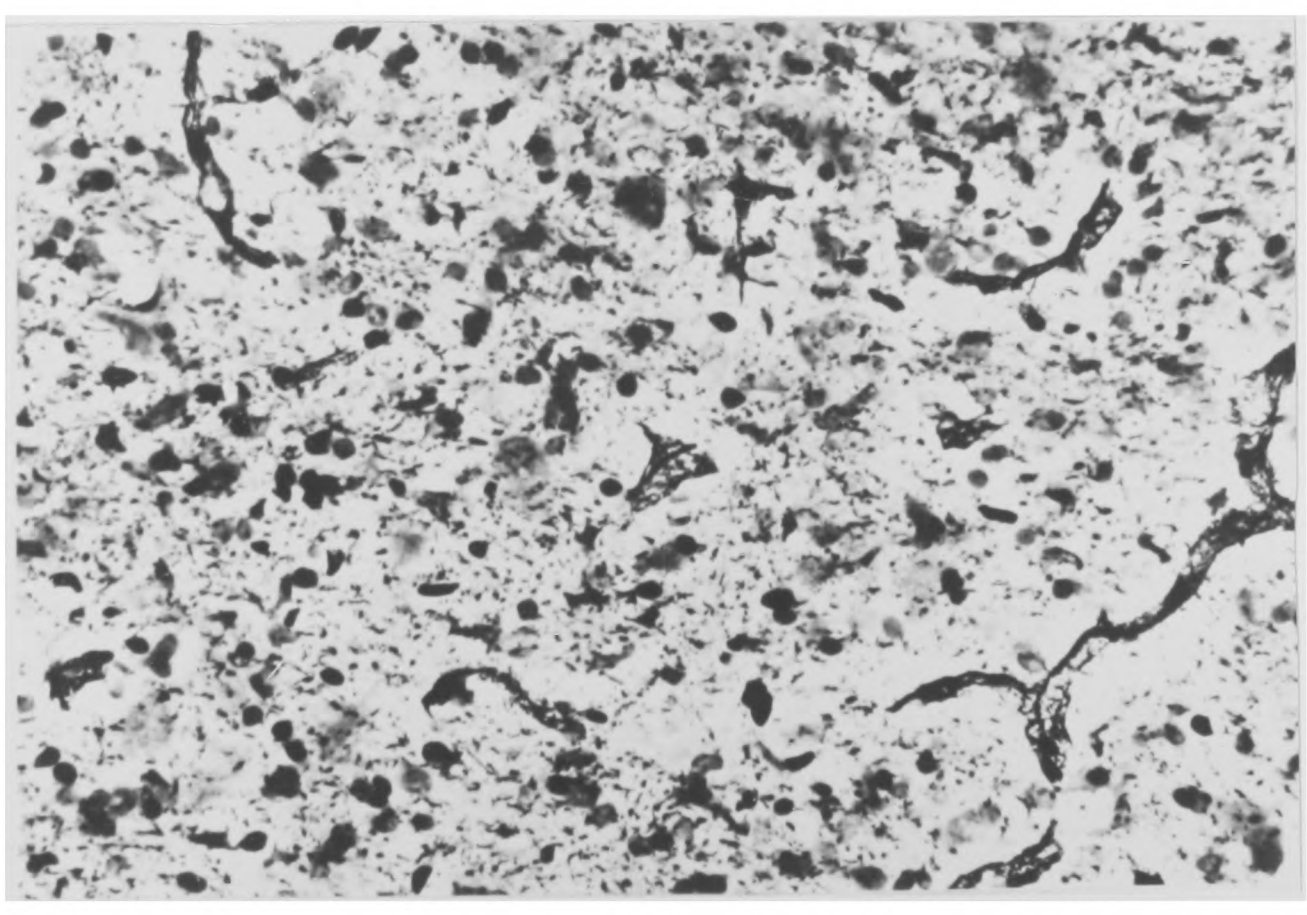


Fig. 32. Photomicrographs of part of a section of the medulla (section the same as that in Fig. 31), from experiment DX2, showing the nucleus gracilis on the same side as that on which the DLF was transected.

Upper:- Magnification 125x.

Lower:- Magnification 310x.

Stain - the silver method of Fink-Heimer.

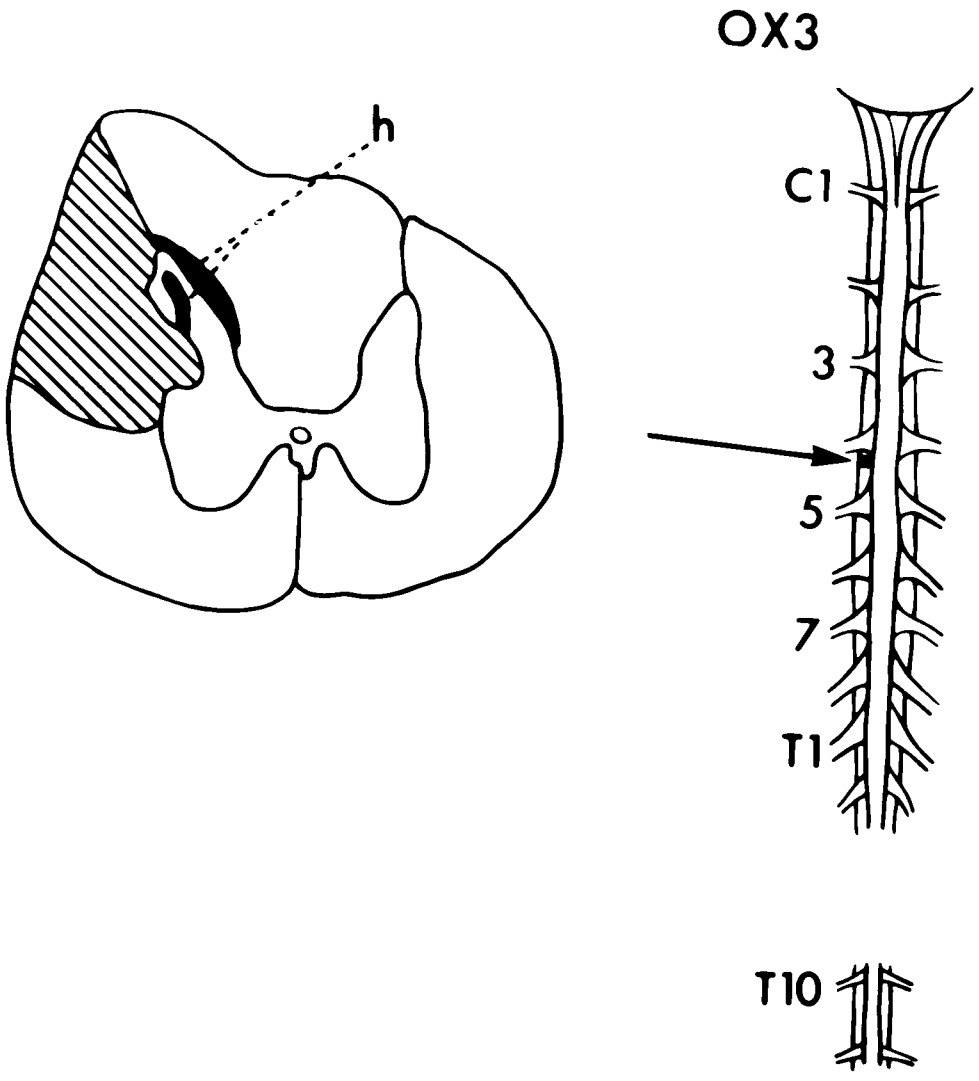

h
OX3
C1
3
5
7
T1
T10

Fig. 33. Diagram showing the site and extent of the lesion of the dorsolateral funiculus in the anatomical experiment OX3. The area of haemorrhage (h) is indicated.

