PHYSIOLOGICAL STUDIES

ON THE

POSTSYNAPTIC DORSAL COLUMN SYSTEM

BY

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DECLARATION

I certify (1) that the authorship of this thesis is entirely my own and (2) that the work presented in the thesis is substantially my own. Some of the material has been published in collaboration with colleagues and reprints are included in the thesis as an appendix. None of the material presented has been submitted for any other degree or professional qualification.

John S. Riddell

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ABSTRACT

This thesis has made an electrophysiological study of segmental and descending influences on identified neurones of the postsynaptic dorsal column (p.s.d.c.) system and has examined aspects of the relationship between the neurones of this projection and the spinocervical tract (s.c.t.). Extracellular single unit microelectrode recordings were made from the axons of p.s.d.c. neurones ascending the dorsal columns of cats anaesthetised with chloralose.

1) The response properties and organisation of the cutaneous receptive fields of p.s.d.c. neurones were investigated using light tactile, and noxious mechanical and thermal stimuli.

The receptive fields of units with input from glabrous skin had a complex organisation and many were discontinuous. These units could be inhibited by both light tactile and noxious cutaneous stimuli. In contrast, units with receptive fields confined to hairy skin of the proximal limb often had a concentric receptive field organisation in which the high threshold excitatory component extended beyond the low threshold area. These units could be inhibited only by light tactile stimuli and their inhibitory receptive fields generally covered an extensive area of skin virtually surrounding the excitatory components.

These observations are contrasted with the

relatively simple receptive field organisation of s.c.t. neurones and are discussed in relation to previous observations of the morphology and ultrastructure of neurones of the p.s.d.c. and s.c.t. systems.

2) A study has been made of the influence of systems descending from the brain on the response properties and receptive field organisation of p.s.d.c. neurones. The cutaneous receptive fields of p.s.d.c. units were investigated both before and during a block of conduction in descending fibres produced by cooling a region of cord rostral to the recording site. The results indicate that both the responsiveness of p.s.d.c. neurones to noxious mechanical and thermal stimuli and the area of skin from which such stimuli may effectively excite these cells are powerfully suppressed by inhibitory controls descending from the brain. The possible functions of these descending actions are discussed.

3) The relationship between neurones of the p.s.d.c. and s.c.t. systems has been investigated. Contrary to recent reports in the literature, it was established that p.s.d.c. and s.c.t. projections arise in substantial part, if not entirely, from separate populations of neurones in the dorsal horn. There is, however, a close relationship between the two systems at the level of the dorsal horn. Evidence was obtained to support the suggestion that some s.c.t. cells make effective excitatory collateral connections with p.s.d.c. neurones.

List of Abbreviations

p.s.d.c.	postsynaptic dorsal column system
s.c.t.	spinocervical tract
d.l.f.-d.c.n.	spinomedullary neurones ascending the dorsolateral funiculus
l.c.n.	lateral cervical nucleus
d.c.n.	dorsal column nuclei
d.l.f.	dorsolateral funiculus
d.c.	dorsal columns
VPL	ventroposterolateral nucleus of the thalamus
NRM	nucleus raphe magnus
Rgc	nucleus reticularis gigantocellularis
Rmc	nucleus reticularis magnocellularis
LC	locus coeruleus
LRF	lateral reticular formation
PAG	periaqueductal grey
e.p.s.p.	excitatory postsynaptic potential
i.p.s.p.	inhibitory postsynaptic potential
HRP	horseradish peroxidase

INTRODUCTION

The postsynaptic dorsal column (p.s.d.c.) and spinocervical tract (s.c.t.) systems are two major ascending spinal pathways in the cat concerned with the processing and transmission of sensory input to the dorsal column nuclei and lateral cervical nucleus respectively.

Neurones of the p.s.d.c. system are contacted by boutons which may participate in axo-axonic contacts, triadic arrangements and glomerular complexes (Bannatyne, 1984; Maxwell, Koerber & Bannatyne, 1985), suggesting that both their coarse and fine fibre inputs are subject to presynaptic modulatory influences. In contrast, neurones of the s.c.t. have a simple ultrastructural organisation and their direct afferent input appears to be free of presynaptic control (Maxwell, Fyffe & Brown, 1982, 1984). This suggests that different mechanisms are involved in the processing of afferent input to these two somatosensory systems and this is likely to be reflected in the response properties and receptive field organisation of p.s.d.c. and s.c.t. neurones. Some differences have already been noted (Brown & Fyffe, 1981; Brown, Brown, Fyffe & Pubols, 1983a) but these studies involved relatively small samples of units most of which had receptive fields on the foot or toes. This thesis has studied the response properties and receptive field organisation of a large sample of identified p.s.d.c.

units including units with receptive fields located on the proximal limb. In view of the ultrastructural organisation of p.s.d.c. neurones, a particular aim of the present study was to investigate the modulatory effect of stimuli applied outside the excitatory field and its interaction with excitatory input.

Dorsal horn neurones are subject to tonic descending influences from the brain which may profoundly modify their modality and receptive field characteristics (Wall, 1967; Hillman & Wall, 1969). While the polysynaptic input to s.c.t. neurones may be profoundly suppressed by descending systems, the boundaries of their receptive fields are relatively unaffected by these actions (Wall, 1967, Brown, 1971). In contrast little is known of the influence of descending systems on the receptive field properties of p.s.d.c neurones although some of these neurones have an extensive subliminal fringe and a minority have labile receptive fields (Brown & Fyffe, 1981; Brown et al., 1983a). This thesis has studied the influence of tonic descending systems on the response properties and receptive field organisation of identified p.s.d.c. neurones.

Although morphological, ultrastructural and physiological studies have established that there are distinct differences between p.s.d.c and s.c.t. neurones (see later), close relationships nevertheless exist between the two systems. Jankowska, Rastad & Zarzecki (1979) have provided electrophysiological evidence for a link at the

level of the dorsal horn. They showed that stimulation of the cervical dorsolateral funiculus produced excitatory postsynaptic potentials in p.s.d.c. neurones and these had latencies compatible with an axon collateral connection from s.c.t. cells. Recently, Maxwell & Koerber (1986) have provided direct ultrastructural evidence for such a link. Most s.c.t. neurones giving rise to axon collaterals respond to both hair movement and pressure on the skin (Brown, Rose & Snow, 1977b) and the response of p.s.d.c. neurones to such stimuli could therefore be mediated in part by neurones of the s.c.t. Work presented in this thesis was aimed at determining the influence of s.c.t. cells on activity in p.s.d.c. units by establishing the efficacy of this link.

Recently the concept of separate s.c.t. and p.s.d.c. projections arising from different populations of dorsal horn neurones, each with distinct characteristics, has been challenged. Lu, Bennett, Nishikawa and Dubner (1985) have provided evidence that some dorsal horn neurones may have branched axons, with one branch ascending the dorsal columns and the other the ipsilateral dorsolateral funiculus. They found that 40% (23) of a sample of dorsal horn neurones could be antidromically activated from both the dorsal columns and dorsolateral funiculi and concluded that many neurones contribute axons to both the p.s.d.c. and s.c.t. systems. However, these workers employed search stimuli of 30V and

observed that the latencies for antidromic activation via the two presumed axons were always similar. This suggests that their stimuli might have spread between the two funiculi. This thesis has reinvestigated the possibility that the p.s.d.c. and s.c.t. projections might, in part, arise from a common population of dorsal horn neurones.

Part A: Laminar Organisation of the Dorsal Horn

The most detailed description of the cyto-architectonics of the dorsal horn is that of Rexed (1952, 1954). On the basis of the shapes, sizes, density and distribution of neuronal cell bodies observed in 100um thick Nissl stained sections, Rexed proposed that the dorsal horn could be divided into six laminae. The boundaries between some of the suggested layers are indistinct and are probably best considered as zones of transition between groups of cells of particular types. Nevertheless the scheme has been useful as a frame of reference for studies of the anatomical and physiological organisation of the dorsal horn.

Extensive golgi studies (Ramon y Cajal, 1909; Scheibel & Scheibel, 1968; Prohansky & Egger, 1977) have suggested that the dendritic organisation of the dorsal horn is composed of a dorsoventral sequence of neuropil fields each of which have particular dendritic organisations. The sequence of layers shows some congruency with the laminae proposed by Rexed (1952, 1954) while the dendritic orientations strongly reflect the organisation of primary afferent fibre collaterals (Scheibel & Scheibel, 1968).

Studies using classical anatomical techniques have provided only limited information about the morphology of primary afferent terminals (Szentagothai, 1964; Scheibel & Scheibel, 1968) but strongly suggest that there is a segregation of input to the dorsal horn with fine fibres

distributed to the superficial horn (lamina I and II) and coarse fibres in deeper layers (lamina III-VI) (LaMotte, 1977; Rethelyi, 1977; Ralston & Ralston, 1979). More recently intracellular staining techniques have enabled investigation of the morphology of axon collaterals associated with electrophysiologically identified afferent units (see Brown, 1981; Light & Perl, 1979; Mense, Light & Perl, 1981; Sugiura, Schrank & Perl, 1985; Sugiura, Lee & Perl, submitted). These studies have confirmed the segregation of coarse and fine fibre inputs and have revealed that different types of afferent unit have characteristic collateral morphologies.

Wall (1960, 1967) has made a systematic study of the functional properties of neurones located in successively deeper laminae. He has suggested that lamina IV, V and VI contain overlapping populations of three main types of cells which have a) progressively larger receptive fields, b) progressively longer central delays, c) increasing modality convergence and d) different segmental and descending controls. These factors were put together to form the 'lamina cascade model' in which it was proposed that afferent input was relayed through cells of successively deeper laminae (Wall, 1967, 1969). However, while some subsequent studies hve supported the cascade scheme (Price & Mayer, 1974; Applebaum, Beall, Foreman & Willis, 1975), others have been unable to detect systematic differences (Gregor & Zimmerman, 1972; Brown, Fuchs & Tapper, 1975).

Part B: Somatotopic Organisation of the Dorsal Horn - The Anatomical Synthesis of Receptive Fields

When the receptive fields of dorsal horn neurones recorded at various locations throughout the dorsal horn of the lumbosacral enlargement are compared, it is apparent that together they form a map of the surface of the hind limb (Wall, 1960; Bryan, Trevino, Coulter & Willis, 1973; Brown, & Fuchs, 1975; Brown, Fyffe, Noble, Rose & Snow, 1980a). The most detailed maps are those from the studies of Brown et al. (1980a) which were compiled by determining the positions of the cell bodies and receptive fields of a large number of identified s.c.t. cells in individual animals. The resulting map consists of a large medial area containing a representation of the toes which is surrounded by a series of crescentyic shells containing the foot, leg and most laterally the thigh and hip.

Major features of the somatotopic arrangement and aspects of dorsal horn organisation by which it is generated are considered below. Much of the work described has used the s.c.t. and its relationship with hair follicle afferents as a model (Brown et al., 1980a; Brown, Rose & Snow, 1980b; Brown & Noble, 1982.)

Organisation of Hair Follicle Afferent Collaterals

Several workers have pointed out that the flame shaped arbours seen in transverse sections are greatly extended in the sagittal plane (Sterling & Kuypers, 1967;

Scheibel & Scheibel, 1968). Intra-axonal staining has identified them as the collaterals of hair follicle afferent fibres and has confirmed that the terminal arbours of successive collaterals overlap in the dorsal horn to form a continuous column of terminals. The full extent of the column is not known but it is at least one centimetre and probably up to three or four centimetres (Brown, Rose & Snow, 1977a).

Scheibel & Scheibel (1968) reported that adjacent flame shaped arbours shift from a virtually upright orientation medially to an inclined position laterally. They therefore form a radial array, perpendicular to the lamina II-III border which curves ventrally at its lateral edge. Similar orientations have been described for individual intracellularly stained hair follicle afferents terminating at various medio-lateral positions in the dorsal horn (Brown , Rose & Snow, 1977b).

The sagittal columns of adjacent hair follicle afferent collaterals therefore form a continuous sheet of terminals throughout lamina III in which the receptive fields of single hair follicle afferent fibres are represented by longitudinal columns of cord.

Distribution and morphology of s.c.t. neurones

Retrograde labelling studies (Craig, 1978; Brown et al., 1980a; Enevoldson, 1982) have shown that neurones of the s.c.t. are distributed in lamina I, III, IV and V with a major concentration in lamina IV. The results of these studies and of electrophysiological mapping

experiments (Brown et al., 1980a) agree that in plan view they are evenly scattered forming a sheet of cells across the dorsal horn.

Though morphologically heterogenous, neurones of the s.c.t. characteristically have well developed dorsally directed dendrites which ascend through lamina III (Jankowska, Rastad & Westman, 1976., Brown, House, Rose & Snow, 1976; Brown et al.,1977a). S.c.t. cells are therefore ideally organised for receiving contacts from the terminals of hair follicle afferent fibres.

Somatotopic organisation of primary afferent fibres

Early accounts of the topographical distribution of dorsal root afferents in the dorsal horn are at variance, perhaps largely because of the different segmental levels studied (reviewed by Rethelyi & Szentagothai, 1973). But there is now good evidence that the terminations of primary afferent fibres are topographically organised and that the somatotopic organisation of dorsal horn neurones is derived largely from this arrangement. Several types of study have provided this evidence. At the single unit level, intracellularly labelled hair follicle afferent fibres terminate in areas where their receptive fields are represented within those of s.c.t. neurones with which they make monosynaptic connections (Brown, 1981). At a gross level, whole cutaneous nerves labelled with HRP distribute to regions of the dorsal horn that are somatotopically appropriate for their electrophysiologically determined fields of innervation (Koerber

& Brown, 1981). And systematic studies of the patterns of degeneration in the dorsal horn following section of each of the lumbosacral dorsal roots has shown that the projections of dorsal root fibres are somatotopically appropriate for their respective dermatomes (P.B. Brown & Culberson, 1981).

Indeed the caudo-ventral progression of the somatotopic map laid out in the lumbosacral dorsal horn is essentially a reflection of the organisation of the dorsal root dermatomes which progress over the hind limb in a spiral-like fashion (Werner & Whitsel, 1967; P.B. Brown & Fuchs; 1978). The sacral dermatomes (S_1-S_2) cover the perineum and tail and progress down the postero-lateral surface of the leg. The L_7 dermatome encompasses both dorsal and ventral surfaces of the foot, with successive rootlets crossing the toes from lateral to medial (Kuhn, 1953; Burton & McFarlane, 1973). These are followed by the L_6-L_5 dermatomes which ascend the antero-medial surfaces of the limb. Within this scheme fibres innervating the proximal limb distribute to lateral regions of the dorsal horn while fibres innervating the distal limb distribute to the medial dorsal horn (Brown, 1981).

Gradients within the somatotopic map

Within the somatotopic representation, about 90% of spinocervical tract cells adjacent in the rostrocaudal plane, have overlapping receptive fields. There is therefore a very gradual change in topography in the

rostrocaudal axis of the cord. In the transverse plane, however, fewer than 50% of adjacent cells have overlapping receptive fields and the resulting somatotopic gradient is therefore steep (Brown et al., 1980a; Brown, Rose & Snow, 1980b).

Scheibel & Scheibel (1968) in proposing a process by which afferent projections could be recruited to form the receptive fields of dorsal horn cells, predicted that the organisation of (hair follicle) afferent arbours would produce a precise segregation of projections from different skin areas in the transverse plane but smearing of the representation in the rostro-caudal axis. However, although the columnar topographical arrangement of s.c.t. neurones is undoubtedly a reflection of the columns formed by primary afferent collaterals, this is not the full explanation.

Brown et al. (1980b) have investigated the relationships between adjacent pairs of s.c.t. neurones both within the columns and in adjacent columns. The neurones were intracellularly labelled after mapping of their receptive fields. Neurones adjacent in the sagittal plane had overlapping or contained receptive fields and their dendritic trees interdigitated. In contrast, pairs of neurones adjacent in the transverse plane had either overlapping receptive fields and interdigitating dendritic trees, or non-overlapping receptive fields and dendrites occupying separate volumes of cord.

The gentle, smeared somatotopic gradient in the sagittal plane, produced by the columns of hair follicle afferent fibres, is therefore exaggerated by the overlapping dendritic domains of sagittally adjacent s.c.t. neurones. In contrast, the steep gradient set up in the transverse plane is maintained by transversely adjacent s.c.t. cells, most of which occupy separate volumes of cord. Even where transversely adjacent neurones make contact with the same hair follicle afferent, the input they receive will be relatively weak (Brown & Noble, 1982).

Factors determining receptive field size

It is clear from the somatotopic map that there are regional variations in the receptive field size of dorsal horn neurones (Brown & Fuchs, 1975; Brown et al., 1980a). Neurones with receptive fields on the proximal limb which are located mainly in the lateral horn have larger fields than those with receptive fields on the distal limb which are located in the medial horn (see also Devor & Wall, 1976). It is also reported that neurones in lamina V have larger receptive fields than those in lamina IV (Wall, 1967; Price & Mayer, 1974; Applebaum, Beal, Foreman & Willis, 1975) though this has been disputed (Brown, Fuchs & Tapper, 1975).

Several investigators have suggested that the configuration of dorsal horn neurones could act as determinants of receptive field size (Wall, 1967; Scheibel & Scheibel, 1968; Tapper, Brown & Moraff, 1973).

If dorsal horn neurones sample groups of adjacent afferent fibre columns to form larger composite receptive fields, then a greater mediolateral dendritic spread would allow recruitment of a larger number of afferent fibres and so produce a larger receptive field. From a quantitative analysis of Golgi stained sections of the dorsal horn, Prohansky and Egger (1977) reported a two-fold increase in mean dendritic spread between neurones in lamina IV and VI and a second gradient within individual laminae where mediolateral spread in particular increased for successively more lateral cells. In addition, neurones in spinal segments L_5 and L_6 (which contain cells with proximal fields) tended to have greater mediolateral dendritic spreads than neurones of the L_7 and S_1 segments.

However, studies, in which s.c.t. neurones were intracellularly labelled with HRP and their receptive fields mapped, have found no correlation between the mediolateral dendritic spread and receptive field size (Brown et al., 1976). Indeed the main axis of orientation of s.c.t. cell dendrites is in the rostrocaudal plane and, furthermore, neurones in the lateral dorsal horn have more extensive rostro-caudal spreads than neurones in the medial horn (Brown et al., 1976; Brown et al., 1977b). These observations suggest that, for the s.c.t. at least, rostro-caudal dendritic spread is correlated with receptive field size. Noble (1981) has therefore suggested that if the primary

afferent columns and rostrocaudally elongated dendritic trees were juxtaposed at a slight angle, then several primary afferents could be recruited from rostral to caudal along the dendritic tree. A more rostrocaudally extensive dendritic tree could recruit more afferent fibres and result in a larger receptive field. In support of this theory, it has been noted (Brown et al., 1977a) that there is a gradual medial shift in the positions at which successive collaterals are distributed from hair follicle fibres coursing rostrally in the dorsal columns.

The theory that dendritic configuration could determine receptive field size is based on an assumption that larger receptive fields are the result of greater afferent recruitment. But quantitative information on the convergence of afferent fibres on to dorsal horn neurones is lacking. Indeed Brown (1981) has pointed out that since changes in the rostrocaudal dimensions of hair follicle collaterals are closely matched by changes in the rostrocaudal spread of s.c.t. cell dendrites, unless there is a gradient across the width of the horn in the density of afferent fibres relative to the number of s.c.t. cells, the convergence on to s.c.t. neurones will be constant (this assumes parallel orientations). Under these conditions the area of the receptive field formed might be determined by the sizes of receptive fields of the afferent fibres recruited. These are greater, on average, for afferents innervating the

proximal limb than for those innervating the distal limb (P.B. Brown & Koerber, 1978).

It is likely that a combination of the factors discussed may determine the receptive field size of dorsal horn neurones.

Homotopy of the somatotopic map

Although the L_7 dorsal root dermatome only extends on to the ankle and most distal leg (Werner & Whitsel, 1967; P.B. Brown & Koerber, 1978), the representation of proximal limb regions on the somatotopic map remains homotopic or continuous (P.B. Brown & Fuchs, 1975; Brown et al., 1980a). This is achieved by a displaced distribution of the overlapping dorsal root dermatomes in the dorsal horn (P.B. Brown & Culberson, 1981). Systematic degeneration studies following section of each of the lumbosacral dorsal roots indicate that the projections of dorsal roots L_4-L_5 spread caudally into lateral regions of the L_6-L_7 spinal segments. Similarly the projections of dorsal roots S_1-S_2 spread rostrally into lateral region of L_6-L_7. Together they overlap to form the crescentric, homotopic representations of proximal limb areas. The distal limb area represented in the L_7 dorsal root demonstrates a similar encroachment into medial regions of L_6 and S_1 spinal segments (P.B. Brown & Culberson, 1981).

Both intercollateral spacing and the rostrocaudal spread of collaterals from a hair follicle afferent vary according to its position in the dorsal horn, with

individual collaterals in the lateral horn covering about twice the extent of those in the medial horn (Brown et al., 1977a). The rostrocaudal spread of the dendritic trees of s.c.t. neurones have been found to follow a similar pattern (Brown et al., 1977b). This expanded organisation of primary afferent and s.c.t. neuropil may account, at least in part, for the extended, homotopic representation of proximal limb areas in the lateral dorsal horn.

Part C: Physiological Mechanisms Involved in the Formation and Control of the Receptive Fields of Dorsal Horn Neurones

Gradients of sensitivity

Wall (1967) reported that when the receptive fields of 'lamina IV type' and 'lamina V type' neurones are investigated with innocuous stimuli, they are found to contain a central region with a low threshold for excitation surrounded by a zone in which the threshold is relatively higher. These cells therefore demonstrate the existence of a gradient of sensitivity to a single submodality from the centre to the periphery of the field. Similar observations have been made for the receptive fields of loosely identified s.c.t. cells investigated with hand held probes (Lundberg & Oscarsson, 1961; Taub, 1964; Zieglegansberger & Herz, 1971). Recently a systematic investigation of the light tactile receptive field profiles of s.c.t. cells has been made using uniform jets of air applied to sequential positions along the proximo-distal and medio-lateral axes of the fields (Brown, Noble & Rowe, 1986). A unimodal gradient of sensitivity was observed in all (18) of the cells studied, the most sensitive area of the field occurring at or near to the centre. The response magnitude declined steadily from the centre to the periphery and abrupt edges to the fields were not found.

Subliminal fringes

The factors forming the edges of receptive fields of dorsal horn neurones have been analysed by Wall and his colleagues. The work has provided evidence that some neurones receive afferent fibre input from areas of skin outside the receptive field (impulse firing zone) determined by natural stimulation.

Wall (1960) and Merrill & Wall (1972) investigated input from dorsal roots to 'lamina IV type' and 'lamina V type' cells in the dorsal horn. They observed that section, cooling or anode block of a single dorsal root was sufficient to abolish the response of a cell to natural cutaneous stimuli. However, when dorsal roots were stimulated electrically, some cells were found to respond over several roots (Merrill & Wall, 1972). Furthermore the results of Devor, Merrill & Wall (1977) and of Mendell, Sassoon & Wall (1978) provided evidence that such responses could be evoked by afferent fibres innervating areas of skin quite distant from the cell's natural receptive field. A minority of cells recorded in the S_1 spinal segment were found to respond to electrical stimulation of upper lumbar dorsal roots (Devor et al., 1977) and, similarly, neurones recorded in spinal segment L_7 with receptive fields on the leg, foot or toes were excited by electrical stimulation of the flank (Mendell et al., 1978). Most of the excitatory effects observed in this series of studies had latencies indicative of polysynaptic pathways.

Wall and his colleagues concluded that there is a highly efficient group of afferent fibres contained in one root which innervates the natural receptive field and that adjacent roots and, for some cells, distant roots contain afferents innervating wider areas of skin which also terminate upon the cells. These 'long ranging afferents' are relatively ineffective and only excite the cells when electrical stimulation produces a synchronous volley and optimal spatial summation. Such an interpretation requires caution however. Intense primary afferent depolarisation may be produced by electrical stimulation of dorsal roots resulting in the generation of impulses in primary afferent fibres and subsequent excitation of dorsal horn neurones (Toennies, 1938; Devor et al., 1977). Also there is known to be considerable overlap of the dorsal root dermatomes (Koerber & Brown, 1978) and of their terminal projections in the dorsal horn (Brown & Culberson, 1981). It is not inconceivable therefore that primary afferent fibres innervating adjacent areas of skin within the naturally evoked receptive field of a dorsal horn neurone might enter the cord from different dorsal roots.

The incidence of weak inputs to dorsal horn neurones has been studied by Pubols, Fogglesang & Kohle-Hinz (1986). They investigated responses to sural nerve stimulation in cells, including some identified p.s.d.c. neurones, with natural receptive fields lying outside the region of innervation of the nerve. About 10% (20) of the

sample of dorsal horn neurones responded to electrical stimulation of the sural nerve but were unresponsive to natural stimulation of the sural nerve region, though only a minority responded with a fixed latency consistent with monosynaptic input. All of the subsample (31) of p.s.d.c. neurones responding to sural nerve stimulation had a receptive field in the sural nerve region. However, electrical stimulation of peripheral nerves has been shown to produce a profound inhibition of p.s.d.c. neurones (Brown, Brown, Fyffe & Pubols, 1983a) which would probably mask weak excitatory inputs. It is interesting in this respect that when condition-testing was used to assess the time course of the inhibitory action, conditioning stimuli applied to ipsilateral nerves sometimes produced an early facilitation, perhaps reflecting a wide subliminal fringe (Brown et al., 1983a).

Direct observations of a subliminal fringe have been made during intracellular recording from dorsal horn neurones. Hongo & Koike (1975) were able to elicit e.p.s.p.'s in response to discrete electrical stimulation of the skin just outside the firing zones of s.c.t. neurones. And Brown, Koerber & Noble (1987c) found that all (10) of a sample of s.c.t. cells examined in detail for their responses to various forms of natural stimuli responded with e.p.s.p.'s from small areas of skin adjacent to the firing zone. A third (6) of a sample of intracellularly recorded p.s.d.c. neurones had an

extensive excitatory subliminal fringe extending beyond the firing zone of the neurone and responding to similar forms of mechanical stimuli (Brown & Fyffe, 1981).

Pharmacologically induced changes in receptive field size

Although there have been numerous studies of the effects of drugs and putative neurotransmitters on the response properties of dorsal horn neurones, only a few have assessed topographical changes in receptive field properties.

Glutamic acid

Expanded receptive fields have been described following electrophoresis of the putative transmitter glutamic acid in the vicinity of neurones with axons ascending the dorsolateral funiculus (Zieglgansberger & Herz, 1971). Interestingly, higher ejecting currents produced a progressive depression which was not due to depolarisation block or current effects. It was suggested that this effect might be mediated by inhibitory interneurones as a result of a spread of the glutamic acid (Zieglgansberger & Herz, 1971).

Glycine & GABA

In the same experiments (Zieglgansberger & Herz, 1971) the inhibitory transmitters glycine and GABA produced a contraction of cutaneous receptive fields.

Strychnine & Picrotoxin

Yokota, Nishikawa & Nishikawa (1979) have investigated the effects of strychnine, a selective antagonist of glycine (Curtis, Duggan & Johnston, 1971),

on the receptive field properties of trigeminal subnucleus caudalis neurones. Intravenous administration of strychnine (0.08mg/kg) produced a marked expansion of the high threshold mechanical receptive fields of (8) convergent neurones but had no effect on the central brush responsive region. In addition, cutaneous, electrical stimuli evoked excitatory responses from previously unresponsive areas of skin. The receptive fields of neurones responding only to low threshold (5) or high threshold (5) stimuli were not affected by strychnine though all were more responsive to electrical stimulation of the skin.

Yokota & Nishikawa (1979) have made a similar study of the effects of the GABA antagonist picrotoxin (1mg/kg) (Kelly & Renaud, 1973). They reported that the low threshold components of (9) convergent neurones in the nucleus caudalis were greatly expanded whereas the high threshold mechanoreceptive components were virtually abolished. The receptive fields of (3) units responding only to light tactile stimuli were similarly expanded while those responding only to high threshold stimuli (2) were not affected. The effects upon inhibitory fields were not reported in these studies.

4-aminopyridine

Saade, Jabbur & Wall (1985) have investigated the effects of the convulsant 4-aminopyridine which facilitates both excitatory and inhibitory connections (Lemeignan, 1972, 1973; Jankowska, Lundberg, Rudomin &

Sykova, 1977; Jack, Redman & Wong, 1981b). The cutaneous receptive fields of 29 of 33 unidentified dorsal horn neurones were markedly expanded by the drug.

Barbiturate anaesthetics

Barbiturate anaesthetics in particular appear to have a pronounced effect upon the receptive fields and response properties of dorsal horn neurones. Mori, Lee, Chung, Edo & Willis (1984) have made a careful study of the effect of pentobarbitone on the response properties of spinothalamic tract neurones in chloralose anaesthetised monkeys and 'spinothalamic tract like neurones' in decerebrate preparations. Small (10mg/kg) intravenous doses of pentobarbitone produced increased responses to noxious pinch and C-fibre volleys, accompanied by expansion of the high threshold excitatory field. Higher doses (15-20mg/kg) had a depressive effect as has been previously reported (Wall, 1967; Kitahata, Ghazi-Saidi, Yamashita, Kosaka, Bonikas & Taub, 1975).

The facilitatory effects of small doses of barbiturate may be the result of interference with descending and segmental inhibitory mechanisms. Frank & Ohta (1971) reported that pentobarbitone (5-10mg/kg) abolished the inhibitory influence of the reticulospinal tract on reflex ventral root potentials. Brown & Short (1974) have reported that cortically produced inhibition of s.c.t. transmission is very sensitive to barbiturate anaesthesia and Taub (1964) noted that pentobarbitone

doubled the threshold of electrical stimulaton required to evoke inhibition of s.c.t. cells from the brain stem. Amongst reports of effects on segmental inhibition, Willis, Trevino, Coulter & Maunz (1974) have observed that the cutaneous inhibitory fields of spinothalamic tract neurones can be abolished by small doses of pentobarbitone and several workers have noted that barbiturates abolish the inhibitory fields of s.c.t. neurones (Lundberg & Oscarsson, 1961; Taub, 1964; Taub & Bishop, 1965).

It is interesting in this regard that inhibitory fields have been described for postsynaptic dorsal column neurones in the chloralose anaesthetized cat (Brown & Fyffe, 1981; Brown et al., 1983a) but not in studies in which barbiturate anaesthesia was used (Uddenberg, 1968; Angaut-Petit, 1975b; Lu, Bennet, Nishikawa, Hoffert & Dubner, 1983).

The depressive effect that barbiturates have upon the inhibition evoked in dorsal horn neurones is difficult to reconcile with the potentiating effect they have upon GABA-mediated presynaptic inhibition (Schmidt, 1963,1964,1971; Nicoll, 1975; Ransom & Barker, 1976; Macdonald & Barker, 1979), but is probably explained by the various other direct and indirect actions that barbiturates have upon synaptic transmission (Weakly, 1969; Nicoll, 1975; Macdonald & Barker, 1979). The overall action of barbiturates is presumably a complex, dose-dependent balance between these effects.

Spontaneous changes in receptive field size

Dubuisson, Fitzgerald & Wall (1979) monitored the receptive field stability of superficial dorsal horn neurones recorded in unanaesthetised, decerebrate preparations. Half (29) of the units examined had receptive fields that expanded during the recording period (5-15 minutes) while the fields of a smaller number of units contracted or moved their position. These observations did not depend on the integrity of descending systems since similar observations were made in spinal animals. Changes in receptive field boundaries were also reported by Devor & Wall (1981) for 'lamina V type' but not 'lamina IV type' neurones recorded in decerebrate, spinal animals. The changes that occurred were reportedly smaller and over a longer period of time (30 minutes to several hours) than for neurones of the superficial dorsal horn (Dubuisson et al., 1979).

Brown et al., (1983a) have reported labile receptive fields for a minority (13%, 5) of p.s.d.c. units recorded in chloralose anaesthetised cats. However, receptive field expansion generally followed natural stimulation of the receptive field or electrical stimulation of peripheral nerves or cervical dorsal columns.

Long term changes in receptive field topography

Wall and his collaborators have used the somatotopic map of the hindlimb laid out in the

lumbosacral dorsal horn as a base on which to investigate possible plasticity of neuronal connections following deafferentation. They conclude that within a month following such lesions many dorsal horn neurones respond to input that would be considered somatotopically inappropriate in the normal animal (Basbaum & Wall, 1976; Mendell et al., 1978; Devor & Wall, 1978, 1981; Lisney, 1983). Wall and his colleagues have interpreted their results as evidence that dorsal horn neurones receive synapses from afferent fibres innervating distant areas of skin beyond their natural receptive fields but which in the normal physiological preparation are ineffective. These are unmasked, it is suggested, by procedures such as deafferentation which might remove a tonic inhibition or produce increased postsynaptic excitability (Devor & Wall, 1981). It is further proposed that this unmasking involves a chemical message mediated by C fibres (Fitzgerald, Wall, Goedert & Emson, 1985) and that such a mechanism might have a physiological role.

In support of this theory they have described other related phenomena. They report that the flexor reflex is enhanced by thermally induced injury (Woolf,1983) and that the receptive fields of dorsal horn neurones expand over periods of 10-15 minutes to incorporate regions of cutaneous injury (McMahon & Wall, 1984). Both of these effects are reported to be mimicked by tetanic C fibre stimulation (Wall & Woolf, 1984; McMahon & Wall, 1984).

However, other workers have not been able to

confirm observations of plastic changes as a result of deafferentation; either for dorsal root section (Pubols & Goldberger, 1980; Pubols and Brenowitz, 1981, 1982; Brown, Brown, Fyffe & Pubols, 1983b), or for peripheral nerve section (Brown, Fyffe, Noble & Rowe, 1984; Pubols, 1984). The explanation for these discrepancies is not obvious and the controversy remains to be resolved.

Synaptic input to dorsal horn neurones

One of the factors that could contribute to the formation of gradients of sensitivity and subliminal fringes in the receptive fields of dorsal horn neurones is a varying strength of synaptic input from the centre to the periphery of the field. This could result from a systematic difference in the convergence of primary afferent fibre input across the field and/or from a varying synaptic efficacy of single afferent fibres. Some evidence for the latter is provided by the work of Hongo & Koike (1975) in which discrete electrical stimuli were applied to the cutaneous receptive fields of intracellularly recorded s.c.t. neurones. Such stimuli evoked complex e.p.s.p.'s which, from their all or none nature, were believed to result from single impulses in single hair follicle afferent fibres. They observed that electrical stimulation within the centre of the receptive field evoked monosynaptic e.p.s.p. components with greater magnitudes and faster rise times than those evoked by stimulation at the periphery.

These observations have been directly confirmed by

simultaneous intracellular recordings from hair follicle afferent fibres synaptically coupled with s.c.t. cells (Brown, Koerber & Noble, 1987c). Single impulses evoked by intracellular stimulation of hair follicle afferent fibres evoked complex e.p.s.p.'s with mono- and poly-synaptic components in s.c.t. cells. All but 1 of 12 Group II afferent fibres innervating the impulse firing zones of s.c.t. cells evoked e.p.s.p.'s with a latency consistent with a monosynaptic connection. Afferent fibres innervating central regions tended to evoke relatively large e.p.s.p.'s with fast rise times while afferent fibres from the periphery produced variable effects including both the largest and the fastest and the smallest and the slowest potentials.

Hongo & Koike (1975) suggested that this variation in synaptic efficacy might be the result of fibres from the periphery terminating on dendrites more remote from the cell soma than fibres from the centre. This has been directly investigated by light microscopic examination of the relationship between intracellularly labelled pairs of hair follicle afferent fibre and s.c.t. cells (Brown & Noble, 1982). When the receptive fields of the hair follicle afferent fibre and s.c.t. cell were located on separate areas of skin (7 pairs) the terminal arborization of the two elements usually occupied separate areas of the cord and no contacts were observed between them. When the receptive field of the hair follicle afferent fibre was contained within that of

the s.c.t. cell (10 pairs) then terminal arborizations from the axon interdigitated with the dendrites of the cell and contacts were always observed between them. Furthermore, where the hair follicle afferent's field was centrally placed there were many (40-60) contacts and these were made with proximal dendrites whereas when the afferent fibre's field was peripherally located there were fewer (2-13) contacts and these were on the distal dendritic tree. Therefore, as predicted by Hongo & Koike (1975), the location of an afferent fibre within the receptive field of an s.c.t. cell is reflected in a differential proximo-distal distribution of its contacts on the neurone's dendritic tree. However, this distribution alone may not be responsible for the relatively small synaptic potentials evoked in s.c.t. cells by peripherally located afferent fibres.

It was at one time considered that, as a result of current leakage and non-linear summation, a synapse on a distal motoneurone dendrite would be only 30% as effective as a synapse located on the soma (Barrett & Crill, 1974). However, Ianseck & Redman (1973) have shown that there is not the expected correlation (Redman, 1973) between the amplitude of a single fibre Ia e.p.s.p. and its time course; the latter being a guide to its electronic location (Redman & Walmsley, 1983a). Analysis of the amplitude variations of single Ia fibre e.p.s.p.'s originating at various electronic locations shows that the larger synaptic currents producing the

more distally originating e.p.s.p.'s are due to units of e.p.s.p. which are greater in amplitude rather than number (Jack, Redman & Wong, 1981a,b; Edwards, Jack & Kullmann, 1983). These units of e.p.s.p. have been attributed to an all-or-nothing action of single synaptic boutons (Jack et al., 1981a,b; Redman & Walmsley, 1983a, b). It seems therefore that excitatory synapses more distally placed on the dendritic tree are no less powerful than proximal ones in increasing the excitability of the cell. Similar observations have been made for monosynaptic contacts from descending fibres on motoneurones (Harrison, Jack & Kullman, 1985) but to what extent this is a general feature of nerve cell organisation is not yet known. It is possible, however, that the smaller synaptic potentials evoked by single hair follicle afferent fibres peripherally located in a s.c.t. cell's receptive field, may be largely explained by the smaller number of contacts made with the dendrites of the neurone rather than their distal location on the dendritic tree.

The preferential distribution of afferent fibre input from the periphery of the receptive field to the periphery of the dendritic tree may be more significant in other respects. It is conceivable that inhibitory synapses appropriately placed on the dendritic tree could selectively suppress input from distally located synapses thus providing a mechanism for the control of receptive field boundaries.

Interest in the segmental control of dorsal horn neurones was largely stimulated by the proposal of the 'gate theory of pain' by Melzack & Wall (1965). Their model for dorsal horn circuitry controlling the transmission of activity leading to the perception of pain was based on interaction between low and high threshold afferent inputs. It was proposed that input over low threshold, large diameter fibres presynaptically inhibited low and high threshold input to 'transmission cells', while activity in high threshold, small myelinated and C fibres facilitated subsequent inputs. It was envisaged that an increasing stimulus intensity would shift the balance between the effects of large and small diameter inputs leading to an increased activity in the 'transmission cells'.

Interaction between A and C fibre inputs to dorsal horn neurones

Mendell (1966) showed that an A and C fibre conditioning volley inhibited the C fibre-evoked component of a succeeding test volley in neurones of the s.c.t. Gregor & Zimmermann (1972) suggested that this inhibition was produced by activity in cutaneous A fibres. They showed, in a sample of unidentified neurones, that electrical stimulation of peripheral nerves at a strength sufficient to activate both A and C fibres produced a larger C fibre-evoked component when

the A fibres were selectively blocked. The inhibitory actions of A fibres have been further investigated by electrical stimulation of their collaterals in the dorsal columns (Hillman & Wall, 1969; Handwerker, Iggo & Zimmerman, 1975; Foreman, Beal, Applebaum, Coulter & Willis, 1976; Lindblom, Tapper & Wiesenfeld, 1977; Chung, Fang, Hori, Lee & Willis, 1984; Duggan & Foong, 1985). These studies have found that activation of dorsal horn neurones by a dorsal column stimulus is followed by inhibition of background activity for a period lasting between 100 and 200ms. This inhibition has also been shown to be effective against activity evoked by both light tactile and noxious cutaneous stimuli.

The interaction between A and C fibre inputs to identified neurones of the s.c.t. have been further studied by Brown and his colleagues (Brown, Kirk & Martin, 1973; Brown, Hamman & Martin, 1975). Electrical stimulation of cutaneous peripheral nerves which do not excite the unit under study produces a profound inhibition of both background and evoked activity (Brown et al., 1973). These effects presumably have a widespread origin since they can be evoked from peripheral nerves of both the ipsilateral and contralateral limb. Conditioning discharges produced by electrical stimulation of peripheral nerves at a strength sufficient only to excite A fibres produces inhibition of both A and C fibre-evoked responses (Brown et al., 1973, 1975). However, the inhibitory effects are particularly

marked for the polysynaptically-evoked A fibre discharges and C fibre-evoked activity (Brown et al., 1973, 1975). The inhibition of C fibre-evoked activity is equally effective in the presence or absence of a preceding A fibre evoked response (Brown et al., 1975).

A similar inhibitory action has been demonstrated in identified p.s.d.c. units following electrical stimulation of ipsilateral and contralateral cutaneous nerves at strengths sufficient only to excite A fibres (Brown et al., 1983a) and also for identified spinothalamic tract neurones recorded in the monkey (Foreman et al., 1976).

In contrast to the inhibitory actions of A fibres, conditioning volleys conducted by C fibres after selective anodal block of myelinated fibres have no effect on the response of s.c.t. cells to A fibre input from different nerves (Brown et al., 1975).

Electrical stimulation of peripheral nerves therefore demonstrates widespread cutaneous inhibitory inputs to neurones of the dorsal horn. For the s.c.t. at least this inhibition is most easily elicited by activity in large diameter afferent fibres and its actions are most effective on polysynaptic input and on responses evoked by small diameter fibres. However, electrical stimulation of whole cutaneous nerves is highly artificial. Natural stimuli are required to determine the cutaneous receptor types involved and the organisation of cutaneous inhibitory input in relation to

excitatory receptive fields. Only then might it be possible to begin to appreciate the functional importance of such inputs.

Receptor types and organisation of cutaneous inhibitory fields

S.c.t. neurones. During extracellular recording the most common types of inhibitory field detected are separated from the excitatory field by skin from which no effects are apparent and are also often located on the contralateral or other limbs (Taub, 1964; Brown & Franz, 1969; Brown, 1971). Noxious mechanical stimulation is most commonly the effective stimulus but low threshold fields have also been described.

Intracellular recording of s.c.t. neurones has detected inhibitory receptive fields which are located near to the excitatory field and which have an eccentric organisation (Taub, 1964; Hongo, Jankowska & Lundberg, 1968; Hongo & Koike, 1975; Brown et al., 1987c). In these studies i.p.s.p.'s were evoked from restricted areas of skin adjacent to and often overlapping the firing zone of the cell. The inhibition was often elicited by gentle mechanical stimulation though noxious mechanical stimuli were occasionally also effective (Brown et al., 1987c). Although both e.p.s.p.'s and i.p.s.p.'s may be evoked by light tactile stimuli in the firing zone of an s.c.t. cell, impulses in single Group II hair afferents do not evoke i.p.s.p.'s (Hongo & Koike, 1975; Brown et al., 1987c). It seems that fibres

innervating other sensitive mechanoreceptors are responsible for the i.p.s.p.'s and Group III fibres innervating down hairs appear a likely candidate (Brown et al., 1987c).

Inhibitory responses to noxious radiant heating of the excitatory receptive field have been described for a small proportion of s.c.t. cells (Cervero, Iggo & Molony, 1977). A further small number of cells gave mixed excitatory and inhibitory responses when the heating was repeated. The effects of noxious thermal stimuli applied to inhibitory receptive fields have not yet been described.

P.s.d.c. neurones. Inhibitory receptive fields were detected in 47% (18) of a sample of extracellularly recorded p.s.d.c. units (Brown et al., 1983a). These were described as of two main types; either small and within or adjacent to the excitatory field, or large and separated from or adjacent to the excitatory field. The effective stimulus for the majority of small fields was noxious stimulation whereas inhibition was produced from the large fields by either low or high threshold stimuli (Brown & Fyffe, 1981; Brown et al., 1983a).

Spinothalamic tract cells. Cutaneous inhibitory fields have been described for spinothalamic tract neurones recorded from the dorsal horn of the monkey. As for cells of the s.c.t., they are most commonly located on the contralateral limb and often occupy a position that mirrors that of the excitatory field (Price & Wagman,

1971; Willis et al., 1974; Gerhart, Yezierski, Giesler & Willis, 1981). Inhibitory fields on the ipsilateral limb lying adjacent to the excitatory field have also been described (Christensen & Perl, 1970; Willis et al., 1974). Although these may be composed of both proximal and distal components they have not been investigated in sufficient detail to determine whether they are organised in a surround fashion (Christenson & Perl, 1970). The types of stimuli that evoke inhibition of background and evoked activity vary between hair movement and intense mechanical deformation of the skin.

'Lamina V type cells' Wall (1967) and Hillman & Wall (1969) have described a particular type of cell with complex excitatory and inhibitory fields which they have termed 'lamina V type' neurones. These neurones have a central low threshold excitatory zone which is overlapped by a more extensive high threshold excitatory area. The excitatory receptive field components are surrounded by an extensive area of skin overlapping part of the high threshold excitatory field from which inhibitory effects may be elicited by light brushing. The identity of these neurones with surround or lateral inhibition has yet to be determined. They do not correspond to any known types of identified s.c.t., spinothalamic tract or p.s.d.c. neurones so far described.

Mechanisms of segmental inhibition

Condition-testing of s.c.t. cells conducted at various intervals indicates that the inhibitory actions

evoked by electrical stimulation of peripheral nerves have a time course of about 200ms and a maximal effect at 20-50ms. (Brown et al., 1973, 1975). Such a time course is observed in both spinal and intact animals (Brown 1971; Brown et al., 1973) and so does not depend on a supraspinal loop. A similar inhibitory time course was observed following condition-testing of spinothalamic tract neurones in intact monkeys, (Foreman et al., 1976) and of p.s.d.c. neurones in cats with lesioned dorsal columns (Brown et al., 1983a). A few p.s.d.c. neurones demonstrated a much longer time course of inhibition with a peak at 100-150ms and a duration of up to 400ms. Such long lasting inhibition suggests the involvement of a supraspinal loop. However, in general the inhibition of dorsal horn neurones evoked by electrical stimulation of peripheral nerves has a time course which is consistent with presynaptic inhibitory mechanisms in the spinal cord (Eccles, Eccles & Magni, 1961; Eccles, Magni & Willis 1962; Eccles, Schmidt & Willis, 1963). Although axo-axonic contacts have been observed on boutons contacting neurones of the p.s.d.c. system (Bannatyne, Brown, Fyffe & Maxwell, 1982; Bannatyne, 1984; Maxwell, Koerber & Bannatyne, 1985) ultrastructural studies of s.c.t. neurones (Maxwell, Fyffe & Brown, 1982, 1984) and of spinothalamic tract neurones in the cat (Snow & Meyers, 1981) have failed to detect such synaptic arrangements.

I.p.s.p.'s have been recorded from neurones of the

s.c.t. (Hongo et al., 1968), p.s.d.c. system (Jankowska et al., 1979) and spinothalamic tract (Foreman et al., 1976) in response to electrical stimulation of cutaneous nerves. In each case the i.p.s.p.'s had a disynaptic latency and a duration too short to account for the longer components of inhibition evoked by electrical stimulation. However, the disynaptic latency may be an artificial result of synchronous activation of whole nerve since disynaptic i.p.s.p.'s have not been observed following natural activation of s.c.t. cells (Brown et al., 1987c).

That segmental inhibition involves both pre- and postsynaptic mechanisms is supported by pharmacological studies by Game & Lodge (1975). They were able to abolish the early and late components of inhibition evoked in dorsal horn neurones by electrical stimulation of skin, using strychnine and bicuculline respectively. However, the relative and respective roles of the two inhibitory mechanisms remain to be resolved. Both mechanisms may of course act upon interneurones interposed in polysynaptic pathways afferent to dorsal horn neurones. Such an action has been demonstrated for neurones of the s.c.t.

The actions of single hair follicle afferent fibres on neurones of the s.c.t.

Neurones of the spinocervical tract show a high degree of synaptic security in response to activity in hair follicle afferent fibres and indeed stimulus

response curves indicate that some amplification occurs (Brown & Franz, 1969). Intracellular recording in s.c.t. cells of the response evoked by impulses in single hair follicle afferent fibres (Hongo & Koike, 1975; Brown et al., 1987c) suggests that the strong excitatory transmission between the two elements is due to a large polysynaptic component in the compound e.p.s.p. from which action potentials arise. Despite this high degree of synaptic security, neurones of the s.c.t. show poor abilities of spatial summation. When hairs are moved by air jets simultaneously at two different sites within the firing zone of a neurone, the response to the combined stimuli is often no greater than to each of the stimuli alone (Brown et al., 1986). Part of this failure of summation may be due to concurrent inhibitory effects from overlapping excitatory and inhibitory fields which involves, at least in part, a postsynaptic inhibitory mechanism (Hongo et al., 1968; Hongo & Koike, 1975; Brown et al., 1987c). However, Brown, Koerber & Noble (1987b,c) have recently provided evidence that powerful inhibitory mechanisms also act upon the interneuronal chain mediating polysynaptic afferent input to neurones of the s.c.t.

Dorsal root ganglion cells of single hair follicle afferent fibres innervating the firing zone of an s.c.t. cell were stimulated intracellularly to produce pairs of impulses. At the same time, single s.c.t. cells were recorded extracellularly from their axons in the d.l.f.

(Brown, Koerber, Noble, Rose & Snow 1984; Brown et al., 1987b) or intracellularly in the dorsal horn (Brown et al., 1987c). When pairs of impulses were generated in hair follicle afferent fibres at intervals of 20-25ms there was a profound depression of the activity evoked by the second impulse of the pair which was reduced on average to only 16% of the control response. The depressive effect remained marked at an interpulse interval of 200ms and had a total duration in the region of 1500ms. Intracellular recordings from s.c.t. neurones indicated that the compound e.p.s.p. evoked by the second impulse was smaller in amplitude than that evoked by the first. The attenuation affected mainly the polsynaptic component of the potential, the early monosynaptic component being relatively unaffected. Furthermore, impulses or pairs of impulses in single Group II hair follicle afferent fibres never gave rise to i.p.s.p.'s (Brown et al., 1987c).

This inhibitory action was not due to a postactivation depression of the neurone since transmission remained depressed even when impulses were not evoked in the cell (Brown et al., 1987c). Recurrent inhibitory effects were also ruled out since direct intracellular stimulation of s.c.t. cells failed to evoke signs of post-synaptic potentials or to condition responses to hair follicle afferent impulses (Brown et al., 1987c). The time course of the depression and the absence of i.p.s.p.'s suggests a presynaptic inhibitory

action. However, the monosynaptic input to s.c.t. cells appears to be relatively unaffected (Brown et al., 1987c). This observation is supported by ultrastructural investigations of the synaptic boutons terminating on s.c.t. neurones (Maxwell et al., 1982, 1984) which have failed to find axo-axonic contacts. The results of this work therefore suggest that transmission of afferent input to neurones of the s.c.t. is suppressed by pre- and/or postsynaptic inhibitory mechanisms which act upon interneurones in polysynatic pathways.

Descending control of dorsal horn neurones

Influence of descending systems on receptive field size

Although there has been much recent interest in the powerful influence that descending systems can exert upon the transmission of afferent input to dorsal horn neurones, comparatively few reports have attempted to assess their effects on receptive field size.

Taub (1964) reported that electrical stimulation of wide regions of the brain stem, including the cerebellar and red nuclei, produced an inhibition of spontaneous and evoked activity in s.c.t. cells which was accompanied by contraction of the receptive field.

A similar contraction limited to the high threshold components of the receptive fields of spinothalamic tract neurones has been reported to be produced by stimulation in the midbrain periaqueductal grey (Hayes,

Price, Ruda & Dubner, 1979).

Zieglegansberger & Herz (1971) reported that the cutaneous receptive fields (particularly the high threshold components) of s.c.t. neurones were expanded following cold block of the cord. Brown (1971) however, was unable to detect changes in the sizes of the excitatory fields of s.c.t. neurones following a similar procedure, although in this study the areas responding to stimuli of a noxious intensity were not assessed.

Wall (1967) reported that cold block produced no observable change in the low threshold receptive fields of 'lamina IV type' neurones though in the same study 'lamina V type' neurones were excited by innocuous stimuli from an expanded receptive field. A similar expansion including both the low and high threshold components of the excitatory fields of 'lamina V type' neurones has been reported by Hillman & Wall (1969).

More recently Dubuisson & Wall (1980) have investigated the effect of electrical stimulation of the dorsolateral funiculus upon the properties of neurones in the superficial dorsal horn. Most of the units they encountered were facilitated by such stimulation and most of these exhibited expanded receptive fields.

Tonic descending inhibition of dorsal horn neurones

The s.c.t. is the only identified system on which the effects of tonic descending impulses have been systematically investigated. In the decerebrate preparation s.c.t cells may be divided into four types:

type I and II units are activated only by movement of tylotrich and guard hairs respectively. Type III units respond to movement of all types of hairs and some also to pressure, while type IV units either have no detectable field or respond weakly to strong pressure (Brown & Franz, 1969; Brown, 1971). In the spinal preparation (Brown & Franz, 1969) or during cold block of the cord (Brown, 1971) types I, II and III are excited by movement of each type of hair and all type II, III and IV units are excited by pressure. In addition, units responding to noxious pinch or heating of the skin do so more vigorously in the spinal state (Brown, 1971; Cervero et al., 1977). Investigation of the response to electrical stimulation of cutaneous nerves before and during cold block of the cord suggests that the inhibitory action of tonic descending systems is particularly effective on polysynaptic and fine fibre inputs to s.c.t. cells (Brown, 1971). This strong suppressive action upon high threshold inputs has been confirmed by others investigating the effects of cold block on unidentified dorsal horn neurones (Hillman & Wall, 1969; Handwerker, Iggo & Zimmermann, 1975; Cervero, Iggo & Ogawa,1976; Bessou, Guilbaud & LeBars 1975; Dickhaus, Pauser & Zimmermann, 1985). There is nevertheless evidence for a more subtle action of tonic descending systems upon the light tactile input to dorsal horn neurones (Brown, 1971; Wall, 1967).

Intraspinal stimulation of descending systems

The presence of bilateral descending pathways influencing transmission through the spinocervical tract has been demonstrated by intraspinal stimulation in the upper cervical cord (Brown, Kirk & Martin, 1973). Inhibitory actions were elicited by stimulation of each of the dorsolateral and ventral funiculi and were most pronounced on the polysynaptic inputs and responses evoked from small cutaneous fibres (Brown et al., 1973; Brown et al., 1975). Condition testing indicated a time course similar to that of presynaptic inhibitory mechanisms in the spinal cord; they did not involve a supraspinal loop since they were observed in animals with high spinal transections. Similar inhibitory effects were elicited by electrical stimulation of the dorsal columns rostral to a dorsal column transection (Brown & Martin, 1973). These effects were found to be relayed through the dorsal column nuclei and parts of the pathways involved the cerebellum and brain stem. It is possible that some of these effects were mediated by spinally projecting cells in the dorsal column nuclei (Dart, 1971; Kuypers & Maisky, 1975, 1977; Burton & Loewy, 1977), some of which have axons descending in the dorsolateral funiculus (Enevoldsen & Gordon, 1984).

The effect of intraspinal stimulation of the dorsolateral funiculus on neurones in the superficial dorsal horn has been investigated by Dubuisson & Wall (1980). More than half of the neurones investigated

were affected by the stimulus and the great majority were excited or facilitated. These effects could also be observed in spinal animals.

The interpretation of the effects of intraspinal stimulation is however complicated by the fact that such stimuli antidromically activate ascending tract neurones, some of which have spinal collaterals (Brown et al., 1977a; Brown & Fyffe, 1981). These may directly or indirectly give rise to excitatory or inhibitory effects.

Descending influences from the cortex and pyramidal tract

The sensorimotor cortex and the pyramidal tract are known to influence activity in the dorsal horn. Electrical stimulation of the sensorimotor cortex produces primary afferent depolarisation in cutaneous nerve terminals (Carpenter, Lundberg & Norrsell, 1963; Anderson, Eccles & Sears, 1964). Wall (1967) and Fetz (1968) observed that electrical stimulation of the pyramidal tract evoked both excitatory and inhibitory effects on dorsal horn neurones, some of which gave rise to the s.c.t. Inhibitory effects were more prominent dorsally and excitatory effects more common ventrally.

The influence of descending activity from the sensorimotor cortex on identified spinothalamic tract neurones in the monkey has been examined (Coulter, Maunz & Willis, 1974; Coulter, Foreman, Beall & Willis, 1976; Yezierski, Gerhart, Schrock & Willis, 1983). Electrical stimulation of the pre- or postcentral gyrus of the sensorimotor hind limb area produced inhibition or

excitation followed by inhibition in about a third of the neurones investigated. In some cases, the inhibition selectively depressed responses to light tactile natural stimuli and had little or no effect on activity evoked by noxious heat or pinch. The inhibition had a time course of around 200ms with a maximal effect at 40-50ms suggesting a presynaptic mechanism. Further experiments using intracortical microstimulation (Coulter et al., 1976; Yezierski et al., 1983) revealed predominantly inhibitory effects from the SI sensory cortex but excitation, or excitation followed by inhibition from area 4 of the motor cortex.

Descending activity from the cortex has also been shown to influence identified neurones of the s.c.t. Surface electrical stimulation of the hind limb areas of the primary and secondary somatic sensory cortex produced a profound inhibition of the responses of s.c.t. cells to electrical stimulation of cutaneous nerves (Brown & Short, 1974). A few cells were also excited but this was thought likely to be due to intense primary afferent depolarisation. Condition testing revealed an inhibitory time course similar to that of the cortically evoked P wave suggesting a presynaptic action. Similar effects upon s.c.t. cells in the cervical enlargement have been demonstrated from forelimb sensorimotor areas (Heath, 1978).

The precise cortical cytoarchitectonic areas contributing to this inhibitory action have been mapped

in detail using intracortical microstimulation (Brown, Coulter, Rose, Short & Snow, 1977). Two main regions were identified; one in the upper bank of the cruciate sulcus centred on cytoarchitectonic area 4y and the other in the medial part of the posterior sigmoid gyrus including areas 3a, 3b, 1, 5a and 5b. The most effective inhibitory sites were in layers III, V and VI of these regions. These layers contain the cell bodies of pyramidal cells (Jones & Powell, 1970) and corticospinal fibres originating in these cytoarchitectonic areas have been shown to terminate mainly in lamina IV and V of the dorsal horn (Nyberg-Hansen & Brodal, 1963; Coulter & Jones, 1977). It is not clear however whether the effects of cortical stimulation are mediated directly by the pyramidal tract, indirectly through reticulospinal pathways (Hongo & Jankowska, 1967), or both. They appear not to be mediated via the rubrospinal tract (Harrison & Jankowska, 1984).

The influence of the corticospinal tract on s.c.t. neurones has recently been investigated by Harrison and Jankowska (1984). Single stimuli to the pyramidal tract evoked a variable number of e.p.s.p.'s some of which, on latency and frequency following criteria, were judged to be monosynaptic. However, the effects of pairs or trains of stimuli were dominated by i.p.s.p.'s. E.p.s.p.'s were also recorded in a similar study of the effects of pyramidal tract stimulation on neurones of the p.s.d.c.

system (Jankowska, et al., 1979). Thus, whatever the mechanisms invoked by cortical stimulation it is clear that the corticospinal tract has postsynaptic actions on dorsal horn neurones.

Raphe spinal system

The midline raphe nuclei (magnus, pallidus, obscurus) in the medial reticular formation of the lower brain stem have been shown to project to the spinal cord (Brodal, Taber & Walberg, 1960; Kuypers & Maisky, 1975; Basbaum & Fields, 1977; Martin, Jordan & Willis, 1978). The majority of fibres descend bilaterally in the dorsolateral funiculi (Martin et al., 1978; Basbaum, Clanton & Fields, 1978) and terminate in two main regions; superficially in lamina I and II and deeper in lamina V and medial VI and VII (Basbaum et al., 1978).

Electrical stimulation of the nucleus raphe magnus has been found to produce primary afferent depolarisation (Proudfit & Anderson, 1974), presynaptic effects upon single C fibres (Hentall & Fields, 1979) and inhibition of dorsal horn neurones (Fields, Basbaum, Clanton & Anderson, 1977; Guilband, Oliveras, Giesler & Besson, 1977; Duggan & Griersmith, 1979) including identified neurones of the spinothalamic tract (Beall, Martin, Applebaum & Willis, 1976; Willis, Haber & Martin, 1977; Gerhart, Wilcox, Chung & Willis, 1981). Inhibitory effects elicited from the medullary raphe are reported to produce a relatively selective depression of the responses of unidentified neurones to noxious cutaneous

stimuli (Fields et al., 1977; Guilband et al., 1977; Duggan & Griersmith, 1979). However, while medullary raphe stimulation preferentially inhibited the long latency (Aδ, C) responses of spinothalamic tract neurones to electrical stimulation of cutaneous nerves, responses to both noxious and non-noxious natural cutaneous stimuli were depressed (Beall et al., 1976; Willis et al., 1977; Gerhart et al., 1981) and these effects involved at least in part a postsynaptic mechanism (Giesler, Gerhart, Yezierski, Wilcox & Willis, 1981).

The midbrain dorsal raphe, the medullary nucleus raphe magnus and its lateral extension the nucleus alatus are rich in 5-hydroxytryptamine (5-HT) or serotonin containing neurones (Dahlstrom & Fuxe, 1965; Hubbard & DiCarlo, 1974). Serotonergic terminals are distributed throughout the dorsal horn but are particularly dense in the superficial laminae (Carlsson, Falk, Fuxe & Hillarp, 1964; Oliveras, Bourgoin, Hery, Besson & Hanson, 1977). Recent light and electronmicroscopic studies have demonstrated that serotonergic terminals are closely associated with and contact both superficial neurones in lamina I and II (Ruda, Coffield & Steinbusch, 1982; Light, Kavookjian & Petrusz, 1983; Maxwell, Leranth & Verhofstad, 1983) and p.s.d.c. neurones in lamina III and IV (Nishikawa, Bennett, Ruda, Lu & Dubner, 1983). Spinal serotonergic terminals are thought to originate almost entirely from descending systems (Dahlstrom & Fuxe, 1965; Oliveras et al., 1977; Bowker, Westlund &

Coulter, 1981; Bowker, Steinbusch & Coulter, 1981; but see Hadjiconstantinou, Panula, Lackovic & Neft, 1984) and 5-HT has therefore been considered a likely candidate for mediating descending inhibitory effects .

In the superficial dorsal horn, iontophoresis of 5-HT has been reported to produce a depression of responses to noxious stimuli in 70% of neurones encountered (Randic & Yu, 1976). However, Todd & Millar (1983) using carbon fibre electrodes and presumably able to record from much smaller neurones, reported that iontophoresed 5-HT had a predominantly excitatory effect. They suggested that these neurones might mediate the inhibitory effect that 5-HT has been shown to have upon cells in the deeper laminae (Belcher, Ryall & Schaffner, 1978; Headley, Duggan & Griersmith, 1978) including identified neurones of the spinothalamic tract (Jordan, Kenshalo, Martin, Haber & Willis, 1978).

The depressive effects of 5-HT on deeper dorsal horn neurones has been shown to be blocked by prior administration of methylsergide (Griersmith & Duggan, 1980). However, it has not so far been possible, using iontophoresis of purported 5-HT antagonists, to consistently block the inhibition produced by electrical stimulation in or near the raphe nuclei (Belcher et al., 1978) even with administration in the superficial horn (Griersmith, Duggan & North, 1981). Some reduction of the inhibition evoked from the dorsal raphe (Guilband, Besson, Oliveras & Liebeskind, 1973) and the

periventricular grey (Carstens, Fraunhoffer & Zimmerman, 1981; Yezierski, Wilcox & Willis, 1982) has been achieved using intravenous administration but the sites of action are unknown and the results difficult to interpret.

It is possible that electrical stimulation excites other, non-serotonergic cells in the raphe or that a different neurotransmitter is involved. About 90% of spinally projecting neurones in the nucleus raphe magnus contain serotonin (Bowker et al., 1981a,b) but there is also evidence for substantial coexistance with various neuropeptides (Ljungdahl, Hochfelt & Nilsson, 1978; Hochfelt, Ljungdahl, Steinbusch, Verhofstad, Nilsson, Brodin, Pernow & Goldstein, 1978).

Medial reticulospinal pathways - Nucleus reticularis gigantocellularis and magnocellularis

The nucleus reticularis gigantocellularis (Rgc) is located dorso-lateral to the NRM in the medial reticular formation (Brodal, 1957), and like the NRM contains serotonergic cells (Bowker, Westlund & Coulter, 1981). The Rgc gives rise to bilateral spinal projections which descend in the ventral and ventrolateral funiculi (Basbaum, Clanton & Fields, 1978; Castiglioni et al., 1978; Abols & Basbaum, 1981). These terminate mainly in the ventral horn but also in dorsal laminae V and VI.

Electrophysiological experiments in which the effects of stimulation in the Rgc and NRM have been compared, report that the depression produced from the two sites is qualitatively similar (McCreery, Bloedel &

Hames, 1979; Gerhart et al., 1981; Gerhart et al., 1984). Thus it is generally reported that stimulation in the Rgc produces inhibition of background activity and of the responses to both light tactile and noxious mechanical stimuli. Similar effects have been observed on neurones of the s.c.t. (Gray & Dostrovsky, 1983) and on spinothalamic tract neurones in both cat (McCreery & Bloedel, 1975; McCreery et al., 1979) and monkey (Haber, Martin, Chung & Willis, 1980; Gerhart et al., 1981; Gerhart et al., 1984). Although some workers have reported that in a minority of spinothalamic tract cells, inhibition is preceded by facilitation (McCreery et al., 1979; Haber et al.,1980).

The nucleus reticularis magnocellularis (Rmc) is located lateral to the NRM and ventral to the Rgc. It gives rise to an ipsilateral projection of fibres which descend in the dorsolateral funiculus and terminate in a similar area of dorsal horn to the raphe spinal system (Basbaum et al., 1978; Abols & Basbaum, 1981).

Stimulation in the Rmc has been reported to produce inhibition of the responses of dorsal horn neurones including some s.c.t. neurones to noxious and innocuous natural cutaneous stimuli (Gray & Dostrovsky, 1983).

Nucleus Locus Coeruleus

The pontine nucleus locus coeruleus (LC) gives rise to a bilateral projection to the spinal cord (Kuypers & Maisky, 1977; Nygren & Olson, 1977; Westlund, Bowker, Ziegler & Coulter, 1983, 1984). Fibres descend in the

ventral and ventrolateral funiculi (Nygren & Olson, 1977; Mokha, McMillan & Iggo, 1986) and terminate most heavily in the ventral horn, but also in lamina I, II, III and IV of the dorsal horn (Nygren & Olson, 1977; Westlund & Coulter, 1980).

Electrical stimulation of the LC is reported to have a predominantly depressive effect upon dorsal horn neurones, although in some units an excitation precedes inhibition and in a small minority excitation alone is observed (Hodge, Apakarian, Stevens, Vogelsang & Wisniki, 1981; Mokha, McMillan & Iggo, 1985, 1986). The inhibition is most prominent in its action upon discharges evoked by noxious cutaneous stimuli or by activation of Aδ and C fibres. For some convergent neurones a selective suppression of nociceptive responses occurs whilst for others a relatively weaker inhibition of background and brush evoked activity is observed (Hodge et al., 1981; Mokha et al., 1985).

One study (Mokha et al., 1985) has compared the inhibition produced from the LC with that evoked from the NRM in the same dorsal horn neurones. It concluded that these were qualitatively and in most cases quantitatively similar. Anatomical and electrophysiological studies have provided evidence for interaction between the two regions; projections from the LC to the NRM (Pickel, Segal & Bloom, 1970; Chu & Bloom, 1974) and from the NRM to the LC (Sakai, Touret, Salvert, Leger & Jouvet, 1977; Segal, 1979) have been demonstrated. However, recent

studies involving various lesions of spinal fascicles and the midline raphe complex suggest that the inhibition of dorsal horn neurones produced by electrical stimulation of the two nuclei are mediated through largely separate pathways (Mokha et al., 1986).

The LC contains cell bodies with a high concentation of noradrenaline (Dahlstrom & Fuxe, 1965; Nygren & Olson, 1977; Commissiong, Hellstrom & Neff, 1978). A substantial proportion of these cells have been shown to project to the spinal cord (Nygren & Olson, 1977; Commissiong et al., 1978; Westlund et al., 1983, 1984) where they terminate largely in the ventral horn but also in lamina I, II, III and VI of the dorsal horn (Nygren & Olson, 1977; Fleetwood-Walker & Coote, 1981). In the monkey and rat these cells constitute the major (80%) spinal catecholaminergic projection from the pons (Westlund et al., 1983, 1984). But in the cat a species difference may occur since the Kolliker-Fuse nucleus is reported to provide the most dense projection (Stevens, Hodge & Apkarian, 1982).

Noradrenaline applied iontophoretically in the dorsal horn is reported to have actions that are similar to those produced by electrical stimulation in the LC. Headley, Duggan & Griersmith (1978) observed an inhibition of responses to both noxious and to a lesser degree innocuous stimuli following iontophoretic application of noradrenaline in the vicinity of lamina IV and V neurones. A more selective suppression of

nociceptive responses was observed when the noradrenaline was iontophoresed in the superficial dorsal horn whilst recording from cells in deeper laminae. A selective action of noradrenaline on nociceptive input has also been reported for identified neurones of the s.c.t. and p.s.d.c. pathways (Fleetwood-Walker, Mitchell, Hope, Molony & Iggo, 1985). Other studies however, (Belcher et al., 1978; Satoh, Kawajiri, Ukai & Yamamoto, 1979) have reported non-selective effects.

Lateral Reticular Formation

Although previous studies have concentrated on the involvement of the midline brainstem structures in the descending control of dorsal horn neurones, several recent studies suggest that the medullary and midbrain reticular formation (LRF) may make a significant contribution.

Morton, Johnson & Duggan (1983) have investigated the effects of electrical stimulation in the medullary lateral reticular regions and reported a selective inhibition of the response of dorsal horn neurones to impulses in unmyelinated primary afferent fibres with no effect on the response to hair deflection. The most effective medullary stimulus sites were in the region of the lateral reticular nucleus; stimulus currents producing inhibition from this region were less effective in the raphe nuclei and generally ineffective at intervening sites. A direct spinal projection from the lateral reticular region by which these effects could be

mediated has been demonstrated by anatomical studies (Basbaum & Fields, 1979; Kuypers & Maisky, 1975).

Inhibition of the responses of dorsal horn neurones has also been described following stimulation in the more rostral midbrain regions of the LRF (Carstens, Klumpp, & Zimmermann, 1980; Carstens, Bihl, Irvine & Zimmermann, 1981). For some neurones the effects of stimulation in the LRF and PAG were directly compared. Stimulation in the LRF was slightly more effective than the PAG in reducing the response of low threshold and convergent neurones to light tactile stimuli. The two midbrain sites were equally effective in reducing responses evoked by noxious thermal stimuli which were always more substantially suppressed than the brush evoked response. Nevertheless, detailed stimulus-response studies revealed qualitative differences between the inhibition evoked from the two regions. Whereas PAG stimulation consistently reduced the slope of the temperature response curve without altering the units' response threshold, stimulation in the LRF generally produced a parallel shift of the stimulus response curve with an increase in response threshold. These qualitative differences were suggested to underly a differential midbrain control of nociceptive spinal transmission (Carstens et al., 1980, 1981).

Inhibition by midbrain LRF stimulation may be mediated by a direct spinal projection (Castiglioni et al., 1978; Tohyama, Sakai, Salvert, Touvet & Jouvet,

1979) or relayed through connections with other midbrain and medullary structures. Projections from the nucleus cuneiformis of the midbrain LRF have been found to terminate in a number of areas involved in the descending control of dorsal horn neurones; these include the nucleus locus coeruleus, reticularis gigantocellularis, raphe dorsalis and the lateral reticular nucleus (Edwards, 1975).

Periaqueductal grey

It is now well documented that electrical stimulation in the periaqueductal grey (PAG) of the midbrain produces inhibition of dorsal horn neurones (Liebeskind, Guilband, Besson & Oliveras, 1973; Oliveras, Besson, Guilband & Liebeskind, 1974; Carstens, Yokota & Zimmerman, 1979; Carstens et al., 1981; Duggan & Morton, 1983), including identified neurones of the s.c.t. (Gray & Dostrovsky, 1983) and spinothalamic tract (Hayes, et al.; Gerhart et al., 1984). However there is some disagreement as to whether these influences are selective for dorsal horn neuronal responses to noxious stimuli or whether responses to non-noxious stimuli are also affected. Some workers have observed inhibition of spontaneous activity and of both light tactile and noxious cutaneous inputs (Liebeskind et al., 1973; Gerhart et al., 1981; Gray & Dostrovsky, 1983). Others however, report relatively greater suppression of the response to noxious compared to innocuous stimuli (Hayes et al., 1979; Carstens et al., 1979, 1981), of C compared

to A fibre-evoked activity (Hayes et al., 1979; Gerhart et al., 1984), or of units responding to convergent (low and high threshold) compared to low threshold inputs (Liebeskind et al., 1973; Oliveras et al., 1974). Duggan and Morton (1983) have compared the inhibition evoked from the PAG and the immediately ventral midbrain tegmentum. They observed a selective inhibition of C fibre-evoked activity from the former but a non-selective inhibition of both nonmyelinated and air jet evoked responses from the latter. These authors attributed the non-selective inhibition observed by others to varying electrode placements and to stimulus spread (Duggan & Morton, 1983).

The PAG appears to exert its inhibitory influence on neurones of the spinal cord through a number of pathways. The existence of a descending connection from the PAG to the medullary raphe has been clearly established. Neurones in the PAG have been retrogradely labelled following HRP injections in the raphe nuclei (Gallagher & Pert, 1978; Abols & Basbaum, 1981; Yezierski, Bowker, Keretter, Westlund, Coulter & Willis, 1982; Chung, Kevetter, Yezierski, Haber, Martin & Willis, 1983) and have been antidromically activated from the NRM (Shah & Dostrovsky, 1980). Furthermore, a proportion of neurones in the NRM, activated antidromically from the spinal cord, can also be activated by electrical stimulation in the PAG (Fields & Anderson, 1978; Lovick, West & Wolstencroft, 1978).

However, recent electrophysiological and lesioning experiments (Morton, Duggan & Zhao, 1984) suggest that a relay through the raphe nuclei may be relatively less important than a projection or relay involving lateral regions of the medulla. When extensive coagulation was produced in the medullary raphe, inhibition elicited from the PAG was reduced by about a quarter. In contrast, limited bilateral lesions of the lateral reticular nucleus produced a much greater reduction in the inhibition (Morton et al., 1984). A substantial projection from the PAG to the ventrolateral medulla is also suggested by anatomical studies (Rose, 1981; Mantyh, 1983).

In addition to the above pathways, autoradiography has demonstrated projections to other brain structures involved in the descending control of dorsal horn neurones, including the LC, Rgc and Rmc (Mantyh, 1983). Furthermore, a small direct projection, once thought not to exist, has now been established (Castiglioni et al., 1978; Mantyh, 1983; Mantyh & Pershanski, 1982).

Sources of tonic descending inhibition

The mechanisms underlying the suppression of spinal reflexes have been extensively studied by Lundberg and his collaborators (reviewed by Lundberg, 1982). Stimulation in the caudal reticular formation reduces transmission from cutaneous afferents and from high threshold and Ib muscle afferents to motoneurones, primary afferent fibres, interneurones and ascending

tract cells (Lindblom & Ottoson, 1955; Holmqvist, Lundberg & Oscarsson, 1960; Carpenter et al., 1963; Carpenter, Engberg & Lundberg, 1966; Engberg, Lundberg & Ryall, 1968a, b). Tonic descending systems have been shown to have similar inhibitory actions (Eccles & Lundberg, 1959; Holmqvist & Lundberg, 1961; Carpenter et al., 1963; Carpenter, Engberg & Lundberg, 1966; Holmqvist et al., 1960) and it therefore seems likely that similar descending pathways are involved.

Tonic descending inhibition has been shown to originate from centres within the ventromedial medullary and pontine brain stem (Holmqvist et al., 1960; Holmqvist & Lundberg, 1961; Carpenter et al., 1965; Engberg, Lundberg & Ryall, 1968c) and to descend through bilateral pathways in the dorsolateral funiculi (Holmqvist & Lundberg, 1959; Holmqvist et al., 1960). Both pharmacological and brain stem lesioning experiments suggest that the raphe spinal system may be one of the pathways involved. Tonic descending inhibition of spinal reflexes is reduced by systemic administration of 5-HT antagonist and enhanced by the use of monamine oxidase inhibitors (Engberg et al., 1968c). Brain stem lesions which essentially destroy all the raphe nuclei substantially reduce tonic descending inhibitory effects (Engberg et al., 1968c). However, since decerebrate inhibition is only totally abolished when the lesions are extended to include the neighbouring medial reticular formation, other brain stem structures such as the Rmc

and Rgc may be involved.

While investigations of the tonic descending control of reflex pathways has centred on the role of medial brainstem structures, recent evidence suggests that the ventrocaudal medulla might play a role in the tonic descending inhibition of dorsal horn neurones (Hall, Duggan, Morton & Johnson, 1982). The degree of tonic descending inhibition of dorsal horn neurones was assessed by the cold block method before and after electrolytic lesions made systematically throughout brain stem regions. Tonic descending inhibition was reduced by bilateral lesions of the ventrolateral caudal medulla in the region of the lateral reticular nuclei but not by lesions in the raphe areas or the PAG of the midbrain (Hall et al., 1982; Morton et al., 1983). Further indirect evidence for the involvement of the reticular formation has been provided by a study of the effects of spinal cold block on the stimulus-response relationship of dorsal horn neurones excited by noxious radiant heat (Dickhaus, Pauser & Zimmermann, 1985). Reversible conduction block usually produced a parallel shift towards higher excitability with an accompanying decrease in threshold temperature. Since such an effect was previously described during electrical stimulation in the LRF but not in the PAG (see above) (Carstens et al., 1981) it was suggested that tonic descending inhibition might be produced by the same LRF system.

The sites of lesions which reduce tonic descending

inhibition are near catecholamine containing neurones in the caudal medulla, but there is as yet no evidence for the involvement of noradrenaline in these actions. Depletion of catecholamines by reserpine administration does not reduce tonic inhibition of the nociceptive responses of dorsal horn neurones (Jurna & Grossman, 1976; Soja & Sinclair, 1983) and the iontophoretic application of selective noradrenaline antagonists does not produce an increase in spontaneous activity (Fleetwood-Walker et al., 1985). Tonic descending inhibition of dorsal horn neurones as measured by the cold block method is not reduced by selective antagonists of enkephalins (Duggan, Hall, Headley & Griersmith, 1977), 5-HT (Griersmith et al., 1981), glycine or GABA (Duggan, Griersmith & Johnson, 1981) whether administered systematically or iontophoretically. It is likely therefore that a variety of neurotransmitters contained in a number of descending and segmental systems are involved.

Part D: The Postsynaptic Dorsal Column System

The existence of long ascending fibres in the dorsal columns originating from the grey matter of the spinal cord was established by the early anatomical work of Munzer & Weiner (1899, 1910 - cited Nathan & Smith, 1959). Some of these fibres were reported to terminate in the cuneate and gracile nuclei in the pigeon, rabbit and dog. Until recently however, the dorsal columns have been considered simply as a pathway to the dorsal column nuclei composed of the collaterals of ascending primary afferent fibres. Renewed interest in the postsynaptic dorsal column projection followed the electrophysiological demonstration of non-primary dorsal column pathways activated from forelimb (Uddenberg, 1968a,b) and hind limb afferents (Petit, 1972). Subsequent anatomical and electrophysiological investigations have established that the post-synaptic dorsal column projection forms one of the major somaesthetic pathways of the spinal cord.

Terminal distribution of p.s.d.c. neurones

The terminal distribution of p.s.d.c. neurones has been studied in cats by observing the degeneration within the medulla following two-stage lesions of the dorsal columns.

Non-primary afferent fibres originating from the lumbar enlargement terminate in the nucleus gracilis and the cuneate rostral pole (Rustioni, 1973; Gordon & Grant, 1982) while fibres originating from the cervical

enlargement distribute to the cuneate nuclei (Rustioni, 1974). Some degeneration has also been reported to occur in the nucleus Z (Rustioni, 1973, 1974) but the use of a discrete dorsal column lesion (Pompeiano & Brodal, 1957; Gordon & Grant, 1982) suggests that this results from the interruption of fibres ascending in the dorsolateral funiculi.

Within the dorsal column nuclei the major termination occurs throughout the rostral reticular region. A less dense degeneration occurs in the base of the middle region while the clusters region is largely free of terminations (Rustioni, 1973, 1974; Gordon & Grant, 1982). A similar distribution is reported to occur within equivalent areas of the dorsal column nuclei of the monkey (Rustioni, Hayes & O'Neill, 1979).

Cells of origin of the p.s.d.c. projection

The cells of origin of the p.s.d.c. projection have been located by retrograde labelling with HRP in the cat (Rustioni & Kaufman, 1977; Enevoldson, 1982; Bennett, Selzer, Lu, Nishikawa & Dubner, 1983), the rat (Pommery, Roudier & Menetrey, 1984; Giesler, Nahin & Madsen, 1984), and the monkey (Rustioni, 1977; Hayes et al., 1979; Bennett et al., 1983).

In the cat, the retrograde labelling of non-primary afferent fibres has been achieved by HRP injections or implants placed variously in the dorsal column nuclei (Rustioni & Kaufman, 1977; Enevoldson, 1982), the cervical dorsal columns (Enevoldson, 1982) or low

thoracic dorsal columns (Bennett et al., 1983). Despite the various methods used the results of these studies are in good general agreement. Arguably the most careful however, are those of Enevoldson (1982) in which restricted unilateral implants were made and the dorsolateral funiculi lesioned as a precaution against labelling s.c.t. and d.l.f.-d.c.n. cells. Labelled cells in the lumbosacral enlargement were concentrated (95%) in the ipsilateral dorsal horn and were located largely in lamina IV and medial V, with only a few in lamina III. Only very rarely were labelled cells observed in lamina I. The contralateral ventral horn contained the remaining 5% of cells lying mainly in medial lamina VII. Some studies using low thoracic implants (Bennett et al., 1983) lay more emphasis on labelled cells in lamina VI. However, it seems likely that most of these can be accounted for by labelling of propriospinal cells (Enevoldson, 1982).

The laminar distribution of p.s.d.c. neurones overlaps that found for retrogradely labelled s.c.t. cells (Craig, 1976; Brown et al., 1980a; Enevoldson, 1982). However, cells of the s.c.t. tend to lie slightly more dorsally in lamina III and IV and in contrast to the p.s.d.c. system, very few are situated in medial lamina V.

Density of cells

Retrograde labelling studies have enabled rough estimates to be made of the numbers of neurones forming the p.s.d.c. projection. These suggest that the

lumbosacral enlargement of the cat contains between 800 and 1200 p.s.d.c. neurones (Enevoldson, 1982; Bennett et al., 1983) and the cervical enlargement between 1700 and 2000 cells (Enevoldson, 1982). The p.s.d.c. projection is therefore similar in size to the s.c.t. (Enevoldson, 1982; Brown, 1980a) and represents one of the major somaesthetic pathways in the cat spinal cord. Similar estimates suggest that it is equally well developed in the rat (Giesler et al., 1984) and the monkey (Bennett et al., 1983).

Morphology of p.s.d.c. neurones

The morphology of p.s.d.c. neurones has been studied by both intracellular injection (Brown & Fyffe, 1981; Bennett, Nishikawa, Lu, Hoffert & Dubner, 1984) and retrograde labelling with HRP (Enevoldson, 1982). Whilst the reports agree that p.s.d.c. neurones demonstrate heterogenous morphologies they nevertheless vary in their emphasis. Brown & Fyffe (1981) and Enevoldson (1982) draw attention to the differences that exist between the majority of cells in their sample and studies of the morphology of s.c.t. neurones (Jankowska et al., 1976; Brown et al., 1977a; Enevoldson, 1982). Bennett et al. (1983) on the other hand stress similarities in morphology between the cells of their sample and s.c.t. cells.

The intracellular sample of Brown and Fyffe (1981) consisted of 17 cells, all of which had axons which could be seen to enter the dorsal columns. Three main types of

neuronal morphology were described, each of which were related to the positions of cells in the dorsal horn.

1) Cells in lamina III-IV had dendrites well developed in the dorsal direction but restricted in mediolateral and rostrocaudal extent; their dendritic trees tended to be contained within a cylindrical or cone shaped volume of tissue. All of these more superficial cells had dendrites that ascended through lamina II, often into lamina I. This is in marked contrast to cells of the s.c.t. where dorsally directed dendrites seldom enter but turn instead to follow the lamina II-III border (Brown et al., 1977a; Enevoldson, 1982).

2) A second type of cell located in ventral lamina IV though having predominantly dorsally directed dendrites, was less restricted in the transverse plane than more superficially located cells.

3) Ventrally located cells particularly those in medial lamina V had dendritic trees that radiated extensively from the cell body but were restricted to the transverse plane. Dendrites extended dorsally into lamina III and ventrally as far as lamina VI or VII.

A common feature of all the cells analysed was that their dendritic trees were equally or better developed in the transverse compared to sagittal plane.

The report of Bennett et al. (1984) differed from the description above in two main respects. Firstly, dorsally directed dendrites were rarely observed to enter lamina II. Secondly, all of the neurones in their sample

had greater rostrocaudal than mediolateral dendritic spreads.

The retrograde labelling study of Enevoldson (1982) although only able to reveal 3rd or 4th order dendrites allowed an assessment of the morphology of a larger, unbiased population of cells. P.s.d.c. neurones having a greater rostrocaudal than mediolateral spread were found to be concentrated in the lateral half of the horn, while cells with equal or greater transverse extents were all contained within the medial half of the horn. Since all but 2 of the (17) neurones investigated by Brown & Fyffe (1981) were located in the medial half of the horn and all but 3 of the (17) cells of Bennett et al. (1984) in the lateral half of the horn, it is conceivable that the discrepant rostrocaudal and mediolateral dendritic dimensions are accounted for in part by biased sample distributions. Because of the limitation of retrograde labelling used in Enevoldson's study, it was not possible to determine the full dorsal extent of dendrites. An important discrepancy therefore remains regarding the degree to which the dorsally directed dendrites of p.s.d.c. neurones penetrate the superficial laminae of the dorsal horn.

Axon collaterals

The majority of p.s.d.c. neurones (85% in the intracellular study of Brown & Fyffe) appear to give rise to between one and three axon collaterals near the cell body (Brown & Fyffe, 1981; Enevoldson, 1982; Bennett et

al., 1984). These arborize ventral to the parent cell but usually cover a greater transverse extent of the dorsal horn. Some collaterals given off in the grey matter have been observed to project in the d.l.f. (Brown & Fyffe, 1981; Enevoldson, 1982).

Ultrastructure of the p.s.d.c. system

The ultrastructure of boutons contacting neurones of the p.s.d.c. system has been investigated by electronmicroscopical analysis of identified neurones intracellularly labelled with HRP and neurones retrogradely labelled from dorsal column implants (Bannatyne, 1984; Bannatyne, Brown, Fyffe & Maxwell, 1982; Bannatyne, Maxwell & Brown, 1987).

Several types of bouton have been observed to make contact with p.s.d.c. neurones, the two most common types were observed on all of the cells (12) analysed. These boutons were electron lucent, made single asymmetrical contacts with dendrites or somata and contained either 1) round agranular vesicles, or 2) flattened agranular vesicles.

1) The boutons containing round vesicles resembled those previously described for primary afferent fibres (Maxwell, Bannatyne, Fyffe & Brown, 1982; Maxwell & Bannatyne, 1983; Bannatyne, Maxwell, Fyffe & Brown, 1984; Maxwell, Bannatyne, Fyffe & Brown, 1984; Ralston, Light, Ralston & Perl, 1984), some of which are known to make monosynaptic contacts with p.s.d.c neurones (Maxwell, Koerber & Bannatyne, 1985). These boutons were sometimes

involved in more complex synaptic arrangements, including axo-axonic contacts, which are thought to mediate presynaptic inhibition (Gray, 1962), and triadic arrangements the functions of which are unknown. Axo-axonic contacts were also observed on the boutons of intraaxonally labelled primary afferent fibres making contact with retrogradely labelled p.s.d.c. neurones (Maxwell et al., 1985).

2) Boutons containing flattened vesicles appeared to be preferentially located nearer the soma of the neurones. Such boutons are not associated with the terminals of primary afferents and are presumably the boutons of interneurones and descending fibres.

Two other types of bouton were less commonly observed to contact p.s.d.c. neurones:

3) One dorsally located neurone was postsynaptic to the central scalloped shaped elements of glomerular complexes in lamina II and III. The central boutons in these complexes are generally thought to be the terminals of small diameter Aδ and C fibres (Gobel, Falls & Humphrey, 1981; Rethelyi, Light & Perl, 1982; Knyihar-Csillik, Csillik & Rakic, 1982). Such fibres therefore appear to make monosynaptic contact with p.s.d.c. neurones.

4) More ventrally located cells with dendrites in lamina IV, V and VI received larger electron lucent bouton terminals containing round agranular vesicles. These made several asymmetric synapses with dendrites or

somata and were also occasionally post-synaptic to other bouton profiles. Large boutons of this type making several synaptic contacts have been described previously on the terminals of identified Pacinian and Group Ia muscle spindle afferent fibres (Maxwell & Bannatyne, 1983; Maxwell et al., 1984; Semba, Masarachia, Malamed, Jacquin, Harris, Young & Egger, 1984).

In contrast to the complex ultrastructure associated with p.s.d.c. neurones, s.c.t. cells are reported to receive contacts from only two main types of bouton (Maxwell et al., 1982, 1984). These boutons are similar to the two most common types observed to contact p.s.d.c. neurones. About two-thirds, a proportion of which degenerate following dorsal root rhizotomy, contain circular agranular vesicles. Many of these are presumably the terminal boutons of hair follicle afferent fibres (Maxwell et al., 1982). The remaining third contain flattened vesicles and are preferentially distributed on proximal dendrites. These survive dorsal root rhizotomy and are presumably the boutons of interneurones and descending fibres. However, in contrast to the boutons contacting p.s.d.c. neurones boutons associated with s.c.t. cells were never observed to be postsynaptic to other bouton profiles. The direct input to the s.c.t. would therefore appear to be free of presynaptic modulatory effects.

The contrasting ultrastructural organisations of these two somatosensory systems suggest that different

mechanisms are involved in the processing of their afferent input. Such differences are likely to be reflected in the response properties and receptive field organisation of p.s.d.c. and s.c.t. neurones.

Physiology of the p.s.d.c. system

The physiology of p.s.d.c. neurones has been studied in less detail than neurones of the s.c.t. in the cat or the spinothalamic tract in the monkey. Recordings have been made from the cuneate (Uddenberg, 1968b) or gracile funiculi (Angaut-Petit, 1975a,b; Brown et al., 1983a) or from neurones in the lumbosacral dorsal horn (Jankowska et al., 1979; Brown & Fyffe, 1981; Lu et al., 1983). As far as can be determined from the brief study of Uddenberg (1968b) there are no obvious differences between units activated from forelimb and hindlimb skin.

a) Response properties and afferent input

P.s.d.c neurones are activated by a wide range of afferent fibre inputs. The majority of neurones may be excited by light mechanical stimulation such as movement of hairs, tapping of the skin and displacement of slowly adapting type I receptors (Uddenberg, 1968b; Angaut-Petit, 1975b; Brown et al., 1983a). Neurones with receptive fields on the foot or toes frequently respond to vibration and pressure applied to glabrous skin (Uddenberg, 1968b; Angaut-Petit, 1975b; Brown & Fyffe, 1981; Brown et al., 1983a). There is direct evidence at the ultrastructural level that several types of sensitive

cutaneous afferent fibre make monosynaptic contact with neurones of the p.s.d.c. system. These include hair follicle, slowly adapting type I and Pacinian afferent fibres (Maxwell et al., 1985).

About 80% of p.s.d.c. neurones are further excited by noxious cutaneous stimuli, including noxious pinch (Uddenberg, 1968b; Angaut-Petit, 1975b; Brown et al., 1983a; Lu et al., 1983) and noxious radiant heat (Angaut-Petit, 1975b; Kamogawa & Bennett, 1986). A small minority of cells (6%) respond exclusively to noxious stimuli (Angaut-Petit, 1975b; Brown et al., 1983a).

Some neurones at least have been shown to respond to electrical stimulation of cutaneous nerves with a burst of long latency impulses consistent with C fibre-evoked activity (Uddenberg, 1968b; Angaut-Petit, 1975b). However, Bennett and his colleagues (Lu et al., 1983; Kamogawa & Bennett, 1986) were unable to evoke C fibre responses by electrical stimulation of the cutaneous receptive field and only observed a response to noxious thermal stimuli after sensitisation by repeated periods of heating. These workers suggest that p.s.d.c. neurones receive nociceptive input from fine Aδ rather than unmyelinated afferent fibres.

In addition to cutaneous input some p.s.d.c. neurones receive input from joint and muscle receptors. Uddenberg (1968b) reported that forelimb units could be excited by electrical stimulation of muscle nerves and by manipulation of tendons and joints after deenervation of

the skin. Jankowska et al. (1979) found that about half of an intracellularly recorded sample of p.s.d.c. neurones could be excited with a mono- and disynaptic latency by Group I and II muscle afferents and by high threshold joint afferents. A monosynaptic input from Group Ia muscle afferents has been directly confirmed at the ultrastructural level (Maxwell et al., 1985).

The physiology of the p.s.d.c. system has been studied mainly in the cat, though one report exists in the rat (Giesler & Cliffer, 1985). More than 60% (18) of the cells in this study, recorded in decerebrate spinalised animals, responded only to light tactile innocuous stimuli. The remainder responded more vigorously to pinch but none were excited by noxious thermal stimuli.

b) Receptive field organisation

Early studies of p.s.d.c. neurones recorded in pentobarbitone anaesthetised cats suggested that receptive fields had a simple organisation (Uddenberg, 1968b; Angaut-Petit, 1975b). Low and high threshold excitatory areas were reported to be coextensive and no inhibitory effects could be detected from surrounding skin. A more recent report has emphasised similar receptive field characteristics (Lu et al., 1983).

However, recordings in the chloralose anaesthetised cat (Brown & Fyffe, 1981; Brown et al., 1983a) have revealed a more complex receptive field organisation. The receptive fields of many units were composed of

separate high and low threshold components and where these involved a number of pads, they were often spatially discontinuous.

About half of the units investigated had inhibitory fields. These were of two main types: either small and within or adjacent to the excitatory field, or large and separated from or adjacent to the excitatory field. Inhibition was generally evoked from the small fields in response to noxious stimulation whereas either low or high threshold stimuli applied to the large fields produced inhibition. There is evidence that both pre- and postsynaptic mechanisms are involved; the time course of inhibition produced by electrical stimulation of cutaneous nerves is suggestive of presynaptic inhibitory mechanisms (Brown et al., 1983a) but i.p.s.p.'s have also been recorded from p.s.d.c. neurones upon adequate stimulation of peripheral cutaneous and muscle nerves (Jankowska et al., 1979).

A minority (13%/5) of units were reported to have excitatory fields that expanded in size during the recording period; generally following electrical stimulation of peripheral nerves innervating the receptive field area or of cervical dorsal columns (Brown et al., 1983a). A related observation was made in an intracellularly recorded sample of p.s.d.c. cells, about a third of which had an extensive subliminal fringe (Brown & Fyffe, 1981). Descending influences on neurones of the p.s.d.c. system have not been studied in detail.

Angaut-Petit (1975b) reported that both background and evoked activity were greater in the spinalised state and Jankowska et al. (1979) have provided evidence of excitation from the corticospinal tract. In view of the marked subliminal fringe and receptive field lability that a proportion of p.s.d.c. neurones demonstrate, this would seem an ideal system in which to investigate the influence of descending systems on the organisation of cutaneous receptive fields.

There are several notable differences between the physiology of cells of the p.s.d.c and s.c.t. projections. S.c.t. cells are activated predominantly, although not exclusively, by hair follicle afferent fibres. They do not receive input from slowly adapting type I mechanoreceptors, neither can they be fired by stimuli applied to glabrous skin (Brown & Franz, 1969). Furthermore, s.c.t. cells responding to both low and high threshold cutaneous stimuli (80%) do so from a single coextensive area of skin (Brown & Franz, 1969). S.c.t. cells are not activated from Group I muscle afferents but some may receive excitatory and inhibitory input from Group II muscle afferents (Harrison & Jankowska, 1984). The inhibitory fields of s.c.t. neurones also differ from those of p.s.d.c. units. Those of p.s.d.c. cells are located on the ipsilateral limb and are often adjacent to the excitatory field. In contrast, inhibition of s.c.t. cells is most easily elicited by noxious stimuli applied to remote areas of skin often on the contralateral limb.

Part E: Relationships Between Neurones of the P.s.d.c. and S.c.t. Systems

Collateral connections betweeen neurones of the s.c.t. and p.s.d.c. pathways

Although the preceding description of the morphology ultrastructure and physiology of p.s.d.c. neurones emphasised some of the differences that exist between this system and neurones of the s.c.t., there are nevertheless close relationships between the two projections. Intracellular staining with HRP has shown that the majority (85%) of spinocervical tract cell axons give rise to one or more collateral branches (Brown et al., 1977; Rastad, Jankowska & Westman, 1977). These arborize in laminae III-VI of the dorsal horn where ultrastructural analysis shows that they make an average of 9 contacts with the dendrites or somata of large dorsal horn neurones (Rastad, 1981a,b; Maxwell & Koerber, 1986).

Jankowska et al. (1979) have provided strong electrophysiological evidence that some of these contacts are made with neurones of the p.s.d.c. system. They were able to record e.p.s.p.'s in p.s.d.c. neurones in response to electrical stimulation of the dorsolateral funiculus (d.l.f.) at Th_9. By comparing the response of the same cells to stimulation of the d.l.f. at C_{3-4} and C_1 and for some cells the pyramids also, they were able to establish that three systems of fibres contribute to

these e.p.s.p.'s: (i) fibres terminating or originating between Th_9 and C_{3-4} segments (ii) fibres terminating or originating between C_{3-4} and C_1 and (iii) fibres of the pyramidal tract. E.p.s.p. components of cervical origin (i.e. (ii)) could be clearly distinguished in at least one third (14) of the sample. They could not be evoked from C_1 (i.e. above the lateral cervical nucleus) and their timing overlapped with the latencies for antidromic activation of s.c.t. neurones. Jankowska et al. (1979) concluded that these observations were compatible with their origin via axon collateral connections from s.c.t. cells.

Recently, Maxwell and Koerber (1986) have provided direct evidence for such connections. The collateral arbour of an intracellularly labelled s.c.t. neurone was shown at the ultrastructural level to form synaptic contacts with a retrogradely labelled p.s.d.c. cell.

Most s.c.t. cells shown to give rise to axon collaterals respond to both hair movement and pressure on the skin, and the responses of p.s.d.c. neurones to such stimuli could therefore be mediated in part by neurones of the s.c.t. However, the functional efficacy of the collateral link remains to be determined.

In addition Svensson, Westman & Rastad (1985), have recently shown that there is a system of spinally projecting cells in the l.c.n. which could also contribute to the excitatory effects observed by Jankowska et al. (1979).

Dorsal horn neurones with bifurcating axons contributing to both p.s.d.c. and s.c.t. systems

While there are distinct differences between many neurones of the s.c.t. and p.s.d.c. projections, it must be admitted that a proportion of neurones might, on inspection of their receptive field properties, be attributed to either. Furthermore, the location of cells of origin of the two systems largely overlap in the dorsal horn as noted by Rustioni and Kaufman (1977).

Recently, the concept of separate s.c.t. and p.s.d.c. projections arising from different populations of neurones in the dorsal horn, each with distinct characteristics, has been challenged. Lu et al. (1983) have stressed the similarities between the receptive field properties of the two sets of neurones and Bennett et al. (1984) have claimed, from a sample of intracellularly stained p.s.d.c. neurones, that there are few morphological differences between them. Furthermore, Lu, Bennett, Nishikawa & Dubner (1985) have provided evidence that some dorsal horn neurones have branched axons, with one branch ascending the dorsal columns and the other the ipsilateral dorsolateral funiculus. They found that 23 of 56 neurones recorded in the lumbar dorsal horn could be antidromically activated from both the dorsal columns and d.l.f. at cervical levels, with 22 only from the dorsal columns and 11 only from the d.l.f. They concluded that many neurones contribute axons to both the p.s.d.c. and s.c.t. systems. This conclusion

was supported in a short note (Jiao, Zhang, Liu, Wang & Lu, 1984) reporting double retrograde labelling of dorsal horn neurones after fluourescent dye injections into the lateral cervical nucleus and dorsal column nuclei.

However, Lu et al. (1985) used an antidromic search stimulus of 30V and observed that the latencies for antidromic activation via the two presumed axons were always similar, differing on the average by only 0.26ms. This suggests that their stimuli might have spread between the ascending tracts, even though they divided the dorsal columns and dorsolateral funiculi away from the cord.

SECTION 1

RESPONSE PROPERTIES AND RECEPTIVE FIELD ORGANISATION OF POSTSYNAPTIC DORSAL COLUMN NEURONES

INTRODUCTION

Previous investigators of the receptive field organisation of p.s.d.c. neurones, recorded in pentobarbitone anaesthetised cats, have reported similarities between these neurones and cells of the s.c.t. (Uddenberg, 1968b; Angaut-Petit, 1975b; Lu et al., 1983). However, recent studies of the morphology (Brown et al., 1977a; Brown & Fyffe, 1981; Enevoldson, 1982) and ultrastructure of neurones of the two systems have revealed important differences between them. P.s.d.c. neurones are contacted by boutons which may participate in axo-axonic contacts, triadic arrangements and glomerular complexes (Bannatyne, 1984; Maxwell et al., 1986), suggesting that both their coarse and fine fibre inputs are subject to presynaptic modulatory influences. In contrast, neurones of the s.c.t. have a simple ultrastructural organisation and their direct afferent input appears to be free of presynaptic control (Maxwell et al., 1982, 1984). This suggests that different mechanisms are involved in the processing of afferent inputs to these two somatosensory systems and this is likely to be reflected in different response properties and receptive field organisations of p.s.d.c. and s.c.t. neurones.