REGISTERED

PART I. SLOW POTENTIAL STUDIES

CONDITIONING OF THE NUCLEAR N WAVE

The experimental arrangement has been described in the methods section. Subsequent examination of the spinal cord sections was carried out in each of these four experiments. In all cases the dorsal column lesion was found to be complete. An example of such a lesion is shown in Figure 2.

In all the experiments the conditioning stimulus was a series of 5 shocks at 500/sec applied to the ipsilateral DLF at C6. The test shock was a single shock applied to the dorsal columns rostral to the dorsal column transection. The resulting N wave was recorded by an electrode inserted into a depth of 1.0 mm in the cuneate nucleus just caudal to the obex. The conditioning stimulus produced a depression in the size of the N wave which was maximal at conditioning-test intervals of 35 - 65 msec and which lasted for 100 - 150 msec. An example of the time course of this conditioning is shown in Figure 3. The results from all experiments were in broad agreement although the magnitude of the depression and the exact time course varied from experiment to experiment and also depended on the sizes of the conditioning and test shocks. When the test shock was large it was observed that there were one or two subsequent negative deflections on the declining part of the N wave. Such deflections were described by Amassian and De Vito (1957) and were

thought to arise due to the second and third discharges of cuneate neurones. With large test shocks it was observed that the conditioning stimulus caused only a small reduction in the size of the large initial wave but that the sizes of the subsequent waves were very substantially reduced.

This depression of the N wave was still present after complete transection of the brain stem immediately rostral to the dorsal column nuclei. The time course of the depression was similar to that seen in intact animals.

It was found that transection of the DLF at C3 abolished the reduction in the size of the N wave caused by a conditioning stimulus applied to the DLF at C6.

These experiments indicate that activation of fibres coursing in the ipsilateral DLF can inhibit the discharge of cuneate neurones and that supraspinal pathways are not necessary for production of this inhibition.

CONDITIONING OF THE MONOPHASIC WAVE RECORDED FROM THE FILLED ENDS OF DORSAL COLUMN FIBRES

In these experiments a test shock was applied from an electrode inserted into a depth of 1.0 mm in the cuneate nucleus just caudal to the obex. This shock activated primary afferent fibres in the cuneate nucleus and resulted in an antidromic volley being discharged down the dorsal columns. This volley was recorded as a positive

monophasic wave from the killed ends of the dorsal column fibres. A conditioning stimulus of 5 shocks at 500/sec was applied to the ipsilateral DLF at C6. Examination of the spinal cord sections showed that in one of these three experiments there was a small untransected fascicle deep in the dorsal columns; in the other two experiments the transection was complete. No difference was observed in the results from the three experiments.

The results from one of these experiments are shown in Figure 4. The size of the test shock was raised, in steps, from values sub-threshold for the production of a response to values which produced a maximal response. At each of these values the test shock was conditioned by a DLF tetanus at a suitable interval. This resulted in the production of two curves: one for a conditioned and the other for an unconditioned test response. Figure 4 was derived from a pair of such curves and shows the increased excitability observed at various test shock strengths.

It was observed that if blocks of 5 conditioned sweeps alternated with 5 unconditioned sweeps the effect of the conditioning diminished after the first or second sweeps. It was also observed that if conditioned and unconditioned sweeps alternated the effects of conditioning were greater at sweep repetition rates of 1/sec than at repetition rates of 2/sec. These phenomena, although not investigated in detail, suggest that the presynaptic depolarization produced by stimulation of the DLF undergoes some accommodatory process.

These experiments show that stimulation of fibres in the ipsilateral DLF can cause presynaptic depolarization of dorsal column fibres which terminate in the cuneate nucleus. This suggests that presynaptic inhibition contributes to the inhibition of cuneate neurones which is produced by stimulation of fibres in the ipsilateral DLF.

PART II. EXPERIMENTS RECORDING FROM SINGLE UNITS IN THE DORSAL COLUMN NUCLEI

In the majority of these experiments subsequent examination of spinal cord sections showed that the transection of the dorsal columns was complete; in a few experiments the transection was complete on the relevant side but some untransected fibres remained on the other side. In some experiments (6 out of a total of 33 unit experiments) there was evidence that the transection of the dorsal columns was incomplete on the relevant side; the untransected fibres invariably lay deep within the dorsal columns. In 14 out of the last 15 unit experiments the dorsal column transection was complete. These 15 experiments yielded more results than the previous 18 experiments, including more cells with receptive fields. In all experiments the DLF stimulating electrodes were placed on the surface of the DLF and hence they were some distance from any untransected dorsal column fibres. In view of this and of the improved yield from later experiments it was decided to combine results from experiments in which the dorsal column transection was complete with those from experiments in which it was incomplete.

The majority of electrode penetrations were made in the cuneate nucleus which offers a much larger volume for exploration than the gracile nucleus. However, with the one exception to be noted later, the results obtained from the gracile nucleus were in agreement with those obtained from the cuneate nucleus and it was thus

decided to treat the gracile and cuneate nuclei as a single functional entity and to combine the results from both nuclei. (As has already been stated in Part I, the slow wave experiments were only performed on the cuneate nucleus.)

The electrodes used in this study discriminated three types of unit response:

(a) Small triphasic responses.

These appeared as a single response of constant latency to a DLF shock. They were triphasic and of very low amplitude, being just discernable above the noise level. Occasionally they were seen to increase in amplitude and become predominantly positive; they were never seen to become predominantly negative potentials.

These responses were thought to be external recordings from single fibres.

(b) Positive, monophasic responses.

Recordings made in the spinal cord and the medial lemniscus with electrodes similar to those used in these experiments have indicated that these responses are recorded from fibres (Brown 1968-71, Brown, Gordon & Kay 1971). These responses probably occur when the electrode tip is very close to the axon membrane.

(c) Responses predominantly negative in phase.

Responses of this type are presumed to indicate that the

electrode is recording from the cell body (Hubel 1957), although it is possible that the smaller responses of this type are recorded from dendrites.