For p.s.d.c. neurones recorded in the chloralose anaesthetised cat, some differences have already been noted (Brown & Fyffe, 1981; Brown et al., 1983a); but

these studies involved relatively small samples of units, most of which had receptive fields on the foot or toes. The experiments to be reported in the present Section were designed to study the response properties and receptive field organisation of a large sample of identified p.s.d.c. units including those with receptive fields located on the skin of the proximal limb. In view of the ultrastructural organisation of p.s.d.c. neurones, a particular aim of the present study was to investigate the modulatory effects of stimuli applied outside the excitatory field and their interaction with excitatory input.

The experiments were designed, as far as possible, to avoid any unnatural stimulation of receptors. The skin of the hindlimbs was left intact and the response properties and receptive fields of p.s.d.c. units were investigated using natural cutaneous stimuli. In order to obtain a large sample of units, and to avoid the possibility that an electrode in close proximity to the cell body might modify the neurones' activity, recordings were made from axons as they ascended the dorsal columns.

METHODS

Preparation of animal

The experiments described in this Section were performed on 23 cats, 2.1-2.7Kg in weight, 14 of which were also used to obtain the results presented in Section 2.

Anaesthesia was induced with 4% halothane in an oxygen, nitrous oxide mixture and a carotid artery and jugular vein cannulated for measuring blood pressure and administering drugs respectively. Chloralose (70mg/Kg) was administered intravenously and the halothane discontinued. The trachea was cannulated and the animal artificially ventilated. The level of anaesthesia was assessed by frequent examination of the pupils of the eyes and of a continuous blood pressure recording and by the absence of a withdrawal reflex in response to strong pinch of the toes. When a steady level of anaesthesia had been achieved, the animal was paralysed with gallamine triethiodide (Flaxedil, 15mg/Kg) to improve recording stability. The effects of gallamine were allowed to wear off periodically, to allow assessment of the state of anaesthesia. Supplementary doses of chloralose (50-100mg) were given when required but were rarely necessary.

The temperature of the animal was continuously measured by a rectal probe and maintained by a thermostatically controlled blanket at between 37 and 39^{o}C. End tidal levels of CO_2 were continuously monitored

and maintained within 3.5-4.5% by adjustment of the stroke rate and stroke volume of the respiratory pump.

The spinal cord was exposed by laminectomies between C_1 and C_3 and between L_4 and S_1 inclusive. The animal was then transferred to an experimental frame in which it was supported by a stereotaxic head holder, by clamps on the spines of thoracic and lumbar vertebrae and by hip pins gripping the iliac crests (Clark & Ramsey, 1975). The dura was opened and retracted and the exposed regions of the spinal cord were covered with warm liquid paraffin (B.P.). The paraffin was poured into a pool formed by securing the flaps of skin surrounding the laminectomy to the recording frame and was kept warm by radiant heat from the operating lamps.

Several procedures were employed to achieve a stable recording situation. In addition to paralysis, a bilateral pneumothorax was performed to reduce respiratory movements; moisture loss was prevented by attaching expansible balloons to polythene tubes placed in the chest incisions. Traction was applied to the cord between the hip pins and the clamp on the lumbar vertebra. The hind feet were secured to a supporting platform by plaster of Paris bandages. The bladder was catheterized and kept empty.

Experiments were discontinued if the mean blood pressure fell below 80mmHg.

Electrical stimulating and recording procedures

A diagrammatic representation of the preparation on which are indicated the positions of stimulating and recording electrodes is shown in Fig. 1.

Electrical stimuli (3V, approx. 250μA, 0.1ms, once every 600ms) were applied to the dorsal columns by bipolar silver ball electrodes. The stimuli were provided by isolated stimulation units (Hi-med HG203) and programmed from a pulse generator/programmer (Hi-med Instruments). Electrodes placed on the dorsal columns at C_1 were used to assess the progress of a sectioning of the dorsal columns at C_{1-2}. The dorsal columns were dissected with watchmaker's forceps until the initial negative component of the cord dorsum potential recorded at L_7 was abolished.

A second pair of electrodes placed at C_{2-3} below the lesion were used to apply search stimuli to the dorsal columns and to identify p.s.d.c. units.

In all experiments cord dorsum potentials were recorded through a monopolar silver ball electrode on the lumbar dorsal columns and amplified (100X) by a low level A.C. amplifier (Tektronix RM122) with low and high pass filters set at 0.2Hz and 10KHz respectively. The amplified cord dorsum potential was displayed on an oscilloscope (Tektronix 5311l). Single unit recordings were made extracellularly from axons in the dorsal columns using glass capillary microelectrodes. These were filled with 4M-NaCl and broken or bevelled to D.C.

resistances of 15-20MΩ. The microelectrode was mounted on a micromanipulator and driven through the cord by a stepping motor drive. The micromanipulator was supported by an arc that spanned the animal transversely and could be adjusted to position the microelectrode at a suitable location and angle for tracking. Potentials recorded by the microelectrode were led through a unity gain D.C. pre-amplifier (WPI) and displayed on one channel of an oscilloscope (Tektronix 5223). The D.C. potentials were further amplified (100X) with an A.C. amplifier equipped with high and low frequency filters set at about 60Hz and 50KHz respectively and then displayed on the second beam of the oscilloscope. The animal was earthed by a silver wire reference electrode inserted into back muscles.

Identification of p.s.d.c. neurones

P.s.d.c. axons were identified by a convergence of input from the periphery and/or by an irregular background activity. These criteria differentiated postsynaptic cells from primary afferent fibres. All units were shown to project at least to upper cervical levels by antidromic activation from the dorsal columns at C_{2-3}. The antidromic impulse was identified both by its ability to follow trains of stimuli at 500Hz and by collision with an orthodromic impulse (Paintal, 1959), see Fig. 2. Since most postsynaptic units were activated orthodromically, it was particularly important that the collision test be performed in such a way as to avoid incorrect identification as a result of collision of

antidromic and orthodromic impulses in primary afferent fibres presynaptic to the unit under investigation. This was achieved by gating an orthodromic impulse recorded from the p.s.d.c. axon, which was then used to trigger the antidromic stimulus. Under these conditions, if collision is observed it can only have occurred between the recording electrode and the cervical stimulating electrode. This criterion therefore differentiates postsynaptic dorsal column neurones from propriospinal fibres.

The purpose of the lesion of the dorsal columns at C_{1-2} was to avoid misidentification as a result of recording from descending axons and, in addition, to avoid bombarding the brain with ascending volleys from the search stimulus.

Cutaneous stimuli

The hair of the hind limbs and tail were clipped and the feet securely attached to a support. The receptive fields of p.s.d.c. units were located by stroking the skin and then investigated using both light tactile and noxious stimuli.

Light tactile stimuli were applied by brushing or tapping the skin with a camel hair brush and by other blunt hand-held probes. A motorized brush and air puffs were also employed. Vibratory stimuli were applied with tuning forks.

Noxious stimuli, that is stimuli that were painful when applied to the skin of the investigator, were

applied in both mechanical and thermal forms. The mechanical noxious stimulus was a sustained pinch produced by a strong clip applied to a skin fold. The noxious thermal stimulus was applied as radiant heat to avoid the contaminating mechanoreceptive response which accompanies the use of a contact thermode. The source of the radiant heat was a halogen bulb with an integral focussing reflector (Beck, Handwerker & Zimmerman, 1974; Fitzgerald & Lynn, 1977). To map the receptive field of a p.s.d.c. unit, it was necessary to move the noxious heat stimulus to a number of different skin positions. It was not therefore practicable to use a feedback control since this would require a thermocouple for measuring skin temperature to be carefully repositioned on each occasion. The source was therefore set at a constant intensity at the beginning of each experiment so that, when positioned above the skin at the focussing distance of the reflector (4cm), it produced a ramp increase in skin temperature to a maximum of 50 - 55^{o}C in 7-8 seconds. Radiant heating was terminated when a clear response was evident, or after 8 seconds in the absence of a response. Such a rapid heating is an effective way of exciting thermal nociceptors which respond most vigorously during the dynamic phase of heating (Kumazawa & Pearl, 1977:C fibres; Georgopoulos, 1976:Aδ fibres) and to rapid (1-2^{o}C/s) compared to slow (0.5^{o}C/s) rises in temperature (Kumazawa & Pearl, 1977). The heat stimulus produced no visible signs of injury to

the skin, provided it was not repeatedly applied to the same location. Studies in which the effects of a similar paradigm were carefully investigated report that it causes transient erythema but not oedema (Mauritz & Henriques, 1947; Campbell, Meyer & LaMotte, 1979).

The areas of skin from which light tactile and noxious stimuli evoked excitatory or inhibitory responses were carefully mapped and were recorded on a photograph of the cat's hind limb.

Analysis

On line analysis was performed using spike discrimination and pulse integration units (NeuroLog; Digitimer). These were used to produce a continuous frequency histogram of impulse activity which was displayed on a pen recorder (JJ Instruments). In addition, all responses were recorded on magnetic tape (Racal Store 7DS) and were analysed off line using a computer (Cromenco Systems III) with which frequency histograms were prepared.

Conduction velocity measurements

Conduction velocities were calculated from the latency of the antidromic impulse measured from the oscilloscope screen and the conduction distance measured between the stimulating electrode at C_{2-3} and the lumbar recording site.

Figure 1

Diagrammatic representation of the experimental arrangement for identifying and recording p.s.d.c. axons.

The drawing represents a dorsal view of the spinal cord exposed by laminectomies at the cervical (C_1-C_3) and lumbar (L_5-L_7) enlargements. SI and SII represent bipolar ball electrodes that were used to apply electrical stimuli to the dorsal funiculi at C_1 and C_2. These stimulation sites were above (C_1) and below (C_2) a lesion of the dorsal columns at C_{1-2}, shown by hatching. Cord dorsum potentials were recorded through a monopolar ball electrode placed on the lumbar dorsal columns (R_{CDP}). Single unit recordings were made extracellularly from axons in the dorsal columns using glass capillary microelectrodes (R_{ME}).

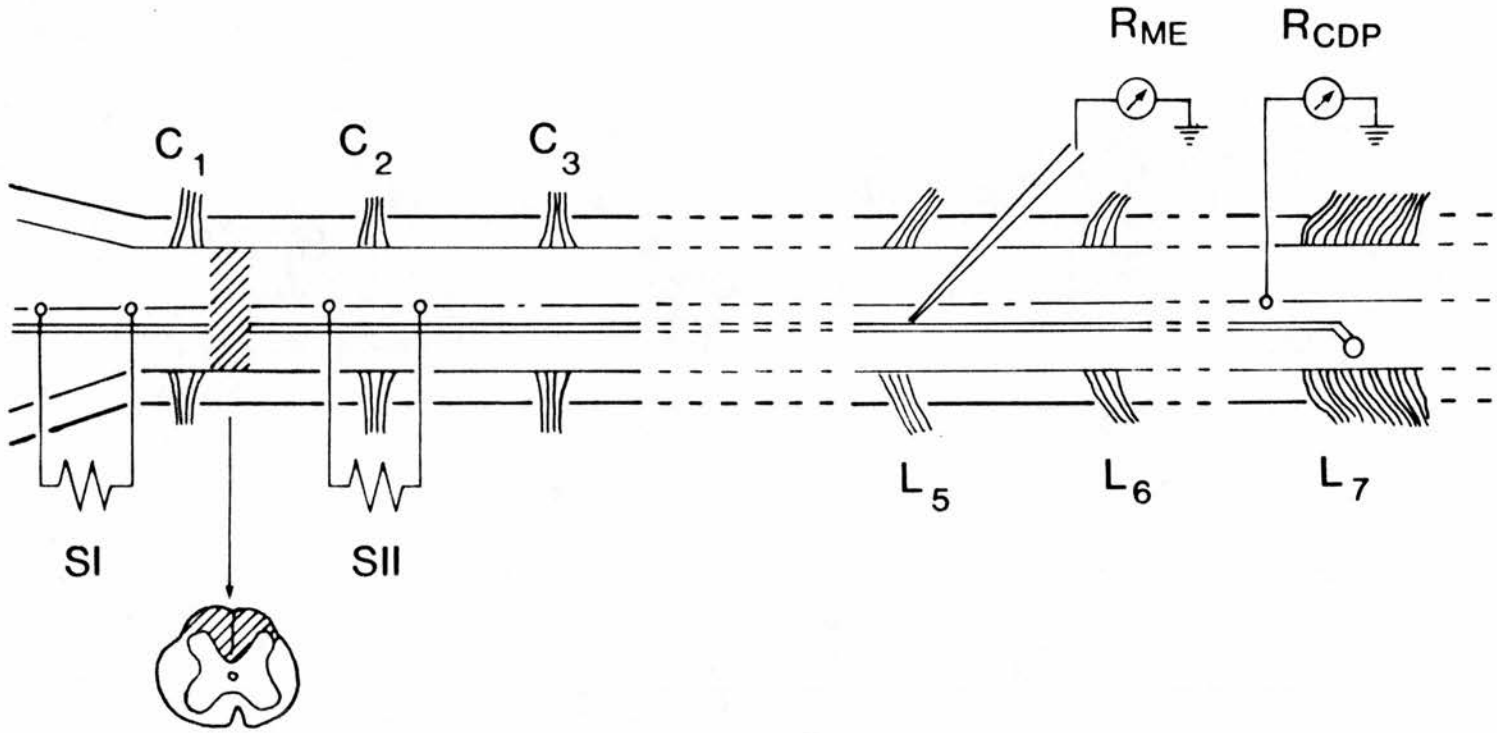

R_ME
R_CDP
C_1
C_2
C_3
L_5
L_6
L_7
SI
SII

Figure 2

Identification of a p.s.d.c. unit; criteria for antidromic activation from the cervical dorsal columns.

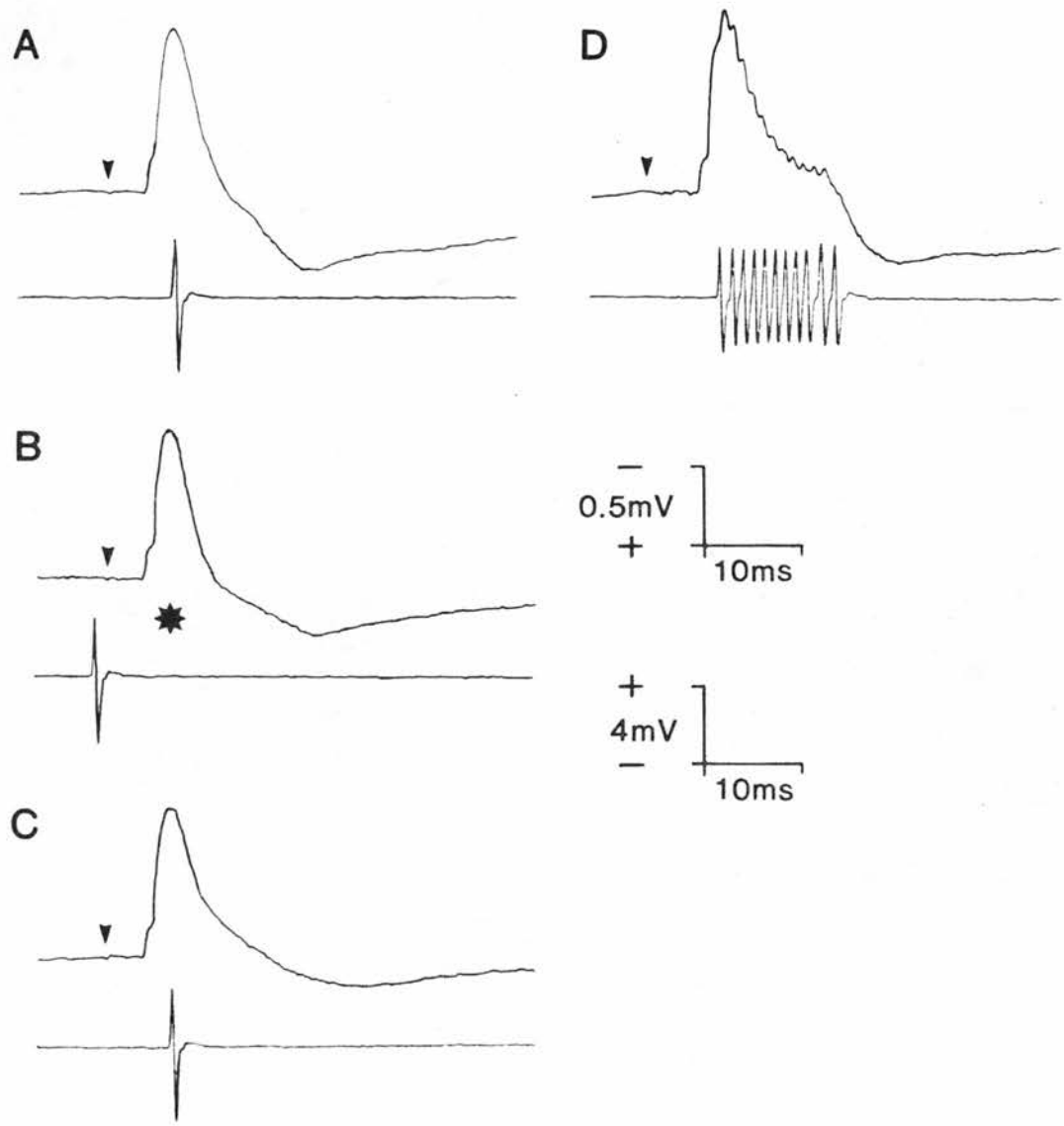
Each pair of traces represents a cord dorsum potential recorded from L_7 (upper trace) and an extracellular single unit recording from an axon in the dorsal columns (lower trace). The arrow heads in A, B and C represent the point at which an electrical stimulus (3V, approx. 250μA, 0.1ms) was applied to the dorsal columns at C_{2-3}. In D the arrow head marks the first in a train of 12 stimuli at 1000Hz. All traces are of single sweeps.

A. Stimulation of the dorsal columns at C_{2-3} excited the unit antidromically.

B. Collision between an orthodromic potential and the antidromic impulse; the asterisk marks the position where the antidromic potential should have appeared.

C. Reappearance of the antidromic impulse in the absence of an orthodromic action potential.

D. The antidromic response following a stimulation frequency of 1000Hz.


A
B
C
D
0.5mV
10ms
4mV
10ms

RESULTS

Detailed investigations were made of the response properties and receptive field organisation of 75 identified p.s.d.c. neurones.

Areas of skin from which brushes and other light tactile stimuli evoked responses were designated low threshold fields.

In early experiments, clips of different force, one judged to be innocuous, the other noxious (when applied to the skin of the investigator) were used to investigate the receptive fields of p.s.d.c. units. All of those units (32) which responded with a slowly adapting discharge to a noxious pinch also responded to an innocuous pinch. Furthermore, it was not possible to differentiate with any certainty between input from low and high threshold slowly adapting mechanoreceptors. Therefore, in subsequent experiments areas of skin from which a sustained noxious pinch evoked a slowly adapting discharge were tentatively designated high threshold fields.

About half the sample of units were also investigated with a selectively noxious stimulus in the form of noxious radiant heat.

Convergence of Input

Convergence of input was a major feature of the p.s.d.c. neurones investigated. Details of these

convergent properties are described below and are summarised in table 1.

1) Sixty-six of the 75 units (88%) received both low and high threshold excitatory inputs. In addition, 48 of these units had inhibitory receptive fields and 15 received input from both hairy and glabrous skin.

2) Eight of the 75 units (11%) received only low threshold excitatory input. However, 7 of these units also had an inhibitory field (of which 4 were high threshold) and 5 responded to stimulation of both hairy and glabrous skin.

3) Only 1 of the 75 units could be excited only by stimuli of a noxious intensity. This unit also had a low threshold inhibitory component.

4) In total, 56 of the 75 units (75%) had inhibitory fields.

5) Twenty of the 75 units (27%) received input (excitatory or inhibitory) from both hairy and glabrous skin.

Skin types forming the receptive field

The extents of both the excitatory and inhibitory receptive fields of the 75 units were carefully mapped. Fifty-two had receptive fields restricted to hairy skin, 3 had receptive fields restricted to glabrous skin and 20 had receptive fields including both hairy and glabrous skin.

Types of unit

Although p.s.d.c. units varied in the degree of convergent input they received, the most marked and consistent differences within the sample were between the properties of those units with receptive fields restricted to hairy skin and those with receptive fields including glabrous skin. These differences included (i) response properties, (ii) receptive field organisation, (iii) pattern of background activity and (iv) conduction velocity. For convenience of description therefore the sample of p.s.d.c. units has been divided into two separate groups:

1) Hairy skin units. This group consists of 52 units all of which had excitatory fields and, where present, inhibitory fields which were restricted to hairy skin.

2) Glabrous skin units. This group consists of 23 units all of which had excitatory and/or inhibitory input from glabrous skin. It should be stressed however, that most of these units (20) also received input from hairy skin.

Each of the receptive field components contributing input to these two types of p.s.d.c. unit are considered in greater detail below.

1) Low threshold excitatory components

All but one of the 75 p.s.d.c. neurones investigated responded with a rapidly adapting discharge to light brushing or tapping of the skin.

Hairy skin units

Examples of the low threshold excitatory components of the receptive fields of hairy skin p.s.d.c. units are shown in Fig. 3.

1) Low threshold excitatory components of the receptive fields of hairy skin p.s.d.c. units varied in their responsiveness to light tactile stimuli such as brushing and air jets.

2) There was a gradient of sensitivity to brushing within the low threshold excitatory areas particularly of those units with larger fields on the proximal limb. However, it was not possible to investigate this systematically using air jets because of the inconsistent nature of responses to air puffs directed at the low threshold area.

3) The boundaries of low threshold excitatory components were diffuse and difficult to map, even in the absence of an obvious low threshold inhibitory area on adjacent skin.

4) Low threshold excitatory components were roughly oval in shape, elongated proximo-distally, and varied in size from the largest areas occupying the thigh

and leg to the smallest areas involving only one or two toes. One unusual unit had two low threshold excitatory components separated by a low threshold inhibitory area of skin.

Glabrous skin units

Examples of the low threshold excitatory components of the receptive fields of glabrous skin p.s.d.c. units are shown in Fig. 4.

1) Of the 23 units with excitatory or inhibitory fields including glabrous skin, 17 responded to tapping of the pads. Twelve of these units were unresponsive to a sustained pinch applied to all, or part, of the tap responsive areas. Therefore, the responses of these units to tapping were most probably a result of rapidly adapting input from the pads.

2) Although very sensitive to tapping of the pads, and even remote parts of the limb and animal frame, none of the units tested (8) followed the vibrations of a tuning fork at a frequency of 384Hz (G) in a one to one fashion.

3) Of the 17 units responding to tap of glabrous skin, 10 also had light tactile input from hairy skin. This usually involved small areas of hairy skin between the responsive pads, so forming a continuous low threshold excitatory component including both hairy and glabrous skin (Figs.4, E & F; 8, A and 9, A).

4) The remaining 7 units, though excited by tapping of the pads, were unresponsive to stimulation of

the hairy skin between them; in this respect, the low threshold excitatory components of these units were discontinuous (Fig. 4, A, B, C & D).

5) The six units with receptive fields including glabrous skin, but with no low threshold input from the pads, all had low threshold excitatory components on the hairy skin.

2) High Threshold Excitatory Components

A. High threshold mechanoreceptive components

Sixty-seven of the 75 units investigated responded with a slowly adapting discharge to sustained noxious pinch produced by a clip applied to the skin.

Hairy skin units

1) Fifty of the 52 units with receptive fields restricted to hairy skin responded with a slowly adapting discharge to a sustained noxious pinch.

2) Responses to pinch were often vigorous and were graded within the field, being strongest at the centre and decreasing towards the edge (Fig. 5).

3) About half (27) of these units had high threshold excitatory components which were roughly coextensive with their low threshold excitatory fields (Fig. 3, C).

4) Sixteen of the units had a high threshold excitatory component which, though overlapping the low threshold component also clearly extended beyond it;

concentrically (3 units), distally (5 units) or proximally (8 units) (Fig. 3, A, B, & D; Fig. 7, A). For 4 of these units the position most responsive to pinch lay outside the low threshold excitatory area. There was no correlation between these observations and the presence of low threshold inhibitory areas on adjacent skin.

5) The remaining seven units had high threshold excitatory components that were smaller than and lay within their low threshold components (Fig. 3, F)

Glabrous skin units

1) Eighteen of the 23 units with receptive fields including glabrous skin responded with a slowly adapting discharge to a sustained noxious pinch.

2) Eleven of these units had high threshold excitatory components restricted to glabrous skin. Where these involved several pads (4 units) the high threshold components were discontinous (Fig. 4, A & B).

3) Four units had a single continuous high threshold component that included both glabrous and adjacent hairy skin.

4) Nine of the units with high threshold excitatory components on glabrous skin could also be excited by gentle tapping of part of the same area (Fig. 4, A & B). The high threshold components on the glabrous skin of the remaining 6 units responded only to stimuli of a noxious intensity.

5) Three units received high threshold excitatory input only from hairy skin (Fig. 4, C).

B. High Threshold Thermoreceptive Components

Thirty-nine of the 75 units were investigated for their responses to noxious radiant heat applied to the skin. Twenty-two of these units were excited, 8 were inhibited (see later) and 11 were unresponsive. (2 units were both excited and inhibited)

Hairy skin units

1) Of the 27 units with receptive fields confined to hairy skin that were tested, 17 were excited, none were inhibited and 10 were unresponsive.

2) All 17 of those units excited by noxious radiant heat were also excited by sustained noxious pinch. Nine of the 10 units unresponsive to noxious heat were nevertheless activated by noxious pinch. There was no clear tendency for those units unresponsive to noxious heat to respond less vigorously to sustained pinch than those units activated by noxious heat.

3) Eleven of the 17 units were excited from areas of skin roughly coextensive with their high threshold mechanoreceptive components (7 of these were also coextensive with their low threshold excitatory components). Two units responded to noxious radiant heat from a wider area of skin than that from which responses to pinch were evoked, whilst 4 responded from a smaller area within that from which pinch was effective.

Glabrous skin units

1) Of 12 units with receptive fields including glabrous skin which were tested for their responses to noxious radiant heat, 5 were excited and 6 were inhibited (see later). The remaining unit was unresponsive.

2) All of the units excited by noxious heat were also excited by noxious pinch from the same area of skin. The 1 unit unresponsive to noxious heat was also unresponsive to pinch.

3) Two of the units excited by noxious heat responded from glabrous skin only, two more responded from hairy skin only and one from both hairy and glabrous skin.

Inhibitory Receptive Fields

All 75 p.s.d.c. neurones were thoroughly investigated for inhibition from skin of the ipsilateral limb in response to light tactile stimuli and sustained noxious pinch. Twenty-seven units were, in addition, investigated for inhibitory responses to noxious radiant heat. A total of 56 units were found to have inhibitory fields. Occasional searches of the contralateral limb did not reveal any inhibitory effects, though this investigation was not made systematically.

Hairy skin units

Thirty-seven of the 52 units (71%) with receptive fields confined to hairy skin were found to receive inhibitory input from areas of skin on the ipsilateral limb.

Effective stimuli: For each of the 37 units, the effective stimulus producing inhibition was light brushing of the hairy skin. Detection of these low threshold inhibitory areas required careful investigation. It was not possible to detect inhibitory input by a single tap or brush stroke; repeated stimulation of an area of skin several cm_2 was required to evoke an effective inhibition of background activity. Although all units were investigated for inhibitory responses to noxious pinch and 27 also to noxious radiant heat, on no occasion did these stimuli produce inhibition of the background activity of units with receptive fields confined to hairy skin.

Inhibition evoked from low threshold inhibitory fields effectively reduced a) background activity, b) activity produced by air puffs directed at the low threshold excitatory area and c) activity evoked by sustained noxious pinch applied to the high threshold mechanoreceptive area (Figs. 6 & 7). Because of the desirability of keeping the duration of noxious thermal stimuli to a minimum, the effect of inhibition on activity evoked by noxious heat was not investigated.

Organisation: Low threshold inhibitory fields generally covered an extensive area of skin which was always adjacent to or overlapping the excitatory field. Twelve of the 37 units with inhibitory input had low threshold inhibitory areas that virtually surrounded their excitatory fields. Most of the units with this surround

type organisation had receptive fields located on the leg or knee regions (Figs. 6, A; 3, A & B).

Eight units had a single low threshold inhibitory area located proximally to their excitatory field. These units had receptive fields on the foot (Fig. 3, E & F).

Similarly, 17 units had a single inhibitory area positioned distally to their excitatory field. However, all of these units had receptive fields on the proximal thigh and hind quarters and some extended as far as the skin flap forming the paraffin pool so that input from skin proximal to the excitatory field could not be investigated (Figs. 3, C & D).

Ten units had low threshold inhibitory fields which overlapped with the edge of their high threshold excitatory components where these extended beyond the low threshold excitatory area (Figs. 6, A; 3,A,B,D & E).

Glabrous skin units

Of the 23 units with receptive fields including glabrous skin, 19 had inhibitory fields.

Effective stimuli: Fourteen units were inhibited by light tactile stimulation of hairy skin. But in contrast to units with receptive fields restricted to hairy skin, glabrous skin units could also be inhibited by stimuli of a noxious intensity (Figs. 8 & 9). Thirteen units were inhibited by a sustained noxious pinch, and 8 of these (all of those tested) were also inhibited by noxious radiant heat. Eight units had both low and high threshold

components to their inhibitory fields (Figs. 4, C, D, E, F & G)

Inhibition evoked by noxious mechanical and thermal stimuli was effective against background activity and against activity evoked by both light tactile and noxious mechanical stimuli. The inhibition was most effective initially though some activity did break through as the response to the noxious stimulus adapted (Fig. 9 and 8,C).

Organisation: Low threshold inhibitory components generally involved small areas of hairy skin around the toe pads (Figs. 4, C & F). They occasionally extended onto the ventral or dorsum surfaces of the foot (Fig. 4, D, E & G) but never included glabrous skin.

All high threshold inhibitory components were located on glabrous skin though those of 2 units also extended on to adjacent hairy skin (Fig. 4, G). Inhibitory fields involving several toe pads were often discontinuous (Fig. A, B, D, E, F & G). The area of skin from which noxious radiant heat was effective, was the same as (4 units), or overlapped with (4 units), that from which inhibition could be evoked by pinch (Fig. 4, A,B,D,E and G). Two units, although inhibited by noxious heat applied to a pad, were weakly excited by pinch of the same pad (Fig. 4, E & G).

Stability of receptive fields

P.s.d.c. axons, for which a thorough examination of cutaneous receptive fields were completed (75), were recorded for periods of between 20 minutes and 1 hour. During this time, the receptive field components were often investigated on several occasions. Although the edges of light tactile excitatory components were often indistinct, particularly when they bordered on light tactile inhibitory areas, unequivocal changes in receptive field boundaries were not detected.

Conduction Velocities

Antidromic conduction valocities were determined for a total sample of 111 identified p.s.d.c. neurones, pooled from each of the three sections of work presented in this thesis. They were measured between the stimulating electrode on the dorsal columns at C_{2-3} and the recording site in the lumbar dorsal columns (105 units), or dorsal horn (6 units). Conduction velocities ranged between 14 and 69ms^{-1} (38.0 $\pm$ 12.1; mean $\pm$ S.D.) (Fig. 10).

Units with input from glabrous skin appeared to have higher conduction velocities than units with receptive fields restricted to hairy skin (Fig. 10, B and C). Since the variances of the two populations were similar, this observation could be investigated by statistical analysis using single factor analysis of variance (see Table 2,A). The difference was found to be highly

significant (at P = 0.001).

However, since all units with input from glabrous skin have receptive fields located on the extremities of the limb, it was possible that this difference in conduction velocity might reflect a systematic variation in the conduction velocity of p.s.d.c. neurones according to the location of the receptive field on the limb. To test this possibility, all units (hairy and glabrous) were divided into four categories according to the location of the centre of their receptive fields. The areas forming these categories were the tail, thigh, leg and foot. All but 2 of the 20 units in the tail category were located on the root or upper third of the tail (Fig. 11). The mean conduction velocity for each category was found to increase progressively from the tail category to the foot, though only 1 of these category means was found to be significantly different. Single factor analysis of variance was used to separate the variation in conduction velocity due to random error from that associated with different receptive field locations (see Table 2,C). The F value was significant (at P = 0.05) and so the method of least significant difference was used to examine the significance of the differences between each of the category means. There was a significant difference (at P = 0.05) between the mean conduction velocity of units with receptive fields on the tail and units in each of the other categories. However, there was no significant difference between the mean

conduction velocities of units in the thigh, leg and foot categories (Fig. 11, right).

Since the group of units with receptive fields on the hairy skin of the tail had significantly slower conduction velocities than all other units, it was possible that this group exaggerated the difference in conduction velocity between hairy skin units and the apparantly faster conducting glabrous skin units. In view of this result, the calculation for analysis of variance between units with input from glabrous skin and those with input only from hairy skin was repeated, but with those units having receptive fields on the tail omitted (Table 2,B). The difference, though reduced, was still highly significant (at $P = 0.01$).

Background Activity

All of the 111 identified p.s.d.c. neurones recorded had a background activity before any manipulation of the receptive field had occurred.

Levels of Activity: for 19 units a systematic investigation was made of the levels of background activity. This was recorded over periods of between 1 and 2 minutes following the minimum manipulation of the receptive field necessary for identification of the unit. The averaged levels of background activity ranged between 0.9 and 22.6 impulses per second (see Table 3 in Section 2). The level of background activity often varied during the recording period as a result of manipulation

of the receptive field. Background levels could be raised or depressed for several minutes following repeated applications of noxious stimuli to excitatory and inhibitory fields respectively. There was no obvious correlation between levels of background activity and other properties of p.s.d.c. neurones.

Patterns of activity: background activity consisted of bursts (4-12 action potentials) of high frequency impulses (>500Hz) interspersed with single or, more rarely, double impulses. This pattern of activity was quite different to that recorded from cutaneous and muscle afferents in the dorsal columns and was one of the criteria used to differentiate p.s.d.c. axons from primary afferent fibres.

For 9 units sufficient background activity was recorded to allow the use of interspike interval analysis; the resulting histograms are shown in Figs. 12 and 13. Analysis with short bin widths (0.25ms) resulted in histograms consisting of an abrupt peak of very short intervals, presumably corresponding to intervals within the bursts (intraburst intervals). The peak intervals were between 0.5 to 1.5ms duration. They were followed by longer intervals presumably corresponding to intervals between bursts, between single impulses, and between bursts and single impulses. (Fig. 12). The shortest intervals recorded varied between 0.25 and 1.0ms duration (0.25ms bins). In each case the longest intervals recorded were in excess of 500ms (Fig. 13).

When the same number of intervals were analysed for each unit in order to facilitate a direct comparison between units, the main variation was in the proportion of very short (intraburst) intervals in comparison to longer (non-burst) intervals. This ratio of intraburst to non-burst intervals was not correlated with the level of background activity of the unit, but units with input from glabrous skin did appear to have a higher proportion of intraburst intervals than did units with receptive fields confined to hairy skin (Fig. 12). Of the 9 units for which interval analysis was performed, the 3 units showing the greatest proportion of short intervals (largest peaks) all had receptive fields including glabrous skin whereas the remaining 6 units, with a smaller number of short intervals, had receptive fields either restricted to hairy skin (5 units) or with hairy skin forming the major part (1 unit).

Unidentified Projecting Units

Nine units were recorded which, though satisfying the identification criteria for p.s.d.c. units, differed in a number of their properties from the units described above. All of the units were shown to project to upper cervical levels and the antidromic impulses of at least three of the units were followed by further impulses with higher stimulus thresholds. However, none of the units appeared to receive convergent input from the periphery and although all had a background discharge, its pattern

differed from that of other types of p.s.d.c. neurones.

These properties suggest two possibilities; either that the units represent a subgroup of the p.s.d.c. neurone population, or that they may not be postsynaptic in origin. For these reasons they have not been included in the previous analysis but are considered here as a separate group of units.

Conduction velocities

Conduction velocities of the nine units ranged from 40-67ms^{-1}. They therefore lay within the upper range of conduction velocities of the sample of p.s.d.c. units described above (compare with Fig. 10).

Background activity

Levels of activity: background activity was recorded from each of the 9 units over periods of 1-2 minutes before any manipulation of the receptive field had occurred. Averaged levels ranged from 2.5 - 36.4 impulses per second. Three units had levels of background activity that were considerably higher (approx. 1.5 times) than the highest levels recorded from other types of p.s.d.c. unit (compare with table 3 in section 2). Background levels did not follow cardiac or respiratory cycles.

Pattern of activity: the background activity of these units did not contain the bursts of impulses characteristic of clearly identified p.s.d.c. units, but was composed predominantly of single impulses interspersed with doublets or more occasional triplets of impulses.

For 7 of the 9 units sufficient activity was recorded to allow the use of interspike interval analysis. The histograms produced differed from those for clearly identified p.s.d.c. units in several respects (compare Fig. 14 with 13 and 12).

1) Five of the 7 units analysed had histograms with sharp peaks of short intervals. However, the duration of the intervals forming the peaks ranged from 3.5 to 5.0ms. These are considerably longer than the intervals forming the peaks in histograms of background activity from identified p.s.d.c. neurones (0.5 - 1.5ms). This suggests that the intervals between the doublets and triplets of activity in the unidentified units are of a longer duration than those between the burst impulses recorded from the clearly identified p.s.d.c. units.

2) There was a markedly greater proportion of longer intervals as a result of the lack of bursts of high frequency impulses within the discharge. Two of the 7 histograms had no clear peak of short intervals.

3) Four of the 7 units showed a tendency towards a bimodal distribution of intervals.

Response Properties

All 9 units responded to tapping of the ipsilateral limb. They were extremely sensitive and could be activated by tapping the frame supporting the animal. They were also activated by tapping remote parts of the animal and localisation of their receptive fields was therefore difficult. The most responsive positions of 5

units were on the leg or foot regions, while 4 units may have responded from glabrous skin of the toe pads. One unit tested responded to air puffs and, in contrast to other p.s.d.c. units, all responded in a 1:1 fashion to a tuning fork vibrating at 384Hz (G) placed against the most responsive area of skin. None of the units could be activated by sustained noxious pinch or noxious radiant heat. Nor did any form of stimuli produce inhibition of background activity. However, for two units, the response to a tuning fork was followed by a period of silence lasting several seconds.

These unidentified units also behaved differently to clearly identified p.s.d.c. neurones during cold block of the spinal cord (see Section 2).

Non-Projecting Units

While tracking in the dorsal columns for p.s.d.c. units, recordings were made from post-synaptic neurones which did not project to upper cervical levels. These neurones received a convergence of input from the periphery and had an irregular background activity. However, none were able to follow stimulation of the cervical dorsal columns at frequencies of 500Hz, nor did impulses evoked by the cervical stimulus collide with orthodromic activity. Though generally discarded, a detailed investigation of the receptive fields of 6 such units was made.

These units were similar to glabrous skin p.s.d.c.

units in terms of their input and receptive field organisation. All 6 units received input from glabrous skin and 5 also from hairy skin. Four units had both low and high threshold excitatory components within their excitatory fields and three units were inhibited by both noxious pinch and radiant heat applied to glabrous skin. One unit received only rapidly adapting excitatory input and one unit only low and high threshold inhibitory input.

Figure 3

Outline of a cat hind limb on which are shown examples of the receptive fields of hairy skin p.s.d.c. units.

Excitatory receptive fields

The excitatory field of each unit was composed of low and high threshold components. The high threshold areas of units A,B,D and E, extended beyond their low threshold components. The high threshold area of unit C was coextensive with the low threshold component, whilst that of unit F was smaller than and lay within the low threshold area.

Only unit C was tested using noxious radiant heat; it responded from a similar area of skin to that over which noxious pinch was effective.

Inhibitory receptive fields

Each of the units illustrated had a low threshold inhibitory field. Those of units A and B virtually surrounded the excitatory field. Those of units C and D were located distally, although the excitatory field of D extended as far as the skin flaps forming the paraffin pool, so that a search of proximal positions was not possible. Units E and F had inhibitory fields which were located proximally to their excitatory fields. The inhibitory fields of units A,B,D and E, overlapped with the edge of their high threshold excitatory areas, where these extended beyond their low threshold components.

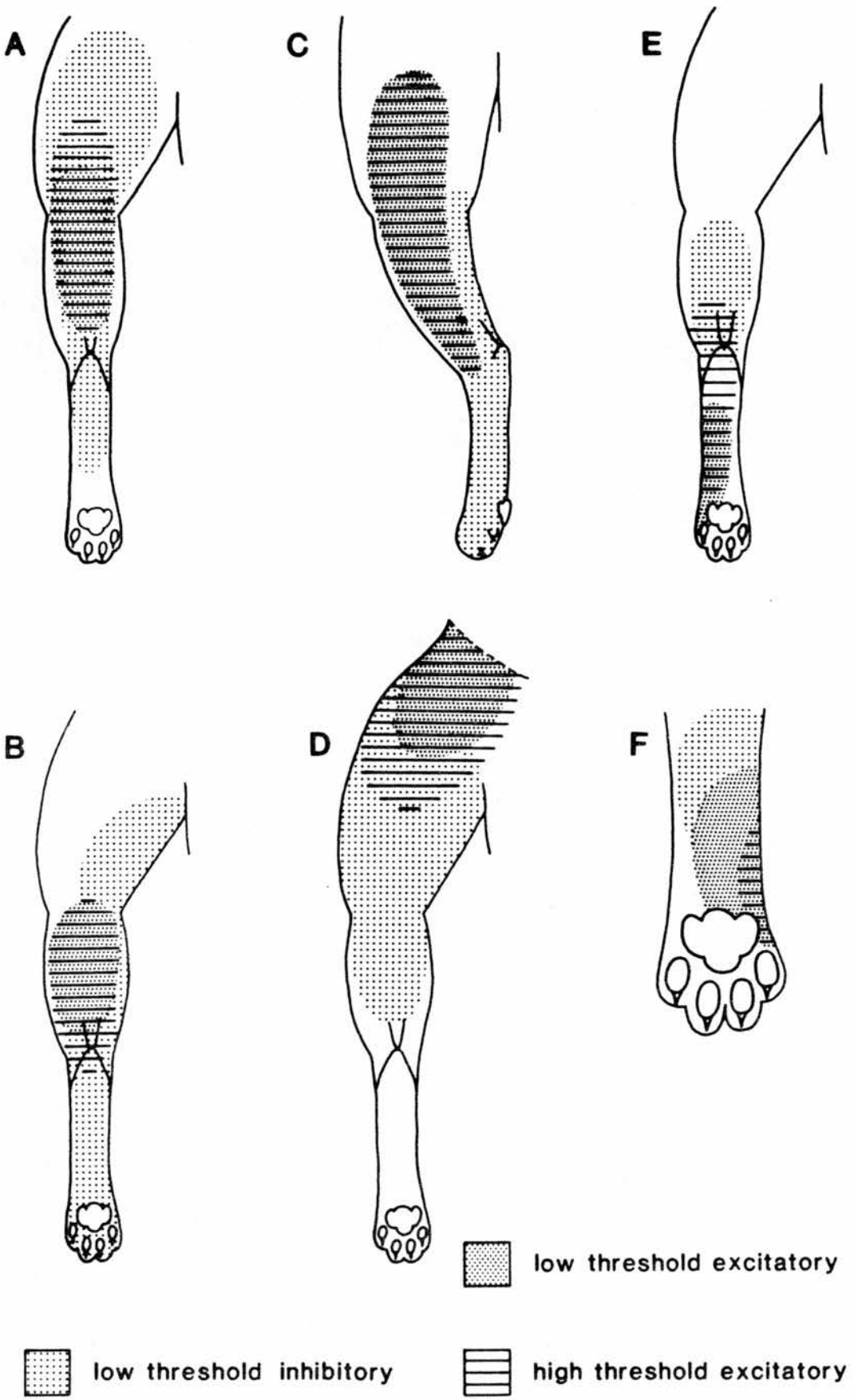

A
C
E
B
D
F
low threshold excitatory
low threshold inhibitory
high threshold excitatory

Figure 4

Outlines of a cat hind paw on which are shown examples of the receptive fields of glabrous skin p.s.d.c. units. Units A and B had receptive fields restricted to glabrous skin while units C,D,E,F and G received input from both glabrous and hairy skin.

Excitatory receptive fields: The excitatory fields of units A and B consisted of overlapping, discontinuous low and high threshold components restricted to glabrous skin. The high threshold areas responded to both pinch and noxious radiant heat.

The excitatory field of unit C consisted of a discontinuous low threshold component involving both hairy and glabrous skin, and a separate high threshold component on hairy skin responding to pinch (noxious heat not tested).

Units D,E,F and G received only low threshold excitatory input. The low threshold component of unit D was discontinuous and restricted to glabrous skin, while those of units E and F were continuous and involved both glabrous and hairy skin. The low threshold area of unit G was restricted to hairy skin.

Inhibitory receptive fields: All of the units illustrated were inhibited by noxious stimuli. Units A and B were inhibited by both noxious pinch and radiant heat from the same area of skin.

Inhibition of unit D was evoked by pinch of each of the pads and by noxious radiant heat applied to pads 4 and 5.

Unit E was inhibited by pinch of the central pad, pads 2 and 3, and the dorsum toes. Noxious heat was inhibitory from the central pad and pads 3,4 and 5. Though inhibited by noxious heat applied to pad 4, pinch evoked a weak excitation.

Unit G was inhibited by pinch of pads 4 and 5, and of the hairy skin of the dorsum toes. Noxious heat applied to each of the pads was inhibitory. Though inhibited by noxious heat applied to the central pad,sustained pinch evoked a weak excitation.

Units C and F were inhibited by pinch but were not tested with noxious radiant heat.

All of the high threshold inhibitory components involved glabrous skin and those of units B,D,E,F and G were discontinuous. The high threshold inhibitory components of units A,B,D,E,F and G overlapped with all, or part of the low threshold excitatory component.

Units C,D,E,F and G also had low threshold inhibitory components; those of C and F involved small areas of hairy skin around the toe pads while those of D,E and F extended on to the dorsum foot.

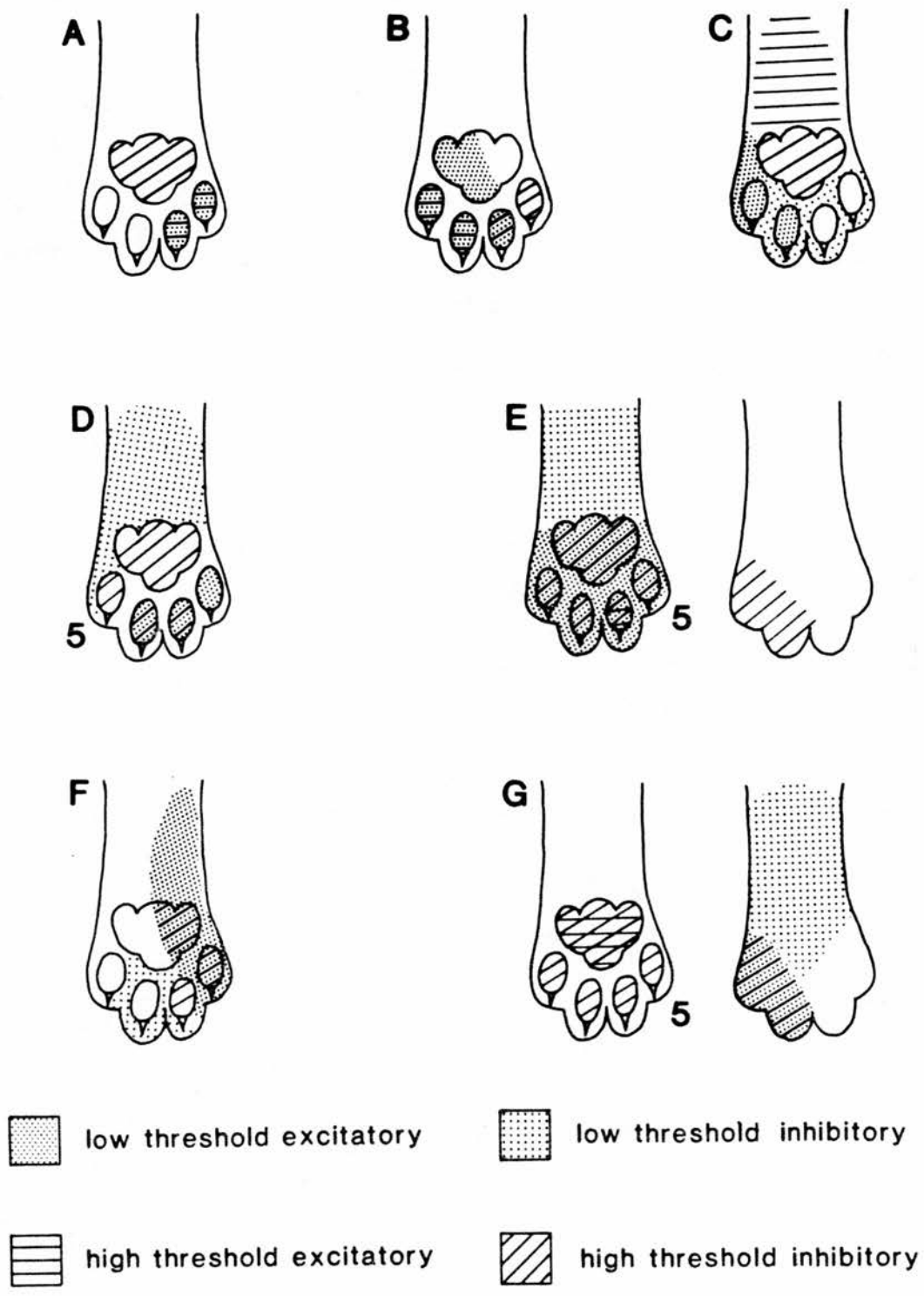

A
B
C
D
5
E
5
F
G
5
low threshold excitatory
low threshold inhibitory
high threshold excitatory
high threshold inhibitory

Figure 5

Examples of typical excitatory responses from a p.s.d.c. neurone with receptive field confined to hairy skin. The diagram shows the gradient of sensitivity within the high threshold excitatory area to noxious pinch.

A. Outline of a cat hind limb on which are indicated the low threshold excitatory and inhibitory fields of a hairy skin p.s.d.c. neurone. The locations labelled A - G represent the positions to which sustained noxious pinch and noxious radiant heat were applied to the skin.

B. Frequency histogram (1ms bins) of a period of recording from the p.s.d.c. unit described in A. On the left is an example of the response to light brushing of the low threshold excitatory field (LTF). This is followed by the graded responses evoked by a noxious pinch applied to each of the skin positions A - G.

C. Frequency histogram (1ms bins) of a period of recording showing the responses evoked by noxious radiant heat applied to each of the skin positions A - G.

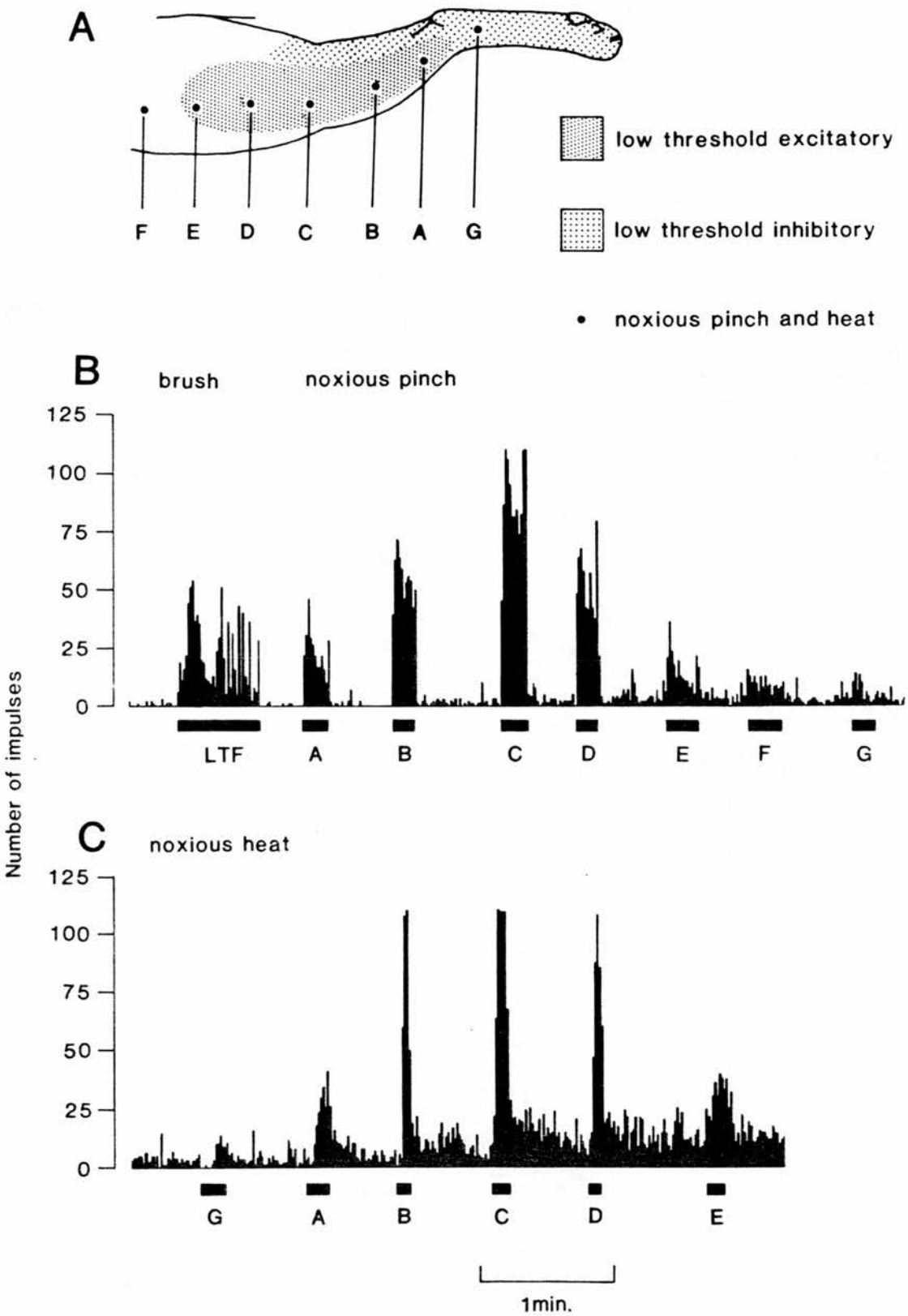

A
F
E
D
C
B
A
G
low threshold excitatory
low threshold inhibitory
noxious pinch and heat
B
brush
noxious pinch
125
100
75
50
25
0
Number of impulses
LTF
A
B
C
D
E
F
G
C
noxious heat
125
100
75
50
25
0
G
A
B
C
D
E
1min.

Figure 6

An example of inhibition evoked by light tactile stimulation of the low threshold inhibitory field of a p.s.d.c. neurone with receptive field confined to hairy skin.

A. Outline of a cat hind limb on which is shown the receptive field of a hairy skin p.s.d.c. neurone. The excitatory field consisted of a low threshold component, overlapped by a high threshold component responding to pinch (noxious heat not tested), which also extended beyond it in a concentric fashion. The excitatory field was surrounded by an extensive low threshold inhibitory area, which overlapped with the edge of the high threshold excitatory component.

B. Frequency histogram (1ms bins) of a period of recording from the p.s.d.c. unit described in A. Light brushing of the low threshold inhibitory field (duration indicated by shaded bar) produced a decrease in the rate of background activity and a marked reduction of activity evoked by sustained pinch of the high threshold excitatory component (black bar).

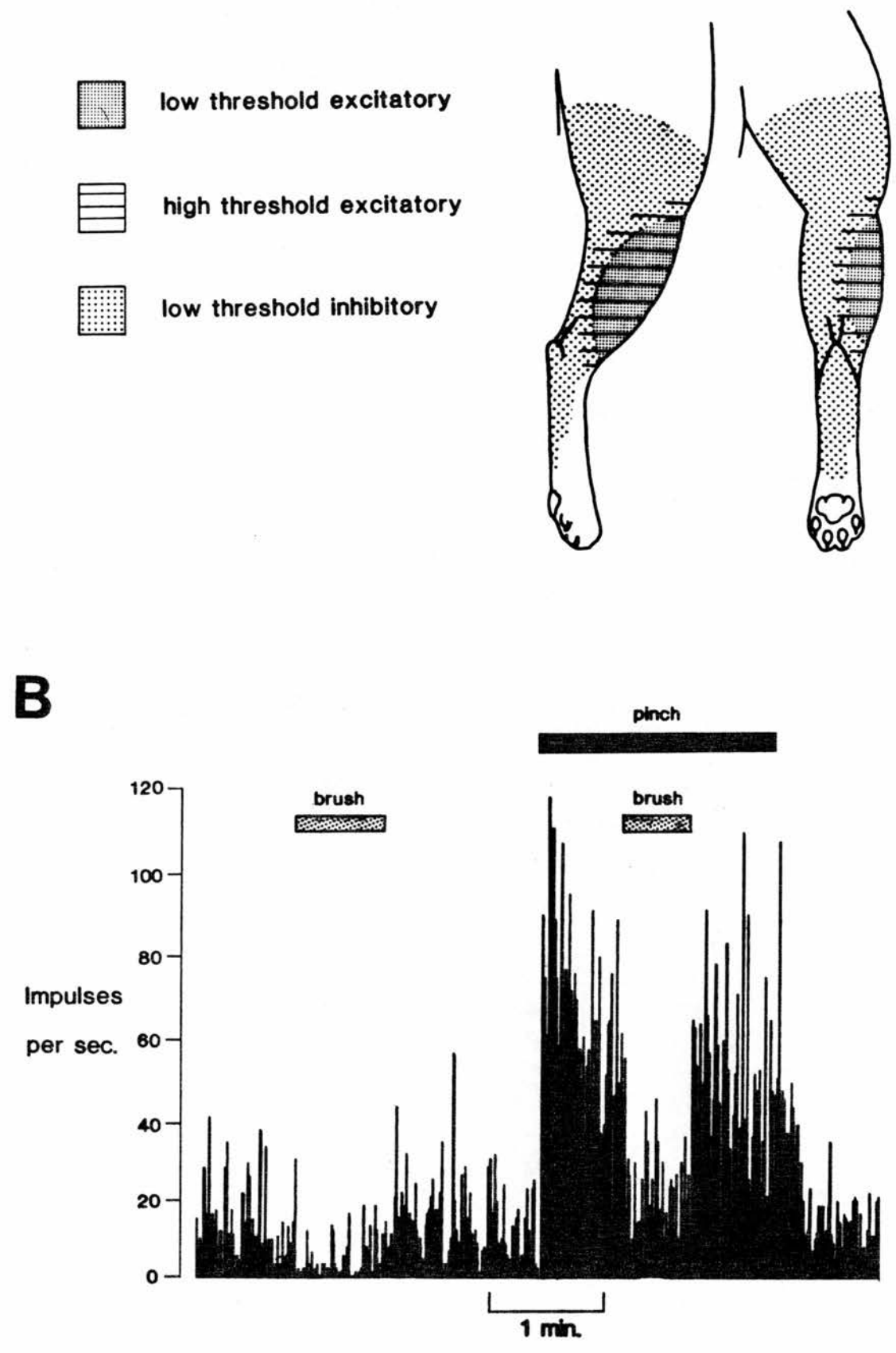

A
low threshold excitatory
high threshold excitatory
low threshold inhibitory
B
pinch
brush
brush
120
100
80
60
40
20
0
Impulses
per sec.
1 min.

Figure 7

An example of inhibition evoked by light tactile stimulation of the low threshold inhibitory field of a p.s.d.c. neurone with receptive field confined to hairy skin.

A. Outline of a cat hind limb on which is shown the receptive field of a hairy skin p.s.d.c. neurone. The unit had an excitatory field consisting of coextensive low and high threshold components, with low threshold inhibitory areas located proximally and distally. However, the unit was lost before the full extent of inhibitory input from between these two areas could be determined.

B. Frequency histogram (1ms bins) of a period of recording from the p.s.d.c. unit described in A. Light brushing of the low threshold inhibitory field (shaded bar) resulted in inhibition of activity evoked by pinch of the high threshold excitatory component (black bar) and of the background discharge of the unit.

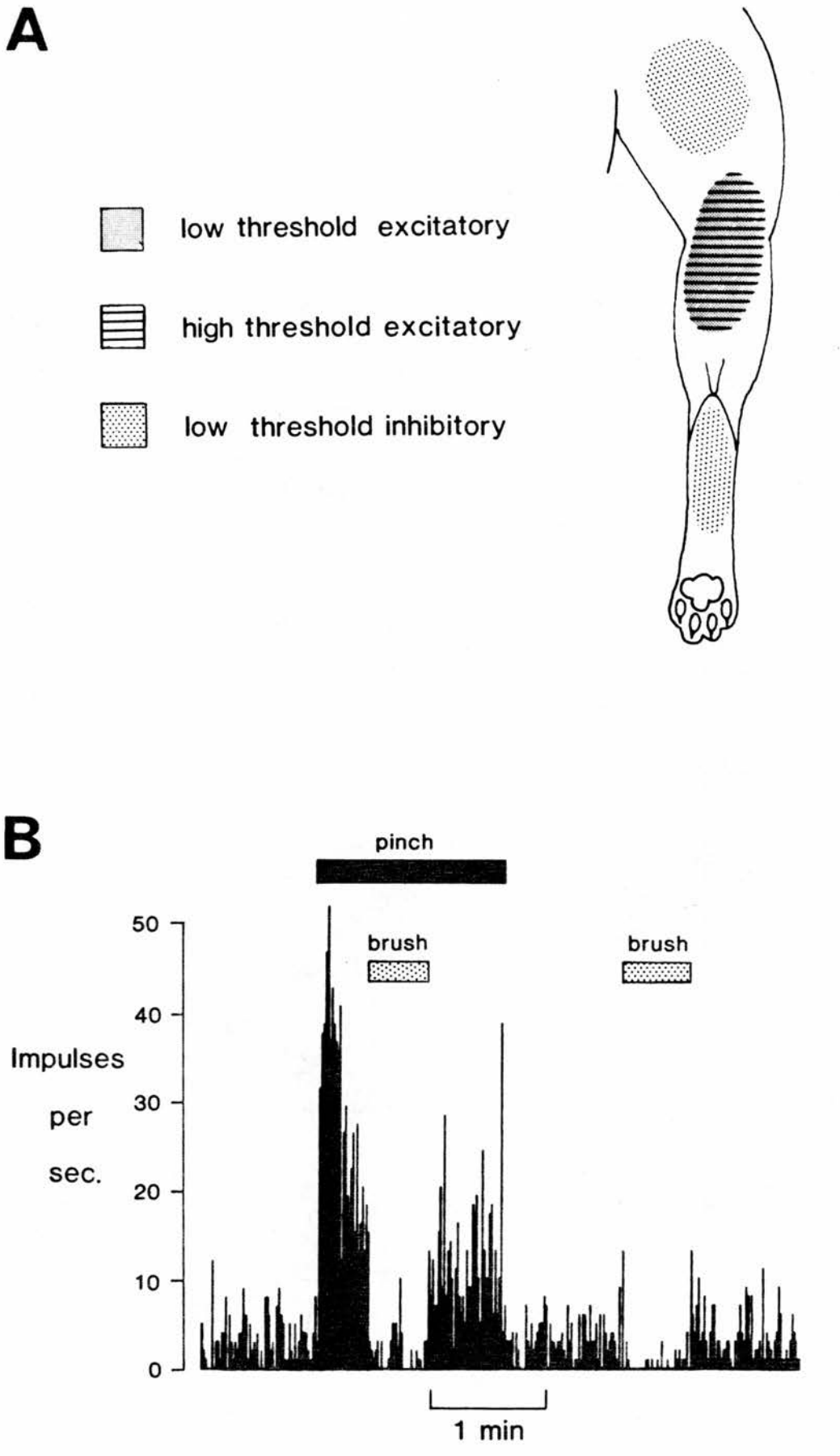

A
low threshold excitatory
high threshold excitatory
low threshold inhibitory
B
pinch
brush
brush
50
40
30
20
10
0
Impulses
per
sec.
1 min

Figure 8

An example of inhibition evoked by noxious pinch of the high threshold inhibitory area of a p.s.d.c. neurone with input from hairy and glabrous skin.

A. Outline of a cat hind paw on which is shown the receptive field of a glabrous skin p.s.d.c. neurone. The unit had a continuous low threshold excitatory component including both hairy and glabrous skin and an overlapping high threshold excitatory component located on a single toe pad. A high threshold inhibitory area located on the central pad also overlapped the low threshold excitatory component

B. Frequency histogram (1ms bins) of a period of recording from the p.s.d.c. neurone described in A. A sustained pinch of the high threshold inhibitory area (hatched bars) resulted in inhibition of both background activity and of activity evoked by tapping the low threshold excitatory component (shaded bar).

C. Frequency histogram (1ms bins) of a period of recording from the same neurone. Sustained pinch of the high threshold inhibitory area (hatched bars) produced inhibition of activity evoked by air puffs (1 every 1.5ms) directed at the low threshold excitatory component (shaded bar); although activity did break through as the response to the noxious stimulus adapted.

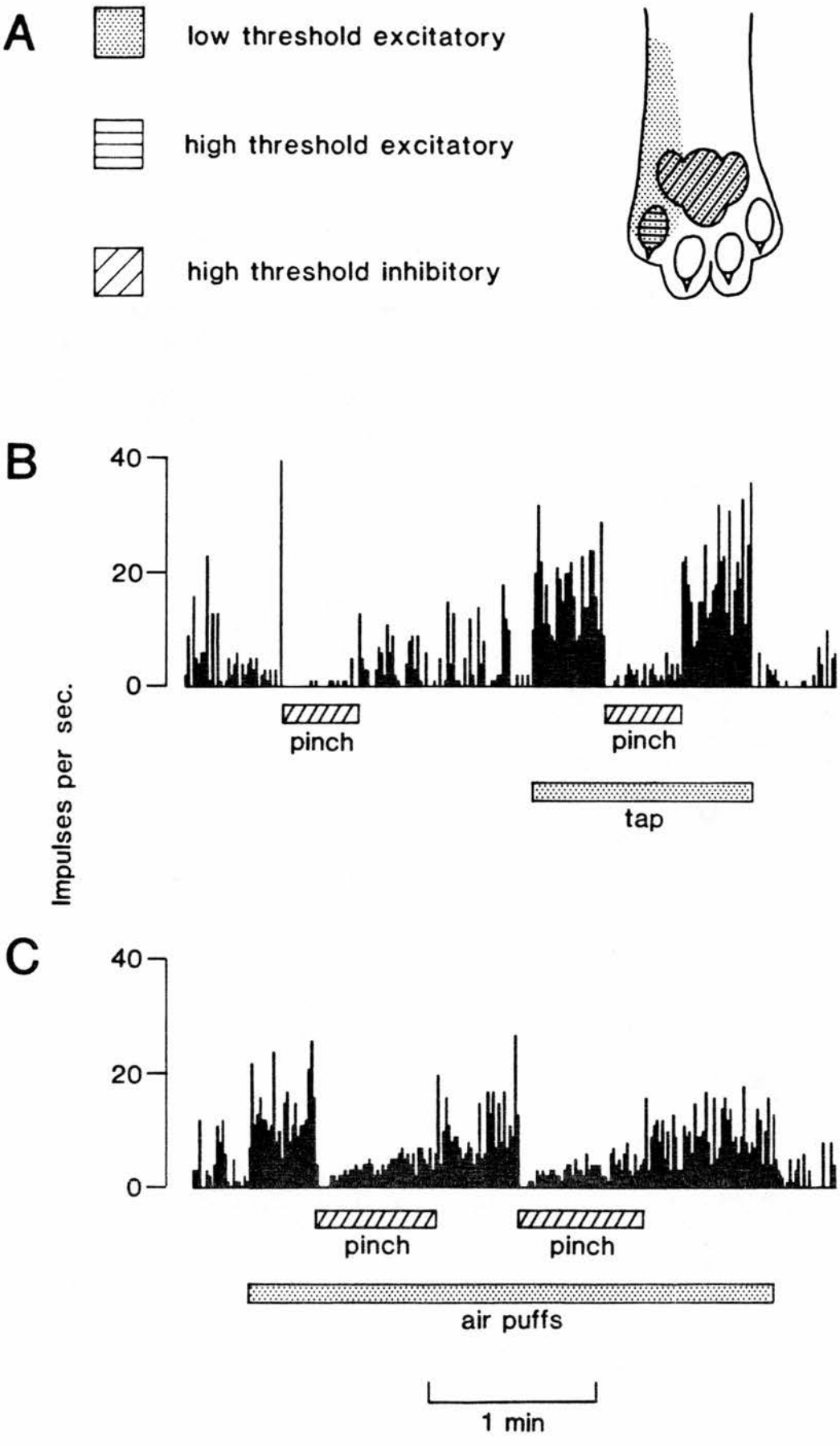

A
low threshold excitatory
high threshold excitatory
high threshold inhibitory
B
40
20
0
Impulses per sec.
pinch
pinch
tap
C
40
20
0
pinch
pinch
air puffs
1 min

Figure 9

An example of inhibition evoked by noxious stimuli from the high threshold inhibitory field of a p.s.d.c. neurone with input from hairy and glabrous skin.

A. Outline of a cat hind paw on which is shown the receptive field of a glabrous skin unit. The neurone had a continuous low threshold excitatory component which included both hairy and glabrous skin. It also had a discontinuous high threshold inhibitory area confined to the glabrous skin of the central pad, C, and each of the toe pads, 2 - 5.

B. Frequency histograms (1ms bins) of a period of recording from the p.s.d.c. neurone described in A, in which is shown the effects of sustained pinch (shaded bars) applied to each of the pads in turn (denoted by symbols below bars). Sustained pinch produced a weak inhibition of the background activity from pads 4, 3 and possibly 2, though activity did break through as the response to pinch adapted. C. Frequency histograms (1ms bins) of a period of recording during which noxious radiant heat was applied to each of the pads in turn. Powerful inhibition of the background activity was evoked from the central pad and each of the toe pads. A rebound excitation followed the inhibition evoked from toe pad 4.

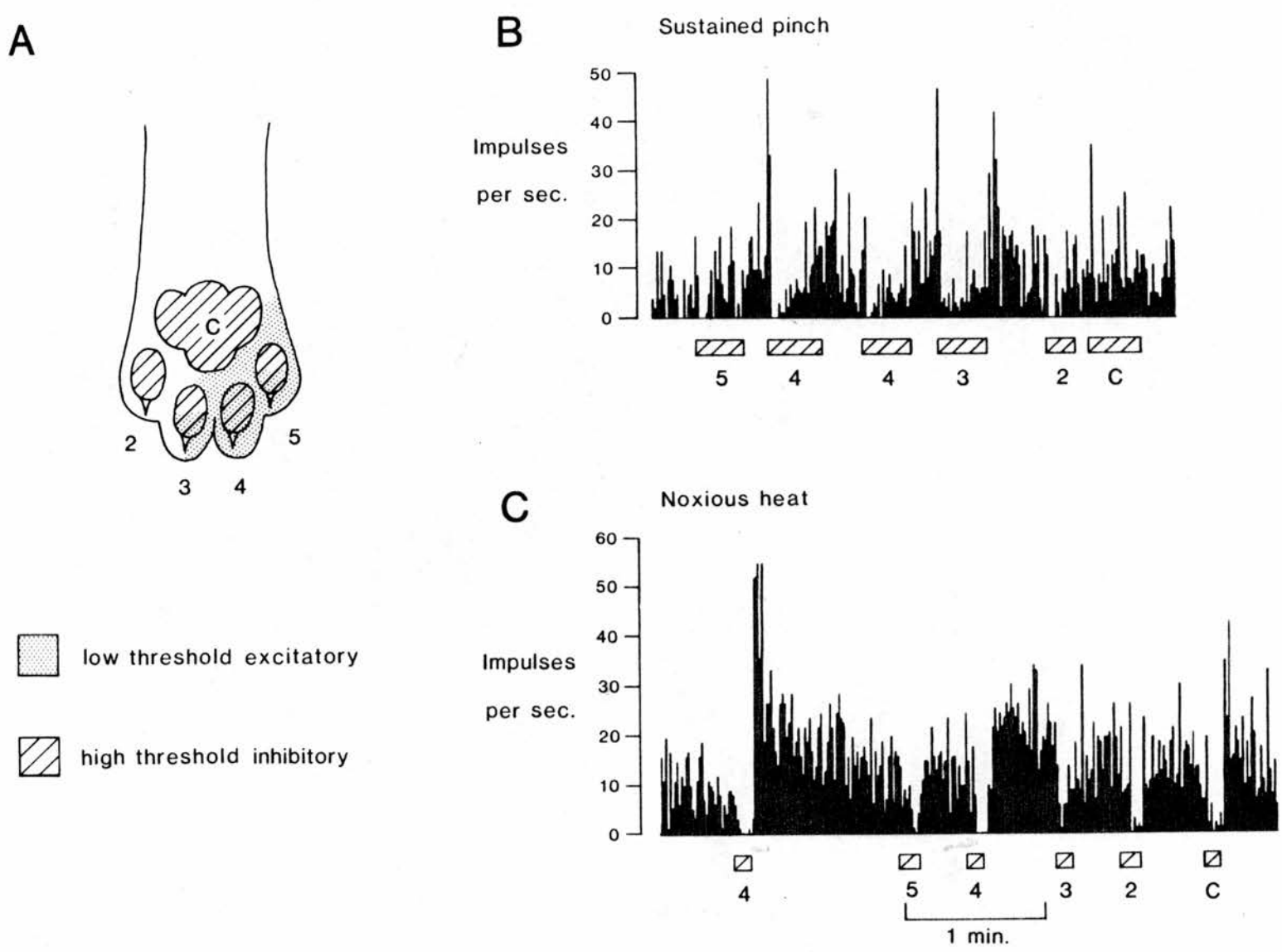

A
C
2
3
4
5
low threshold excitatory
high threshold inhibitory
B
Sustained pinch
Impulses
per sec.
50
40
30
20
10
0
5
4
4
3
2
C
C
Noxious heat
Impulses
per sec.
60
50
40
30
20
10
0
4
5
4
3
2
C
1 min.

Figure 10

Frequency histograms of the conduction velocities of p.s.d.c. neurones, measured between a stimulating electrode on the dorsal columns at C_{2-3} and the lumbar recording site. (x=mean conduction velocity, n=number of units).

A. Distribution of conduction velocities of total population of p.s.d.c. neurones recorded.

B. Distribution of conduction velocities of p.s.d.c. neurones with receptive fields confined to hairy skin.

C. Distribution of conduction velocities of p.s.d.c. neurones with receptive fields including glabrous skin.

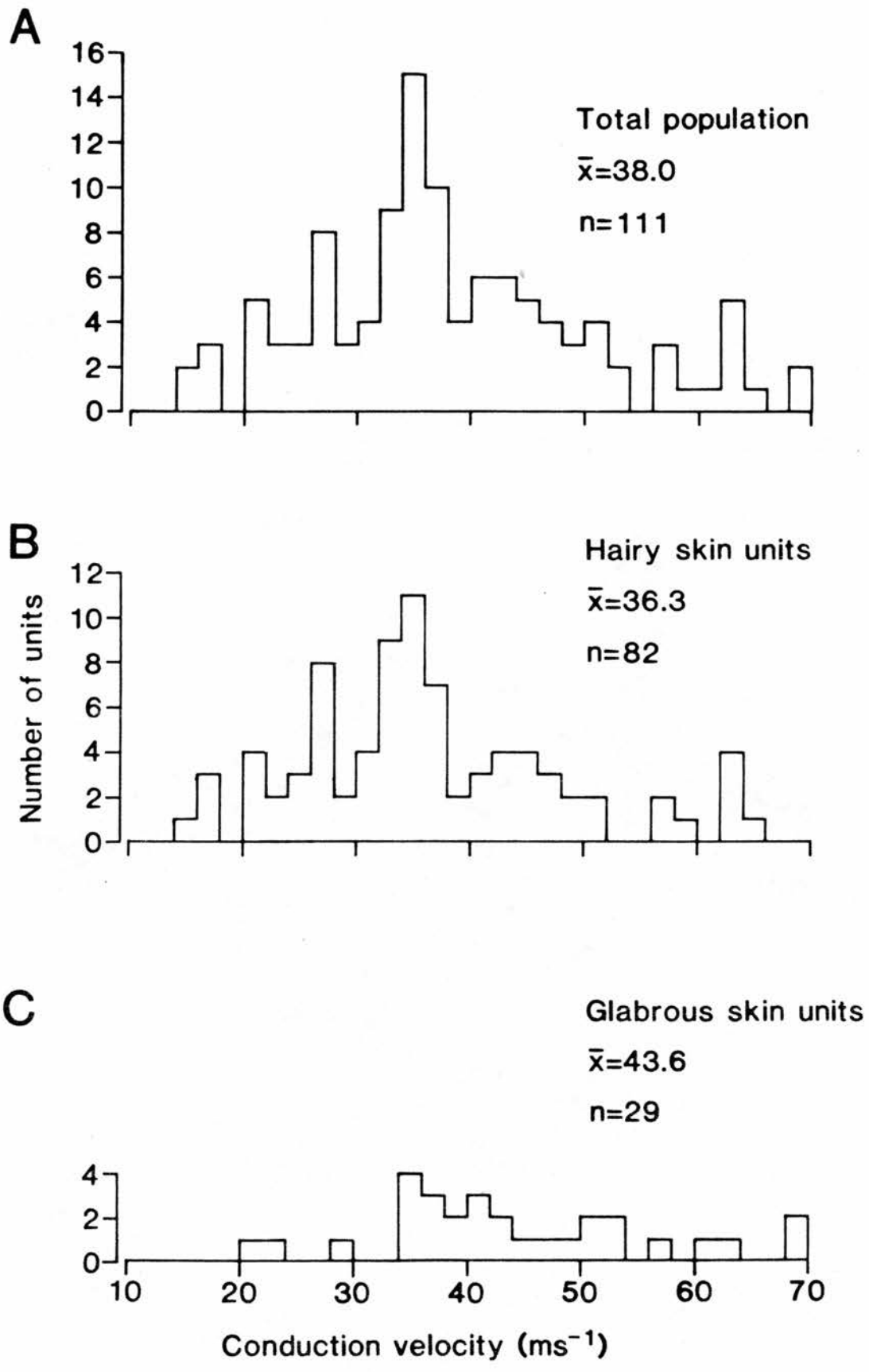

A
16
14
12
10
8
6
4
2
0
Total population
x̄=38.0
n=111
B
Number of units
12
10
8
6
4
2
0
Hairy skin units
x̄=36.3
n=82
C
Glabrous skin units
x̄=43.6
n=29
4
2
0
10
20
30
40
50
60
70
Conduction velocity (ms⁻¹)

Figure 11

Frequency histograms of the conduction velocities of p.s.d.c. neurones grouped according to the location of the centre of their receptive field. On the left, the areas representing each group are indicated; these are the tail, thigh, leg and foot. In the bottom histogram, those units with receptive fields including glabrous skin are indicated by diagonal shading.

On the right are shown the number of units (n), and the mean conduction velocity for each category. Those means which are not significantly different from one another, as determined by the method of least significant differences (L.S.D.=1.96 at P=0.05), are joined by a bracket.

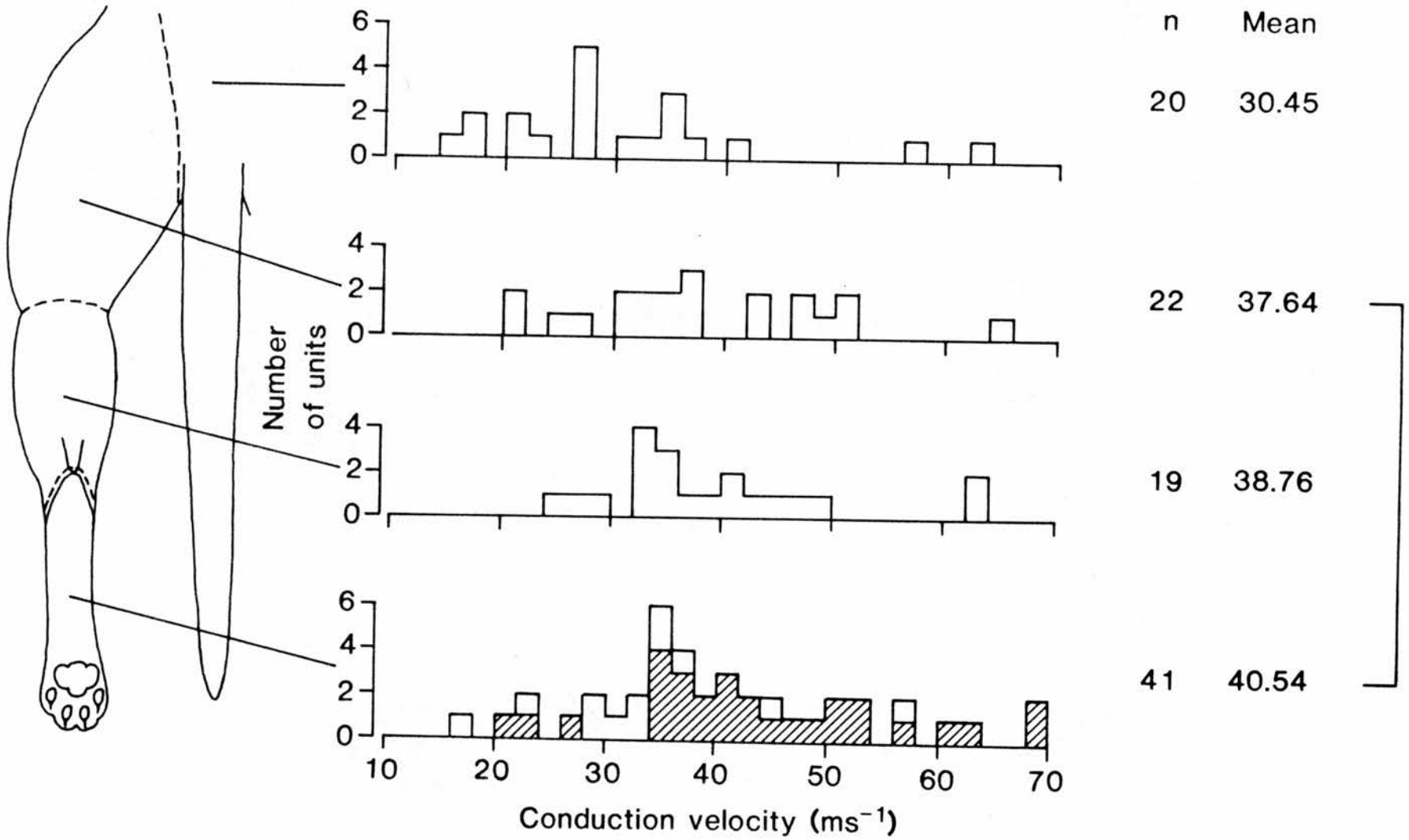

n
Mean
20
30.45
22
37.64
19
38.76
41
40.54
Number of units
Conduction velocity (ms⁻¹)
10
20
30
40
50
60
70

Figure 12

Interspike interval histograms of the background activity of six p.s.d.c. neurones. In order to allow direct comparison, all of the histograms are an analysis of 450 intervals, all have a bin width of 0.25ms and all are at the same scale.

On the left hand side are shown three units with a high proportion of very short (intraburst) intervals in their discharge. On the right hand side are shown three units with a greater proportion of longer intervals in their discharge.

The pattern of activity was not correlated with the level of background activity which is indicated in impulses per second above each histogram.

However, units with input from glabrous skin (left) tended to have a higher proportion of short (intraburst) intervals than did units with receptive fields restricted to hairy skin (right). The excitatory receptive fields of each unit are indicated on the accompanying figurines.

Intervals longer than 20ms were counted but are not displayed; but see Fig. 13.

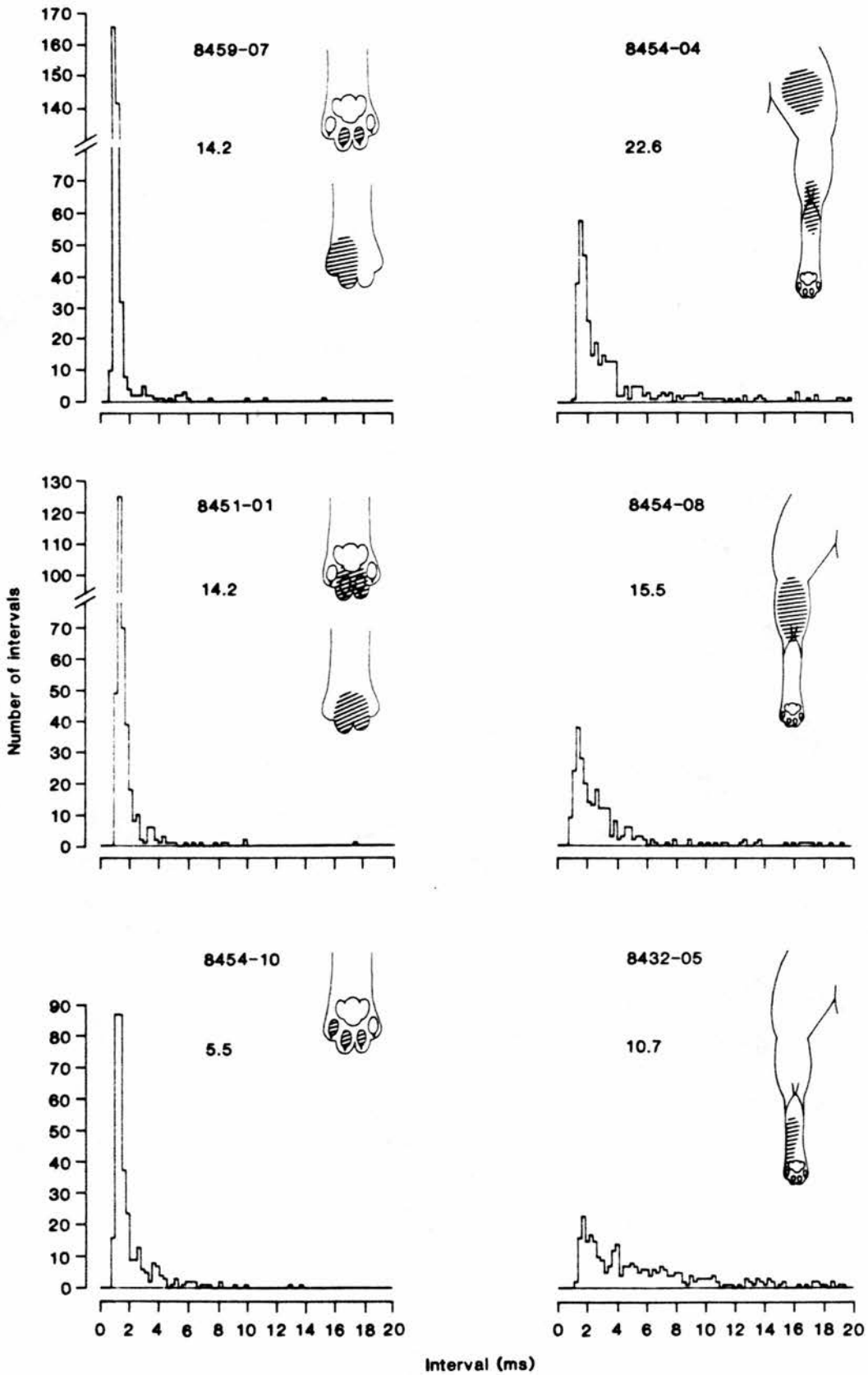

8459-07
14.2
8454-04
22.6
8451-01
14.2
8454-08
15.5
8454-10
5.5
8432-05
10.7
Number of intervals
Interval (ms)

Figure 13

Interspike interval histograms of the background activity of four p.s.d.c. neurones. A bin width of 5ms has been used for each of the histograms in order to demonstrate the distribution of longer (non-burst) intervals within the discharge. The longest interval recorded was, in each case, in excess of 500ms duration.

8432-05, 1200 intervals; 8454-07, 400 intervals; 8434-07, 450 intervals; 8459-07, 800 intervals. The level of background activity in impulses per second is given above each histogram.

For comparison an analysis of the shorter intervals within the background activity of units 8432-05 and 8459-07 is shown in figure 12.

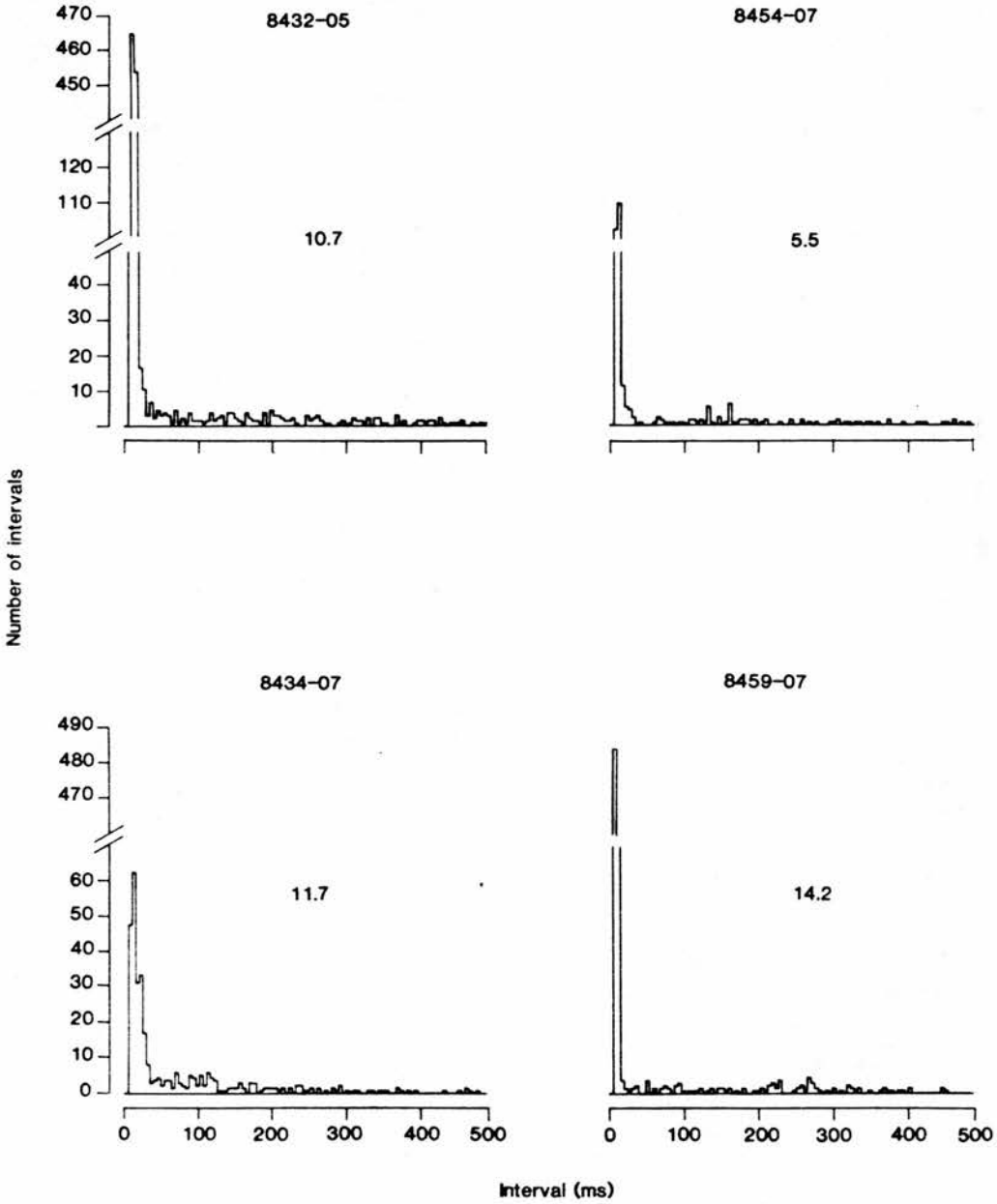

8432-05
8454-07
8434-07
8459-07
10.7
5.5
11.7
14.2
Number of intervals
Interval (ms)
470
460
450
120
110
40
30
20
10
490
480
470
60
50
40
30
20
10
0
0
100
200
300
400
500

Figure 14

Interspike interval histograms of the background activity of unidentified projecting units.

The pattern of background activity recorded from these units differed in a number of respects from that of clearly identified p.s.d.c. neurones. These differences are reflected in the histograms:

1) The duration of peak intervals were considerably longer than those in histograms from identified p.s.d.c. units (compare histogram 8452-05 with Fig. 12).

2) There was a markedly greater proportion of longer intervals resulting from the absense of high frequency bursts of impulses (compare with Fig. 19, left).

3) There was a tendency towards a bimodal distribution of intervals in the histograms of some units. This tendency is particularly clear in histograms 8458-08 and 8452-05.

8458-08, 1500 intervals; 8452-05, 800 intervals; 8518-01, 950 intervals; 8458-06, 500 intervals; 8459-01, 800 intervals; 8517-01, 200 intervals.

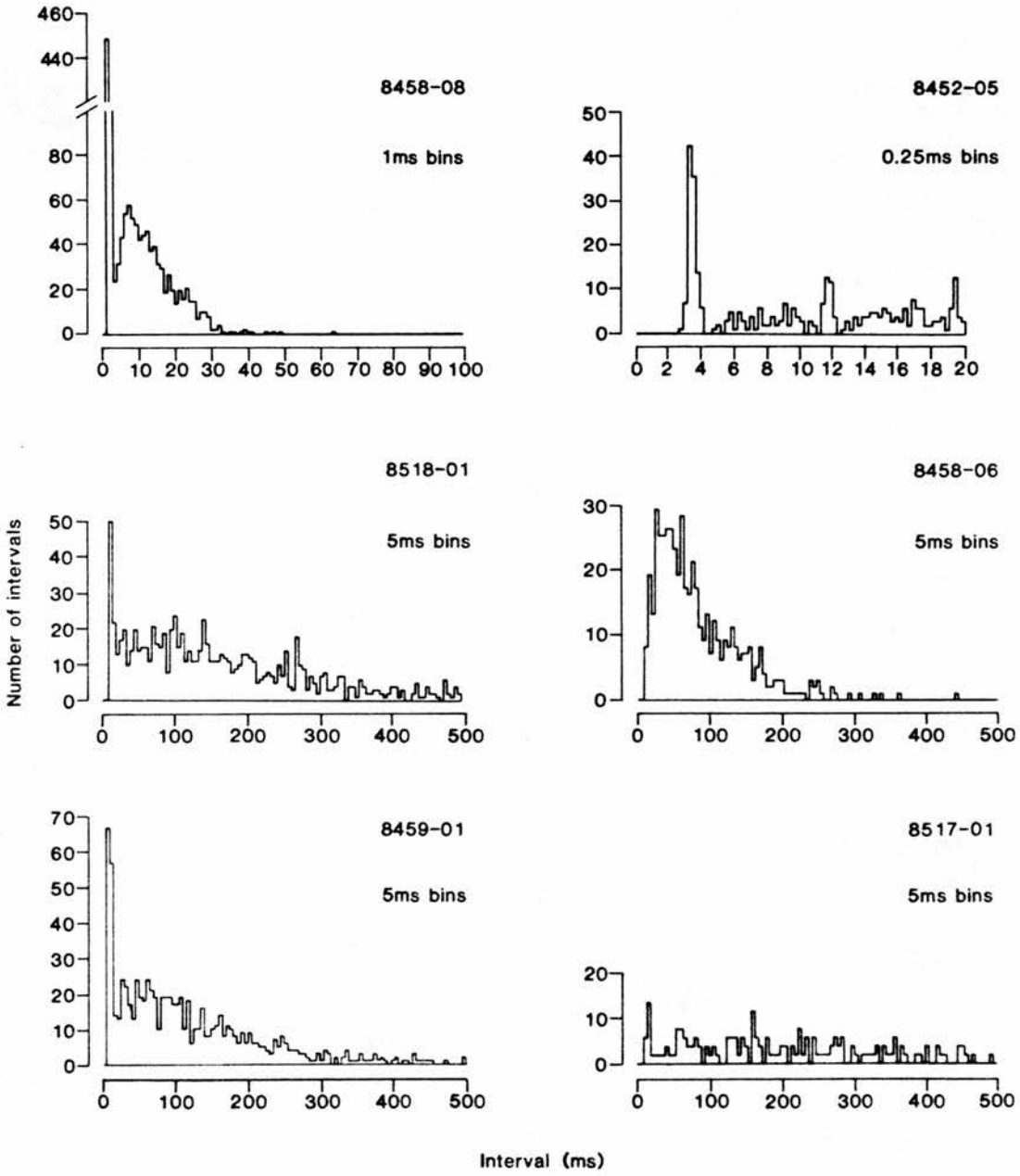

8458-08
1ms bins
8452-05
0.25ms bins
8518-01
5ms bins
8458-06
5ms bins
8459-01
5ms bins
8517-01
5ms bins
Number of intervals
Interval (ms)

Table 1

Summary of the convergent properties of 75 identified p.s.d.c. neurones.

Units have been grouped according to the excitatory input they received (column 1). The number of units within each group and the proportion they form of the total population are shown in column 2. The number of units of each group with inhibitory fields are shown in column 3. In the remaining three columns are shown the skin types on which the receptive fields of neurones in each of the groups were located. The location of both excitatory and inhibitory fields are included in this analysis.

TABLE 1

Excitatory receptive field type	Number of units (%)	Number with inhibitory fields (%)	Receptive field location		
			hairy skin	glabrous skin	hairy and glabrous skin
low threshold	8 (11)	7	2	1	5
high threshold	1 (1)	1	1	0	0
low threshold and high threshold	66 (88)	48	49	2	15
Total	75 (100)	56 (75)	52	3	20

Table 2

Tables showing analysis of variance for the conduction velocities of p.s.d.c. neurones.

A. Single factor analysis of variance for conduction velocities of units with receptive fields a) including glabrous skin and b) restricted to hairy skin. The F-value indicates a highly significant difference between the conduction velocities of these two groups of neurones.

B. Single factor analysis of variance as described for A, but in this case those units with receptive fields on the tail (with significantly slower conduction velocities) were omitted from the sample with receptive fields confined to hairy skin. The F-value is still highly significant.

C. Single factor analysis of variance for the conduction velocities of p.s.d.c. neurones grouped according to the location of the centre of their receptive field. The F-value is significant.

TABLE 2

A.

Source of variation	Sum of squares	Degrees of freedom	Mean square	Variance ratio (F)
Between categories	1513.16	1	1513.16	11.38***
Error	13302.33	100	133.02	
Total	14815.49	101	*** P=0.001	

B.

Source of variation	Sum of squares	Degrees of freedom	Mean square	Variance ratio (F)
Between categories	864.30	1	864.30	7.03**
Error	9838.30	80	122.98	
Total	10702.60	81	** P=0.01	

C.

Source of variation	Sum of squares	Degrees of freedom	Mean square	Variance ratio (F)
Between categories	1383.57	3	461.19	3.36*
Error	13431.92	98	137.06	
Total	14815.49	101	* P=0.05	

DISCUSSION

Identification Criteria

The identification criteria employed (page 87) were designed to ensure that only postsynaptic units with axons ascending the dorsal columns to high cervical levels were identified as postsynaptic dorsal column neurones. The adequacy of these criteria is discussed below.

Sampling bias

It is possible that the strict application of the identification criteria may have led to the omission of certain types of postsynaptic dorsal column unit from the sample. P.s.d.c. units receiving only low threshold excitatory input and without a background discharge would, under the criteria employed, be indistinguishable from rapidly adapting primary afferent fibres. In the present sample of p.s.d.c. neurones, only 8 units (11%) were excited by low threshold input alone. However,it seems unlikely that this type of unit is significantly underrepresented since all of the units recorded, including the 8 excited only by light tactile stimuli, had an irregular background activity.

Unidentified projecting units

A group of units were recorded that, while satisfying the criteria for identification as p.s.d.c. neurones, had a number of unusual characteristics. These units raise the possibility that the criteria

employed may be insufficient to distinguish between p.s.d.c. neurones and certain types of primary afferent fibre.

None of these units showed modality convergence, and although all had a background discharge this differed from that of clearly identified p.s.d.c. units in two main respects: 1) the activity was more regular, with a bimodal tendency in some interval histograms and 2) the activity lacked high frequency bursts of impulses.

Several of these units responded with more than one impulse to stimulation of the dorsal columns, but it is not safe to assume that this represents synaptically evoked activity. Pairs of impulses were frequently evoked in units that were clearly primary afferent fibres and this presumably represents the equivalent of the dorsal root reflex (Toennies, 1938; Eccles, Kozak & Magni, 1961). Thus, while it is conceivable that these units represent a subgroup of the p.s.d.c. neuronal population, it was not possible to demonstrate conclusively that they were postsynaptic in origin. The possibility therefore exists that they were primary afferent fibres.

All of the units were extremely sensitive and, unlike clearly identified p.s.d.c. units responded in a 1 to 1 fashion to a vibrating tuning fork placed against the skin as well as to gentle tapping of the frame supporting the animal; these are properties commonly described for Pacinian and Krause afferent fibres (Janig,

Schmidt & Zimmermann, 1968; Lynn, 1971; Iggo & Ogawa, 1977). In this respect these units are similar to two of the units in the sample of Brown et al. (1983a) which were reported to respond as if excited by Pacinian corpuscles alone.

A background activity in rapidly adapting primary afferent fibres has rarely been reported, but Hunt (1961) noted that some Pacinian corpuscle fibres recorded from the interosseous nerve had a random pattern of discharge in the absence of applied stimuli. This was apparently associated with slight vibration of the table revealed only by a sensitive microphone and with vibration of the air produced by an audio monitor. It is therefore possible that the present units represent Pacinian corpuscle afferents which, because of their location and extreme sensitivity, have an ongoing activity. In support of this possibility, the conduction velocities of these units are all faster than the average for clearly identified p.s.d.c. units and fall within the range reported for Pacinian and Krause afferent fibres in the dorsal columns (Brown, 1968; Janig et al., 1968; Uddenberg, 1968a).

Conduction Velocities

The present sample of p.s.d.c. axons had conduction velocities ranging between 14 and 69ms^{-1} and averaging 38ms^{-1}. This is similar to the range reported by Angaut-Petit (1975b) for a sample of p.s.d.c. neurones

recorded from the gracile funiculus. Uddenberg (1968b) measured the conduction velocity of only a small sample (10) of p.s.d.c. neurones from the cuneate funiculus, these spanned a narrower range and none conducted at slower than $40ms^{-1}$.