FIBRE RESPONSES

The responses dealt with in this section are predominantly the small triphasic responses already described. The size of these responses was not large enough to permit any investigation of receptive fields. Those large positive responses which discharged a single impulse of constant latency to a DLF shock are also included in this section. Repetitive fibre responses or single fibre responses with a variable latency are discussed in the next section.

Thus all the responses in this section discharged a single impulse of constant latency in response to a DLF shock. In addition, all those tested could discharge at constant latencies to each stimulus when the stimulus repetition frequency was raised to 50/sec. On the basis of these observations these responses are thought to represent direct fibre connections between the dorsal column nuclei and the DLF. It is not possible to determine from these results whether these fibres are afferent to, or efferent from, the cells of the dorsal column nuclei.

Figure 5 shows a histogram of the latencies of these responses. Twelve of these responses were of the large positive monophasic type. The histogram may be biased in favour of low latency values because

the small triphasic responses were more easily detected visually on the oscilloscope face when near the stimulus shock escape. The conduction distance between stimulating and recording sites in these experiments was approximately 50 cm.

CELL RESPONSES

Most of the responses described in this section were predominantly negative in phase and were thus typical of responses recorded from cells. In addition, a few responses were recorded from fibres which either responded with a repetitive discharge or with a variable latency to a DLF shock and hence were not included in the previous section. Some of these fibres could be antidromically activated by stimulation of the contralateral mid-brain and were thus thought to be axons of projecting dorsal column nuclei cells. These responses are included in this section but omitted from that part of it which deals with the anatomical positions of recorded cells. All other fibre responses have been omitted from this analysis.

Towards the end of this series of experiments the presence of dorsal column nuclei cells whose axons project into the ipsilateral DLF was discovered. As a consequence of this discovery the results from previous experiments were reinvestigated and a number of cells with properties compatible with a projection into the spinal cord were found. These two categories of response will be described separately.

CELLS TRANSYNAPTICALLY ACTIVATED BY STIMULATION OF THE IPSILATERAL DLF

Figure 6 shows a cell transynaptically activated by a single shock applied to the ipsilateral DLF. The latency of the cell shows a slight variation and the cell gives a repetitive discharge in response to a single shock. These properties indicate that the cell is transynaptically, rather than antidromically, activated.

1. Latencies

The latencies of units transynaptically activated by stimulation of the ipsilateral DLF are shown in the top histogram of Figure 7. (This information was inadvertently lost for 4 cells; all 4 of these cells had receptive fields and one of them projected into the contralateral mid-brain.) A few units could only be activated when the DLF was stimulated by two shocks; rarely a tetanus was needed. The latencies in both these cases were measured with respect to the second shock. The conduction distance from the stimulating to recording electrodes in these experiments was approximately 50 mm.

In one experiment the brain stem was transected just rostral to the dorsal column nuclei. Cells were recorded in this experiment with long latencies (greater than 10 msec.). This indicates that whatever the mechanism for production of these late responses, it does not depend on pathways coursing rostral to the dorsal column nuclei.

The shaded areas in the histograms of Figure 7 indicate the

latencies of cells which discharged repetitively.

2. Fields

Of the 219 units which were synaptically activated by stimulation of the ipsilateral DLF, 79 were found to have peripheral excitatory receptive fields. All the units described in this section are cells. The middle histogram in Figure 7 shows the latencies of these cells in response to transynaptic activation by stimulation of the DLF.

In the majority of these experiments the dorsal columns were transected at C4; in a few cases the transection was made at C3. The drawings in Figure 8 are taken from the paper of Hekmatpanah (1961) and show the dermatomal distribution of segments C3 and C4 in the cat. All the fields described in this analysis were found at sites on the cat's body caudal to the area shown for the C4 dermatome.

The excitatory receptive fields of these cells are described briefly below. Unless otherwise stated all receptive fields described below were ipsilateral with respect to the recording site.

Hairs (23)

Some cells within this category required movement of most of the hairs within their receptive fields for activation, others required movement of only a few hairs. Fields on the trunk and on the proximal parts of the limbs were found to be much larger than those which were found on the distal parts of the limbs and

on the feet. For three of these cells the evoked discharge could be inhibited by firm squeezing of one or more of the cat's paws. In two of these cases the inhibition could be produced by firmly squeezing any of the cat's paws. The excitatory and inhibitory receptive fields of the third such cell are described in the next section.

Hair and Pad (3)

These three cells had small receptive fields located on the paws. They were activated by movement of hairs and also by delicate mechanical stimulation of one or two adjacent pads.

Pad (2)

Both these cells responded to delicate mechanical stimulation of a single pad. Both responses were very quickly adapting.

Skin Pressure (11)

These cells responded with a slowly adapting discharge when pressure was applied to the skin. The receptors were thought to be in cutaneous rather than deep structures because these cells also discharged when pressure was applied to flaps of skin lifted free of the underlying structures. One cell responded to transverse, but not longitudinal, stretching of the skin over the dorsal surface of the ipsilateral foreleg between the elbow and the ankle; these properties suggest that it may have been activated from a type II receptor. For two other cells the discharge frequency increased as the stimulus intensity was increased from moderate to intense pressure.

Noxious (15)

Fourteen of these cells responded to firm squeezing of an ipsilateral paw. The remaining cell responded to such stimulation of a contralateral paw. These cells tended to lie deeper than other cells with excitatory receptive fields. The histogram in Figure 9 compares the depths of cells with noxious fields with those of cells with hair, and pad and hair, receptive fields. The depths were obtained from readings taken during the experiments from a dial indicating the vertical movement of the microelectrode. Depths determined in this way are probably slightly larger than the true depths. There are two reasons for this. Firstly, the presence of a layer of fluid over the brain stem makes it impossible to determine accurately the exact surface of the nuclei. Secondly, there is often indentation of the nuclei by the recording electrode. Nevertheless, there is undoubtedly a difference between the depths of the two populations. It is suggested that many of these noxious cells may be inhibitory interneurones. It is of interest that no cells of this type were found in the gracile nucleus.

Deep (6)

These cells were activated when pressure was applied to structures deep to the skin. Four were activated when pressure was applied to muscle bellies. The other two cells were activated when pressure was applied to one of the paws. They differed from the "noxious" class because only light pressure was needed.

Tap (8)

These cells could only be activated by a brief tap applied to the relevant limb. Their receptive fields could not be further delineated. For one of these cells the discharge evoked by tapping the limb could be inhibited by firm squeezing of the paw of that limb. Inhibition was also produced by squeezing the other three paws but these were less effective.

Positional (1)

This cell was activated by flexion of the elbow; the discharge produced in this way was slowly adapting. Extension of the elbow caused cessation of the discharge.

Miscellaneous (5)

One of these cells was activated by pressure applied to the skin of the foreleg between the shoulder and the proximal part of the foot. Activation was achieved when moderate pressure was applied to skin flaps but the discharge frequency was higher when firm squeezing was employed. The discharge produced by the skin pressure was slowly adapting. A discharge of a few impulses was also produced when the elbow was moved quickly from mid-flexion to full flexion. No discharge was produced by extension. The discharge produced by joint movement may have been spurious and due to activation of receptors at other sites.

The four other cells in this class could be activated by peripheral mechanical stimulation, but no conclusion was reached

as to the relevant receptors or the actual receptive field sites.

Four cells with excitatory receptive fields were inhibited by squeezing one or more paws (see above). Inhibition of the "surround type" was not found for any of these cells.

Squeezing one or more paws was found to inhibit the discharge evoked by stimulation of the DLF in a further nine cells for which no excitatory receptive fields could be found.

Although not systematically studied, cells were commonly encountered with a spontaneous activity which could be inhibited by stimulation of the DLF. The inhibition in some of these cases was also produced by squeezing one or more paws.

3. Projection of transaynaptically activated cells

A projection into the contralateral mid-brain was demonstrated for 47 units out of 157 tested (four of these units were fibres). In all cases the criterion used for identification of activation as antidromic was that of the collision technique. An example of collision is shown in Figure 10. The shock to the contralateral mid-brain is preceded by a shock to the DLF. When the orthodromic impulse produced by stimulation of the DLF falls within the critical cancelling interval, the impulse produced by the mid-brain shock fails to occur. This demonstrates that the mid-brain shock antidromically activates this cell.

The latencies of these units in response to transynaptic activation by stimulation of the DLF are shown in the bottom

histogram in Figure 7. The latencies for antidromic stimulation of these units from the contralateral mid-brain are shown in Figure 11. (In three cases this information was inadvertently lost.) Of particular interest is the unit with a latency of 17 msec. The axon of this cell was presumably unmyelinated.

Eighteen of these units were found to have excitatory peripheral receptive fields. These are shown in the table below. This table also shows the total number of cells in each class which were found in experiments in which projection was investigated.

RF Type	No. found to project into the contra-lateral mid-brain	Total no. found in experiments in which projection was investigated
Hairs	9	20
Hair and pad	1	1
Pad	1	1
Deep	3	4
Noxious	1	7
Skin pressure	2	8
Tap	1	5
Positional	0	1
Misc.	0	1

Mechanical stimulation was found to inhibit the evoked discharge of six of these cells. In all cases the effective mechanical

stimulus was squeezing one or more of the cat's paws. Only one of these cells had an excitatory receptive field. This cell was activated by movement of hairs on the lateral side of the hindlimb from the ankle down to the most lateral digit. The cell was inhibited by squeezing the three remaining digits of the ipsilateral hindfoot. In the other five cases no excitatory receptive fields could be found but the discharge evoked by stimulation of the ipsilateral DLF was inhibited by squeezing the ipsilateral, homologous paw (3 cells) or any of the three paws (2 cells).

The antidromic activation of two cells was inhibited by a preceding shock applied to the ipsilateral DLF. One of these cells was activated by a twin shock applied to the DLF with a latency of 10 msec with respect to the second of the two shocks. It was activated by stimulation of the contralateral mid-brain with a constant latency of 1.2 msec and collision was observed to occur at the correct time interval. With longer DLF-mid-brain shock separations the antidromic response appeared consistently, as expected. However, with shock separations of from 30 - 70 msec there was failure of antidromic activation of the cell. A similar sequence was observed for the other cell but the time course of the effect was not investigated. It is supposed that the explanation of this phenomenon is that the antidromic activation of the cell is prevented by postsynaptic inhibition which occurs following the shock applied to the DLF. A number of other cells which were not

activated by stimulation of the DLF but which were activated with short constant latencies by stimulation of the contralateral mid-brain were found to have this activation prevented by a preceding shock to the DLF. It is likely, but not proven, that the responses to mid-brain stimulation were antidromic and that postsynaptic inhibition resulting from stimulation of the DLF prevented antidromic invasion of these cells. These observations suggest that part of the inhibitory action produced by DLF stimulation on the cells of the dorsal column nuclei is postsynaptic in nature.

The stimulating arrangements of the grid inserted into the contralateral mid-brain have been described in the methods section. With this arrangement it is possible to determine the transverse position across the mid-brain at which the axon of the cell under study can be excited with the minimum threshold. The anatomical location of this point can be found by subsequent study of the histological sections of the mid-brain. The results from all experiments have been combined and are shown in Figures 12 and 13. It was usually found that the grid had been inserted into a more rostral region than had been intended. This was probably because the atlas of Jasper and Ajmone-Marsan, which was used in these experiments as a guide to the position of the medial lemniscus, was probably slightly inaccurate for the small cats used. It is for this reason that the projection sites are shown on drawings of slides which, according to the atlas of Jasper and Ajmone-Marsan, are A 4.5 and A 6.0. Representative slides at these two levels

were projected onto a screen and traced. The other slides were then projected onto these tracings and those points from which cells could be activated with the lowest threshold were marked. The tracings were then converted into drawings and then photographed. One projecting cell was recorded in an experiment in which recordings were made from the left dorsal column nuclei. This cell was antidromically activated from the contralateral mid-brain and its projection site has been transposed from one side of the mid-brain to the other by inversion of the tracing.

Some cells were lost before the details of antidromic activation had been investigated and hence their projection sites do not appear in Figures 12 and 13.

The minimum thresholds obtained in these experiments varied between 0.08 and 3.0 mA; most of them being in the range 0.1 - 0.9 mA. The higher values tended to be found when an axon could only be activated from the one or two most medial positions of the grid. This suggests that the most medial projection sites shown in Figures 12 and 13 may not be as accurate as the rest of the projection sites. Since the depth of the lemniscal grid was not adjusted except at the start of an experiment, the dorso-ventral locations of projection sites shown in Figures 12 and 13 are not as accurate as the medio-lateral locations. The majority of the projection sites shown are within or around the medial lemniscus. Most of the medial positions are just dorsal to the red nucleus.

4. Cells transynaptically activated by stimulation of the contralateral mid-brain

Seven cells, which were transynaptically activated by stimulation of the DLF, were also transynaptically activated by stimulation of the contralateral mid-brain. The identification of the latter activation as transynaptic was based on a variability in latency and an absence of collision between mid-brain and DLF evoked impulses. The latencies of these cells in response to stimulation of the mid-brain are given below, together with their receptive fields. The latencies given are the lowest which were observed in each case. The cells with latencies of 10 and 17 msec may have been activated by transcortical routes or by fibres descending in the contralateral mid-brain; the five other cells were presumably activated by stimulation of fibres descending in the mid-brain.

Latency	Field
17.0	Inhibited by squeezing ipsilateral paw
3.0	-
5.5	-
3.0	-
2.0 and 4.0 (two impulses)	-
10.0	Skin pressure
3.0	Skin pressure and elbow flexion

Figure 14 shows the mid-brain positions from which five of these cells were activated with minimum thresholds. Three of these positions are just dorsal to the red nucleus; the other two are in the medial part of the medial lemniscus. The latter two sites indicate the positions from where the cells with latencies of 10 and 17 msec were activated.