The range of conduction velocities of p.s.d.c. axons in the gracile funiculus falls within that reported for various primary afferent fibres ascending the dorsal columns and reaching high cervical levels ($10-85ms^{-1}$) (Brown, 1968; Petit & Burgess, 1968; Uddenberg, 1968a). The p.s.d.c. pathway does not, however, conduct as fast as the s.c.t. where the average conduction velocity for neurones originating in the lumbosacral cord is $60ms^{-1}$ and where a significant proportion of fibres conduct at between 80 and $100ms^{-1}$ (Brown & Franz, 1969). Primary afferent input processed in parallel by the two systems, will therefore, generally reach high cervical levels earlier through the s.c.t. than the p.s.d.c. system. This difference in average conduction velocity is maintained in the subsequent relays of the two systems. Axons projecting through the medial lemniscus from cells in the l.c.n. conduct on average at $28ms^{-1}$ (Craig & Tapper, 1978) whereas d.c.n. relay cells have average conduction velocities of $20ms^{-1}$ (Cooper & Dostrovsky, 1985). Furthermore, neurones in the rostral region of the d.c.n., including those activated by non-primary afferents in the d.l.f., tend to have conduction velocites even slower than the average (Gordon & Jukes,

1964; Kleider, 1974).

The present results suggest that p.s.d.c. neurones with receptive fields located on successively more distal areas of the hind limb might, on the average, have progressively faster conduction velocities, as if some compensation may occur for the greater conduction distances involved in the transmission of impulses to the brain. However, except for the category with receptive fields on the root of the tail, the differences between the groups proved not to be statistically significant. Similar suggestive results were obtained by Heath (1978) for a pooled sample of s.c.t. cells with receptive fields located on various areas of the forelimb, hindlimb and trunk; but here again the mean differences in conduction velocity were not statistically significant. Heath (1978) did however detect a significant difference between the conduction velocities of a small sample of forelimb and hindlimb s.c.t. cells recorded in the same experiment and it is possible that the trend revealed in the present experiments would reach significance if a large sample of results were obtained from a single animal.

The present results did however demonstrate a highly significant difference between the conduction velocities of units with receptive fields restricted to hairy skin and a faster conducting group of units with input from glabrous skin.

Background Activity

All of the p.s.d.c. units recorded had a background discharge. Interval histograms of this activity consisted of an abrupt peak of very short intervals followed by gradually declining numbers of longer intervals. A similar distribution of intervals has been described for the background discharge of unidentified dorsal horn neurones (Brown, Moraff & Tapper, 1973) and for s.c.t. cells (Brown & Franz, 1970). The peaks in the present histograms occurred for intervals of around 1ms in duration suggesting that the bursts of discharges within the background activity have frequencies of about 1000Hz.

The profiles of the interval histograms of background activity varied from one unit to another. The main difference was in the proportion of very short (less than 3ms) intervals forming the peaks of the histogram compared to the number of longer intervals (greater than 3ms). This suggests that p.s.d.c. neurones demonstrate varying degrees of bursting in their background discharges. Clearly a more detailed analysis than the present would be required to determine whether this variation is in the frequency with which bursts occur, the number of impulses within each burst, or both. The degree of bursting was not correlated with the level of background activity, but there was a tendency for those units with input from glabrous skin to contain a higher

proportion of burst impulses within their background activity than those with receptive fields confined to hairy skin. This may reflect different properties in the dorsal horn networks responsible for mediating the background activiy in the two different types of unit. Alternatively it may be a result of the different afferent input that these neurones receive. Rapidly adapting receptors in glabrous skin are extremely sensitive and may respond with several impulses to extraneous stimuli (Hunt, 1961). If activity in these rapidly adapting fibres is more effective in triggering bursts of impulses than say the activity in hair afferent fibres, then this may explain why those units receiving afferent input from glabrous skin tend to contain a higher proportion of burst impulses within their background activity.

Convergent properties

Since the present study has been concerned predominantly with the receptive field organisation of p.s.d.c. neurones, no attempt was made to precisely identify the types of receptors involved. Because of this limitation the results are presented with certain caveats.

1) Eighty-eight percent of the present sample of p.s.d.c. units were found to respond to both light tactile stimuli and with a slowly adapting disharge to maintained noxious pinch. For some units, these

responses could be elicited from partly or entirely separate areas of skin and so could confidently be presumed to represent input from rapidly and slowly adapting mechanoreceptors respectively. However, for about two-thirds of the sample, the area of skin from which responses could be evoked by light tactile stimuli were completely overlapped by an area responsive to maintained pinch. As a result, it was not possible to determine whether rapidly or slowly adapting receptors were involved in mediating the light tactile response.

2) Similarly, since a slowly adapting disharge could be elicited by pinch of both an innocuous and noxious intensity, it was not possible to differentiate with any certainty between input from sensitive slowly adapting mechanoreceptors and from high threshold mechanoreceptors. For the purpose of analysis it has tentatively been assumed that units responding with a slowly adapting disharge to a sustained noxious pinch received high threshold mechanoreceptive input.

If this assumption is made then 88% (66) of the sample of p.s.d.c. neurones investigated received input from both low and high threshold mechanoreceptors. In addition, more than half of the neurones of this type, when tested, were excited by noxious radiant heat. Eleven per cent (8) of the sample received only low threshold rapidly adapting excitatory input and only one unit required a stimulus of a noxious intensity for activation. These observations are in broad agreement

with those of Angaut-Petit (1975b) for a large population of p.s.d.c. neurones recorded from the gracile funiculus in the pentobarbitone anaesthetised cat.

In addition to this high degree of convergence from low and high threshold excitatory input, 75% (56) of neurones in the present sample received further input from an inhibitory receptive field. Angaut-Petit (1975b) failed to detect inhibitory fields for p.s.d.c. neurones recorded in the pentobarbitone anaesthetised cat but Brown et al. (1983a) have reported inhibitory fields in about half of a smaller sample of p.s.d.c. neurones from the chloralose anaesthetised cat.

Response properties and receptive field organisation

Excitatory receptive fields

Qualitatively the responsiveness of p.s.d.c. neurones to light brushing of hairy skin varied considerably. Some responded briskly like s.c.t. cells but the majority were relatively unresponsive, some failing to respond to an air jet stimulus. Light tactile receptive fields had diffuse boundaries and the larger light tactile areas, when investigated carefully, appeared to have a gradient of sensitivity. It was not possible however, to confirm these qualitative judgements by systematic analysis using an air jet stimulus as has been performed for neurones of the s.c.t. (Brown et al., 1986) since the responses of most p.s.d.c. neurones to an air jet were too inconsistent, even when the jet was directed at the centre of the light tactile receptive

field.

It has been reported (Kamogawa & Bennett, 1986) that p.s.d.c. neurones are relatively unresponsive to noxious thermal stimuli and are excited only after sensitisation by prolonged (30s) and repeated (3-7 trials) heating to between 50 and 56°C. However, the present results, in agreement with those of Angaut-Petit (1975b), have shown that about 50% of p.s.d.c. neurones may be excited by noxious radiant heat. Furthermore, in the present preparation, vigorous responses could be elicited without prior sensitisation. There are no obvious reasons for this discrepancy; both Angaut-Petit (1975b) and Kamogawa & Bennett (1986) used pentobarbitone anaesthetised preparations and both used a contact thermode to provide the thermal stimuli. Furthermore, the rates of rise and range of temperatures employed by Kumogawa and Bennett are similar to those used in the present experiments.

The vigorous responses to noxious mechanical and thermal stimuli observed in the present study are consistent with reports that the dendrites of p.s.d.c. neurones frequently enter lamina II and even I (Brown & Fyffe, 1981) and that these dendrites may participate in glomerular synaptic complexes (Bannatyne et al., 1982; Bannatyne, 1984). The central terminals of these glomeruli are thought to originate from Aδ or C primary afferent fibres (Gobel et al., 1981; Rethelyi et al., 1982; Kniyihar-Csillik, et al, 1982) which suggests that

p.s.d.c. neurones may receive a direct input from nociceptive afferent fibres.

In contrast to neurones of the s.c.t. (Brown & Franz, 1969) and of the spinothalamic tract in the cat (Ferrington, Sorkin & Willis, 1986), p.s.d.c. neurones with receptive fields on the distal limb often received excitatory input from the glabrous skin of toe and foot pads.

The present study has been predominantly concerned with the receptive field organisation of p.s.d.c. neurones. Previous studies of these neurones recorded in the pentobarbitone anaesthetised cat (Uddenberg, 1968b; Angaut-Petit, 1975b; Lu et al., 1983) have reported that the low threshold mechanoreceptive and nociceptive components of their excitatory fields are coextensive as is the case for s.c.t. cells (Brown & Franz, 1969). In the present sample however the low and high threshold components were commonly composed of a central area responsive to low threshold stimuli superimposed on a larger area responsive to noxious input. About half of the sample of units with receptive fields restricted to hairy skin had this concentric type of organisation. It has been a fairly common observation that for some dorsal horn neurones the high threshold excitatory component may extend beyond or around a central low threshold area. This type of receptive field organisation has been described for spinothalamic tract neurones in the monkey (Willis et al., 1974; Price, Hayes, Ruda & Dubner, 1978)

and is also characteristic of certain unidentified dorsal horn neurones in the cat (Taub & Bishop, 1965; Wall, 1967). These have been referred to by Wall as 'lamina V type' neurones (Wall, 1969; Hillman & Wall, 1969; Devor & Wall, 1976).

In the present sample, hairy skin p.s.d.c. units rarely had more than a single excitatory field, whereas the excitatory receptive fields of units with input from glabrous skin often consisted of several discontinuous areas of skin. Some of these areas contained both low and high threshold components but equally as often the two components were located on entirely separate areas of skin. A small minority of units with spatially separate excitatory fields have been reported previously in samples of unidentified dorsal horn neurones (Devor & Wall, 1976; Pubols & Goldberger, 1980; Brenowitz & Pubols, 1981) but the receptive fields of these units have always been located on the most proximal regions of the limb. Indeed, apart from previous studies of this system in the chloralose anaesthetised cat (Brown & Fyffe, 1981; Brown et al., 1983a) there are no reports in the literature of dorsal horn neurones with complex receptive fields of the kind that have been observed for glabrous skin p.s.d.c. units.

Inhibitory receptive fields

Previous investigations of the receptive fields of p.s.d.c. neurones have not always revealed inhibitory areas. Several studies in the pentobarbitone

anaesthetised cat have failed to detect inhibitory fields even though it is clear from the reports that attempts were made to do so (Uddenberg, 1968b; Angaut-Petit, 1975b; Lu et al., 1983). Inhibitory fields have however been reported for about half of a sample of p.s.d.c. neurones recorded in the chloralose anaesthetised cat (Brown et al., 1983a). These inhibitory areas were on the ipsilateral limb and were often adjacent to or overlapped the excitatory field. Inhibition was generally evoked from small fields by noxious stimuli and from large fields by either noxious or light tactile stimuli (Brown & Fyffe, 1981; Brown et al., 1983a).

The present experiments have confirmed that a large proportion of p.s.d.c. neurones in the chloralose anaesthetised cat, 75% of the present sample, have inhibitory receptive fields on the ipsilateral limb. Previous observations have been extended by an investigation of the inhibitory input to p.s.d.c. neurones with proximally located receptive fields. This has established that, in contrast to neurones with receptive fields including glabrous skin which may be inhibited by both light tactile and noxious stimuli, p.s.d.c. units with proximally located receptive fields restricted to hairy skin may be inhibited only by light tactile stimuli.

The glabrous skin units in the present study had small inhibitory fields adjacent to or overlapping the excitatory field. Light tactile inhibitory components

involved either a small area of hairy skin between the toe pads or extended proximally on to the foot. High threshold inhibitory components, for which effective stimuli included both noxious pinch and radiant heat, always involved glabrous skin and were often spatially discontinuous. The inhibitory fields of these glabrous skin p.s.d.c. units therefore resembled those described previously (Brown & Fyffe, 1981; Brown et al., 1983a).

P.s.d.c. units with proximally located receptive fields confined to hairy skin could be inhibited only by light tactile stimuli. Inhibitory fields generally covered an extensive area of skin adjacent to the excitatory field and in some cases overlapped with the high threshold excitatory component. At least one-third of the hairy skin units inhibited by light tactile stimuli had inhibitory fields that virtually surrounded the excitatory area.

Surround inhibition has been described previously in samples of unidentified dorsal horn neurones and is a characteristic feature of the 'lamina V type' neurones described by Wall (1967) and Hillman & Wall (1969). A surround inhibitory organisation has also been described for neurones at other stages in the dorsal column system; in the dorsal column nuclei (Gordon & Jukes, 1964a; Andersen et al., 1970; Bystrzycka, Nail & Rowe, 1977; Aoki, 1981) in the thalamus (Poggio & Mountcastle, 1963; Gordon & Manson, 1967; Baker, 1971; Janig et al., 1979) and in the somatosensory cortex (Mountcastle & Powell,

1959; Baker, Tyner & Towe, 1971; Laskin & Spencer, 1979). Surround inhibition has generaly been considered to produce a spatial sharpening of the transmission of somatosensory information and thus to provide a mechanism for improving the spatial discrimination of tactile stimuli (Mountcastle & Powell, 1959; Gordon & Paine, 1960; Anderson, 1962).

Surround inhibitory fields have not so far been described for any other identified dorsal horn neurones: neurones of the s.c.t. in the cat and spinothalamic tract in the monkey most commonly have inhibitory fields located on the contralateral limb (Brown & Franz, 1969; Willis et al., 1974; Gerhart et al., 1981). Nor has surround inhibition been reported in the lateral cervical nucleus (Oswaldo-Cruz & Kidd, 1964; Horrobin, 1966; Fedina, Gordon & Lundberg, 1968) or in thalamic relay cells of the spinocervico-lemniscal pathway (Andersen, Andersson & Landgren, 1966). Intracellular recording of s.c.t. cells has, however, revealed restricted eccentrically located inhibitory fields (Hongo et al., 1968; Brown et al., 1987c) and Hongo et al. (1968) have suggested that this asymmetrical inhibitory field geometry might provide a mechanism for detecting the direction of motion of a tactile stimulus on the skin. There are no reports of directional sensitivity in s.c.t. or any other dorsal horn neurones, but this possibility remains to be rigorously tested.

Whatever the precise functional role of inhibitory

input to dorsal horn neurones, the different inhibitory field geometries of p.s.d.c. and s.c.t. neurones suggest that sensory processing in the two systems may be specialised for detecting different features of a cutaneous stimulus.

The present study has not provided any information about the mechanisms of the inhibitory action elicited from these inhibitory fields although it has been established that background activity and activity evoked by both light tactile and noxious mechanical stimuli are reduced. Both pre- and postsynaptic mechanisms seem likely to be involved since electrical stimulation of cutaneous peripheral nerves inhibits activity in p.s.d.c. neurones with a time course similar to presynaptic inhibitory actions in the spinal cord (Brown et al., 1983a) but may also evoke i.p.s.p.'s (Jankowska et al., 1979).

In view of the extensive nature of these low threshold inhibitory fields and their surround organisation, it seems improbable that inhibition is evoked only from the inhibitory field; rather it seems likely that the excitatory field may be superimposed on a larger area, the whole of which generates inhibition. 'In field' inhibition has been demonstrated for cells in the somatosensory cortex (Andersson, 1965; Whitehorn & Towe, 1968; Innocenti & Manzoni, 1972; Laskin & Spencer, 1979), the thalamus (Iwamura & Inubushi, 1974; Janig, Spencer & Younkin, 1979), the dorsal column nuclei (Andersen,

Eccles, Oshima & Schmidt, 1964; Andersen, Etholm & Gordon, 1970; Janig, Schoultz & Spencer, 1977) and for s.c.t. cells in the dorsal horn (Brown et al., 1986, 1987b,c). For spinocervical tract cells it has been shown that different circuitry mediates the inhibitory actions originating from the inhibitory field and from within the excitatory field (Brown et al., 1987c) (see introduction page 38). It was a common observation in the present experiments that inhibition of p.s.d.c. units could be evoked from within the high threshold excitatory component where this extended beyond the light tactile excitatory area. An attempt to investigate inhibitory actions within the light tactile excitatory field using an air jet stimulus-test paradigm was unsuccessful because of the inconsistent responses of p.s.d.c. neurones to these stimuli. An intracellular study of p.s.d.c. neurones is required to provide further information concerning both the mechanisms of the inhibitory action and its precise spatial relationship to the light tactile excitatory field.

Stability of receptive fields

In a previous study of p.s.d.c. neurones from the chloralose anaesthetised cat a small minority of units had receptive fields that expanded during the recording session, suggesting that the receptive field boundaries of p.s.d.c. neurones might be dynamically modulated (Brown et al., 1983a). In the present experiments the

receptive fields of p.s.d.c. axons were thoroughly examined for periods varying from 20 minutes to an hour. During this time receptive field components were often reinvestigated on a number of occasions. The edges of receptive fields, particularly those of light tactile excitatory components which bordered on inhibitory fields, were often diffuse; but, unequivocal changes in receptive field boundaries were not detected. However, in the present experiments the skin of the hind limbs was left intact and electrical stimulation of peripheral nerves, which apparently triggered some of the changes observed by Brown et al. (1983a), was not employed.

Correlations of physiology with lamina distribution and morphology

The lamina distribution of p.s.d.c. neurones differs from that of s.c.t. cells in that additional groups of p.s.d.c. units are labelled in medial lamina V of the ipsilateral dorsal horn and medial lamina VII of the contralateral ventral horn (Brown et al., 1980a; Enevoldson, 1982; Bennett et al., 1983). The cells in medial lamina V are ideally located to receive input from rapidly adapting mechanoreceptors or Pacinian corpuscle afferent fibres, the terminals of which are distributed in lamina III-VI of the medial dorsal horn (Brown, Fyffe & Noble, 1980c). These neurones presumably correspond in part to those p.s.d.c. units described in the present study with receptive fields including the glabrous skin.

Furthermore, an examination of the morphological categories of Brown & Fyffe (1981), for which receptive field data were also obtained, suggests that hairy skin units and glabrous skin units may have morphological correlates in the dorsal horn. Most of the cells examined by Brown & Fyffe (1981) lay in the medial half of the dorsal horn. Cells located in lamina III and IV of the horn had primarily dorsally directed dendrites and although these receptive fields were on the toes, they were restricted to hairy skin (Figs. 4 & 5 of Brown & Fyffe). In contrast more ventrally located cells had extensive radiating dendrites and receptive fields that included glabrous skin (Figs. 6, 7 & 8 of Brown & Fyffe). Although the receptive fields of the retrogradely labelled cells studied by Enevoldson (1982) cannot of course be known, his results support the idea of two main morphological categories of p.s.d.c. neurone. One category of units which occurred throughout lamina III and IV had primarily dorsally directed dendrites whilst the second main group which had dendrites radiating in all directions were restricted in their location to medial lamina V.

About 5% of neurones retrogradely labelled by unilateral injections of HRP into the d.c.n. are located in lamina VII of the contralateral ventral horn and have axons that cross in the ventral commissure at their segment of origin (Enevoldson, 1982). All of the units in the present sample had receptive fields located on the

ipsilateral limb. However p.s.d.c. units were occas$ionally recorded for which there was no obvious cutaneous receptive field on the hind limbs. It is possible that cells in the contralateral ventral horn receive input predominantly from subcutaneous structures and that a cursory search of the skin of the contralateral limb therefore failed to activate them. The physiology of this group of p.s.d.c. neurones therefore remains to be determined.

Summary and Conclusions

The present sample of p.s.d.c. neurones was characterised by a high degree of modality convergence. Eighty-eight percent of units were excited by both light tactile and noxious mechanical stimuli and 50% of those tested were excited by noxious radiant heat. In addition, 75% of neurones received input from inhibitory receptive fields.

The receptive field organisation of the p.s.d.c. system is summarised in Fig. 15. Units with input from glabrous skin had complexly organised receptive fields many of which were discontinuous. These units could be inhibited by both light tactile and noxious cutaneous stimuli.

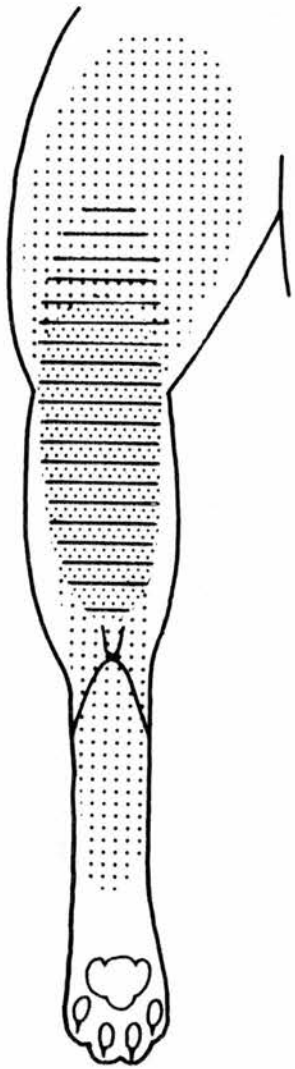
Units with receptive fields restricted to hairy skin often had a concentric receptive field organisation in which the high threshold excitatory component extended beyond the low threshold area. These units could be

inhibited only by light tactile stimuli and their inhibitory fields generally covered an extensive area of skin, virtually surrounding the excitatory field.

These properties contrast with the relatively simple receptive field organisation of s.c.t. cells where low and high threshold excitatory components are coextensive and where inhibitory fields are positioned either separate from, or eccentric to, the excitatory field (Brown & Franz, 1969; Brown et al., 1987c). These observations emphasise the differences that exist between p.s.d.c. and s.c.t. neurones and suggest that the two systems may employ different strategies of sensory processing. Thus, while several receptor types may activate neurones of the p.s.d.c and s.c.t. systems in parallel, it seems likely that each may be specialised to respond to different aspects of the same stimulus.

Figure 15

Summary diagram of the receptive field organisation of p.s.d.c. neurones descriptions of which are given in the text.

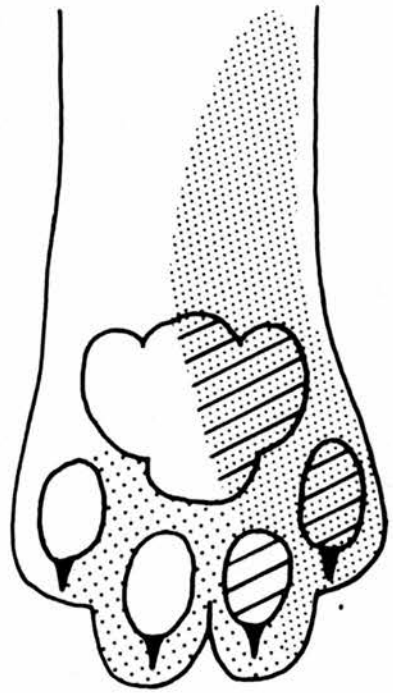


low threshold excitatory

high threshold excitatory

low threshold inhibitory

high threshold inhibitory



SECTION 2

DESCENDING INFLUENCES ON THE RESPONSE PROPERTIES AND RECEPTIVE FIELD ORGANISATION OF POSTSYNAPTIC DORSAL COLUMN NEURONES

INTRODUCTION

Dorsal horn neurones may be influenced by a variety of systems descending from the brain (see earlier) some of which are tonically active in animals prepared for electrophysiological recording (Wall, 1967; Brown, 1971). It is now well established that these systems may profoundly modify the response modalities of dorsal horn neurones (Hillman & Wall, 1969; Brown, 1971; Handwerker et al., 1975; Dickhaus et al., 1985) and there is also evidence that they may influence the receptive field borders of certain neurones (Wall, 1967; Hillman & Wall, 1969).

Whilst it has been shown that polysynaptic input to s.c.t. neurones is profoundly suppressed by descending systems, the boundaries of their receptive fields are considered to be relatively unaffected by these actions (Wall, 1967; Brown, 1971). These observations have been interpreted as implying that there is little or no subliminal fringe for s.c.t. cells (Brown, 1971, 1981), although in a recent study restricted subliminal receptive field components were demonstrated (Brown et al., 1987c).

In contrast, little is known of the influence of descending systems on either the response properties or receptive field organisation of p.s.d.c. neurones. However, these cells have an extensive subliminal fringe (Brown & Fyffe, 1981) and a minority are reported to have

labile receptive fields that expand following such procedures as electrical stimulation of peripheral nerves (Brown et al., 1983). These properties suggest that p.s.d.c. neurones may be amongst those dorsal horn cells with receptive field boundaries under the control of descending systems and the experiments described in this Section were designed to investigate this possibility. Recordings were made from axons of p.s.d.c. neurones in chloralose anaesthetised preparations. The response properties and receptive field organisation of each of the units were investigated both before and during a reversible block of descending impulses produced by cooling the spinal cord rostral to the recording region.

METHODS

Preparation of animal

The experiments were performed on 11 cats, 2.1 - 2.6Kg in weight, anaesthetized with chloralose and paralysed with gallamine triethiodide. Procedures for the general preparation and physiological maintenance of the animal were as described in Section 1.

Electrical stimulating and recording procedures

A diagrammatic representation of the preparation on which are indicated the positions of stimulating and recording electrodes is shown in Fig. 16. The set up and procedure for identifying and recording from axons of p.s.d.c. neurones was the same as that described in detail in Section 1.

Reversible block of impulse conduction in the spinal cord

A reversible block of the conduction of impulses through the spinal cord was achieved by cooling a region of thoracic cord rostral to the recording site. The cold block was produced by a thermoelectric thermode with a cooling surface shaped to surround the dorsal half of the spinal cord (Brown, 1971). A thermocouple junction mounted on the cooling surface was used to monitor its temperature throughout the cold block procedure.

An additional laminectomy was performed at T_{11} to L_1 and the device lowered over the dorsal surface of the cord at about T_{13}; to achieve a close fit it was occasionally necessary to cut one pair of dorsal roots.

Care was taken to avoid exerting pressure on the cord which might impede blood flow or produce pressure block or damage to superficial fibres. A cord dorsum potential recorded from L_7 in response to stimulation of the dorsal columns at C_4 was monitored for signs of impairment of conduction past the thermode whilst it was placed in position .

The thermode could produce cold block of the cord within 5 - 10 minutes at thermode temperatures of between 0 and -5°C. The precise time and temperature required varied between experiments and depended on the closeness of apposition of the cooling surface to the cord. Provided that the temperature of the cord was not allowed to fall below that at which cold block was initially achieved, there was no indication (from the cord dorsum potential) of permanent damage to the cord. The block could therefore be maintained for up to 45 minutes and repeated several times in a single experiment.

Assessment of the block of impulse conduction through the spinal cord

The effectiveness of the cooling procedure in blocking the conduction of impulses through the spinal cord was assessed by monitoring recordings from both the cord dorsum and the single unit under study (Fig. 17).

Cord dorsum potential Throughout the blocking procedure a cord dorsum potential was recorded from L_7 (below the cooling device) in response to stimulation of the dorsal columns at C_2 (above the cooling device). As cooling of

the cord progressed, the latency of both negative and positive waves of the potential were increased whilst their amplitudes were decreased. Eventually, at temperatures between 0 and -5°C, both negative and positive waves were abolished.

Antidromic single unit responses

An antidromic response to stimulation of the dorsal columns at C_2 was recorded from each of the single units studied. As cooling of the cord progressed the latency of the antidromic impulse lengthened. Eventually the antidromic impulse failed and was replaced by non-synchronous background activity which was enhanced by cooling the cord.

Neither the cord dorsum potential nor the antidromic impulse was consistently more sensitive to cooling than the other: the first potential to be abolished varied between different units recorded during the same experiment and probably reflected the differing locations of the axons of p.s.d.c. units within the dorsal columns. Cooling of the cord was therefore continued until both the cord dorsum potential and the antidromic single unit response were abolished. At this point it was assumed that fibres in at least the dorsal half of the cord were incapable of conducting impulses.

Although no other criteria were used in assessing the effectiveness of the block, two further observations provided evidence of its efficacy. The cooling device was situated caudal to the major cardio-sympathetic

outflow to avoid the instability produced by cardiovascular disturbances. Nevertheless, the cold blocking process and its reversal were accompanied by marked changes in blood pressure (Fig. 18). In addition, cold block of the cord produced changes in the background activity, response properties and receptive field size of p.s.d.c. units which are the subject of this section of work.

Cutaneous stimuli

The response properties and receptive field organisation of p.s.d.c. units were investigated both before and during block of impulse conduction through the cord. Full details of the cutaneous stimuli employed are given in Section 1.

Assessment of receptive field size

A particular aim of the present experiments was to assess the effects of blocking descending impulses on the spatial properties of receptive fields.

Low threshold components were investigated with brushes, blunt probes and air jets both before and during cold block of the cord. The responsive areas detected in each of the states were outlined on a photograph of the hind limb.

High threshold components were assessed by applying noxious pinch and radiant heat to a range of skin positions. The stimulus locations were chosen so that they overlapped and extended beyond areas of skin from which slowly adapting responses could be evoked before

cold block of the cord. To enable the same stimuli to be accurately repeated at the same skin locations during cold block of the cord, the locations were recorded on a photograph of the cat's hind limb. Noxious stimuli were generally applied only twice to each of the skin positions, before and during the block of descending impulses. The interval between the two stimuli was therefore at least 8 minutes. All responses were recorded on magnetic tape and were analysed on and off line by plotting continuous impulse frequency histograms, as described in Section 1.

Figure 16

Diagrammatic representation of the experimental arrangement for investigating the effect of spinalisation on the responses and receptive fields of p.s.d.c. neurones.

The drawing represents a dorsal view of the spinal cord exposed by laminectomies at the cervical (C_1-C_3) and lumbar (L_5-L_7) enlargements. SI and SII represent bipolar ball electrodes that were used to apply electrical stimuli to the dorsal funiculi at C_1 and C_2. These stimulation sites were above (C_1) and below (C_2) a lesion of the dorsal columns at C_{1-2} shown by hatching. Cord dorsum potentials were recorded through a monopolar ball electrode placed on the lumbar dorsal columns (R_{CDP}). Single unit recordings were made extracellularly from axons in the dorsal columns using glass capillary microelectrodes. A reversible spinalisation could be produced by cooling the cord with a thermoelectric thermode placed over the dorsal half of the spinal cord at Th_{13}.

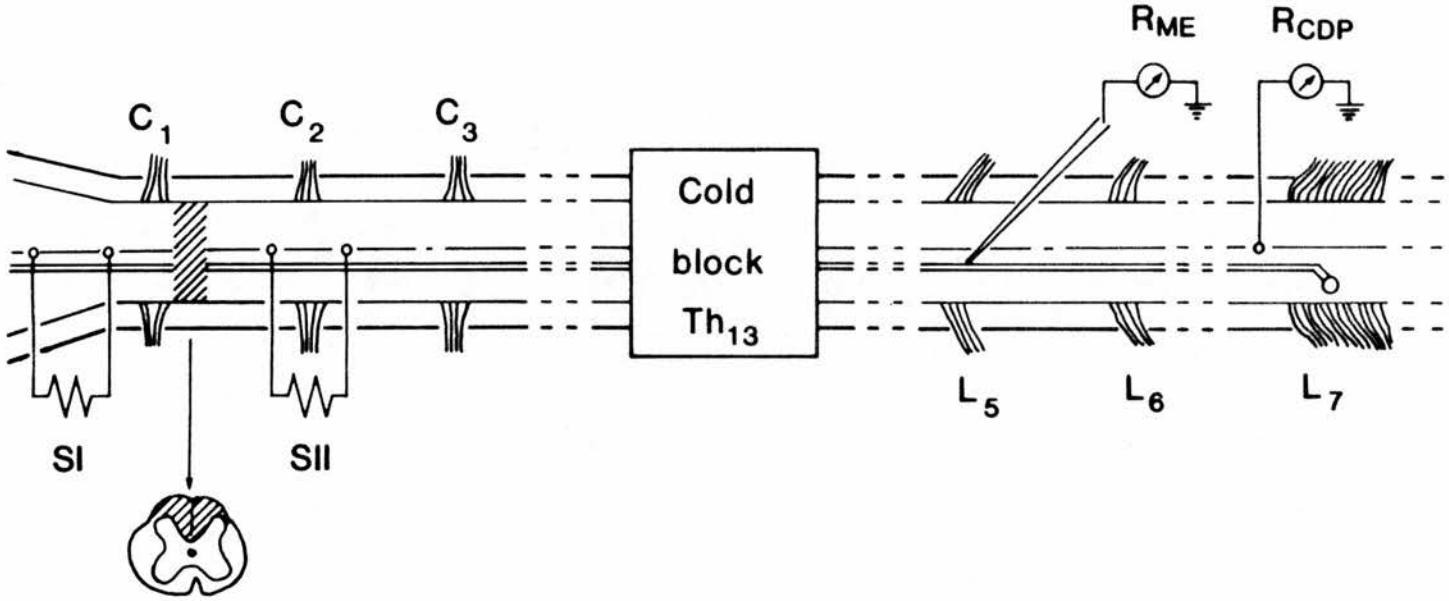

R_{ME}
R_{CDP}
C_1
C_2
C_3
Cold
block
Th_{13}
L_5
L_6
L_7
SI
SII

Figure 17

Assessment of the block of impulse conduction through the spinal cord.

Each pair of traces represents a cord dorsum potential recorded at L_7 (left) and a single unit recording from a p.s.d.c. axon (right) at various stages during cold block of the cord. The arrowheads mark the point at which a stimulus (3V, 0.1ms) was applied to the dorsal columns at C_2. All traces are of single sweeps.

A. Cord dorsum potential and antidromic impulse recorded before cooling the cord.

B. Cord cooled to 10°C: the latency of the cord dorsum potential lengthened and its amplitude decreased. The latency of the antidromic impulse was also increased.

C. Cord cooled to 2°C: the latency of the cord dorsum potential was further lengthened and its amplitude further reduced. The antidromic impulse failed and was replaced by background activity.

D. Cord cooled to 0°C: in this example both the cord dorsum potential and the antidromic impulse were abolished at this temperature. At this point at least the dorsal half of the spinal cord was assumed to be cold blocked.

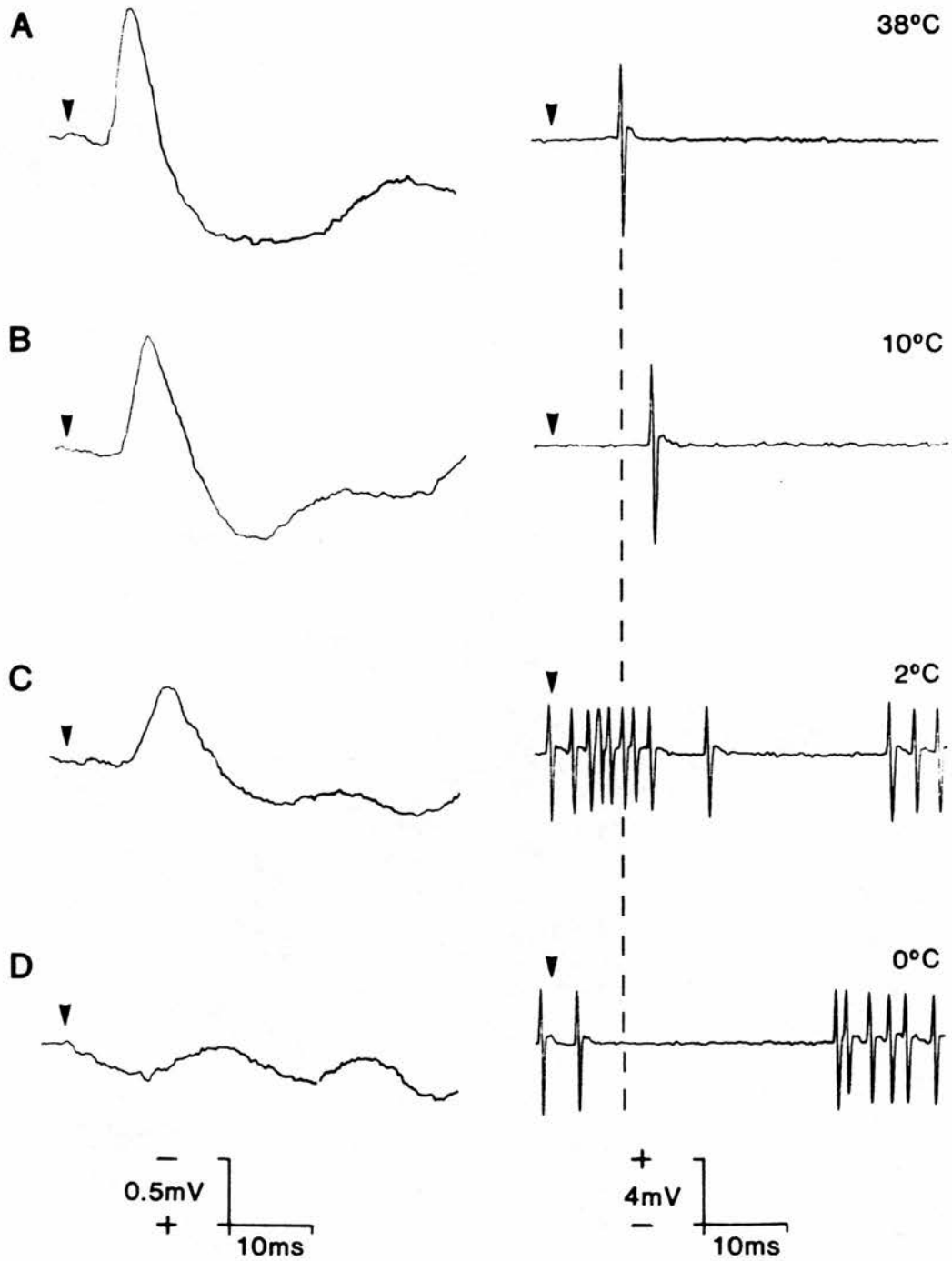
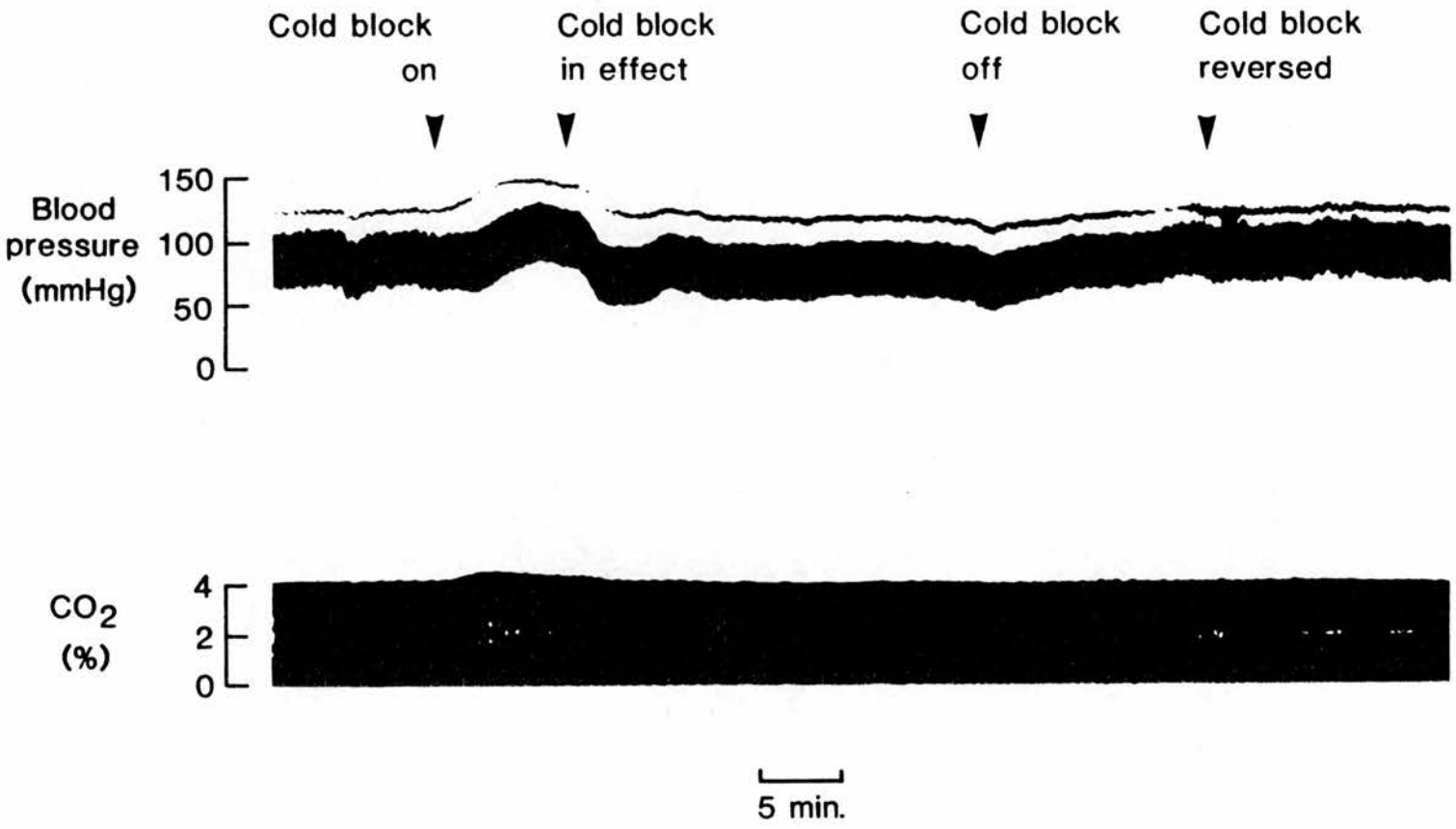

A
38°C
B
10°C
C
2°C
D
0°C
0.5mV
10ms
4mV
10ms

Figure 18

The effect of cooling the spinal cord on the levels of blood pressure and end tidal carbon dioxide.

The top trace is a continuous record of blood pressure from a cannula in a carotid artery and the lower trace a continuous record of the end tidal level of CO_2.

The first arrow indicates the point at which cooling of the cord began and the second arrow the point at which cold block of the cord was achieved. Cold block was maintained until the position of the third arrow, at which point the thermoelectric thermode was switched off and the cord allowed to recover. The fourth arrow marks the point at which a full reversal of the spinalisation had occurred.


Cold block on
Cold block in effect
Cold block off
Cold block reversed
Blood pressure (mmHg)
150
100
50
0
CO_2 (%)
4
2
0
5 min.

RESULTS

An investigation was made of the influence of activity in descending fibres on the cutaneous input to 19 p.s.d.c. neurones. The response properties and receptive field organisation of each unit were analysed both before and during cold block of the spinal cord.

The Sample of Units

When the 19 units were analysed before cold block of the cord, their response properties and receptive field organisation were representative of the types of unit within the larger sample of p.s.d.c. neurones described in Section 1.

1) Skin types forming the receptive field

The sample consisted of 11 units with receptive fields (excitatory and inhibitory) confined to hairy skin, 3 units with receptive fields confined to glabrous skin and 5 units with receptive fields including both hairy and glabrous skin. As described in Section 1, those units with receptive fields restricted to hairy skin are referred to as 'hairy skin units' whilst those units with input from glabrous skin are termed 'glabrous skin units'. It should be stressed however that a large proportion of the latter group of neurones also received input from hairy skin. The response properties and receptive field organisation of these two groups of units were typical of those described in Section 1.

2) Convergence of input

Sixteen of the 19 units received both low and high threshold excitatory inputs. Twelve of these units also had inhibitory fields and 4 received input from both hairy and glabrous skin.

Three of the 19 units received only low threshold excitatory input. However, 2 of these units also had an inhibitory field and 1 received input from both hairy and glabrous skin.

Eleven of the 19 units had inhibitory receptive fields.

3) Conduction velocities

The conduction velocities of the 19 units lay between 17 and 62ms^{-1} and therefore covered a similar range to that recorded from the larger sample of units in Section 1 (14 - 69ms^{-1})

The Effect of Blocking Descending Activity in the Spinal Cord on the Background Activity of P.s.d.c. Neurones

A comparison was made of both the level and pattern of background activity recorded from each of the 19 p.s.d.c. units, before and during cold block of the cord. Background activity was recorded before cold block, over periods of between 1 and 2 minutes, following the minimum manipulation of the receptive field nescessary to identify the unit. Background activity from the same neurones was recorded over similar periods in the spinal state, as soon as the cold block was judged to be fully

effective, but before reinvestigation of the receptive field. The levels and pattern of activity recorded from p.s.d.c. neurones in the intact spinal cord are described in section 1; the changes produced by a block of descending impulses are described below.

levels of activity: table 3 shows the averaged levels of background activity recorded before and during cold block of the cord.

The level of activity of 15 of the 19 units was increased during cold block of the cord. The increases ranged from a few impulses per second to 104 impulses per second. When calculated as a proportion of the level of activity recorded before cold block, increases ranged between 1.7 and 18.7 times (Table 3). The increase in activity did not depend on the level of activity recorded before cold block, nor were large increases associated only with those units with response properties or receptive fields affected by cold block.

Two of the 19 units had a reduced background activity in the spinal state. These units were not of any particular type and their response properties were not unusual before or after cold block; 1 unit became responsive to noxious heat after spinalisation, the other was unaffected.

The background activities of 2 units were virtually unchanged by cold block. These units were not unusual in their response properties either before or during the block; both became responsive to noxious radiant heat in

the spinal state.

Pattern of activity: For 9 units sufficient background discharge was recorded to allow a comparison of the pattern of activity in each state using interval analysis; the resulting histograms are shown in Figs. 18 and 19.

The shortest intervals detected and the durations of the peak (intraburst) intervals were the same in each state. However, two main changes in the pattern of activity were observed.

1) For 5 of the 9 units, cold block produced a decrease in the proportion of very short (intraburst) intervals compared to longer ($\geq$3ms) non-burst intervals (Fig. 19). This change in pattern was most marked for those units with large increases in background activity, as a result of cold block. For the remaining 4 units analysed, there was little or no change in the proportion of intraburst to non-burst intervals in the background activity.

2) All of the 9 units analysed had a larger number of short to medium intervals (20 - 100ms duration) but fewer long intervals. Before cold block of the cord, the background activity of all 9 units contained intervals in excess of 500ms. However, during cold block of the cord, the longest intervals recorded were between 80 and 400ms (Fig. 20).

The Effects of Blocking Descending Activity in the Spinal Cord on the Response Properties and Receptive Field Organisation of P.s.d.c. Neurones

Excitatory receptive fields

1) Low threshold excitatory components

All 19 p.s.d.c. neurones were investigated for their responses to light brushing and tapping, both before and during cold block of the spinal cord. In general, few changes in either response properties or receptive field size could be detected during cold block of the cord.

Response properties

1) Before cold block of the cord all 19 units could be excited by light tactile stimuli applied to a low threshold excitatory area. However, during cold block of the cord 2 of these units could no longer be excited; they were instead inhibited by light tactile stimulation of the same area of skin. For 1 unit this modification resulted from the increased effectiveness, in the spinal state, of previously undetected inhibitory input. The inhibition was evoked by light tactile stimulation of an area of skin overlapping that where excitatory input had previously been detected (Fig. 21 top). A similar change, in the response of a second unit, resulted from the expansion of a low threshold inhibitory component (Fig. 21 bottom).

2) During cold block of the cord 2 units developed mixed excitatory and inhibitory responses, to light tapping. The excitatory response to tap being followed by a depression of background activity lasting about a second.

3) Cold block of the cord had no detectable effect on the response of the remaining 15 units to light tactile stimuli.

Receptive field size

Apart from the two units described above, which were excited by light tactile stimuli before cold block but inhibited from the same area of skin in the spinal state, the interruption of descending impulses produced no detectable change in the size of the low threshold excitatory areas of p.s.d.c. neurones.

2) High threshold excitatory components

A) High threshold mechanoreceptive components

All 19 p.s.d.c. neurones were investigated for their responses to sustained noxious pinch, both before and during cold block of the spinal cord. The predominant effect of interrupting descending impulses was to enhance the responsiveness of p.s.d.c. neurones to noxious pinch.

Response properties

1) Before cold block of the cord, 16 of the 19 units responded to sustained pinch with a slowly adapting discharge; 10 were hairy skin units and 6 glabrous skin units. All of these units remained responsive to

sustained pinch during cold block of the cord. In addition, a glabrous skin unit previously unresponsive was excited by noxious pinch of a single toe pad. However, the response evoked was very weak and noxious heat applied to the same pad produced inhibition.

2) Eleven of the 16 units, excited by noxious pinch before cold block of the cord, responded more vigorously to the same clip applied to the same skin position in the spinal state; even when changes in background activity were taken into account. Eight were hairy skin units and 3 were glabrous skin units (Fig. 22).

Receptive field size

1) During cold block of the cord, 8 units responded to noxious pinch of areas of skin outside those from which such stimuli were previously effective; that is, they responded from a larger area of skin. The high threshold mechanoreceptive components of 5 hairy skin units expanded to include a larger area of hairy skin (Fig. 22); while those of 2 units, previously unresponsive to pinch of the pads, expanded to include glabrous skin (Fig. 23). The high threshold mechanoreceptive components of 3 glabrous skin units were also expanded; 2 to include a greater area of glabrous skin (Fig. 24) and 1 an increased area of hairy skin.

2) The high threshold mechanoreceptive field of one glabrous skin unit changed position in the spinal state. This unit responded to noxious pinch of the

central pad and pad 5 before cold block of the cord, but responded to pinch of toe pad 5 and also pad 4 in the spinal state but was no longer responsive to stimuli applied to the central pad.

Six units responded both more vigorously to pinch and from a larger area of skin during cold block of the spinal cord.

B) High threshold thermoreceptive components

Eleven of the 19 p.s.d.c. neurones were tested for their responses to noxious radiant heat both before and during cold block of the cord. These included 8 hairy skin units and 3 glabrous skin units. Interrupting the conduction of descending activity revealed excitatory responses to noxious heat from units unresponsive before the block.

Response properties

1) Before cold block of the cord, only 4 of the 11 units tested were excited by noxious radiant heat; 2 hairy skin units and 2 glabrous skin units. During cold block of the cord, however, 5 of the 7 units previously unresponsive were excited by noxious radiant heat; all of these were hairy skin units (Fig. 25).

2) During cold block of the cord, 3 of the 4 units previously excited by noxious heat responded more vigorously to stimuliation of the same skin positions (Fig. 26).

Receptive field size

Two of the 4 units excited by noxious heat before cold block of the cord, responded from a larger area of skin in the spinal state (Fig. 26 and Fig. 27).

Several units were more responsive to both noxious mechanical and thermal stimuli in the spinal state. All of those units which responded to noxious heat more vigorously (3) or from a larger area of skin (2), were also more responsive to noxious pinch in the spinal state. Three of the 5 units which became responsive to noxious heat during cold block of the cord were also more responsive to noxious pinch.

Inhibitory Receptive Fields

1) Low threshold inhibitory components

Eighteen of the 19 p.s.d.c. units were tested for inhibitory input from the skin of the ipsilateral limb in response to light brushing both before and during cold block of the cord. Though difficult to assess, the effectiveness of low threshold inhibitory input was maintained or enhanced after blocking the conduction of descending impulses.

Response properties

1) Before cold block of the cord 9 of the 18 units, 7 hairy skin and 2 glabrous skin, were found to have low threshold inhibitory areas. During cold block of the cord, all 9 of these inhibitory fields remained

effective. In addition, a further 4 units, 2 hairy skin and 2 glabrous skin, developed low threshold inhibitory areas which had not previously been detected. The low threshold inhibitory component of one of these units occupied an area where a low threshold excitatory component had been detected before cold block (Fig. 21 top).

2) Because of the increase in background activity that usually occured during cold block of the cord, it was difficult to compare the effectiveness of inhibition evoked by light tactile stimuli in the two states. However, 2 units which had a low threshold inhibitory area before cold block of the cord appeared more effectively inhibited by motorised brushing of the same area in the spinal state (Fig. 28).