5. The afferent pathway

At the end of a number of experiments the ipsilateral DLF was transected rostral to the transection of the dorsal columns. This transection was made when a small group of cells were being activated by the stimulus to the DLF and was made with as little disturbance to the preparation as possible. The transection was continued in small steps until the evoked responses were no longer obtained. As the effects of transection were observed upon a small number of cells recorded at the same time, it is unlikely that their disappearance was an artifact caused by any mechanical disturbance of the preparation which this procedure produced. Subsequent examination of spinal cord sections revealed the extent of the lesions. Determination of the full extent of these lesions required study of several serial sections in each case as the full extent of the lesion was never apparent from a single section. The upper two records in Figure 15 were obtained before transection of the DLF, the lower two records were obtained after the transection. The extent of the DLF lesion is shown in the

accompanying drawing. This drawing was produced in the following way. A slide of the spinal cord, from the region of the DLF lesion, was projected onto a screen and traced. The other slides from this region were then projected onto this tracing and the area of the lesion shown in each slide was marked onto the tracing. In this way the full extent of the DLF lesion was depicted. In some cases it appeared that the evoked response was abolished by a lesion which did not transect fibres coursing in the dorsomedial area of the DLF, but only transected those fibres travelling more laterally. It is difficult to know whether this observation is valid, because the medial fibres, although not transected, may have been damaged by the lesion to an extent sufficient to prevent them transmitting impulses. However, if this observation is valid it would be of importance because the SCT courses in the dorsomedial part of the DLF (Mann 1971).

In three experiments the ipsilateral anterior lobe of the cerebellum was stimulated to investigate the possibility that collaterals of spinocerebellar tract fibres might course to the dorsal column nuclei and hence be responsible for the transynaptic activation of dorsal column nuclei cells produced by stimulation of the DLF. The techniques used in these three experiments have been described in the methods section. A total of 17 cells, transynaptically activated by stimulation of the DLF, were found in these experiments. None of these cells were transynaptically or

monosynaptically activated by stimulation of the anterior lobe of the cerebellum. This indicates that in these three experiments activation of cells in the dorsal column nuclei by stimulation of the DLF did not take place by way of collaterals of direct spinocerebellar fibres. These experiments do not exclude a contribution from this source in other experiments nor a contribution from collaterals of indirect spinocerebellar fibres.

6. Histological reconstruction of recording positions

In four experiments reconstruction of recording sites was based on readings of electrode position taken during the experiment; at the end of these experiments the electrode was positioned so that its tip was at the point of bifurcation of the dorsal column nuclei and the reading of this position was noted. With these readings it is possible to reconstruct the rostro-caudal position of each electrode recording position with respect to the point of bifurcation of the dorsal column nuclei. In five other experiments the distance between the point of bifurcation of the dorsal column nuclei and the obex was measured; the average value for this distance was 1.0 mm. With this information it is possible to convert recording positions measured with respect to the point of bifurcation of the dorsal column nuclei to values with respect to the obex.

In all other experiments reconstruction of recording positions was based on marking electrolytic lesions made during the experiment.

These lesions were then found on subsequent examination of transverse medulla sections, although in a few cases this was not so and in these cases reconstruction of recording positions was not possible. Examination of medulla sections also revealed the position of the obex. Since sections were cut at 50μ and since all sections were serially numbered it was then possible to determine the rostro-caudal distance between the lesion and the obex. This was then converted to an *in vivo* value by allowing for the tissue shrinkage which occurred during fixation. In six experiments two lesions were made sufficiently far apart (in a rostro-caudal plane) to allow determination of the percentage by which the tissue had shrunk (the relative movement of the electrode from one recording position to the next was always noted in every experiment). In these six experiments the value for shrinkage determined as described was used in each case; in all other experiments the average value from these six experiments was used. This value indicated a shrinkage in the rostro-caudal axis of 20%. As has already been described, during the course of an experiment the relative movement of the electrode from one recording site to another was noted. Thus since the position of one or more tracks could be related to the position of the obex and since the positions of other recording sites could be related to the position of those tracks with lesions, the positions of all tracks could be found with respect to the obex. Reconstructions of the positions of those tracks without lesions had to be made

with respect to those tracks with lesions because the electrodes used were rather fine and hence they were often not visible in the sections. Since electrode penetrations were not in excess of 2.5 mm no allowance has been made for the 8° tilt with which the electrode was inserted into the nuclei (see methods section).

The top histogram in Figure 16 shows the rostro-caudal positions of all those transynaptically activated cells for which reconstruction of recording position was possible. The zero on the abscissa of the histogram indicates the position of the obex. The middle histogram shows the rostro-caudal position of those cells for which excitatory receptive fields were found; the bottom histogram indicates the rostro-caudal position of cells which projected into the contralateral mid-brain. These histograms indicate the sites, in the rostro-caudal axis of the nuclei, at which these cells were found, but they do not indicate their absence from other sites. This is because electrode tracks tended to be made in regions in which it was known, from the results of previous experiments in the series, that responses to DLF stimulation could be expected. The histogram in Figure 17 shows the distribution of electrode tracks along the rostro-caudal axis of the nuclei; it can be seen that the distribution of cellular positions shown in Figure 16 parallels the distribution of electrode penetrations.

The actual lesion sites marking the positions of cells which projected into the contralateral mid-brain are shown in Figures 18-21.

Those in Figures 18 and 19 were for cells which were found to have peripheral excitatory receptive fields, whilst those cells marked in Figures 20 and 21 did not have receptive fields. The photomicrographs in Figure 22 show one such lesion. The drawings shown in Figures 18-21 were produced in the following way. Photographs of slides containing lesions were taken and the negatives printed. Tracings were then made of the outlines of the brain stem and of the nuclei and the positions of the lesions marked. The tracings so obtained were then inked over and then photographed; they appear in Figures 18-21. The most interesting feature of these lesion sites is that the majority of them appear around the periphery of the nuclei.

CELLS ANTIDROMICALLY ACTIVATED BY STIMULATION OF THE IPSILATERAL DLF

The existence of cells in the dorsal column nuclei whose axons project into the ipsilateral lateral columns was discovered towards the end of this series of experiments. The discovery of this descending projection was made when it was observed that a cell which discharged a single impulse of constant latency in response to a shock applied to the DLF was also activated by a shock to the dorsal columns, but with a longer and variable latency. The activation of the cell by the DLF shock was then shown to be antidromic by the collision technique; the orthodromic impulse being provided by a shock applied to the dorsal columns. A similarly conclusive example of a cell with a descending projection

was seen on one further occasion. Investigation of results from previous experiments revealed two other cells for which there was strong evidence of a descending projection. These four cells are discussed in detail below.