Receptive field size

It was not possible to detect low threshold inhibitory input, by a single tap or brush stroke to a small area of skin. Simultaneous movement of many hairs (or other receptors) was required to evoke an effective inhibition of background activity. Since it was therefore necessary to repeatedly stroke an area of skin several cm^2, accurate mapping of changes in inhibitory areas was not possible. However, the low threshold inhibitory area of 1 unit was clearly expanded in size since it occupied an area of skin where light tactile stimuli had previously excited the unit (Fig. 21).

2) High threshold inhibitory fields

P.s.d.c. units were tested for high threshold inhibitory input from skin of the ipsilateral limb both before and during cold block of the cord. Eighteen units were tested for their response to noxious pinch and 11 units further investigated for their response to noxious heat. Blocking descending activity enhanced the inhibitory effects of noxious stimuli on some units.

Response properties

Before cold block of the cord 2 neurones, both glabrous skin units, were inhibited by both noxious pinch and radiant heat. During cold block of the cord, a further two units, both with input from glabrous skin, were also inhibited by noxious stimuli (Fig. 29). One unit could be inhibited by noxious pinch (noxious heat not tested) and the other by both noxious pinch and noxious heat.

Receptive field size

Both of the units that were inhibited by noxious stimuli before cold block of the cord could be inhibited more effectively, from an expanded area of skin, in the spinal state. In each case, the high threshold inhibitory components expanded to include additional glabrous skin of the toe or foot pads.

Control Observations

Reversal of spinalisation

Reinvestigating the responses of p.s.d.c units after reversing the spinal cord block would represent an ideal control. Such a procedure could produce evidence that the modified response properties observed during cold block of the cord were a direct result of the interruption of descending activity. However, due to the time consuming nature of the detailed receptive field analysis and the changes in blood pressure which accompanied the cold bock process (Fig. 18), it proved difficult to obtain a stable recording of sufficient duration to enable such observations to be made. The background activity of 3 units and the receptive field of 1 unit were adequately analysed after reversing the cold block.

Background activity

The background activity of 3 p.s.d.c. units was recorded for periods of between 1 and 2 minutes after reversal of the cold block process. Recovery from cold block was judged to have occurred, when the cord dorsum potential recovered its previous shape and amplitude and the unit could be antidromically activated with the same latency as before the block.

Each of the 3 units had an increased rate of background activity in the spinal state. After recovery from the cold block, the rate of activity of two units returned to pre-block levels while that of the remaining

unit, though much reduced, had not fully returned at the time of analysis (Table 3).

Receptive field analysis

Only one unit was recorded for sufficient duration after reversing the spinal cord block to complete a reanalysis of its receptive field properties. During cold block of the cord this unit responded to noxious radiant heat from a larger area of skin than previously. After reversal of the spinalisation the responsive area contracted to its original size (Fig. 27).

Additional control observations

The most consistent modification of the response properties of p.s.d.c. units, produced by cold block of the cord, was the appearance of an excitatory response to noxious radiant heat from units which were not previously responsive. However, occasional inconsistencies in the responses of some units to noxious radiant heat were observed. Three units, though excited by noxious radiant heat from one skin position, responded from an adjacent position only after a second application of the stimulus (see for example Fig. 26, B). Because of these observations and also because of the problems of maintaining a stable recording following recovery from cold block, further control observations were considered desirable.

Five p.s.d.c. neurones were recorded (4 hairy skin units, 1 glabrous skin unit) from 3 cats. These units

were selected for their lack of response to noxious radiant heat. They were tested in the usual manner by applying noxious radiant heat to a number of skin positions some of which overlapped areas of skin from which pinch was effective. After 8 to 10 minutes, which is the usual period required to produce a cold block of the cord, each of the 5 units were tested again at the same skin positions. All of the 5 units tested in this way remained unresponsive to noxious heat.

Unidentified Projecting Units

In Section 1 a group of 9 units was described that, whilst satisfying the criteria for identification as p.s.d.c. neurones, had unusual properties. These suggested either that they might form a separate subgroup of the p.s.d.c. neuronal population or that they may not be post-synaptic in origin. Five of these units were also investigated following cold block of the cord.

Background activity

A comparison was made of both the level and pattern of background activity, recorded from each of the 5 unidentified units, both before and during cold block. Background activity was recorded before cold block, over periods of 1 - 2 minutes, following the minimum manipulation of the receptive field necessary to identify the units. Background activity was recorded from the same neurones in the spinal state over similar periods, as soon as the cold block was judged to be fully effective.

Levels of activity: In contrast to clearly identified p.s.d.c. units, the background activity of 3 of the 5 unidentified units was decreased during spinalisation while that of one unit was slightly increased. The background activity of the remaining unit was too low to measure and remained so during cold block of the cord.

Pattern of activity: The pattern of background activity was one of the features by which these units differed from clearly identified p.s.d.c. neurones (see Section 1). For each of the 5 units, sufficient background activity was recorded in both states to allow interval analysis to be used to investigate the effect of spinalisation on the pattern of activity. The resulting histograms are shown in Fig. 30.

Cold block did not alter the pattern of activity as assessed by the distribution of intervals within the histograms. However, there was a general increase in the duration of intervals recorded from those units in which the rate of background activity was decreased.

Receptive fields

Although investigated with both light tactile and noxious stimuli, there were no detectable changes in the responses or receptive fields of these 5 unidentified units. They remained responsive only to rapidly adapting low threshold input.

Figure 19

Interspike interval histograms of the background activity of three p.s.d.c. neurones, recorded before (left) and during (right) cold block of the spinal cord.

In order to allow comparison of the pattern of activity in the two states, each pair of histograms represents an analysis of the same number of intervals; 8459-07, 800 intervals; 8434-07, 450 intervals; 8454-09, 250 intervals. Bin width = 0.25ms. Intervals of longer than 20ms were counted but are not displayed; but see Fig. 20. The figures above each histogram represent the level of background activity in impulses per second, in each state.

The histograms illustrate the shift in pattern towards activity with a smaller proportion of burst intervals compared to non-burst impulses, which occurred during cold block of the cord. The change was particularly marked for units with a substantially increased rate of background activity in the spinal state.

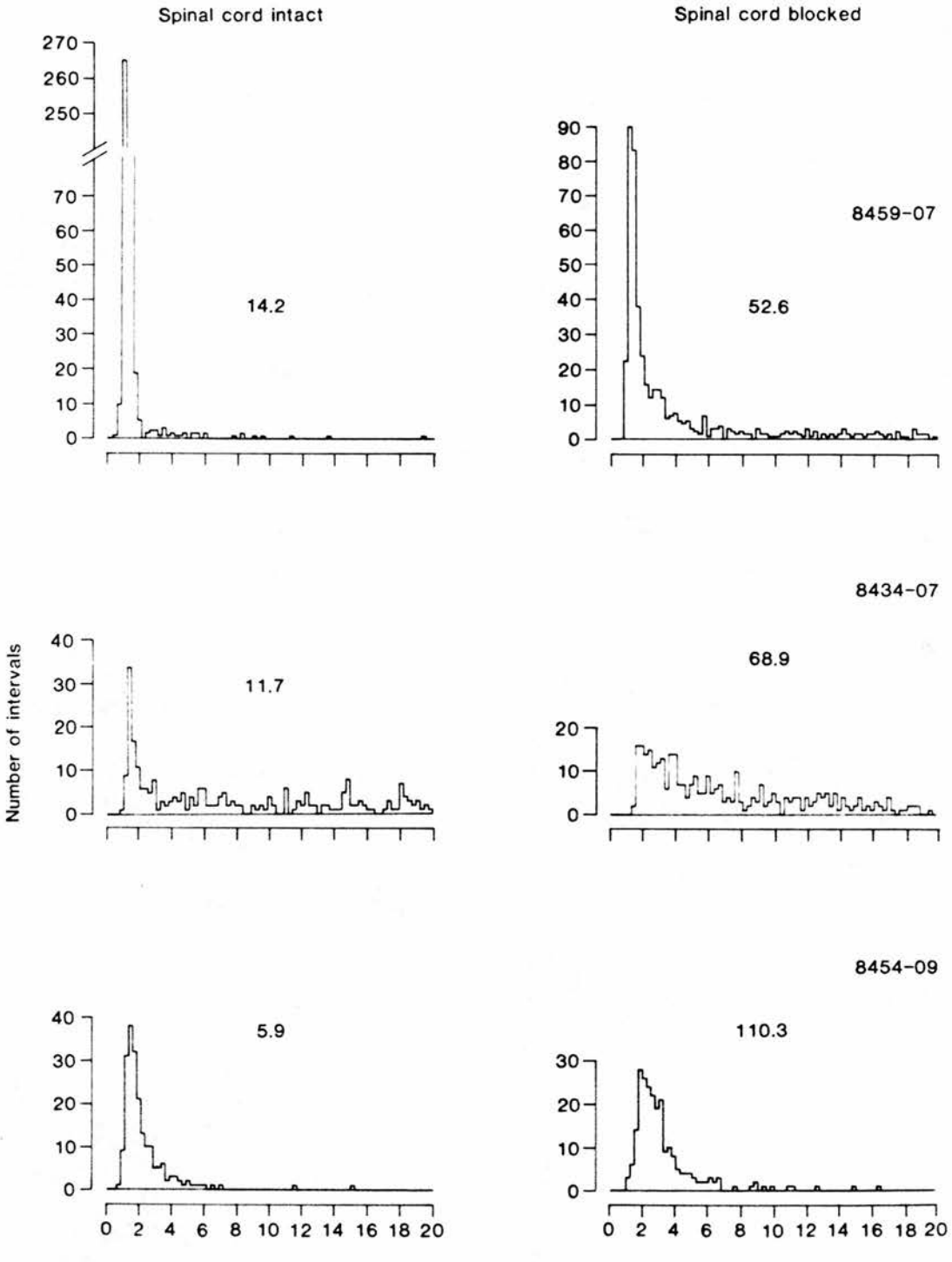

Spinal cord intact
Spinal cord blocked
270
260
250
70
60
50
40
30
20
10
0
14.2
90
80
70
60
50
40
30
20
10
0
8459-07
52.6
8434-07
Number of intervals
40
30
20
10
0
11.7
20
10
0
68.9
8454-09
40
30
20
10
0
5.9
30
20
10
0
110.3
0 2 4 6 8 10 12 14 16 18 20
0 2 4 6 8 10 12 14 16 18 20
Interval (ms)

Figure 20

Interspike interval histograms of the background activity of three p.s.d.c. neurones, recorded before (left) and during (right) cold block of the cord.

In order to allow comparison of the pattern of activity in the two states, each pair of histograms represents an analysis of the same number of intervals; 8459-07, 800 intervals; 8432-05, 1200 intervals; 8434-07, 450 intervals. Bin width = 5ms. The level of background activity in each state is given in impulses per second above each histogram.

The histograms illustrate the shortening of the intervals between non-burst impulses, which occurred as a result of cold block of the cord. While histograms for activity from p.s.d.c. neurones in the intact cord (left), contain intervals of at least 500ms duration, the longest intervals recorded during cold block of the cord (right), were less than 300ms in duration.

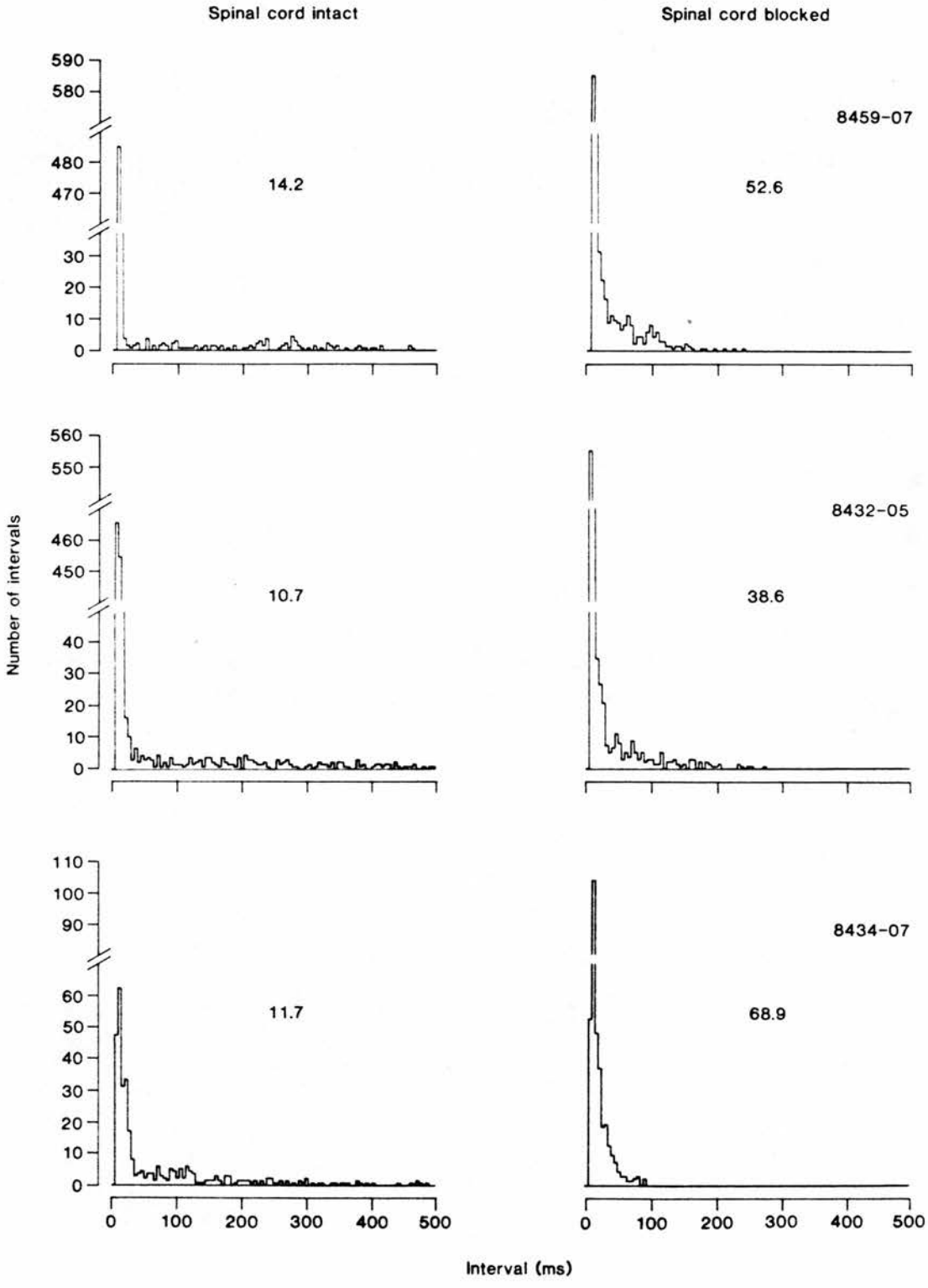

Spinal cord intact
Spinal cord blocked
590
580
480
470
30
20
10
0
14.2
8459-07
52.6
560
550
460
450
40
30
20
10
0
10.7
8432-05
38.6
110
100
90
60
50
40
30
20
10
0
11.7
8434-07
68.9
0
100
200
300
400
500
Number of intervals
Interval (ms)

Figure 21

The effect of blocking descending impulses on the organisation of the low threshold excitatory and inhibitory receptive field components of two p.s.d.c. neurones.

On the left are outlines of a cat hind limb on which are shown the receptive field components of two p.s.d.c. neurones investigated before cold block of the cord. On the right are shown the receptive fields of the same units during cold block of the spinal cord. Those pads from which noxious pinch produced excitatory responses are shown filled in, other symbols are shown in the key.

Before cold block (left), both units had low threshold excitatory components and one (lower unit) a low threshold inhibitory area. During cold block of the cord (right), the low threshold excitatory components of both units were replaced by the appearance (upper unit), or expansion (lower unit), of a low threshold inhibitory field which occupied the same area of skin.

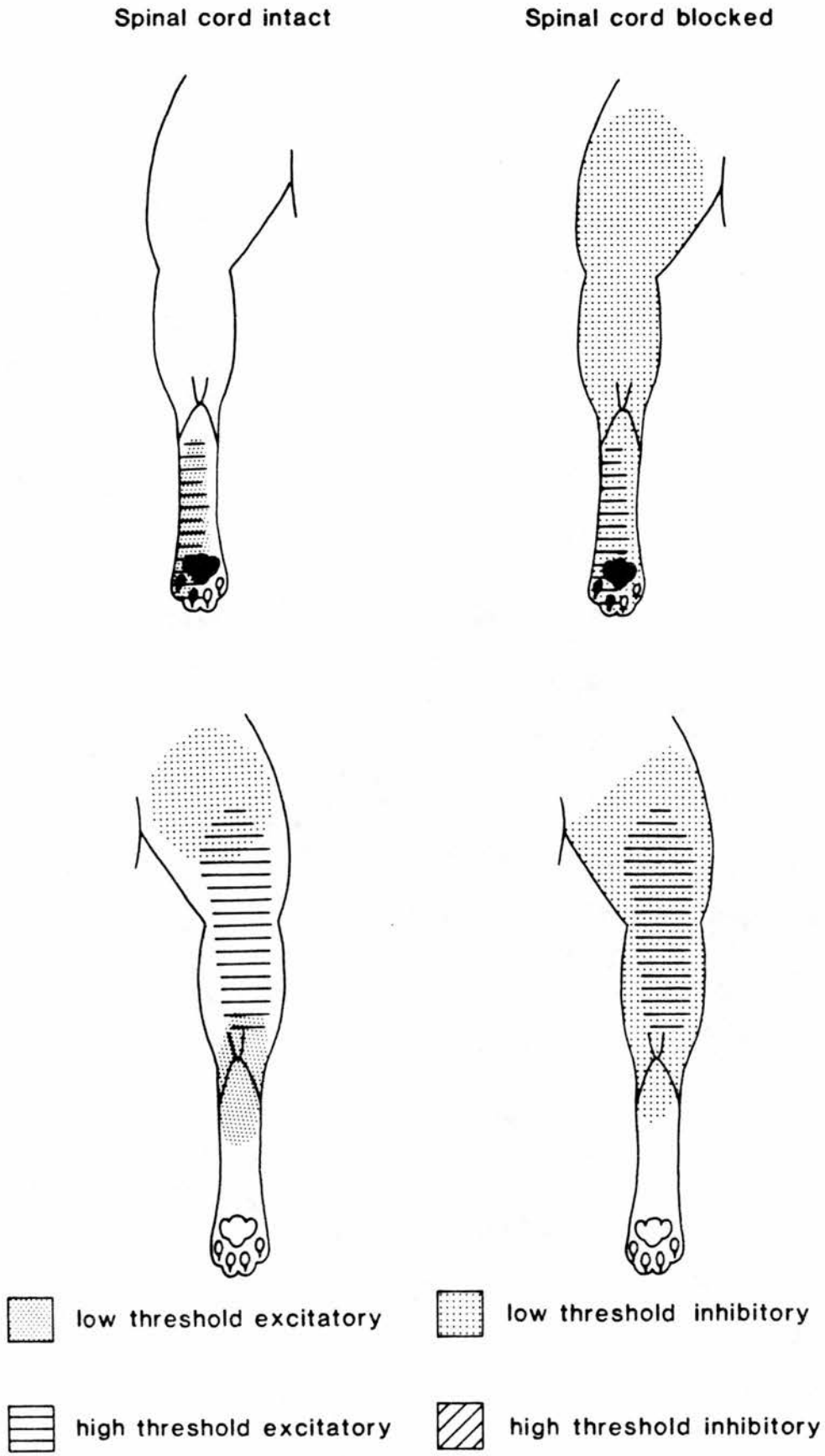

Spinal cord intact
Spinal cord blocked
low threshold excitatory
low threshold inhibitory
high threshold excitatory
high threshold inhibitory

Figure 22

The effect of blocking descending impulses on the high threshold mechanoreceptive component of the excitatory field of a p.s.d.c neurone.

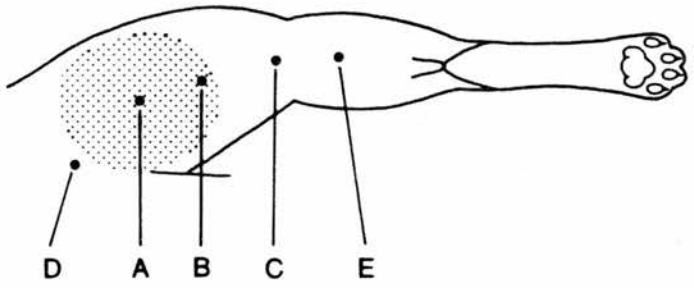
A. Outline of a cat hind limb on which is shown the low threshold excitatory component (shaded area) of the excitatory field of a p.s.d.c. unit. The locations labelled A - E represent the positions to which sustained noxious pinch was applied to the skin. A low threshold inhibitory field has been omitted for clarity.

B. Frequency histogram (1ms bins) of a period of recording from the unit shown in A made before cold block of the cord. Noxious pinch evoked a weak excitation from position A and D but little or no response from positions B and C.

C. Frequency histogram (1ms bins) of a period of recording from the same unit during cold block of the cord. Background activity was increased and the same clip applied to the same skin positions A and D evoked more vigorous responses than previously. In addition, the same clip which was not previously effective when applied to position B, now evoked a vigorous response; indicating an expansion of the area of skin from which the unit could be effectively excited by pinch.

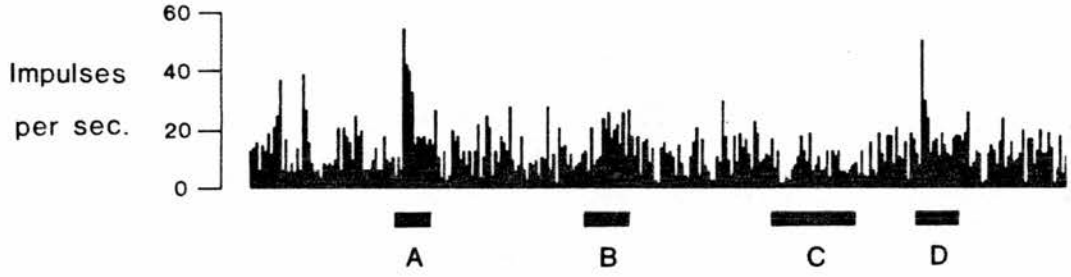
Sustained pinch.

A



B

Spinal cord intact.



C

Spinal cord blocked.

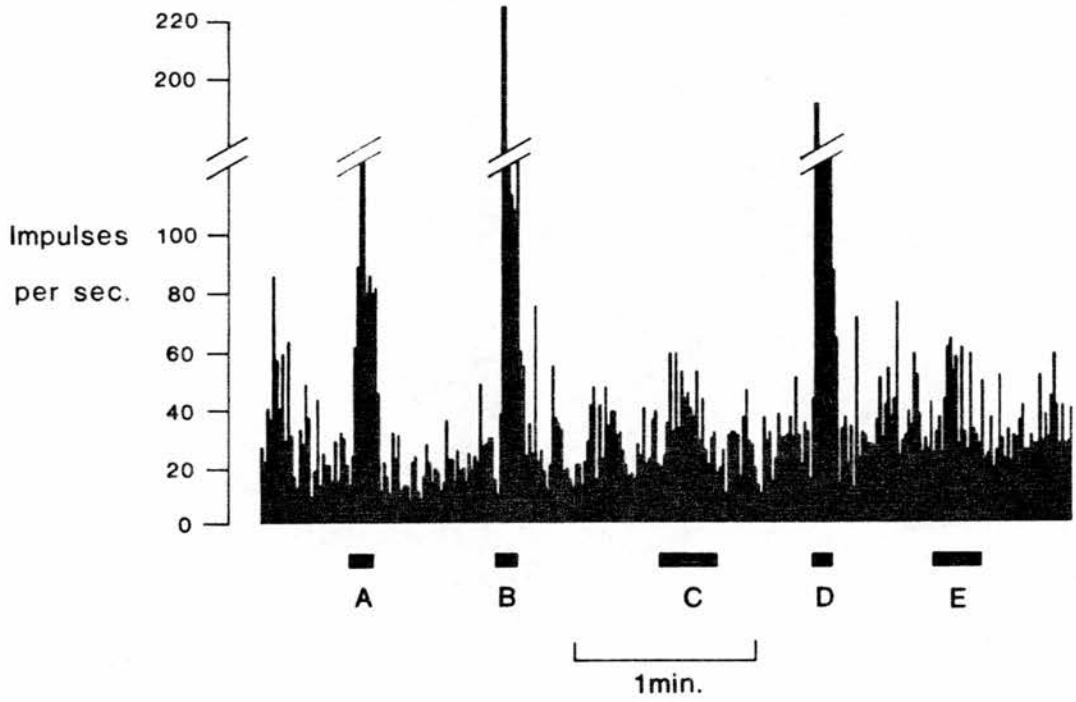


Figure 23

Expansion of the high threshold excitatory components of two hairy skin p.s.d.c. units to include input from glabrous skin.

On the left are outlines of a cat hind limb on which are shown the receptive field components of two p.s.d.c. neurones recorded before cold block of the cord. On the right are shown the receptive fields of the same units in the spinal state.

Before cold block, the high threshold mechanoreceptive components of the receptive fields of both units were restricted to hairy skin. Cold block produced an expansion of the high threshold mechanoreceptive components so that they also included glabrous skin. Those pads from which noxious pinch evoked excitatory responses are shown filled in. Other symbols used appear in the key.

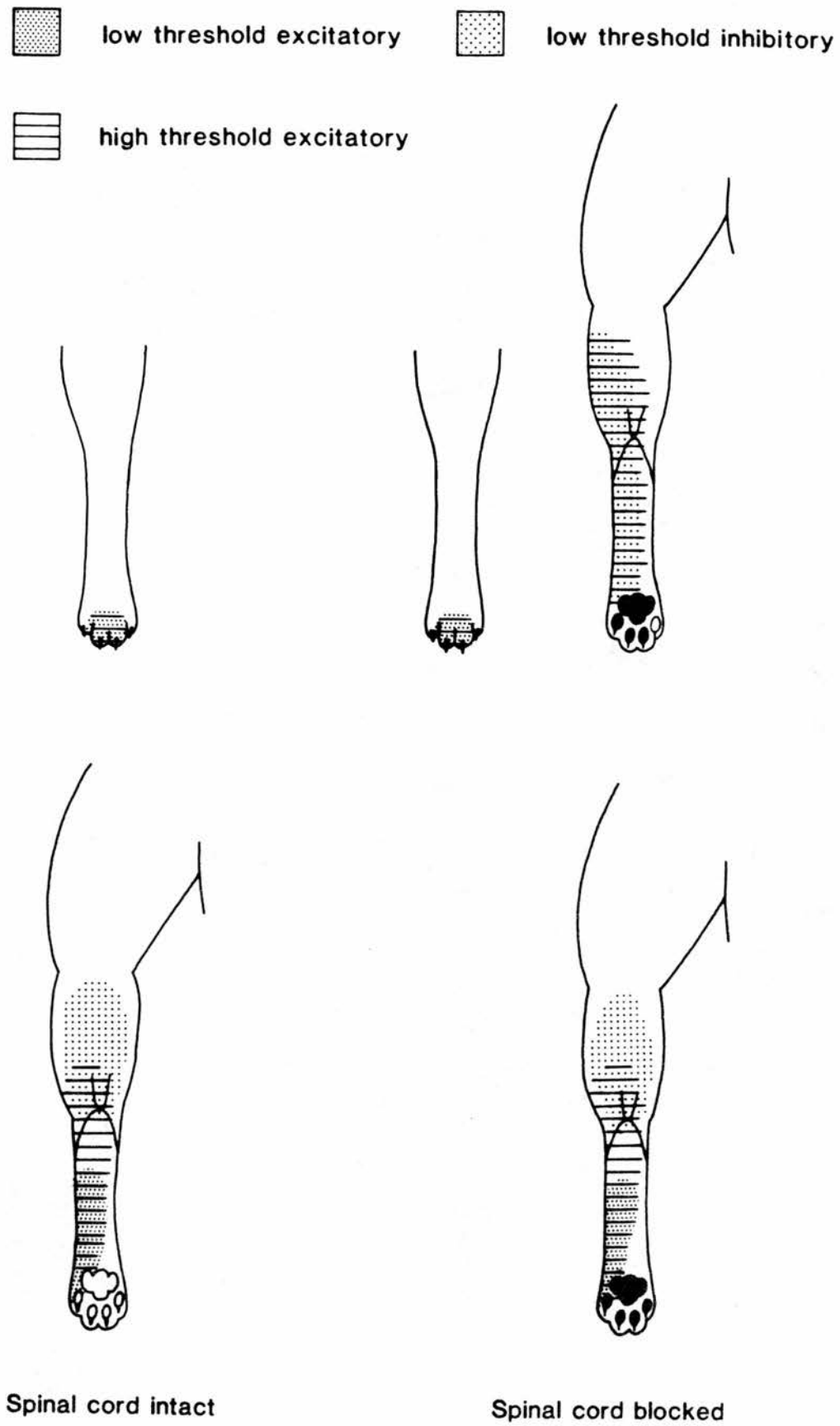

low threshold excitatory
low threshold inhibitory
high threshold excitatory
Spinal cord intact
Spinal cord blocked

Figure 24

The effect of blocking descending activity on the high threshold mechanoreceptive component of the excitatory field of a glabrous skin p.s.d.c. neurone.

A. Frequency histogram (1ms bins) of a period of recording made from a p.s.d.c. unit. Before cold block noxious pinch (duration indicated by bars), applied to each of the pads in turn (symbols beneath bars), evoked an excitatory response only from pad 4.

B. The locations of each of the pads and the position of of the high threshold mechanoreceptive component before cold block of the cord are indicated on an outline of a cat hind paw. Low threshold excitatory and inhibitory components have been omitted for clarity.

C. Frequency histograms (1ms bins) of a period of recording made from the same unit during cold block of the spinal cord. Background activity was increased and noxious pinch now evoked vigorous responses from each of the toe pads and possibly a weak response from the central pad. This indicates an expansion of the area of skin from which the unit could be effectively excited by noxious pinch.

D. The expanded area of the high threshold mechanoreceptive field during cold block of the cord is shown on an outline of the cat hind paw.

The peaks of the responses have been truncated.

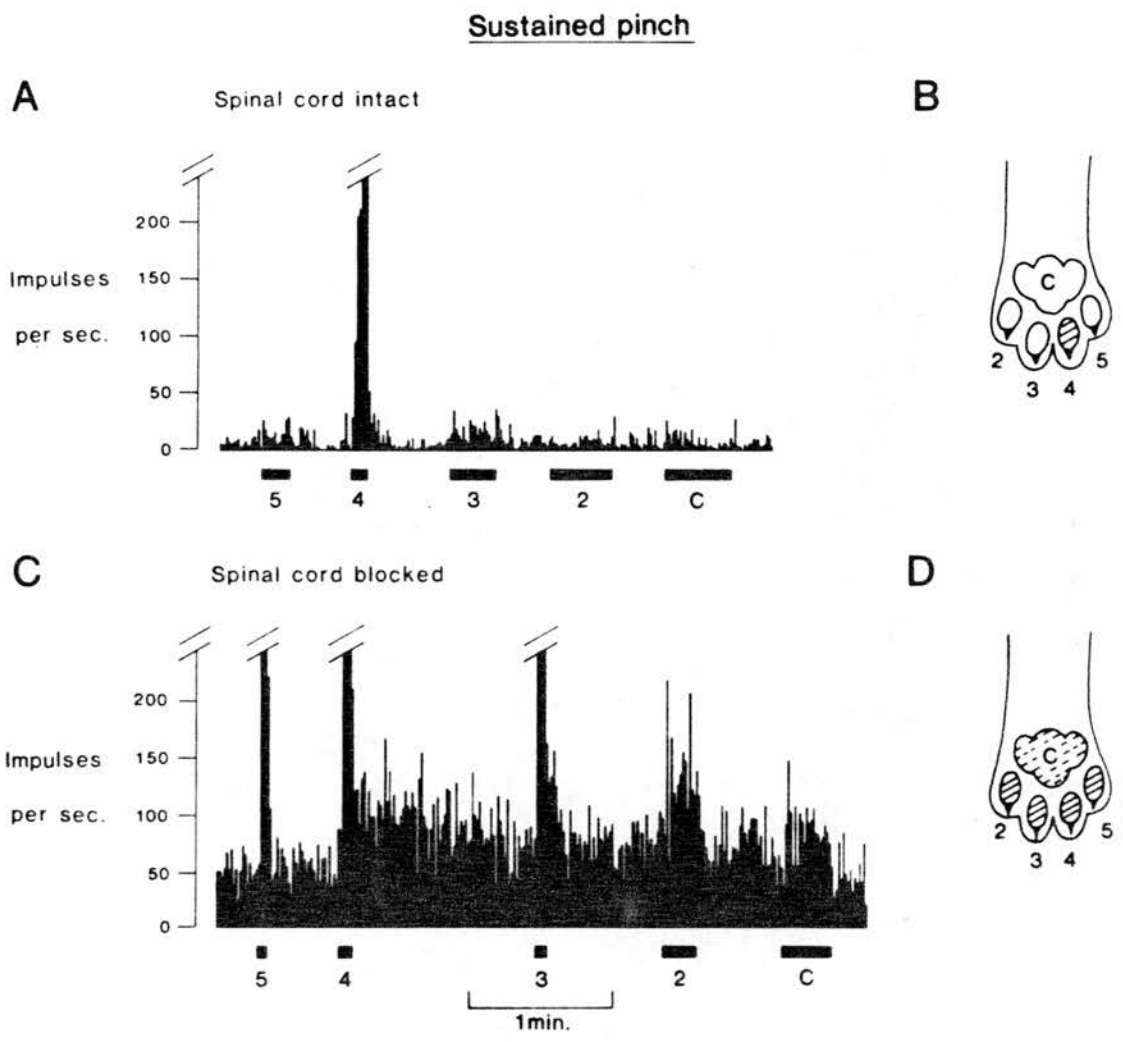

Sustained pinch
A
Spinal cord intact
B
Impulses
per sec.
200
150
100
50
0
5
4
3
2
C
2
3
4
5
C
Spinal cord blocked
D
1min.

Figure 25

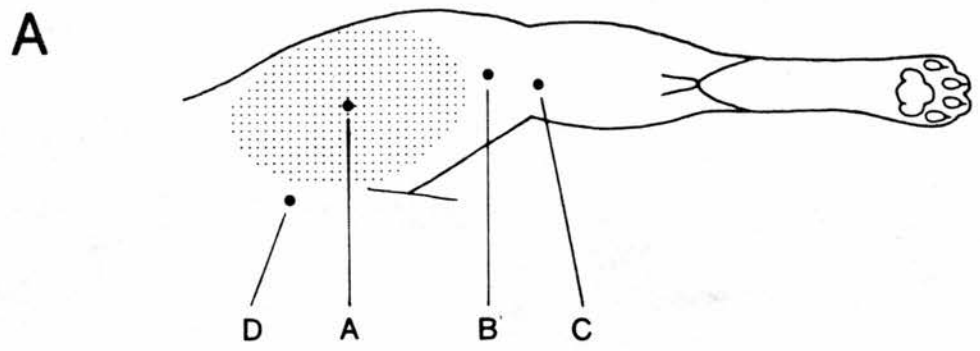
The effect of cold block of the cord on a p.s.d.c. unit previously unresponsive to noxious radiant heat.

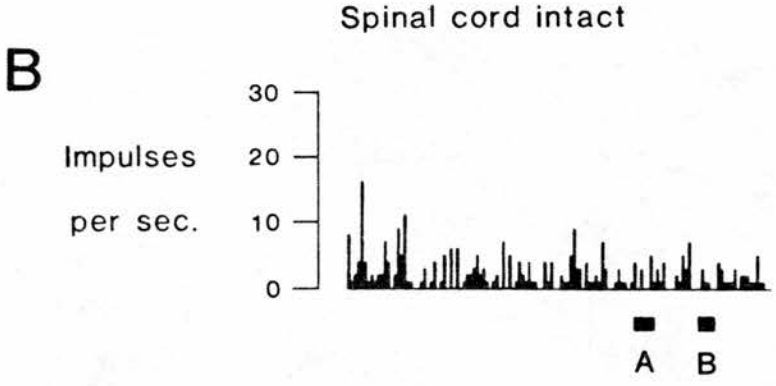
A. Outline of a cat hind limb on which is shown the low threshold excitatory component (shaded area) of the receptive field of a p.s.d.c. neurone. The locations labelled A - D represent the positions to which noxious radiant heat was applied to the skin.

B. Frequency histograms (1ms bins) of a period of recording from the unit shown in A. Before cold block of the cord noxious heat (duration indicated by bars) applied to position A, at the centre of the low threshold excitatory area and to position B, just outside it, were both ineffective.

C. Frequency histogram (1ms bins) of a period of recording from the same unit during cold block of the spinal cord. Background activity was increased and noxious radiant heat now evoked excitatory responses when applied to both positions A and B, though it remained ineffective at the more distant positions C and D.

Noxious radiant heat





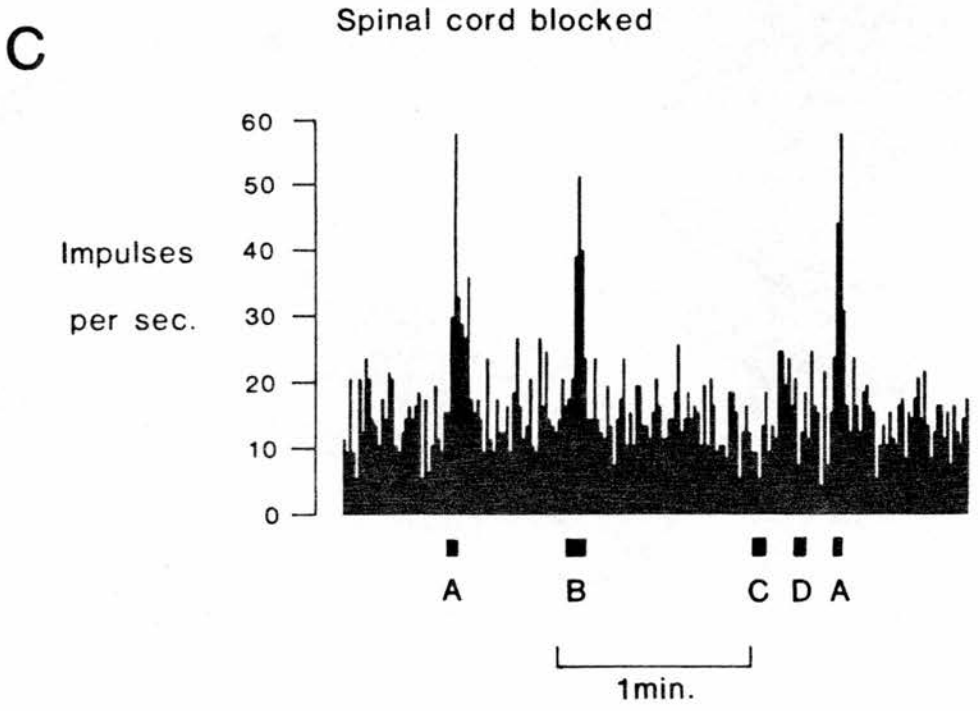


Figure 26

The effect of blocking descending impulses on the excitatory response of a p.s.d.c. neurone to noxious radiant heat.

A. Outline of a cat hind limb on which is shown the low threshold component (shaded area) of the excitatory field of a p.s.d.c. neurone. The locations labelled A - E represent the positions to which noxious radiant heat was applied to the skin. A low threshold inhibitory field has been omitted for clarity.

B. Frequency histogram (1ms bins) of a period of recording from the unit shown in A. Before cold block of the cord noxious heat (duration indicated by bars) applied to position A, at the centre of the low threshold excitatory area and to position B, at its edge, evoked weak excitatory responses. There was no response to noxious heat applied to positions C and D outside the low threshold excitatory field.

C. Frequency histogram (1ms bins) of a period of recording from the same unit during cold block of the spinal cord. Background activity increased and noxious radiant heat evoked more vigorous responses from positions A and B within the low threshold excitatory area. In addition, clear responses were evoked from positions C, D and E outside the low threshold excitatory area and well beyond the area from which responses could be evoked before cold block.

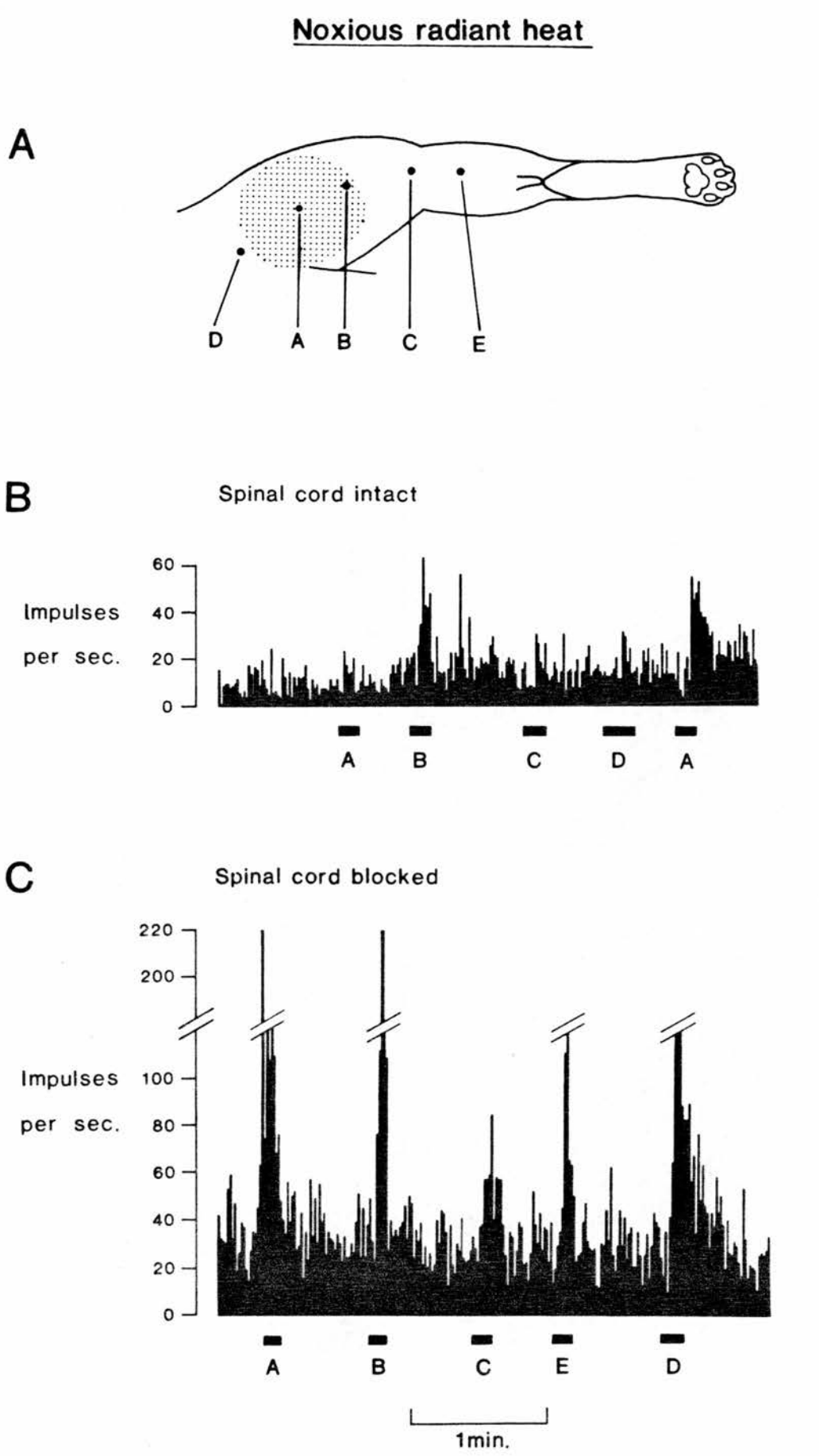

Noxious radiant heat
A
D
A
B
C
E
B
Spinal cord intact
Impulses
per sec.
60
40
20
0
A
B
C
D
A
C
Spinal cord blocked
Impulses
per sec.
220
200
100
80
60
40
20
0
A
B
C
E
D
1min.

Figure 27

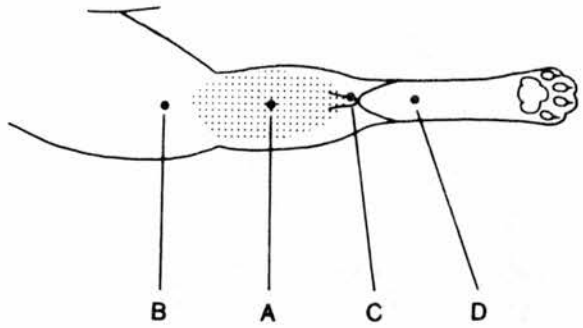
The effect of blocking descending impulses on the excitatory reponse of a p.s.d.c. neurone to noxious radiant heat.

At the top is an outline of a cat hind limb on which is shown the low threshold component (shaded area) of the excitatory field of a p.s.d.c. neurone. The locations labelled A - D represent the positions to which noxious radiant heat was applied to the skin. A low threshold inhibitory field has been omitted for clarity.

Below are shown frequency histograms (1ms bins) of periods of recording made from the same neurone, before (left), during (centre) and after (right) cold block of the spinal cord. Before cold block noxious radiant heat (duration indicated by bars) was only effective when applied to position A at the centre of the low threshold excitatory area. During cold block of the cord noxious heat applied to the same skin positions evoked responses not only from position A but also from position B at the edge of the low threshold area and positions C and D well outside, indicating an expansion of the high threshold thermoreceptive component. After reversal of the cold block the unit responded to noxious heat only from position A; indicating a contraction of the high threshold thermoreceptive field to its original size.

The background activity which was increased in the spinal state is given in impulses per second above each histogram.

Noxious radiant heat.



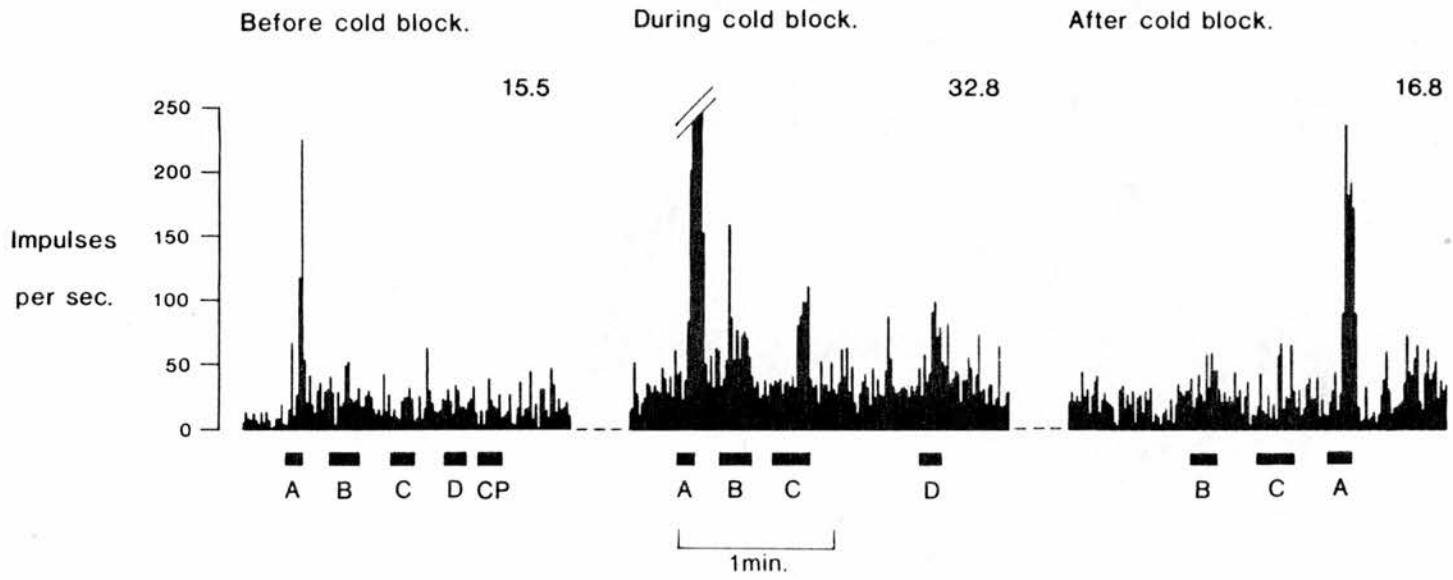


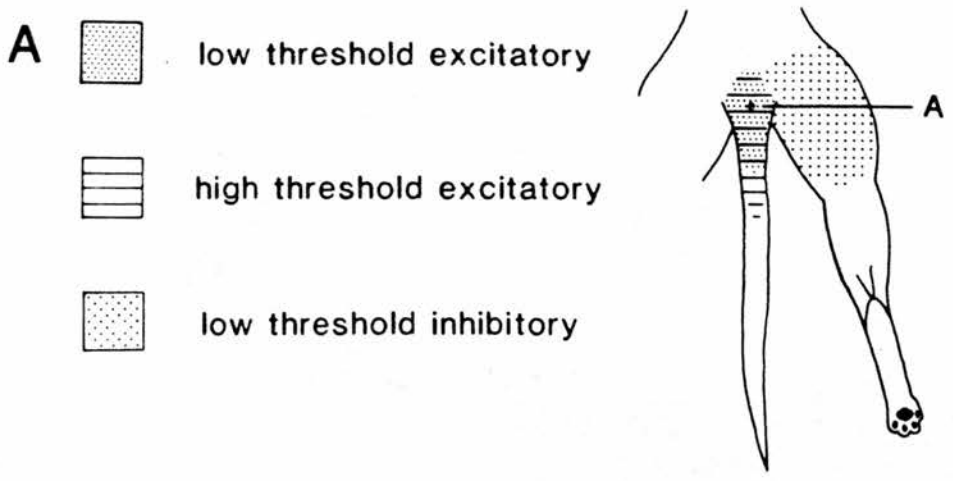
Figure 28

The effect of blocking descending activity on the low threshold inhibitory input to a p.s.d.c. neurone.

A. Outline of a cats hind quarters on which are shown components of the receptive field of a p.s.d.c. neurone. The point labelled A is the position to which a noxious pinch was applied to the skin.

B. Frequency histograms (1ms bins) of a period of recording made from the unit shown in A before cold block of the cord. Repeated brushing (shaded bar), of hairy skin on the thigh, produced inhibition of the background activity, while a noxious pinch (solid bar), applied at A, evoked an excitatory response.

C. Frequency histogram (1ms bins) of a period of recording from the same unit during cold block of the cord. In the spinal state, repeated brushing (shaded bar) evoked a more effective inhibition of a raised background activity while noxious pinch applied at A evoked a more vigorous excitatory response.


A
low threshold excitatory
high threshold excitatory
low threshold inhibitory
A

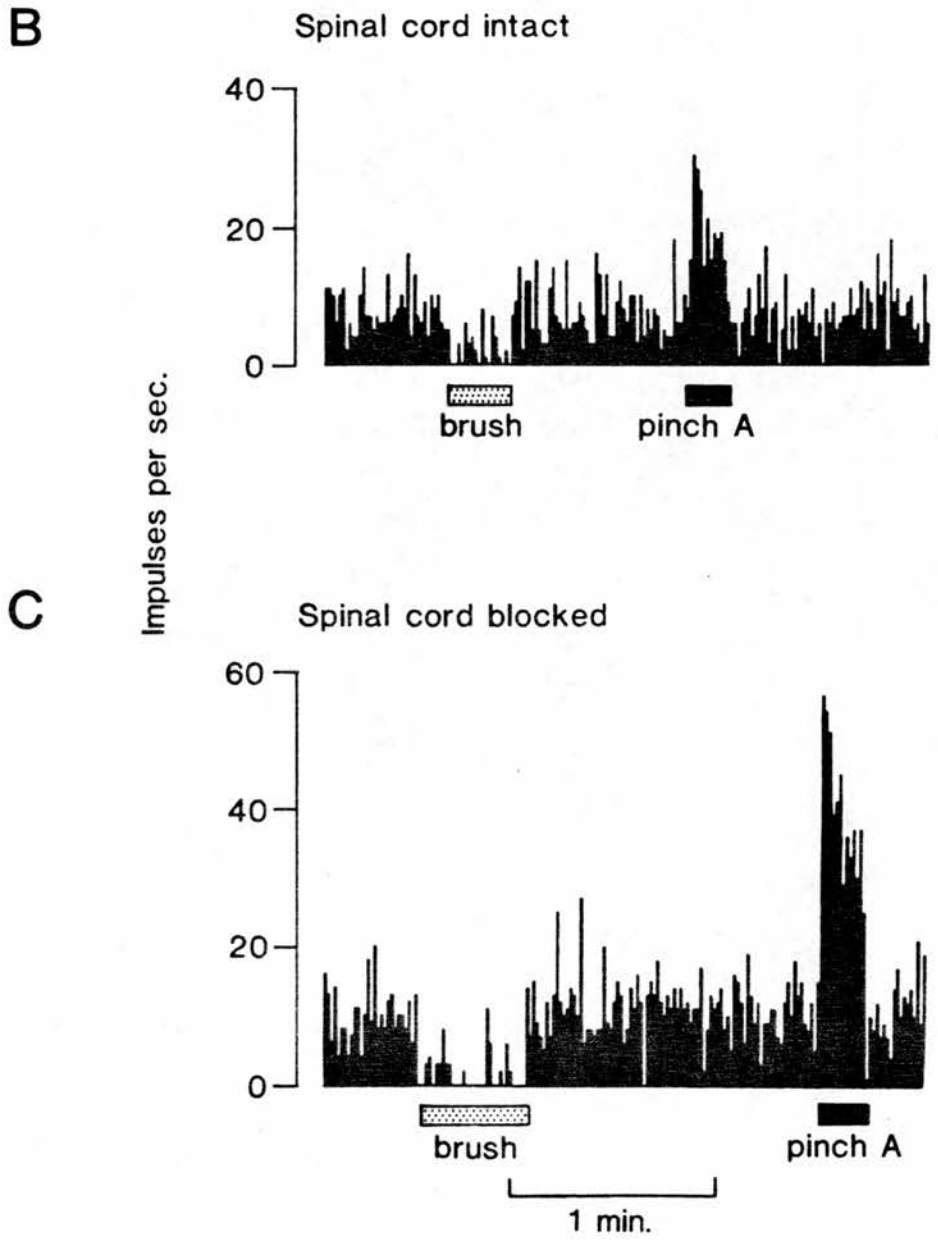

B
Spinal cord intact
40
20
0
brush
pinch A
Impulses per sec.
C
Spinal cord blocked
60
40
20
0
brush
pinch A
1 min.

Figure 29

The effect of blocking descending activity on the response of a glabrous skin p.s.d.c. unit to noxious pinch.

A. Outline of a cat hind paw on which are shown the receptive field components of a p.s.d.c. unit with input from glabrous skin.

B. Frequency histogram (1ms bins) of a period of recording from the unit shown in A. Before cold block of the cord noxious pinch evoked a weak excitatory response from pad 5 but no clear response from the remaining pads.

C. Outline of cat hind paw on which are shown the receptive field components of the same unit during cold block of the cord. A high threshold inhibitory component, not previously detected, became evident.

D. Frequency histogram (1ms bins) of a period of recording from the same unit during cold block of the spinal cord. Noxious pinch evoked a stronger excitatory response from pad 5, but in addition, noxious pinch of each of the remaining pads evoked clear inhibitory responses. The background activity was also raised in the cold blocked state and it is possible that this aided the detection of the inhibitory responses.

Sustained pinch

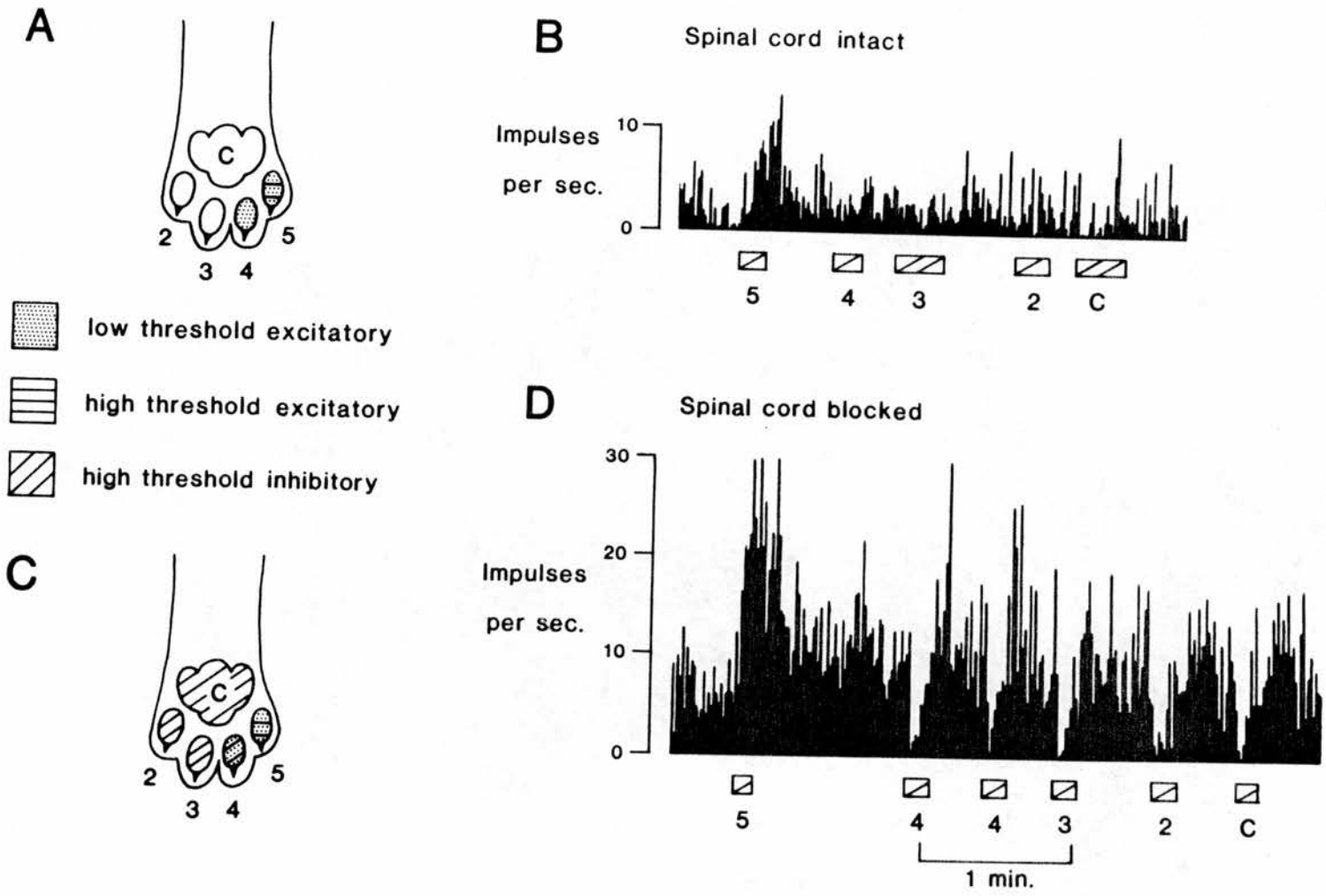


Figure 30

The effect of blocking descending impulses on the pattern of the background activity of unidentified projecting neurones.

Interspike interval analysis of background activity recorded from three unidentified projecting units both before (left histograms) and during (right histograms) cold block of the spinal cord. In order to allow direct comparison of the pattern of background activity in the two states, each pair of histograms is an analysis of the same number of intervals; 8458-06, 500 intervals; 8458-08, 800 intervals; 8452-05, 350 intervals. The rate of background activity recorded from each unit, in both the intact and spinal states, is given in impulses per second above each histogram.

In each case the rate of background activity was reduced by cold block and as a result there was a general increase in the duration of intervals. But the pattern of activity, as assesed by the distribution of intervals within the histograms, remained similar.

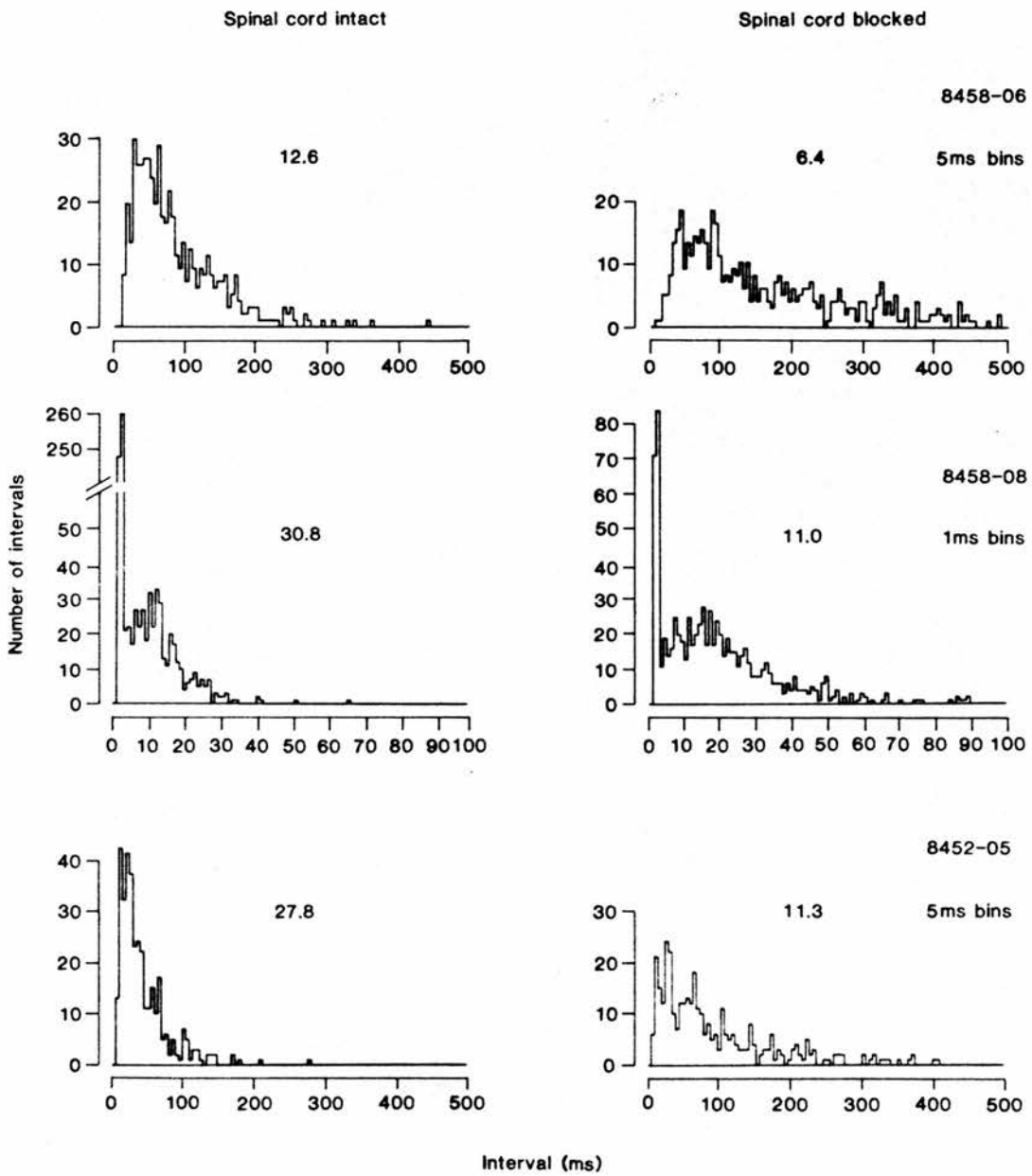

Spinal cord intact
Spinal cord blocked
8458-06
12.6
6.4
5ms bins
30
20
10
0
0 100 200 300 400 500
20
10
0
0 100 200 300 400 500
Number of intervals
260
250
50
40
30
20
10
0
30.8
0 10 20 30 40 50 60 70 80 90 100
80
70
60
50
40
30
20
10
0
8458-08
11.0
1ms bins
0 10 20 30 40 50 60 70 80 90 100
8452-05
40
30
20
10
0
27.8
0 100 200 300 400 500
30
20
10
0
11.3
5ms bins
0 100 200 300 400 500
Interval (ms)

Table 3

The effect of cold block on the rates of background activity of a sample of 19 p.s.d.c. neurones.

On the left are shown the averaged rates of background activity recorded over periods of between 1 and 2 minutes before, during and after (3 units) cold block of the spinal cord.

Changes in the rate of activity resulting from the interruption of decending impulses are shown on the right both in impulses per second (absolute change) and as a proportion of the rate of activity recorded before the block (proportional change). + = increase, - = decrease, * = no change.

TABLE 3

Unit Number	Background Rate (impulses/second)			Changes	
	Before	During	After	Absolute	Proportional
8432-05	10.7	38.6		+ 27.9	3.6 X
8434-05	14.2	43.1		+ 28.9	3.0 X
8434-07	11.7	68.9		+ 57.2	5.9 X
8449-01	3.1	11.2		+ 8.1	3.6 X
8449-02	2.3	7.1		+ 4.8	3.1 X
8451-01	14.2	23.5		+ 9.3	1.7 X
8452-01	0.9	5.4		+ 4.5	6.0 X
8452-04	16.7	14.4		- 2.3	1.2 X
8454-04	22.6	23.6		* 1.0	1.0 X
8454-07	5.5	21.5		+ 16.0	3.9 X
8454-08	15.5	32.8	16.8	+ 17.3	2.1 X
8454-09	5.9	110.3	28.6	+104.4	18.7 X
8454-10	5.1	26.3	3.9	+ 21.2	5.2 X
8455-01	5.4	30.6		+ 25.2	5.7 X
8455-04	7.4	52.0		+ 44.6	7.0 X
8456-01	7.9	8.0		* 0.1	1.0 X
8456-03	16.1	12.5		- 3.6	1.3 X
8457-01	11.6	27.9		+ 16.3	2.4 X
8459-07	14.2	52.6		+ 38.4	3.7 X

DISCUSSION

The main aim of the present study was to investigate the influence of descending systems on the receptive field organisation of p.s.d.c. neurones and in particular to determine whether their receptive field boundaries are under the control of descending systems. The main findings of the study indicate that both the responses of these neurones to noxious stimuli and the area of skin from which they may be excited by such stimuli are subject to strong inhibitory controls descending from the brain.

Effects of descending impulses on receptive fields

Low threshold excitatory components

Previous studies (Wall 1967; Hillman & Wall, 1969) have reported that the low threshold receptive field components of certain unidentified dorsal horn neurones, recorded in the decerebrate preparation, expand during cold block of the cord. Such an expansion has not, however, been observed for neurones of the s.c.t. (Wall, 1967; Brown, 1971).

In the present experiments no obvious expansion of the light tactile components of p.s.d.c. neurones could be detected. Indeed, with the exception of two units (see later) the low threshold areas of p.s.d.c. neurones appeared unaffected by cold block of the cord.

However, in view of the indistinct nature of the low threshold receptive field boundaries of p.s.d.c. neurones, it is possible that small changes below the limits of resolution of the present process of assessment may have occurred. Furthermore the present study concentrated primarily on the receptive field organisation of p.s.d.c. neurones and did not attempt to identify the contribution of input from individual receptor types. The results of a detailed study of the effects of descending impulses on transmission through the s.c.t. (Brown, 1971) suggest that a careful investigation within the low threshold receptive field components of p.s.d.c. neurones may reveal subtle descending actions on light tactile input.

High threshold excitatory components

Both the sensitivity of p.s.d.c. neurones to noxious stimuli and the area of skin from which such stimuli could effectively excite these neurones were profoundly modified by descending activity.

Two thirds of the p.s.d.c. units in the present sample responded more vigorously to the same clip applied to the same receptive field location during a block of descending impulses. Furthermore, the strength of this descending inhibitory action was sufficient to suppress completely the thermal nociceptive input to some units; responses to a noxious radiant heat stimulus becoming evident only when spinal conduction was blocked. These observations have confirmed and extended those of

previous studies on unidentified neurones (Wall, 1967; Hillman & Wall, 1969; Handwerker et al., 1975; Dickhaus et al., 1985) and on neurones of the s.c.t. (Brown, 1971; Cervero et al., 1977).

A previous investigation of the effect of descending impulses on the receptive fields of unidentified dorsal horn neurones (Hillman & Wall, 1969) indicated that the area of skin from which these neurones could be excited by noxious pinch was restricted by the actions of descending systems. The observation that p.s.d.c. neurones had an extensive subliminal fringe (Brown & Fyffe, 1981) suggested that these neurones might be amongst those with receptive field boundaries under the control of descending systems. The present results have shown this to be the case. The high threshold excitatory components of the receptive fields of half of the p.s.d.c. neurones in the present sample were found to expand during cold block of the cord. Furthermore, this is likely to be an underestimate since the stimulus locations used to assess receptive field sizes were separated by between 2.0 and 3.0cm and changes smaller than this would not have been detected. In addition, for those units which were responsive to thermal stimuli, the expanded receptive field could be confirmed using noxious radiant heat, a stimulus which avoids the possibility that sensitive mechanoreceptors could be excited from a distance.

It is unlikely that the substantial modifications of

response properties and receptive field areas observed in the present study could be explained by the sensitisation of nociceptors (Burgess & Perl, 1967; Beitel & Dubner, 1976; Croze, Duclaux & Kenshalo, 1976; Fitzgerald & Lynn, 1977) since noxious stimuli were not generally applied to a single receptive field location more than once in each state. This view is also supported by control observations in which p.s.d.c. neurones, initially unresponsive to noxious heat, were found to remain so when noxious heat stimuli were repeated.

Inhibitory receptive field components

Little is known about the interaction of descending systems with segmental inhibitory processes. Furthermore there are conflicting reports of the effect of cold block on the cutaneous inhibitory fields of dorsal horn neurones. Hillman & Wall (1969), on the one hand, report that the light tactile inhibitory zones of 'lamina V type' neurones are almost completely suppressed during cold block of the cord whilst the light tactile excitatory zone is concomitently expanded. Brown (1971), on the other hand, has reported the direct opposite of this action; inhibition of s.c.t. cells being more easily elicited by light tactile or noxious stimuli in the spinal state.

In the present experiments in a chloralose anaesthetised preparation, both low and high threshold inhibitory field components, detected under conditions of normal spinal conduction, remained effective when

descending impulses were blocked. Direct comparisons of the efficacy of inhibitory actions in the two states was complicated by the increased levels of background discharge in the spinal state, against which inhibition is more easily observed. However, some evidence for enhanced inhibitory actions was obtained: the light tactile excitatory regions of two p.s.d.c. units shrank during cold cold block of the cord as a result of the appearance or expansion of light tactile inhibitory components. These observations suggest that for some p.s.d.c. neurones at least, descending systems may, by an influence on light tactile inhibitory areas, be able to control the size of low threshold excitatory components.

It seems therefore, that the cutaneous inhibitory fields of p.s.d.c. neurones do not depend on a supraspinal loop for their actions though their effectiveness may be modulated by systems descending from the brain.

Effects of descending impulses on background activity

All of the p.s.d.c. units in the present sample had a background activity upon isolation. In agreement with the reports of previous investigators (Wall, 1967; Hillman & Wall, 1969; Brown, 1971), the majority of units exhibited a greater rate of discharge during the block of descending impulses. Interval analysis suggested that in the present study the raised activity resulted predominantly from an increase in the number of

individually occurring impulses rather than from an increase in burst activity.

Unidentified projecting units

In the previous section a group of fibres were described which satisfied the identification criteria for p.s.d.c. neurones but could not conclusively be shown to be postsynaptic. From a consideration of their response properties it was suggested that they might be Pacinian or Krause afferent fibres with an ongoing activity. In this Section it has been shown that while the response properties of these units are not obviously affected by cold block of the cord, their levels of background activity may be modified (1 increased, 3 decreased). Although this might suggest that these units receive a tonic descending influence, it is possible that the modified activity results from circulatory changes that occur during the cold block procedure. Freeman & Rowe (1981) have shown that the circulatory changes associated with electrical stimulation of sympathetic efferents or with arterial occlusion may produce either an increase or decrease in the sensitivity of cutaneous Pacinian afferent fibres to vibrating stimuli. These effects are presumably a result of the influence of temperature changes on the generator potential of the receptor (Imai & Peruzzi, 1961). It therefore remains possible that the units in the present study are Pacinian afferent fibres

which because of their location and extreme sensitivity have an ongoing activity.

The source of tonic descending influences

It seems likely that the effects described in the present study may be derived from several descending systems. The cold block technique interrupts descending fibres in at least the dorsal half of the spinal cord but can of course only reveal the actions of those systems which are tonically active in an animal prepared for electrophysiological recording. Tonic descending inhibiton of spinal reflex pathways in the decerebrate cat has been shown to originate from the raphe and juxta-raphe regions of the medial reticular formation (Engberg et al., 1968c), while tonic descending inhibition of dorsal horn neurones in the barbiturate anaesthetised cat emanates largely from the brain stem lateral reticular formation (Hall et al., 1982; Morton et al., 1983). This work might suggest that different descending systems are responsible for the control of dorsal horn neurones and for suppression of spinal reflex pathways; but it also raises the possibility that tonic descending influences might originate from largely separate descending systems in anaesthetised and decerebrate preparations. This possibility should be considered when comparing the results presented here, which were obtained in the choralose anaesthetised cat, with previous studies of the influence of descending

systems on the receptive fields of dorsal horn neurones, all of which used decerebrate preparations (Wall, 1967; Hillman & Wall, 1969; Brown, 1971).

The activation of tonic descending systems

Whilst the present study has revealed the potential of descending systems for modifying the response characteristics and receptive field sizes of p.s.d.c. neurones, little is known of the circumstances under which such influences are exerted. Clarke (1985) has suggested that tonic inhibition in the medullary dorsal horn of the trigeminal nucleus may result from procedures necessary to prepare an animal for electrophysiological recording. Transmission through the jaw opening reflex was found to be progressively depressed during various stages of the surgical preparation of a cat and its insertion into a stereotaxic frame. These results were obtained whether the preparation remained anaesthetised or was subsequently decerebrated and some release from this inhibition could be achieved by lesioning the brain stem lateral reticular formation. It was therefore suggested (Clarke, 1985) that tonic descending inhibitory systems might be activated in response to the trauma produced by these procedures.

Such a hypothesis requires the operation of mechanisms involving a spino-bulbo-spinal loop. Electrophysiological recordings in brain stem regions, which give rise to descending systems inhibiting dorsal

horn neurones, have shown that cells in these regions can be activated by cutaneous stimuli. Neurones of the raphe and adjacent reticular nuclei, some of which were shown to project to the spinal cord, could be activated by noxious mechanical and thermal stimuli from large receptive fields, often including all four limbs (Moolenhaar, Holloway & Trouth, 1976; Anderson, Basbaum & Fields, 1977). These neurones were found to be tonically active in the decerebrate cat (West & Wolstencroft, 1982; Wolstencroft & West, 1982), but it is not clear what drove their activity under these conditions.

Le Bars and his colleagues have accumulated evidence for a spino-bulbo-spinal inhibitory phenomenon in the rat, which is triggered by noxious somatic inputs (Le Bars, Dickenson & Besson, 1979a, b). Activity in convergent dorsal horn neurones can be inhibited by noxious stimuli applied to widespread areas of the body, by mechanisms which involve a supraspinal loop (Le Bars et al., 1979) and probably relay through the nucleus raphe magnus (Dickenson, Rivot, Chaouch, Besson & Le Bars, 1982). A mechanism such as this could produce the tonic descending inhibiton which is observed in animals prepared for electrophysiological recording, although a relay through the raphe nuclei seems unlikely in view of the apparent source of tonic descending inhibition in the dorsal horn (Hall et al., 1982; Morton et al., 1983).

Speculation on the functions of descending systems

The point has often been made that the suppressive effects of descending systems on the nociceptive input to dorsal horn neurones may be of survival value to animals in a potentially injurious environment. Duggan & Morton (1983), for example, have noted an association between the inhibition of C-fibre input to dorsal horn neurones evoked by electrical stimulation of the PAG and changes in the peripheral circulation which involve an increased perfusion of muscles. They suggest that gating noxious inputs to the spinal cord would allow motor commands to proceed uninterrupted by reflex responses, while an increased muscle perfusion would enhance motor performance.

Electrical stimulation of various brain stem and midbrain sites producing inhibition of the response of dorsal horn neurones to noxious stimuli (see introduction) have been found to produce analgesia in conscious animals (Mayer, Wolfle, Akil, Carder & Liebeskind, 1971; Oliveras, Redjemi, Guilbaud & Besson, 1975; Oliveras, Guilbaud & Besson, 1979). Suppression of nociceptive input as a result of injury might therefore serve to reduce the sensation of pain and prevent attention from being diverted from a motor task such as taking evasive action. It is well known, for example, that battlefield or accident victims are often initially oblivious to serious injuries (Wall, 1979) and it is possible that tonic descending inhibitory mechanisms

activated by trauma are involved in this type of response to injury.

Whilst tonically active descending influences may be a response to tissue damage, it seems likely that the descending systems by which they are mediated might be activated not only by noxious somatic inputs but also by other regions of the central nervous system, perhaps according to the motivational state of the animal. Although a barrage of sensory input is continually transmitted to the brain by receptors of different modalities, responding to various aspects of the animals environment, selective processing occurs so that only a fraction of this input is consciously perceived. It seems resonable to assume that, in the somatosensory pathway, the mechanisms of this selection process may include an action at the level of the spinal dorsal horn by systems descending from the brain.

It has long been known that mass potentials recorded in conscious animals at various stages of the visual, auditory and somatosensory pathways, may be depressed or facilitated according to the animal's motivational state (see Hernández-Peón, 1959). In the somatosensory system (Hernandez-Peon & Brust-Carmona, 1961) it was found that massed potentials recorded from the spinal lateral columns of conscious cats in response to electrical cutaneous stimuli, could be dramatically depressed if the animals attention was distracted by mice or fish odour! More recently, investigations have been

made of the influence of behavioural variables on the activity of single convergent neurones in the medullary dorsal horn of conscious monkeys (Hayes, Dubner & Hoffman, 1981). The monkeys were trained to perform two tasks, one of which involved responding differently to innocuous and noxious thermal stimuli and the other detection of a variable intensity light. Behaviourally relevant thermal stimuli, that is stimuli presented during performance of the thermal task, evoked a greater neuronal response than when the same stimulus was applied in between performance of the task or during the visual task. Behaviourally relevant noxious thermal stimuli also produced a neuronal response when applied outside of receptive fields that had been determined when the stimulus was irrelevant. Furthermore, these effects were enhanced when the attentional demands made upon the animal during the visual task were increased by reducing the intensity of the light. These results suggest that the sensitivity and receptive field size of dorsal horn neurones responding to noxious thermal stimuli are modulated in freely moving animals according to their attentive behaviour. As has been emphasised by the present study, the sensitivity of dorsal horn neurones to noxious thermal stimuli and the area of skin from which such stimuli effectively excite cells, are profoundly modified by descending systems. These systems therefore have the potential to mediate the behaviourally directed modulation of sensory processing.

SECTION 3

RELATIONSHIPS BETWEEN SPINOCERVICAL TRACT AND POSTSYNAPTIC DORSAL COLUMN NEURONES

INTRODUCTION

Experiments described in this section of the thesis were aimed at investigating two aspects of the relationship between neurones of the p.s.d.c. and s.c.t. systems.

A. It has been established that the p.s.d.c. and s.c.t. systems are linked at the level of the dorsal horn. Jankowska et al. (1979) have provided electrophysiological evidence for excitatory actions on p.s.d.c. neurones via an axon collateral link from s.c.t. cells and recently Maxwell and Koerber (1986) have provided direct ultrastructural evidence that the required contacts exist. The aim of experiments described in this section was to determine the influence that s.c.t. cells have on activity in p.s.d.c. units by providing further information about the efficacy of this link.

B. The concept of separate s.c.t. and p.s.d.c. projections arising from different populations of dorsal horn neurones, each with distinct characteristics, has recently been challenged. Lu et al. (1985) have claimed that some dorsal horn neurones can be antidromically activated from both the dorsal columns and the dorsolateral funiculus. They conclude that these neurones have branched axons and contribute to both the p.s.d.c. and s.c.t. projections. However, these workers employed search stimuli of 30V and observed that the latencies for antidromic activation via the two presumed

axons were always similar. This suggests that their stimuli might have spread between the two funiculi even though they were each dissected away from the cord. The aim of experiments described in this section was to reinvestigate the possibility that the s.c.t. and p.s.d.c. projections might, in part, arise from a common population of dorsal horn neurones. The experimental preparation chosen, which did not involve physical separation of the dorsal and dorsolateral funiculi, was expected to bias the experiment in favour of stimulus spread between the two parts of the cord.

METHODS

Preparation of animal

The experiments were performed on 8 cats, 2.2-3.1Kg in weight, anaesthetized with chloralose and paralysed with gallamine triethiodide. The procedures for the general preparation and physiological maintenance of the animal were as described in Section 1.

Electrical stimulating and recording procedures

A diagrammatic representation of the preparation, on which the positions of stimulating and recording electrodes are indicated, is shown in Fig. 31.

The spinal cord was exposed by laminectomies at C_1-C_4 and L_3-L_7 inclusive. Bipolar silver-ball stimulating electrodes placed on the dorsal columns at C_{2-3} were used to assess the progress of a sectioning of the dorsal columns at caudal C_3. The dorsal columns were dissected with watchmaker's forceps until the initial negative component of the cord dorsum potential recorded at L_7 was abolished. At the end of one experiment the section of cord containing the lesion was removed and fixed (Karnovsky, 1966). Serial frozen sections (90μm) were cut and examined under a microscope to check the extent of the lesion (Fig. 32).

Stimulating electrodes were placed on the dorsal columns at C_4, below the dorsal column lesion, in order to locate and identify p.s.d.c. neurones, and on the dorsolateral funiculi at C_1 and C_3, to locate and identify s.c.t. neurones. The electrodes on the

dorsolateral funiculi were also used to investigate orthodromic effects on p.s.d.c. neurones.

Search stimuli (3V, approx. 250μA, 0.1ms, once every 600ms) were applied either to the dorsolateral funiculus at C_3, or to the dorsal columns at C_4, depending on the location of the recording site. Stimuli of this strength applied to the dorsolateral funiculus at C_3 are known to be capable of antidromically exciting all s.c.t. neurones (Brown, Fyffe, Noble, Rose & Snow, 1980a).

In six cats, recordings were made from single axons, in both the lumbar dorsal columns and left dorsolateral funiculus, using glass capillary microelectrodes. The electrodes were filled with 4M-NaCl and broken or bevelled to D.C. resistances of 15-20MΩ. In the remaining two cats recordings were made using similar electrodes with lower impedances, from neurones in the left lumbar dorsal horn.

In all experiments, cord dorsum potentials were recorded through a monopolar silver ball electrode on the dorsal columns at L_7.

Identification of p.s.d.c. and s.c.t. units

P.s.d.c. axons were identified by a convergence of input from the periphery and/or by an irregular background activity. All units were shown to project to cervical levels by antidromic activation from C_4 below the dorsal column lesion. None of these units, including those from the dorsal horn, could be activated

from the dorsal columns above the lesion.

S.c.t. units were identified by antidromic activation from the dorsolateral funiculus at C_3 and either failure to respond from C_1 (13 of the 33 units) or an antidromic response of longer latency, indicating a drop in conduction velocity of at least one third (17 of 33 units). All of these units had an irregular background activity.

All antidromic responses were identified by the collision test between orthodromic and antidromic impulses and by their ability to follow high frequency stimulation (at least 7 stimuli at 500Hz).

Tests for branched axons

Units recorded from the dorsal columns identified as p.s.d.c. neurones were tested for an axon branch ascending the dorsolateral funiculus. Stimuli of progressively increasing strength were applied to the dorsolateral funiculi at C_3 and at C_1 until an antidromic response was observed or to some maximal voltage with no response.

Units recorded from the dorsolateral funiculus identified as s.c.t. neurones were similarly tested for an axon branch in the dorsal columns by stimuli of increasing strengths applied to the dorsal columns at C_4 and C_{2-3}.

Antidromic responses were identified by the collision and frequency following tests; this was particularly important for s.c.t. units, which were

nearly all (31 of 33) excited orthodromically from the dorsal columns at C_4. Threshold voltages required to evoke antidromic responses were carefully determined and the latencies of antidromic impulses carefully measured from the oscilloscope screen. Cerebrospinal fluid that accumulated around the cervical cord was removed repeatedly during an experiment.

This preparation in which the dorsal columns and dorsolateral funiculus were not physically separated should have biassed the experiment in favour of stimulus spread between these two parts of the cord.

Tests for orthodromic effects from the dorsolateral funiculus on p.s.d.c. units

P.s.d.c. units were tested for orthodromic effects from the dorsolateral funiculus with stimuli in trains of 5 shocks at 333Hz, 0.1ms duration and 3V (approx. 250μA) in amplitude, applied every 1500ms. The stimuli were applied at both C_1 and C_3 above and below the lateral cervical nucleus. A clip was applied to the receptive field of some units in order to raise their level of activity. All responses were recorded on magnetic tape and both on-line and off-line analysis was carried out with a CED 1401 interface (Cambridge Electronic Design, England) and BBC 'B' microcomputer with which peri-stimulus time histograms were prepared. All latency and duration measurements were taken from the time of the first stimulus in the train. At the end of each experiment the conduction distances from the

stimulating electrodes (cathodes) to the recording sites were measured.

Cord dorsum potential and single unit traces used to produce the diagrams were plotted with a pen chart recorder (JJ Instruments) from a digital oscilloscope (Tektronix 5223).

Figure 31

Diagrammatic representation of the experimental arrangement by which a) p.s.d.c. and s.c.t. neurones were identified and investigated for bifurcating axons ascending both the dorsal and dorsolateral funiculi and b) the presumed effects of s.c.t. cells on p.s.d.c. neurones were examined.

The drawing represents a dorsal view of the spinal cord exposed by laminectomies at the cervical (C_1-C_4) and lumbar (L_5-L_7) enlargements. S1 and S2 represent bipolar ball electrodes used to apply electrical stimuli to the dorsolateral funiculi at C_1 and C_{2-3}. S3 and S4 represent bipolar ball electrodes used to apply electrical stimuli to the dorsal funiculi at C_{2-3} and C_{3-4} above and below a lesion of the dorsal columns at C3 (indicated by hatching). Cord dorsum potentials were recorded through a monopolar ball electrode placed on the lumbar dorsal columns (R_{CDP}). Single unit recordings were made in the lumbar region from axons in the dorsal and dorsolateral funiculi or from cell bodies in the dorsal horn, using glass capillary microelectrodes (R_{ME}).

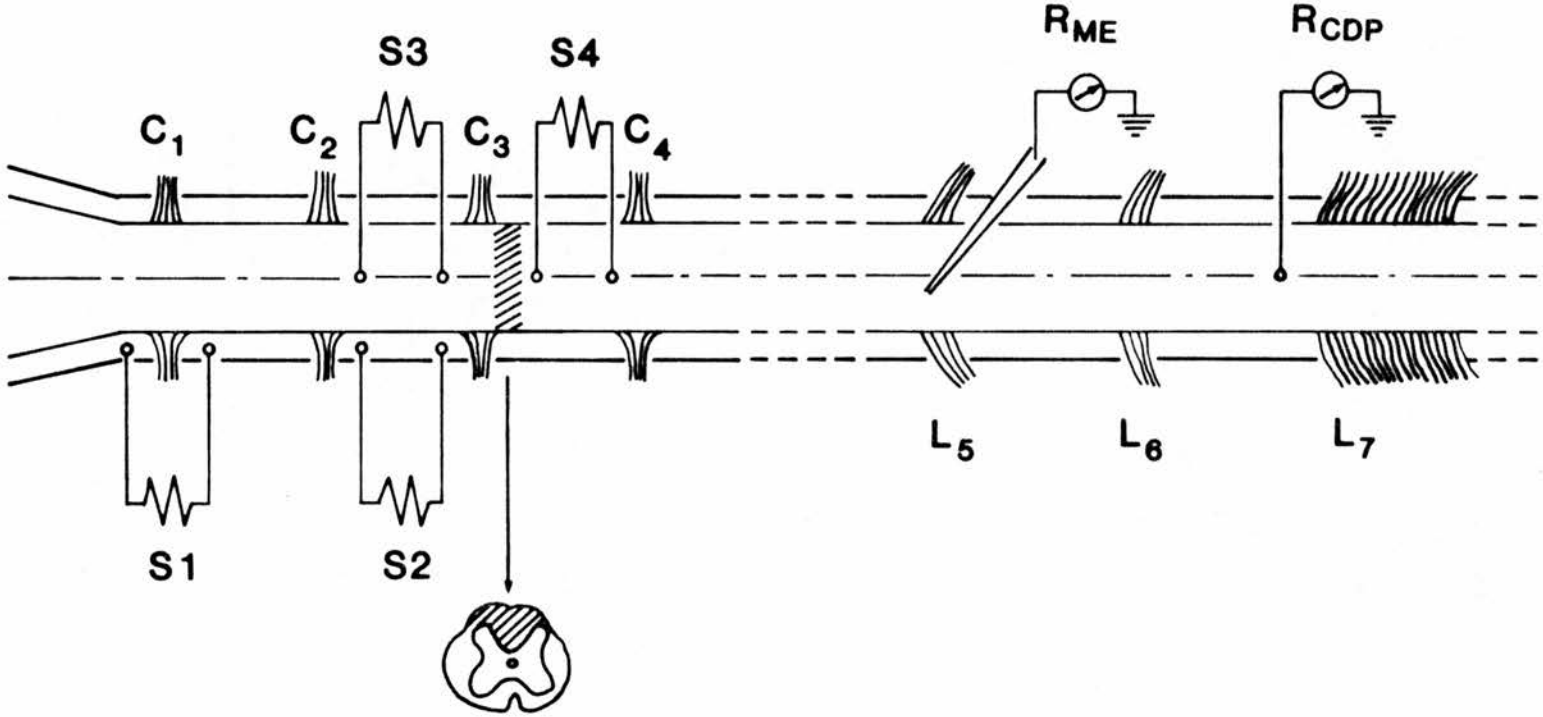
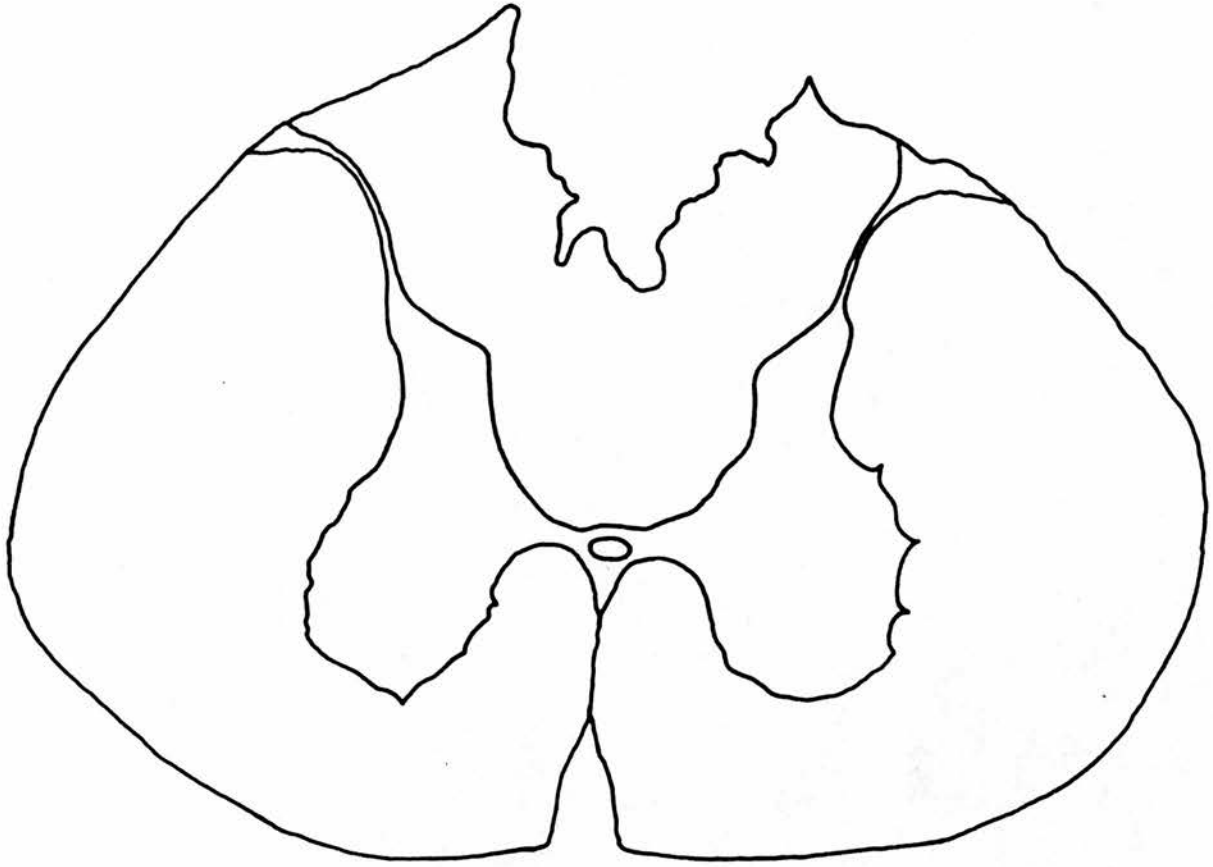

S3
S4
R_{ME}
R_{CDP}
C_1
C_2
C_3
C_4
L_5
L_6
L_7
S1
S2

Figure 32

Camera lucida drawing of a section through the cervical region of the spinal cord at the location of the dorsal column lesion.

The lesion was made by dissection of the dorsal columns at C_3 with watchmakers forceps. The drawing is made from a single 90μm frozen section and shows the maximum extent of the lesion which involved only a part of the dorsal columns corresponding in position to the dorsal half of the funiculus gracilis. The lesion did not encroach upon the dorsolateral funiculi.


1mm

RESULTS

A. Tests for Branched Axons

Cord dorsum potentials

In order to assess possible stimulus spread between the dorsal columns and dorsolateral funiculi, cord dorsum potentials were recorded from L_7 in response to electrical stimulation of each of the stimulus sites on the cervical region of the cord. The stimulus parameters used were the same as those employed when searching for p.s.d.c. and s.c.t. neurones; 3V, approx 250μA, 0.1ms duration.

Stimulation of the dorsal columns at C_4 produced a potential with a short duration negative wave (N wave) followed by a long duration positive wave (P wave, Fig. 33, A bottom). This is similar to the the well documented negative-positive cord dorsum potential evoked by stimulation of cutaneous nerves, at a stimulus strength sufficient to excite mainly large diameter (Aα-β) afferents, (Eccles, Kostyuk and Schmitt, 1962; Beall, Applebaum, Foreman and Willis, 1976). Stimulation of the dorsal columns at C_3 and stimulation of the dorsolateral funiculus at both C_1 and C_3, all of which were above a lesion of the dorsal columns, each produced a similar cord dorsum potential (Fig. 33). These potentials were almost completely positive going and peaked at about the same time as the P wave of the potential evoked from the

dorsal columns below the lesion. The P wave evoked from the dorsal columns above the lesion is presumably due to stimulus spread to the dorsolateral funiculus. Since no negative wave was recorded in response to stimulation of the dorsolateral funiculus at the same stimulus strength, nor indeed at a stimulus strength of up to 30V (see Fig. 35), the dorsal column lesion was presumably sufficient to prevent the effects of any stimulus spread in this direction.

The sample of units

Recordings were made from 63 single units. The sample consisted of 30 units identified as belonging to the p.s.d.c. system, 24 recorded from the dorsal columns and 6 from the dorsal horn; together with 33 units belonging to the s.c.t., 26 recorded from the dorsolateral funiculus and 7 from the dorsal horn. Two of the dorsal horn recordings were intracellular, the rest extracellular.

Conduction velocities: The sample of units covered the range of both p.s.d.c. and s.c.t. axonal conduction velocities. Figure 33 shows histograms for the two samples including those recorded from the dosal horn. The conduction velocities of p.s.d.c. units ranged from 26 to 62ms^{-1} and therefore fell within the range recorded from the population of units described in Section 1. The conduction velocities of s.c.t. units ranged from 27 to 95ms^{-1}; more than half of the units having faster

conduction velocities than the fastest conducting p.s.d.c. neurones.

Response properties and receptive fields: Although detailed investigations of receptive fields were not made, the reponse properties of most units were investigated in order to subsequently determine a) whether p.s.d.c. or s.c.t. units with bifurcating axons were of any particular type and b) whether those p.s.d.c. neurones receiving excitatory effects from the dorsolateral funiculi had particular characteristics.

P.s.d.c. units: The sample of p.s.d.c. neurones consisted of 22 units with receptive fields restricted to hairy skin and 5 units with receptive fields including glabrous skin. One unit had a receptive field which appeared to lie beneath the plaster supporting the feet and the receptive fields of 2 units were not investigated. All 27 units tested responded to light tactile stimuli and all but 1 responded with a slowly adapting discharge to a sustained noxious pinch. In addition, 11 of 15 units tested were excited by noxious radiant heat and 7 of 17 units investigated had inhibitory fields.

S.c.t. units: Twenty-three of the 33 s.c.t. units were investigated for their responses to light tactile and noxious mechanical stimuli. Three units responded only to light tactile stimuli, 1 unit only to noxious pinch and 19 units to both light tactile and noxious stimuli.

Activation of P.s.d.c. and S.c.t. Neurones From the Dorsolateral Funiculus and the Dorsal Columns

P.s.d.c. units

The 30 p.s.d.c units could all be excited antidromically from the dorsal columns at C_4 at stimulus strengths between 0.05 and 2.6V. But none of them could be excited antidromically from either the dorsal columns at C_3 or from the ipsilateral dorsolateral funiculus at C_3 (Fig. 35), both of which were above the level of the dorsal column section. All but 2 of the units were tested with dorsolateral funicular stimulation of at least 20V, with 18 tested at 30V and 1 at 40V. The remaining units were tested at only 6V and 10V. All but 3 of the units were tested with stimuli of at least 20V applied to the dorsal columns at C_3. In the same experiments however, s.c.t. units were antidromically activated from the dorsolateral funiculus at low stimulus strengths (see below).

S.c.t. units

The 33 s.c.t. units were excited antidromically from the ipsilateral dorsolateral funiculus at C_3 with stimuli of 0.3-3.3V. Of this sample, 13 could not be antidromically fired from the dorsal columns at C_4 with stimuli of at least 20V, 4 units being tested at 30V. A further 7 units were not activated with stimuli up to 5V, but were not tested at greater stimulus strengths.

Thirteen units however, including 4 of the 7 recorded from the dorsal horn, could be excited

antidromically from the dorsal columns at C_4 (Fig. 36). However, 8 of these 13 units required a dorsal column stimulus of at least 17 times the strength required to activate them from the dorsolateral funiculus, 3 required stimuli of 6-9 times the dorsolateral funiculus threshold and 2 required only 2.3 and 3.5 times threshold. All of the 13 units that could be excited antidromically from both the dorsolateral funiculus at C_3 and the dorsal columns at C_4 had antidromic latencies from the two sites within 0.3ms of each other. The latency from the C_4 stimulus was always less than that from the C_3 stimulus.

Seventeen of the units identified as belonging to the s.c.t., including 10 of those antidromically excited from the dorsal columns at C_4, could be excited antidromically from the dorsal columns at C_3, above the dorsal column lesion. The strengths of stimulation required were, in general, less than those required for antidromic activation from the dorsal columns at C_4. Twelve of the 17 units required stimuli at the C_3 dorsal columns of less than 8 times the threshold for activation from the dorsolateral funiculus at C_3. And for 7 of the 10 units which were antidromically activated from both C_3 and C_4, the stimulus srength required at C_3, above the lesion, was less than at C_4 below it. The C_3 dorsal column electrodes were placed rostral to the C_3 dorsolateral funicular electrodes and the antidromic latencies from the dorsal columns were either the same (7

units) or up to 0.3ms longer (9 units). One unit had a latency from the C_3 dorsal columns 0.8ms longer than from the C_3 dorsolateral funiculus.

Recordings from dorsal horn neurones

It is possible that neurones with bifurcating axons, one ascending the dorsolateral funiculus and the other the dorsal columns, are present in the dorsal horn but that an antidromic impulse conducted down one branch fails to invade the other; in this case axonal recording would not reveal the branching. For this reason, in addition to the axonal recordings, 13 units in the sample were recorded extracellularly (and 2 of them intracellularly) from the dorsal horn (Fig. 36). The results obtained from units recorded in the dorsal horn were no different to those obtained with axonal recording.

B. Effects of Stimulation of the Dorsolateral Funiculus on P.s.d.c. Neurones

The effects of stimulation of the ipsilateral dorsolateral funiculus on the activity of 25 p.s.d.c. units were investigated. Nineteen of the units were recorded from axons in the dorsal columns and 6 from cells in the dorsal horn. Both excitatory and inhibitory effects were observed.

Excitatory effects

1) Stimulation of the dorsolateral funiculus at C_3

For 13 of the 25 units peri-stimulus time histograms revealed clear excitatory effects in response to

electrical stimulation of the dorsolateral funiculus at C_3 (5 stimuli at 333Hz, 0.1ms, 3V, approx. 250μA). Examples of these histograms are shown in Figures 37 and 38. The effects could be observed against both background activity (Fig. 37, A) and a raised level of discharge produced by a sustained innocuous pinch of the receptive field (Fig. 37, B and 38, A and B).

The excitatory effects had latencies of between 3 and 16ms (measured from the first stimulus in the train) and lasted for between 6 and 22ms. The effectiveness of stimulation of the dorsolateral funiculus at C_3 varied between units, having a weak effect on some cells (Fig. 38, B) and a much stronger effect on others (Fig. 37, A) even within the same experiment.

2) Stimulation of the dorsolateral funiculus at C_1

Eleven of the 13 units with an excitatory response to stimulation of the dorsolateral funiculus at C_3 were also tested for their response to stimulation of the dorsolateral funiculus at C_1. For six of these units, peri-stimulus time histograms revealed similar excitatory effects although in each case the excitation was less than that evoked from C_3 (Fig. 37).

There was a tendency for those units excited by stimulation of the dorsolateral funiculus to have higher conduction velocities than those units not excited (Fig. 39). Since the variances of the conduction velocities for these two groups of units were similar, this observation was tested using analysis of variance (see

Table 4), a significant difference was found (at P=0.05). However, there were no obvious differences between the response properties of those units excited and those apparently not excited by stimulation of the dorsolateral funiculus. Excited units included both those with receptive fields restricted to hairy skin and those with input from glabrous skin. All of the units had both low threshold and high threshold excitatory components to their receptive fields.