Cell 1

This cell (Fig. 23) responded to a stimulus to the DLF with a single impulse at a constant latency of 1.5 msec. The response to the dorsal column (DC in Fig. 23) shock was of longer and variable latency. In the left hand block of sweeps in Figure 23 the impulse evoked by stimulation of the dorsal columns falls outside the critical cancelling interval and consequently the impulse produced by stimulation of the DLF occurs. In the right hand block of sweeps the impulse produced by stimulation of the DLF is cancelled because the impulse produced by stimulation of the dorsal columns falls within the critical cancelling interval.

Cell 2

This cell responded at a constant latency of 2.0 msec when a shock was applied to the ipsilateral DLF. Stimulation of the dorsal columns, rostral to the transection, activated the cell with a latency of about 3 msec. When the impulse produced by stimulation of the dorsal columns fell within the critical cancelling interval, DLF stimulation failed to activate the cell.

An additional phenomenon was observed in this case which was not found for cell 1. It was found that the threshold stimulus

strength required for dorsal column activation of the cell was lower when the dorsal column stimulus was preceded by a shock to the DLF. This facilitation was observed at DLF stimulus strengths which did not antidromically activate the cell. This indicates that DLF stimulation not only antidromically activated this cell but also produced an orthodromic excitatory action; this was, however, not powerful enough to cause the cell to discharge an impulse. The facilitation was found to last for 30 msec.

Cell 3

At a DLF stimulus repetition frequency of 2/sec this cell was found to discharge repetitively to each shock; the first impulse occurred at a latency of 3.5 msec. This cell could also be activated by mechanical stimulation of the skin on the ventral surface of the forearm between the elbow and the forefoot. The response produced by stimulation of the skin was rapidly adapting but the receptors did not appear to be hairs. It was also found, during the course of the experiment, that the cell could discharge to each of a series of DLF shocks when these were given at high repetition frequencies. The exact extent of this "following" was not appreciated at the time of the experiment but it was sufficient to suggest that the DLF activation might be antidromic (the repetitive discharge seen at lower frequencies of stimulation could have been due to a subsequent orthodromic activation). In order to test this idea the cell was activated by skin electrodes and

an attempt was made to cancel the first of the evoked impulses. This was not successful.

Subsequent analysis of the data, performed after the experiment, revealed that the cell could respond, with a single impulse, to each of five DLF shocks delivered at a frequency of 1100/sec. This seemed to indicate antidromic activation of the cell but such an explanation was at variance with the failure to demonstrate collision. It was observed, however, that the latency of the cell to each shock of the tetanus was 4.0 msec. The cell also responded at stimulus repetition frequencies of 20 and 50/sec with a single impulse at a latency of 4.0 msec. Collision was investigated at a stimulus repetition frequency of 2/sec and at this frequency the cell discharged repetitively, the first impulse being at 3.5 msec. The explanation suggested for these findings is that the cell had both afferent and efferent fibres coursing in the DLF and that orthodromic activation of the cell had a shorter latency than antidromic activation so that the antidromic impulse was cancelled by the first orthodromic impulse. The orthodromic impulse was, however, unable to "follow" higher stimulus repetition frequencies so that the antidromic activation of the cell was then apparent. The top 3 records in Figure 24 show the orthodromic activation of the cell which occurs at stimulus repetition frequencies of 2/sec; the first impulse occurs at a latency of 3.5 msec and it is supposed that this cancels the antidromic impulse which would

otherwise occur at 4.0 msec. When the stimulus repetition frequency is raised to 50/sec (lower records in Fig. 24) the orthodromic impulse cannot follow and consequently the antidromic impulse appears.

Cell 4

When initially encountered this cell could only be activated by a twin shock applied to the DLF. The latency fluctuated around a value of 2.5 msec with respect to the second of the two shocks. The cell was also activated by pressure applied to the skin of the tail and the posterior aspect of the ipsilateral hindleg. The cell was shown to project into the contralateral mid-brain; it was antidromically activated from the mid-brain with a latency of 2.4 msec.

During the investigation of the receptive field the response of the cell to the DLF stimulus changed so that it responded with a constant latency of 2.0 msec to a single DLF shock. The cell discharged an impulse at a latency of 2.0 msec to each shock of a series of five delivered at a frequency of 500/sec. It was found that the DLF evoked impulse was cancelled by a skin evoked impulse when the latter fell just within the critical cancelling interval.

The explanation suggested for these findings is that the afferent supply to this cell came from the DLF and that its axon branched, one branch travelling to the contralateral mid-brain and the other into the ipsilateral DLF. It is further supposed that during the course of investigation of the cell slight movement

of the DLF stimulating electrodes occurred with respect to the surface of the spinal cord. Thus, whilst earlier the DLF stimulating electrodes activated the afferent supply to this cell, later, after the supposed slight movement of the electrodes, they activated the descending branch of its axon.

It is interesting to observe that three of the four cells described above had afferent, as well as efferent, fibres coursing in the DLF.

In addition to the four cells described a further twenty eight cells were found with properties which suggest that their activation by a DLF stimulus was antidromic. These cells responded to each DLF shock with a single impulse of short, constant latency. It is not possible to conclusively state whether these cells were antidromically or transynaptically activated by stimulation of the DLF but their response characteristics suggest that most of them were probably antidromically activated.

The latencies of all 32 cells included in this section are shown in the histogram of Figure 25.

The histological reconstruction of the positions of cells which project into the spinal cord was made in the same way as for cells transynaptically activated by stimulation of the DLF. Figure 26 shows a histogram indicating the rostro-caudal positions of these cells. The photomicrograph in Figure 27 shows the lesion marking the position of cell 2; Figure 28 shows the positions of

cells 1 - 4. The other two lesion sites shown in Figure 23 indicate the positions of two cells which responded with short, constant latencies to shocks applied to the PLF.

PART III ANATOMICAL EXPERIMENTS

Three cats were used in these experiments; in two of them the method of successive degeneration was used, whilst in the third there was solely a lesion of the DLF. The details of the time intervals between dorsal column and DLF lesions, and between DLF lesions and death, were given in the methods section. The methods section also contains an account of the staining procedures used. The results from the three experiments are described individually below. In all three experiments the DLF was only transected on one side so that the contralateral dorsal column nuclei provided a control situation.

CX1

Figure 29 shows the extent of both the DLF and the dorsal column lesions and indicates the rostro-caudal levels at which these lesions were made. It can be seen that there was a small untransected fascicle deep within the dorsal columns. The DLF lesion was made at T10 and resulted in terminal degeneration in the gracile nucleus; the details of this degeneration will be described below. Because of the possibility that the DLF lesion could have damaged gracile fibres which subsequently coursed through the undamaged fascicle in the C4 - C5 region (the site of the dorsal column lesion) and hence resulted in the appearance of degeneration within the gracile nucleus, the region of the untransected fascicle

at the C4 - C5 level was examined for degenerating fibres; none were found. This indicates that there was no damage to any dorsal column fibres which subsequently coursed through the untransected gracile fasciole and hence degeneration within the gracile nucleus cannot be explained on this basis.

Examination of the medulla sections showed that at a level corresponding to the transition between the middle and caudal thirds of the gracile nucleus, degenerating fibres were found in a manner as if coursing from the DLF dorsomedially towards the gracile nucleus. Also at this level the first degenerating fibres appeared, lying around the gracile nucleus. Signs of terminal degeneration, however, were not found until 1 mm caudal to the obex; but from this level terminal degeneration was found at all levels up to the most rostral pole of the nucleus. No degeneration was found in the cuneate nucleus in this experiment.

OX2

Figure 30 shows the extent of both the dorsal column and the DLF lesions. The dorsal column lesion was made at C4 - C5 and the DLF lesion at C7. The dorsal column lesion, in this case, was complete.

The features of the degeneration in the gracile nucleus were the same as those found for OX1. In addition degenerating fibres were found in the cuneate nucleus. Terminal degeneration was present in the cuneate nucleus from 1 mm caudal to the obex up to the

rostral pole of the nucleus. The terminal degeneration in the cuneate nucleus was more diffuse than in the gracile nucleus; this was possibly because the DLF transection was at C7 which would have left any contribution from more rostral cervical segments untransected whereas the lesion at T10, in OX1, probably transected all the fibres running to the gracile nucleus.

The photomicrographs in Figure 31 are of the nucleus gracilis contralateral to the side on which the DLF was transected. Those in Figure 32 are of the nucleus gracilis ipsilateral to the side on which the transection was made. In both Figures the upper photomicrographs are at a magnification of approximately 125x and the lower ones at a magnification of approximately 310x. Comparison of the two higher power pictures indicates the presence of degenerating fibres on the operated side and their absence from the control side. OX3

In this case there was solely a transection of the DLF at C5 (Fig. 33) with no preceding transection of the dorsal columns. The degeneration found in the gracile nucleus was similar to that found in OX1 and OX2. In a restricted lateral part of the cuneate nucleus there was an area of heavy degeneration; elsewhere the pattern of degeneration resembled that found in OX2. The area of heavy degeneration found laterally in the cuneate nucleus probably resulted from damage to fibres in the cuneate funiculus of the dorsal columns at C5 caused by haemorrhage produced at the time of

the DLF transection. The area of this haemorrhage is shown in Figure 33.

These three anatomical experiments demonstrate the presence of fibres which course from the ipsilateral DLF to the rostral parts of both the cuneate and gracile nuclei. It was suggested in Part II that the small triphasic responses of constant latency recorded in the dorsal column nuclei in response to DLF stimulation represented direct fibre connections between the DLF and the dorsal column nuclei. It was stated in that section that it was impossible to know whether they represented fibres afferent to, or efferent from, the cells of the dorsal column nuclei. The discovery of cells in the dorsal column nuclei which project into the spinal cord indicates that some of them may have been efferent fibres and the results from these anatomical experiments indicates the presence of direct afferent fibres.

The results from these anatomical experiments do not indicate the functional type of cell with which these direct afferent fibres synapse. Thus these fibres may synapse with inhibitory interneurones, with cells projecting into the mid-brain or the spinal cord, or with cells which themselves synapse with cells of any of these categories. In the electrophysiological experiments the "following" frequencies of cells were only rarely investigated. However, one cell which projected into the contralateral mid-brain and which was excited by hair movement, was shown to respond to

each of five shocks delivered at 400/sec. This suggests that this cell was monosynaptically activated and indicates that some of these direct afferent fibres do synapse with cells which project into the mid-brain. On another occasion a cell which was activated by squeezing the ipsilateral paw was found to respond to each of five shocks delivered to the DLF at 330/sec. Projection was not tested for this cell but its properties suggest that it was probably an inhibitory interneurone; the "following" frequency again indicates monosynaptic activation.

A comparison of the sites of terminal degeneration with the location of cells transynaptically activated by stimulation of the DLF is not really valid because of the biased sampling involved in the electrophysiological experiments. Thus, although 64% of cells were found rostral to -2 mm, 63% of electrode tracks were also rostral to -2 mm. It is, however, of interest to consider the possible reasons why cells, transynaptically activated by stimulation of the DLF, were recorded at sites caudal to those where terminal degeneration was found. There are two main possibilities (experimental error in the compilation of recording positions is discounted because there is no reason why such an error should be systematically in the direction of indicating more caudal recording positions than was actually the case). Firstly, it is possible that those fibres which course directly to the rostral parts of the nuclei subsequently activate interneurones

so that the field of activation in the nuclei is thereby increased. Such a spread of activation by way of interneurones is more likely to be the explanation if it should transpire that DLF activated cells are not found at much more caudal levels than those found in these experiments. The second possibility is that in addition to the direct fibre pathway from the DLF to the dorsal column nuclei there are one or more other pathways which synapse before reaching the dorsal column nuclei; such indirect pathways would not, of course, be demonstrated by the anatomical experiments performed.

C O N C L U S I O N S

Stimulation of the dorsolateral funiculus of the spinal cord produces both excitatory and inhibitory effects on the dorsal column nuclei. The inhibitory system will be described first.

Evidence has already been presented which indicates that both presynaptic and postsynaptic inhibitory mechanisms are involved in the inhibitory component of this system. Lesion experiments have shown that the pathway responsible courses in the ipsilateral DLF. In some cases inhibition was produced by squeezing one or more of the cat's paws. Cells were found, deep in the cuneate nucleus, which were activated by such stimuli; of the seven such cells tested only one was found to project into the contralateral mid-brain. It is thus suggested that many of these "noxious" cells may have been inhibitory interneurones. None of these "noxious" cells were found in the gracile nucleus; this may simply have been due to the much smaller total number of cells recorded in the gracile nucleus, although on the other hand, it may be that cuneate "noxious" cells inhibit cells in both nuclei. This inhibitory input to the dorsal column nuclei probably corresponds to the "widespread cutaneous inhibition" of Jabbur & Banna (1970). The results of Davidson & Smith (1970) suggest that a similar inhibitory system occurs in the rat.

The excitatory input from the ipsilateral DLF to the dorsal column nuclei probably includes that described by Tomasulo & Emmers (1970). However, the present demonstration that some of the

activated cells are relay cells conclusively proves the existence of a genuine excitatory effect, in addition to the inhibitory effect already described. In this study receptive fields were found for approximately one-third of the cells transynaptically activated by stimulation of the DLF. A number of cells were found to be activated by stimulation of the dorsal columns, rostral to the lesion, in addition to being activated by stimulation of the DLF. This indicates that some of the cells found to be activated by stimulation of the DLF were partially deafferented by the dorsal column lesion; this partial deafferentation may partly explain the relatively low percentage of cells found to have receptive fields. The majority of cells with receptive fields were found to be excited by cutaneous stimulation.

The identity of the afferent path (or paths) from the ipsilateral DLF to the dorsal column nuclei has not been elucidated by the present experiments. Some of the possibilities are discussed below.

1. Collaterals of SCT fibres

Tomasulo & Emmers (1970) presented evidence that collaterals of SCT fibres were responsible for the effects that they described (see Introduction). It is possible that this is also the case for the results which have been presented here but there is no experimental support for this suggestion in the present study. Indeed, in some experiments in which the DLF was transected whilst

a small group of cells was being activated by DLF stimulation, it was found that the responses were abolished when only the superficial part of the DLF had been transected. There is evidence that the SCT runs in a dorsomedial region of the DLF (Lundberg & Oscarsson 1961, Mann 1971); this suggests that on some occasions the responses were abolished by lesions which did not transect the SCT.

2. Collaterals of direct spinocerebellar paths

Evidence has already been presented which suggests that collaterals of DSCT and RSCT fibres are not responsible for the effects produced by stimulation of the DLF.

3. Antidromic activation of descending paths

A stimulus to the DLF could cause effects on the dorsal column nuclei by antidromic activation of descending fibres which sent collaterals to the dorsal column nuclei. Although this explanation cannot be excluded there are a number of reasons for regarding it as unlikely; particularly for those cells with receptive fields. Of the various paths descending in the DLF the corticospinal tract can probably be excluded because there is evidence that in the cat corticospinal axons do not send collaterals into the dorsal column nuclei (Gordon & Miller 1969); a contribution from other tracts, such as the rubrospinal, cannot be excluded. The excitatory and inhibitory effects produced on cells by mechanical stimulation of the skin could have been produced by cerebrofugal fibres but this

seems very unlikely since in the majority of these experiments the animals were anaesthetized with barbiturate; this anaesthetic is known to exert a very depressant action on the cerebral cortex. Direct evidence against the mediation of effects by cerebrofugal fibres was provided by the finding of receptive fields in the unit experiment in which the brain stem was transected.

4. Other paths

A separate tract may exist which courses in the DLF and terminates in the dorsal column nuclei; it is also possible that some of the effects described could have been mediated by a path which did not directly project to the dorsal column nuclei but only did so after relaying elsewhere.

The results from the anatomical experiments indicate the presence of a direct path from the DLF to the ipsilateral dorsal column nuclei but, as has already been stated, they do not exclude the presence of indirect paths as well. There is no evidence from the anatomical experiments as to whether the direct input to the dorsal column nuclei is formed from collaterals of another tract or whether it exists as a separate entity. One of the most interesting properties of the tract demonstrated by the anatomical experiments is that it terminates solely in the rostral parts of the cuneate and gracile nuclei; other distinguishing features of the rostral parts of these nuclei have been described in the Introduction.

The electrophysiological experiments revealed the existence of a descending projection from cells of the dorsal column nuclei into the ipsilateral DLF. Some of these cells were also orthodromically exited by stimulation of the DLF and it is tempting to speculate that these cells projected to the cells of origin of the afferent path and thereby modulated their activity. Such an idea is, however, only a speculation since the sites of termination of the axons of these cells are unknown.

In summary it can be stated that these experiments have demonstrated the existence of an ascending input to the dorsal column nuclei which courses in the DLF, and of a descending projection from some cells of the dorsal column nuclei into the dorsolateral white matter of the spinal cord. This reciprocal connection between the dorsal column nuclei and other sensory structures of the dorsal part of the spinal cord shows that it is now unjustified to regard the dorsal column system with its nuclei as an isolated functional entity even at the level of the first relay.

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A B S T R A C T

Electrophysiological experiments have shown that stimulation of the ipsilateral DLF, caudal to a transection of the dorsal columns (at C4), inhibits cells in the dorsal column nuclei. The presence of such inhibition was shown both by focal potential, and single unit, recording. It was found that the amplitude of a volley, conducted down the dorsal columns in response to a shock applied to the cuneate nucleus and recorded from the killed ends of dorsal column fibres at the rostral end of a transection of the dorsal columns, was increased by a preceding tetanus applied to the ipsilateral DLF. This evidence of depolarisation of dorsal column fibre terminals suggests that presynaptic inhibition contributes to the inhibition produced by DLF stimulation. A contribution from postsynaptic inhibitory mechanisms was suggested by the observation, made on several occasions, that antidromic activation of a unit from the contralateral mid-brain could be prevented by a preceding shock applied to the ipsilateral DLF. In some cases inhibition of units was produced by squeezing one or more of the cat's paws; some of these units projected into the contralateral mid-brain.

In addition to an inhibitory action from the ipsilateral DLF on the cells of the dorsal column nuclei, electrophysiological experiments have also demonstrated the presence of an excitatory action. The majority of the cells transynaptically activated by

stimulation of the DLF were found in the region -3 to +2 mm (the obex being zero); however this may have been because the majority of electrode penetrations were also made in this region. Many of the units so excited were shown to project into the contralateral mid-brain, thereby demonstrating the existence of a genuine excitatory effect on the dorsal column nuclei. Approximately one third of the units excited by stimulation of the DLF were also excited by peripheral mechanical stimulation. In the majority of cases the effective stimulus was cutaneous stimulation. A number of units, deep in the cuneate nucleus, were found to be excited by "noxious" mechanical stimulation; no such units were found in the gracile nucleus. Only one of those tested was found to project into the contralateral mid-brain, suggesting that these units may be inhibitory interneurones.

The excitation and inhibition, produced by stimulation of the ipsilateral DLF, were abolished by transection of the DLF. They were not affected by transection of the brain stem at a level immediately rostral to the dorsal column nuclei. None of the cells transynaptically activated by stimulation of the DLF were also activated by stimulation of the anterior lobe of the cerebellum; this suggests that dorsal column nuclei cells were not excited by collaterals of direct spinocerebellar tract fibres.

The presence of direct connections between the dorsal column nuclei and the DLF was demonstrated electrophysiologically by the recording, in the dorsal column nuclei, of short constant latency

responses with properties indicative of external recordings from fibres. Whether such fibres were afferent to, or efferent from, the cells of the dorsal column nuclei could not be established from such recordings. However, evidence for the existence of both such categories was found.

Some cells in the dorsal column nuclei were antidromically activated by stimulation of the ipsilateral DLF. Some of these cells were orthodromically activated by afferents coursing in the DLF. The presence of such orthodromic activation of these cells led to the speculation that the cells with descending projections may synapse, directly or indirectly, with the cells of origin of the afferent pathway, and thereby form a feed-back circuit within this system.

Anatomical experiments have demonstrated the existence of direct afferent fibre connections between the DLF and the dorsal column nuclei. Terminal degeneration was found, after lesions of the DLF, in the rostral parts of both cuneate and gracile nuclei. The terminal degeneration extended from 1 mm caudal to the obex up to the rostral poles of both nuclei. Such anatomical evidence of a direct afferent pathway does not, of course, exclude the presence of indirect pathways; such pathways, if synapsing before reaching the dorsal column nuclei, would not be demonstrated by anatomical methods. It is not possible, from the results described, to determine whether the direct pathway is formed by collaterals from a tract already

known, such as the spinocervical tract, or whether it exists as a separate entity.