Inhibitory effects

In addition to the excitatory effects, stimulation of the ipsilateral dorsolateral funiculus, both at C_3 and at C_1, produced profound inhibition of the background or pinch evoked activity of p.s.d.c. neurones. Inhibition was evoked in 24 of the 25 units investigated for their response to stimulation of the dorsolateral funiculus at C_3 and in 10 of the 11 units tested from C_1; 1 unit was not inhibited by stimulation of either site.

For those units which were not excited by stimulation of the dorsolateral funiculus, the inhibition began at between 8 and 26ms after the first stimulus in the train (Fig. 38, C and D). In those units both excited and inhibited by stimulation of the dorsolateral funiculi the inhibition immediately followed the excitatory effects (Figs. 37 and 38). The resting or pinch evoked discharge was virtually silenced for between 93 and 145ms and a full recovery of activity did not occur until after about 250-300ms (Fig. 40). There were

no differences between the inhibitory effects produced from C_3 and from C_1.

Figure 33

Cord dorsum potentials recorded from the dorsal columns at L_7 in response to electrical stimulation of the cervical spinal cord.

A. Stimulation of the dorsal columns (DC) at C_3, above the dorsal column transection, and at C_4 below the transection.

B. Stimulation of the dorsolateral funiculus (DLF) at C_1 and at C_3, above and below the lateral cervical nucleus.

All records are single traces, negativity upwards, and all stimuli were of 3V strength. Stimulation of the dorsal columns at C_4 evoked a large negative wave of short duration, followed by a positive wave of long duration. Stimulation of the dorsal columns above the lesion, and also of the dorsolateral funiculus at both C_1 and C_3, evoked clear cord dorsum potentials consisting of a single positive wave. The response to stimulation of the dorsal columns at C_3 was presumably due to stimulus spread to the dorsolateral funiculus. Since the negative wave evoked by stimulation of the dorsal columns at C_4 was absent from the responses to stimulation of the dorsolateral funiculus, the dorsal column lesion was presumably sufficient to prevent the effect of stimulus spread in this direction.

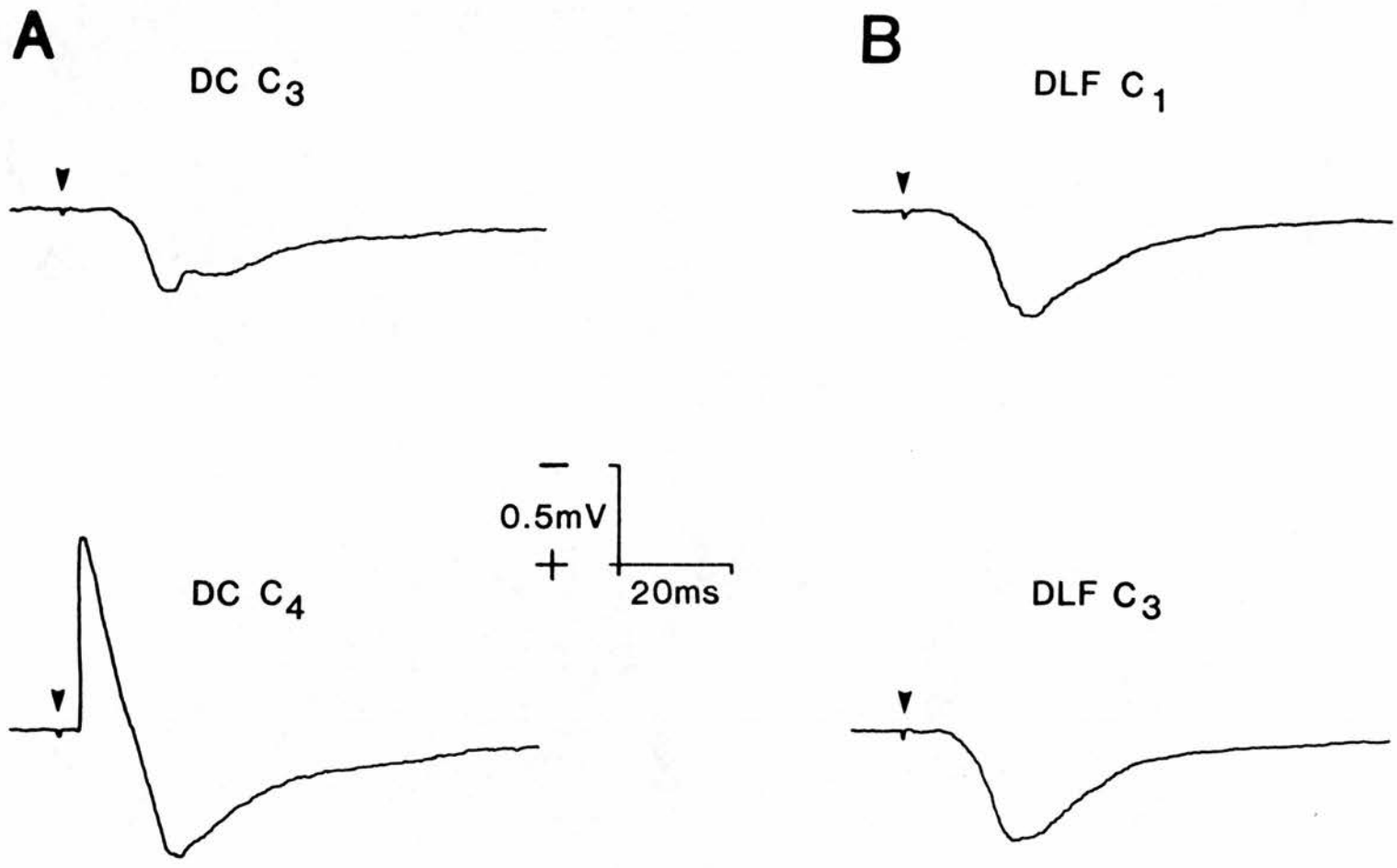

A
DC C_3
DC C_4
0.5mV
20ms
B
DLF C_1
DLF C_3

Figure 34

Conduction velocities of the samples of post-synaptic dorsal column (PSDC, n=30) and spinocervical tract (SCT, n=33) units. The total samples are shown as clear histograms which include the units recorded from the dorsal horn (stippled).

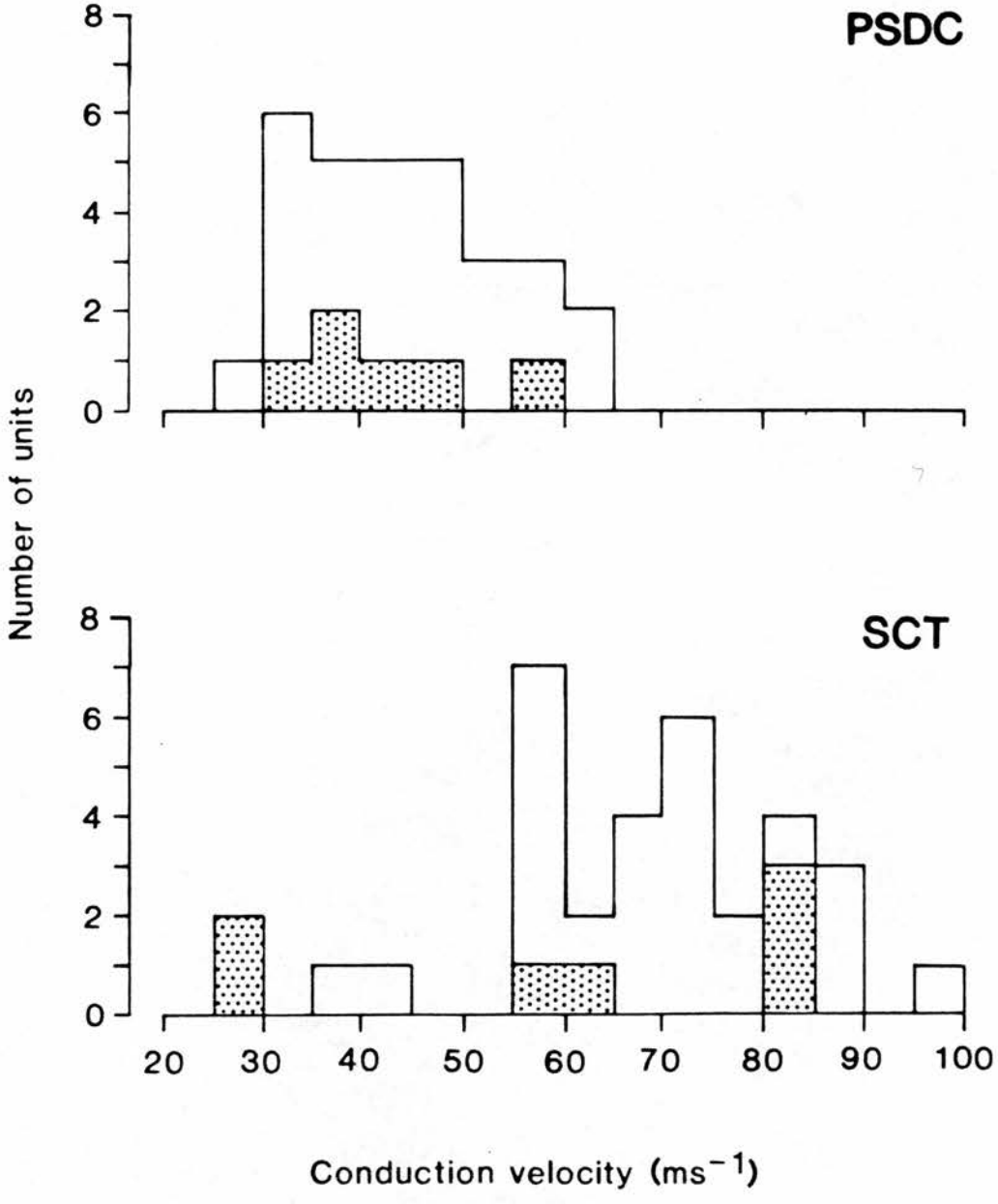

PSDC
SCT
Number of units
0
2
4
6
8
20
30
40
50
60
70
80
90
100
Conduction velocity (ms⁻¹)

Figure 35

Tests for antidromic activation of a p.s.d.c. unit from the cervical dorsal columns and for an axon branch in the dorsolateral funiculus.

Each pair of traces shows a cord dorsum potential recorded from L_7 (upper trace) and an extracellular single-unit recording from an axon in the dorsal columns (lower trace). The arrow heads mark the positions of the stimulus artefacts. All traces are of single sweeps.

Criteria for identifying the antidromic response of a p.s.d.c. neurone, to stimulation of the dorsal columns (DC) are shown in the right hand panel. Stimulation of the dorsal columns at C_4 excited the unit antidromically at 3V (threshold for activation was 1.1V) as shown in the top pair of traces. Collision of an orthodromic impulse with the antidromic action potential is shown in the second pair of traces; the asterisk marks the position where the antidromic action potential should have appeared. The third trace shows its reappearance in the absence of an orthodromic potential. The bottom pair of traces shows the unit following a train of 12 stimuli at a frequency of 1000Hz.

Tests for an axon branch in the ipsilateral dorsolateral funiculus (DLF) are shown in the left hand panel. Stimulation of the DLF at strengths of 10, 20 and 30V failed to excite the unit.

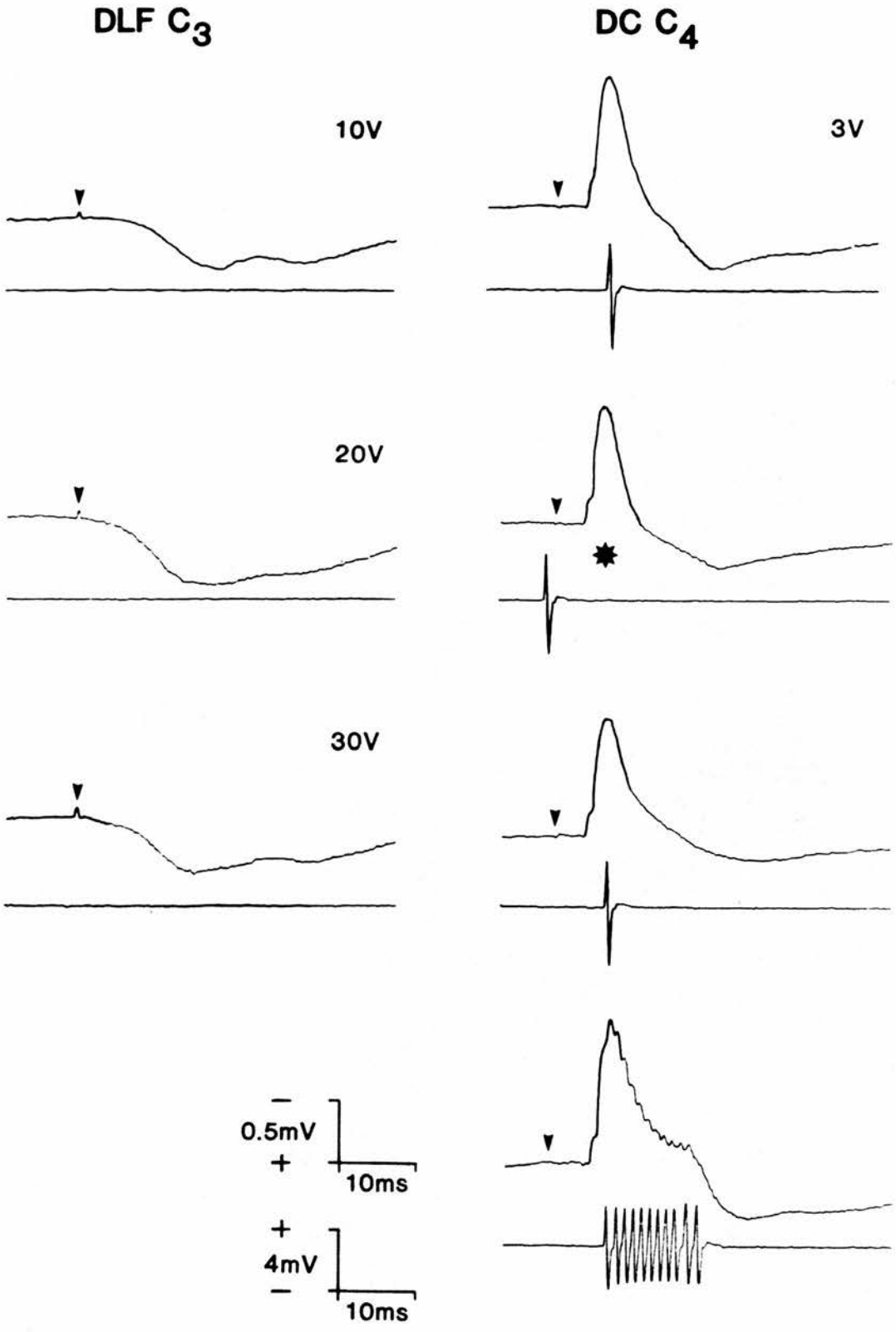

DLF C_3
DC C_4
10V
3V
20V
30V
0.5mV
10ms
4mV
10ms

Figure 36

Tests for antidromic activation of an s.c.t. unit from the cervical dorsolateral funiculus and for an axon branch in the dorsal columns.

Each pair of traces shows a cord dorsum potential recorded from L_7 (upper trace) and an intracellular recording from a s.c.t. neurone in the lumbar dorsal horn (lower trace). The arrow heads mark the positions of the stimulus artefacts. All traces are of single sweeps.

Criteria for identifying the antidromic response of a s.c.t. neurone, to stimulation of the ipsilateral dorsolateral funiculus (DLF) at C_3, are shown in the left hand panel. As shown in the top pair of traces, the unit had a threshold for antidromic activation of 0.3V. The second pair of traces shows collision of an orthodromic impulse with an antidromic action potential (the expected position of the antidromic impulse is marked with an asterisk) and the third pair the reappearance of the antidromic action potential in the absence of an orthodromic impulse. The bottom pair of records shows the unit following a train of 7 stimuli at 500Hz.

Tests for an axon branch in the dorsal columns (DC) are shown in the right hand panel. A stimulus of 3V (top pair of traces) and of 10V (second pair of traces), applied to the DC at C_4, evoked an orthodromic response. At 17V (third pair of traces) an antidromic impulse was also evoked which could be shown to collide with an orthodromic action potential (bottom traces).

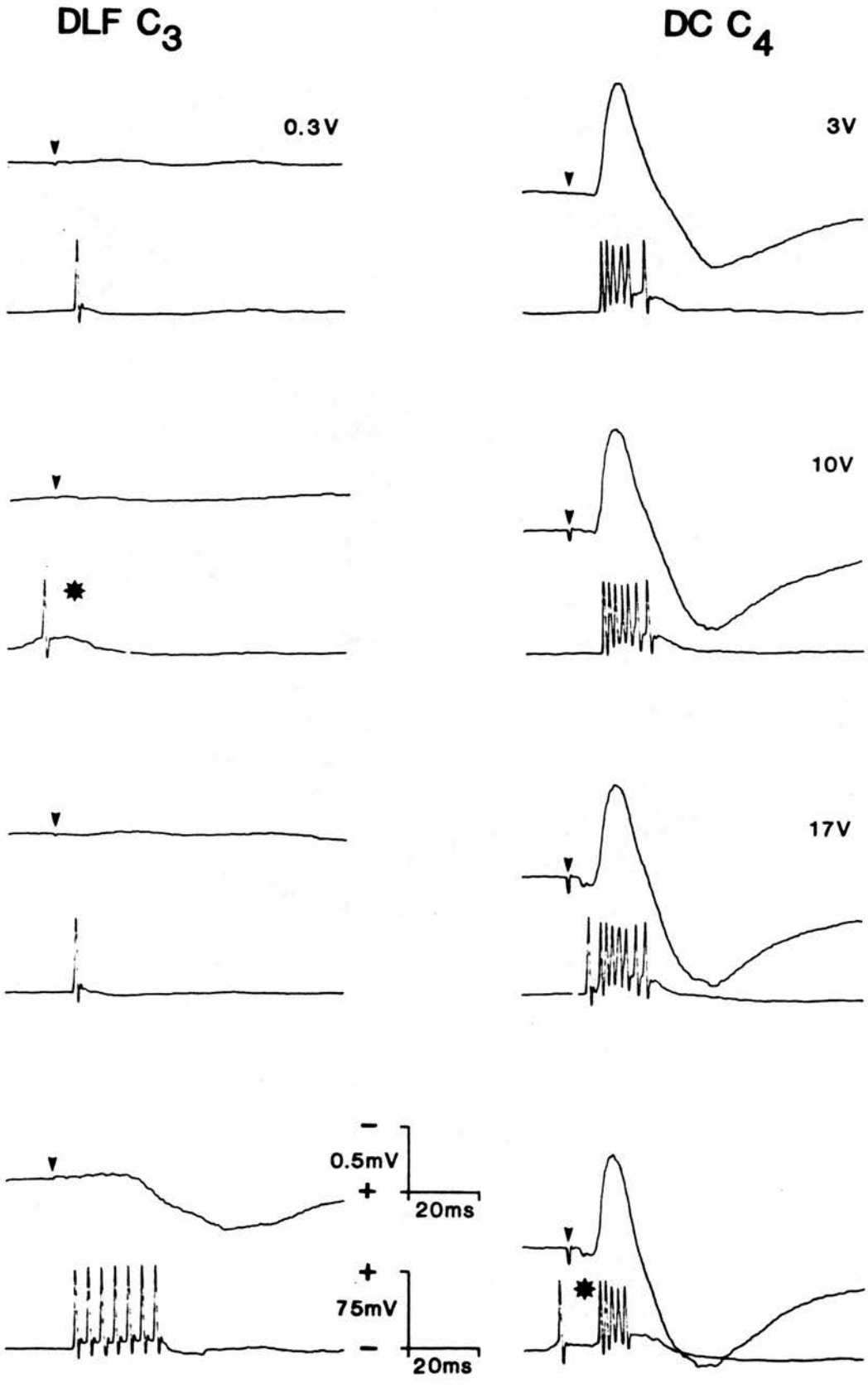

DLF C_3
DC C_4
0.3V
3V
10V
17V
0.5mV
20ms
75mV
20ms

Figure 37

Excitation of p.s.d.c. units produced by electrical stimulation of the dorsolateral funiculus.

Peri-stimulus time histograms show the effects on two p.s.d.c. neurones (A and B) of stimulating the dorsolateral funiculus (DLF) at C_3 (left) and C_1 (right). Onset of stimulus train (5 stimuli, 333Hz) is indicated by arrows. Impulses are accumulated in 1ms time-bins. In B background activity was elevated by a sustained pinch to the excitatory receptive field.

Both units were facilitated by stimulation of the DLF at C_1 and at C_3, though the effects of stimulation at C_1, above the lateral cervical nucleus, were weaker than from C_3 below it. A strong inhibition of background activity followed the excitation.

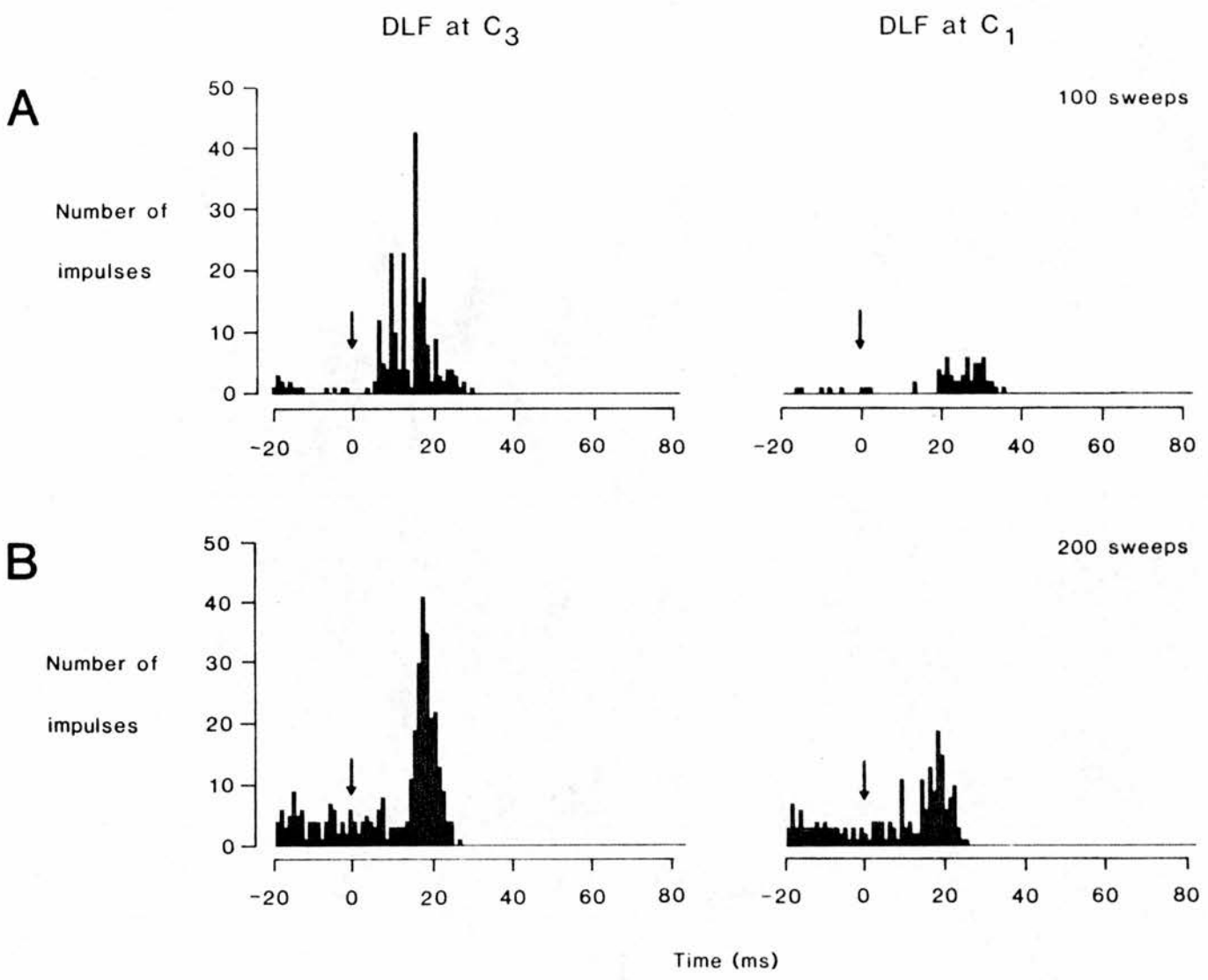

DLF at C_3
DLF at C_1
A
B
100 sweeps
200 sweeps
Number of impulses
Number of impulses
50
40
30
20
10
0
-20
0
20
40
60
80
Time (ms)

Figure 38

Excitation and inhibition of p.s.d.c. units produced by electrical stimulation of the dorsolateral funiculus.

Peri-stimulus time histograms show the effects on single p.s.d.c. units of stimulating the ipsilateral dorsolateral funiculus (DLF). The onset of the stimulus train (5 stimuli, 333Hz) is indicated by arrows. Impulses are accumulated in 1ms time-bins. In A and B activity was elevated by a clip applied to the receptive field.

A and B show the response of two different units to stimulation at C_3 (left) and C_1 (right). In both cases a clear facilitatory effect was evoked from C_3 but not from C_1. A strong inhibition of background activity was produced from C_3 and C_1.

C and D show the response to stimulation of the DLF at C_3 of different units, neither of which was excited. Both units were, however, profoundly inhibited.

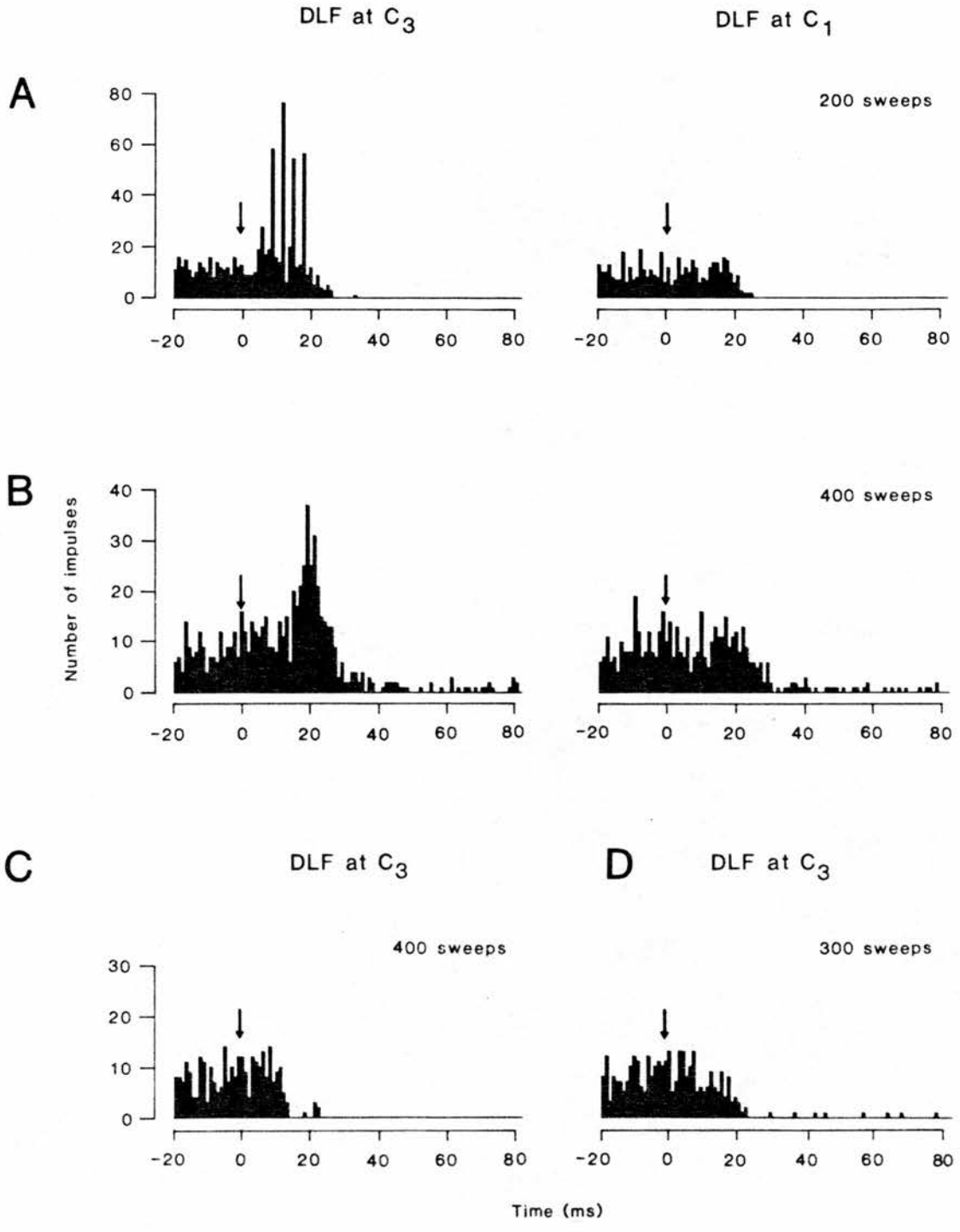

A
DLF at C_3
DLF at C_1
200 sweeps
B
400 sweeps
Number of impulses
C
DLF at C_3
400 sweeps
D
DLF at C_3
300 sweeps
Time (ms)

Figure 39

Frequency histograms of he conduction velocities of p.s.d.c. neurones measured between a stimulating electrode on the dorsal columns at C_{2-3} and the lumbar recording site.

The top histogram shows the distribution of conduction velocities for those p.s.d.c. units which were not apparantly excited by stimulation of the dorsolateral funiculus at C_3. Those units which were also excited by stimulation of the dorsolateral funiculus at C_1 are shaded.

The bottom histogram shows the distribution of conduction velocities for those p.s.d.c. units which were not apparently excited by stimulation of the dorsolateral funiculus at C_3.

x= mean conduction velocity, n= number of units.

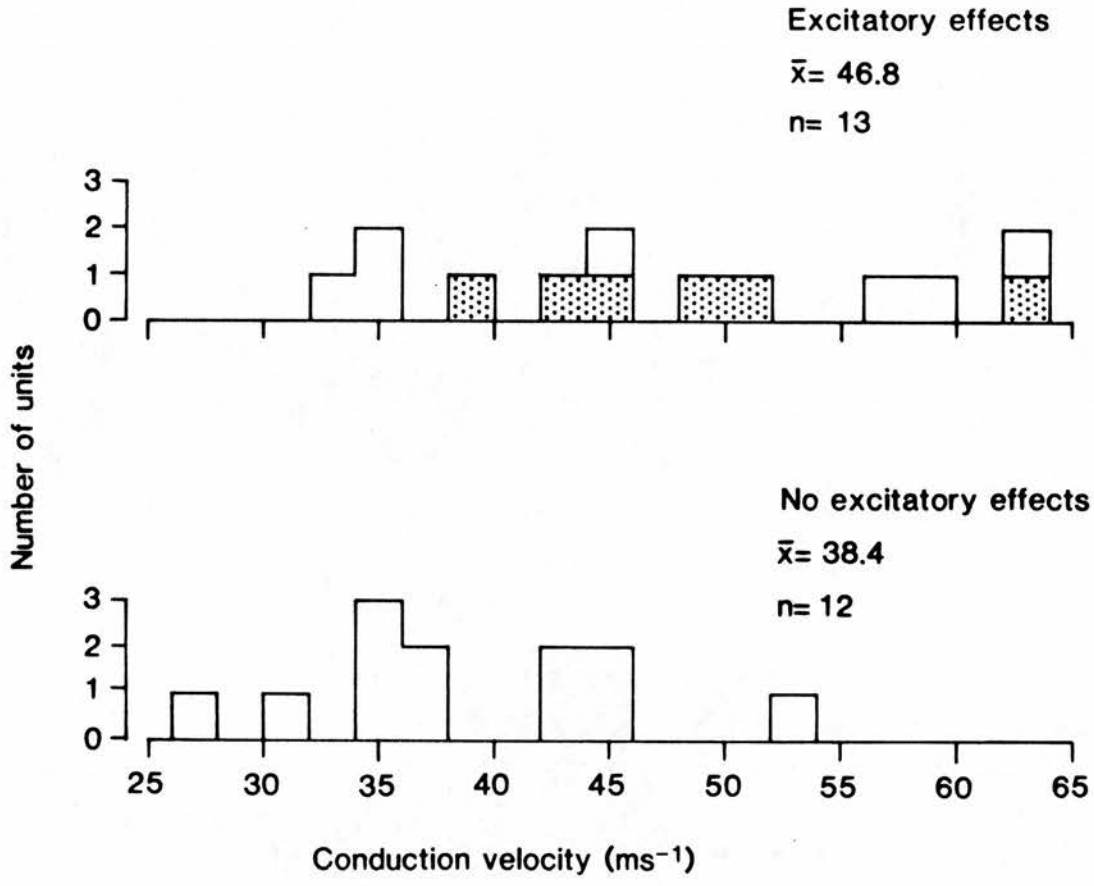

Excitatory effects
x̄= 46.8
n= 13
No excitatory effects
x̄= 38.4
n= 12
Number of units
0
1
2
3
25
30
35
40
45
50
55
60
65
Conduction velocity (ms⁻¹)

Figure 40

Time course of inhibitory effects on p.s.d.c. neurones produced by stimulation of the dorsolateral funiculus.

Peri-stimulus time histograms show the response to stimulating the dorsolateral funiculus (DLF) at C_3 (A, C and D) and at C_1 (B). The arrows indicate the onset of the stimulus train (5 stimuli, 333Hz). Impulses are accumulated in 2ms time-bins.

A, B and C are responses from the same unit; A and B with background activity elevated with a sustained pinch and C without. The histograms show the time course of a strong inhibition of the background activity, which immediately followed the excitatory effect.

D shows the time course of inhibition in a p.s.d.c. unit which showed no excitatory response.

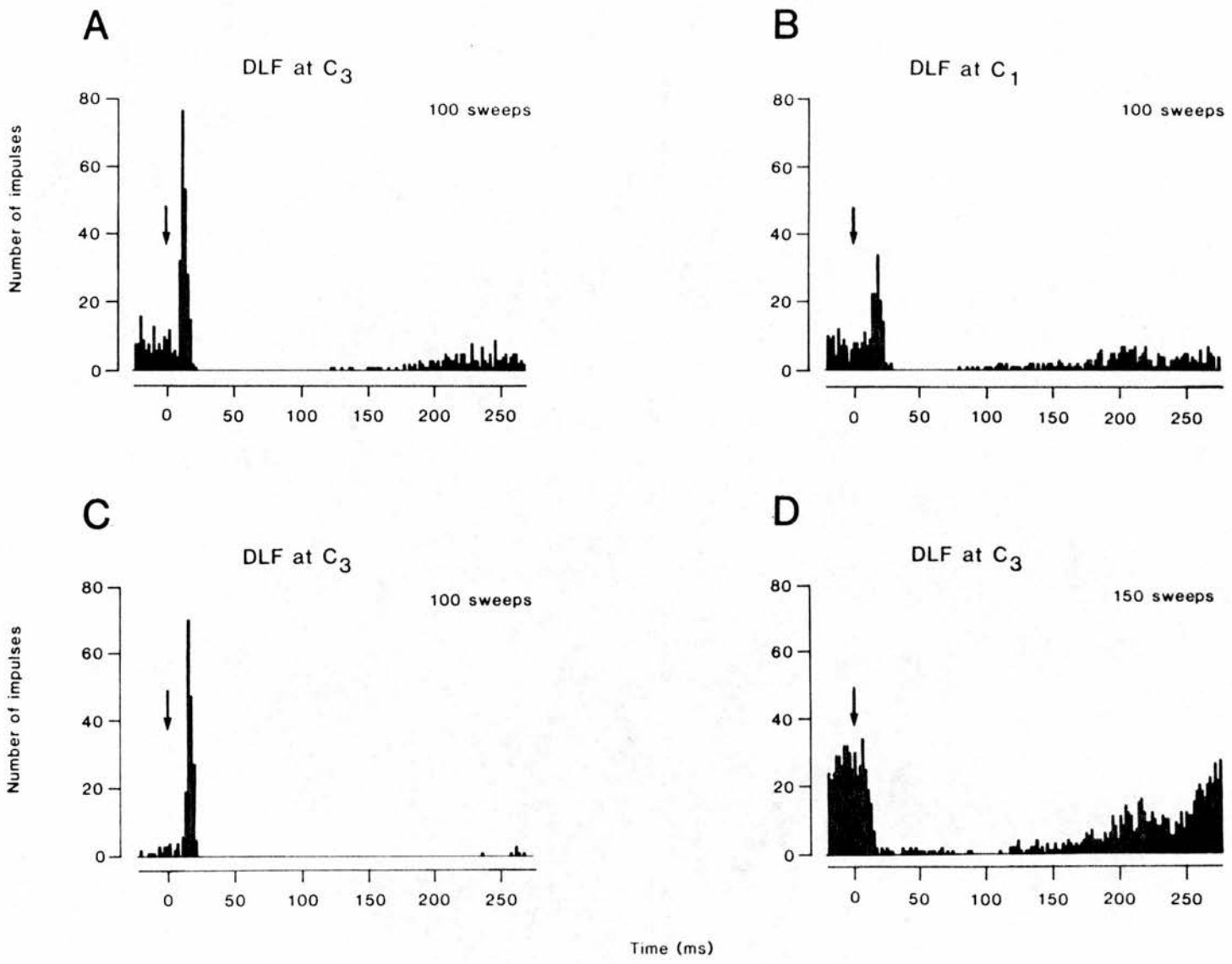

A
DLF at C_3
100 sweeps
B
DLF at C_1
100 sweeps
C
DLF at C_3
100 sweeps
D
DLF at C_3
150 sweeps
Number of impulses
Number of impulses
0
20
40
60
80
0
50
100
150
200
250
Time (ms)

Table 4

Table showing single factor analysis of variance for the conduction velocities of p.s.d.c. units. Those units excited by stimulation of the dorsolateral funiculus had significantly faster conduction velocities (P=0.05) than those units apparantly not excited.

TABLE 4

Source of variation	Sum of squares	Degrees of freedom	Mean square	Variance ratio (F)
Between categories	443.39	1	443.39	5.38*
Error	1896.61	23	82.46	
Total	2340.00	24	* P=0.05	

DISCUSSION

Do some dorsal horn neurones have bifurcating axons with one branch contributing to the s.c.t. and the other to the p.s.d.c. pathway?

Evidence for dorsal horn neurones with bifurcating axons, one branch ascending the d.l.f. and the other the d.c.'s comes largely from the report of Lu et al. (1985). In their experiments the upper cervical dorsal columns and dorsolateral funiculus were each dissected free from the rest of the cord and separated from it with a sheet of plastic. Each dissected component was stimulated electrically, using a pair of needle electrodes with stimuli of 0.2 - 0.5ms width and 30V amplitude in order to search for dorsal horn neurones excited antidromically from each of the funiculi. Stimulus spread between the dorsal columns and d.l.f. was assessed by field potential recording in the dorsal horn at lumbosacral levels.

Cord dorsum potentials

The field potential recording performed by Lu et al. (1983, 1985) appears to be insensitive. They claim that stimulation of the d.l.f. does not evoke a field potential in the lumbosacral dorsal horn unless the stimulus spreads to the dorsal columns. But as has been shown in the present work, stimulation of the d.l.f. produces an obvious cord dorsum potential in the lumbosacral cord, and one that is clearly different from that evoked by stimulation of the dorsal columns (Fig.

33). The cord dorsum potential evoked from the d.l.f. consists largely of a positive potential whereas that evoked from the dorsal columns has a large negative component followed by a positive one, the positive one being of a similar time course to that recorded from the d.l.f.

The field potentials illustrated by Lu et al. (1983) are unusual. Although the initial negativity reverses at about 2mm (as would be expected) the following positivity, which is clear in the records shown in Fig. 33 of this thesis as it is in records produced by stimulating peripheral cutaneous or mixed nerves, is inconspicuous in their surface records and only apparent at depths of 1.0 and 1.5mm whereas a clear reversal at between 0.4 and 0.8mm would be expected (see for example Coombs, Curtis & Landgren, 1956; Eccles, Kostyuk & Schmidt, 1962). It appears, therefore, that the field potential recordings performed by Lu et al. (1983, 1985) as a test for stimulus spread were comparatively insensitive and may have missed any spread that occurred.

In the present experiments in which the dorsal column and dorsolateral funiculi were left in situ, recordings of cord dorsum potentials suggested that some stimulus spread occurred from the dorsal columns to the dorsolateral funiculus but that the dorsal column lesion was sufficient to prevent the effects of stimulus spread from the d.l.f. to the dorsal columns, even at very high stimulus strengths (up to 30V).

Dorsal column lesion

The main function of the dorsal column lesion at caudal C_3 was to limit the effect of stimulus spread from the d.l.f. to the dorsal columns. This lesion was always made by teasing apart, with watchmakers' forceps, the minimum amount of tissue necessary to abolish the initial negative component of the cord dorsum potential evoked from the dorsal columns at C_{2-3}. Whilst a complete dorsal column lesion would produce a clearer interpretation of the effects of the stimulus spread, the integrity of the dorsolateral funiculus is crucial to the rationale of the experiments and particular care was therefore taken to avoid damage to the d.l.f. In one experiment the extent of the lesion was verified histologically (Fig. 32). It was found to involve only a dorsally and centrally located portion of the columns and not to encroach upon the d.l.f.

Tests for bifurcating axons

In the present experiments, with conditions chosen such that there was a bias in favour of stimulus spread between the dorsal and dorsolateral funiculi, no evidence could be found that neurones belonging to the p.s.d.c. or s.c.t. systems had bifurcating axons with branches ascending both the ipsilateral d.l.f. and the dorsal columns and reaching the cervical stimulation sites. For the sample of p.s.d.c. neurones the results were unequivocal. None of the units identified as belonging

to the p.s.d.c. system could be antidromically excited from the dorsolateral funiculus at C_3 even at stimulus strengths some seventy times threshold for activation from the dorsal columns. For the sample of s.c.t. neurones however, about one third could be antidromically excited from both the d.l.f. and dorsal columns; but, for the following reasons, it is most likely that this can be accounted for by stimulus spread:

1) All but 2 of these units required stimuli to the dorsal columns that were considerably greater than the threshold stimulus required to activate them from the dorsolateral funiculus.

2) All but three of these units could also be activated by stimuli to the dorsal columns at a location above the level of the dorsal column lesion. Once again this required levels of stimuli greater than the threshold for antidromic activation from the d.l.f., and unless some fibres cross from the d.l.f. to the dorsal columns above the level of the lesion, then this result could only be due to stimulus spread.

3) None of the units identified as belonging to the p.s.d.c. system, and recorded either in the dorsal columns or the dorsal horn, could be antidromically activated by stimuli applied to the d.l.f. at C_3. This was probably because this stimulus location was also above the level of the dorsal column lesion, and the effects of stimulus spread from the d.l.f. to the dorsal columns would have been contained above the transection.

4) When s.c.t. units could be antidromically excited from both the dorsal columns and the dorsolateral funiculus the antidromic latencies from each site were almost identical. This observation, which is similar to that reported by Lu et al. (1985), would mean that if there are neurones with bifurcating axons, then each of the axonal branches would have to be of the same diameter. There are, therfore, no obvious reasons why one branch should be any less excitable than the other; and yet s.c.t. units that were antidromically activated from the dorsal columns required stimuli considerably greater than the threshold stimulus required to activate them from the d.l.f.

5) In their experiments, Lu et al. (1985) used search stimuli of at least 0.2ms in duration and 30v in amplitude. In the present experiments, however, a search stimulus of around 3V (0.1ms duration) was used to search systematically for units belonging to the spinocervical tract or postsynaptic dorsal column system. This level of stimulation was chosen because it had previously been shown by combined electrophysiological and retrograde labelling experiments (Brown et al., 1980a), to be capable of activating all s.c.t. cells in the lumbosacral dorsal horn. It is unlikely therefore, that a population of units was missed by not using search stimuli of a greater strength. Furthermore, in the experiments of Lu et al. (1985), the neurones which they claimed had bifurcating axons were not of a particularly fine

diameter; the conduction velocities of each of the presumed axonal branches were, on average, $50ms^{-1}$. This is faster than the average conduction velocity of p.s.d.c. axons ($38ms^{-1}$).

It might be argued that neurones with bifurcating axons would not be revealed by axonal recording, since an antidromic impulse conducted down one branch may fail to invade the other. However, in the present experiments, the results obtained from the 13 units recorded in the dorsal horn were no different to those obtained with axonal recording. Furthermore, in previous experiments (Brown, Fyffe, Noble & Rowe, 1984 - unpublished observations) neurones were tested for antidromic responses from both the cervical dorsal columns and ipsilateral d.l.f. in the same way as in the present experiments. Of 12 units belonging to the s.c.t. and 8 belonging to the p.s.d.c. system, none showed any evidence of bifurcating axons. In addition, Jankowska et al. (1979) investigated the effect of stimulation of the d.l.f. on identified p.s.d.c. neurones recorded in the dorsal horn. They did not report the presence of antidromic activation from the d.l.f.

In support of their claim that some neurones have bifurcating axons ascending both the dorsal columns and d.l.f., Lu et al. (1985) note that double labelling of dorsal horn neurones has been reported following injection of different fluorescent dyes into the l.c.n. and d.c.n. (Jiao et al., 1984). However, these results

are inconclusive since they give no indication of the pathways by which the axons of these neurones project. It is known that there are neurones with axons projecting in the d.l.f. which nevertheless terminate in the dorsal column nuclei (Dart & Gordon, 1973; Gordon & Grant, 1982). If these axons give off collateral branches to the lateral cervical nucleus, as has been suggested by Craig and Tapper (1978), then such double labelling would be expected.

Conclusion

From the present results it is concluded that the s.c.t. and p.s.d.c. systems form in substantial part, if not entirely, separate populations of neurones in the dorsal horn.

Implications for other work

The results presented here must cast doubts upon the ability of the protocol employed by Bennett and his collaborators (Bennett et al., 1983; Lu et al., 1983, 1985) to distinguish between neurones contributing to the s.c.t. and p.s.d.c. projections. It seems most likely that the high stimulus strengths employed by these workers (30V) resulted in stimulus spread between the dissected dorsal and dorsolateral funiculi. In the introduction (pages 66, 74, 79) reference was made to discrepancies concerning reports of the morphology and physiology of p.s.d.c. neurones. Lu et al. (1983) have stressed the similarities between the receptive field properties of p.s.d.c. and s.c.t. neurones and Bennett et

al. (1984) have claimed, from a sample of intracellularly stained p.s.d.c. neurones that there are few morphological differences between the two sets of neurones. However, since the same protocol was employed in these studies as that which led them to identify some neurones as having bifurcating axons (Lu et al., 1985), it is likely that the neuronal samples they studied consisted of both s.c.t. and p.s.d.c. units. This may explain why their observations suggest similarities between the two systems.

Relationships between the p.s.d.c. and other projections

Now that it has been established that the p.s.d.c. and s.c.t. projections arise from separate populations of neurones in the dorsal horn, related questions concerning the relationship of each of these systems to other ascending projections can be more clearly addressed. In particular their relationship with the substantial projection through the d.l.f. to the d.c.n. (Rustioni & Molenaar, 1975; Gordon & Grant, 1982) remains to be determined. It has been suggested (Dart & Gordon, 1973; Craig & Tapper, 1978) that some or all of the d.l.f. axons terminating in the d.c.n. might be collaterals of s.c.t. fibres. Craig and Tapper (1978) reported that electrical stimulation in the d.c.n. synaptically excited some cells in the l.c.n. and a few of these responses could be occluded by stimulation of the d.l.f. However, since stimulus spread from the medullary electrode to the d.l.f. could not be ruled out, these results are

supportive rather than conclusive. Preliminary anatomical evidence also supports the suggestion that some or all d.l.f. fibres terminating in the d.c.n. are collaterals of s.c.t. cells since they show a greater morphological resemblance to neurones of the s.c.t. than p.s.d.c. system (Enevoldson, 1982).

On the other hand, the pattern of termination of d.l.f.-d.c.n. and p.s.d.c. fibres within the d.c.n. show a striking similarity, though the former also terminate in other medullary structures including the nucleus X, nucleus Z and external cuneate nucleus (Rustioni, 1973, 1974; Rustioni & Molenaar, 1975; Gordon & Grant, 1982). This raises the possibility that these two projections might be parts of the same population of neurones ascending both the dorsal and dorsolateral fascicles. Clearly, if this is the case, then the physiological evidence presented in Section 1 of this thesis together with morphological and ultrastructural evidence reviewed in the introduction (pages 66 & 69), suggests that only a small minority of these neurones could make collateral connections with the l.c.n. Indeed the possibility remains that the d.l.f.-d.c.n. projection is derived from a population of dorsal horn neurones which is separate, in whole or in part, from both the s.c.t. and p.s.d.c. systems. Further physiological and morphological studies are required to resolve this question.

Finally, Hayes and Rustioni (1979, 1981) have demonstrated by a double labelling technique, that a few

neurones in lateral lamina V and VI of the lumbosacral dorsal horn of monkeys, project both to the ipsilateral d.c.n. and to the contralateral thalamus. The paths of axonal projection of these neurones are unknown. They could therefore be a subpopulation of either the p.s.d.c. projection or, if they exist in the monkey, of the d.l.f-d.c.n. projection.

Effects of stimulation of the dorsolateral funiculus on the activity of p.s.d.c. neurones

Excitatory effects from C_3

The present results comfirm and extend the observations of Jankowska et al. (1979) who showed that stimulation of the ipsilateral dorsolateral funiculus produced excitatory postsynaptic potentials in p.s.d.c. neurones. Jankowska et al. (1979) were able to establish that one of the systems of fibres giving rise to these e.p.s.p.'s terminated or originated between C_1 and C_3. On the basis of latency measurements they proposed that the e.p.s.p.'s originated via an axon collateral link from spinocervical tract cells which terminate in the l.c.n. at C_{1-2}. Maxwell and Koerber (1986) have provided direct ultrastructural evidence for the connections between the two sets of neurones as required by the hypothesis of Jankowska et al. (1979) but Svensson, Westman and Rastad (1985) have described neurones in the l.c.n. with descending axons, as far as L_6 at least.

Obviously the effects described by Jankowska et al. (1979) and those described in the present work may have originated via the s.c.t. or the newly described descending pathway. Since the direct connections do exist (Maxwell & Koerber, 1986) it seems reasonable to suppose that at least some of the effects from the dorsolateral funiculus at C_3 are evoked via the spinocervical tract.

Efficacy of the collateral link

The stimulus parameters used to activate d.l.f. fibres (5 stimuli at 333Hz) represents a pattern of discharge that must often occur naturally in s.c.t. cells, either as bursts within background discharge or in response to natural peripheral stimuli. The excitatory effects following application of this stimulus to the d.l.f. at C_3 were often sufficient to cause p.s.d.c. cells to fire and were certainly sufficient to facilitate ongoing background or pinch evoked activity. However, the convergence of s.c.t. collaterals on to a single p.s.d.c. neurone remain an unknown factor as does the contribution of fibres descending from the l.c.n.

Not all s.c.t. cells can be involved in this action on p.s.d.c. neurones. About 30% of s.c.t. cells do not have collateral axons near the segmental level of their cell bodies (Brown et al., 1977b). Neurones in this group are excited by hair movement alone. In contrast, neurones which give off collateral axons near their cell body include some neurones responding only to hair

movement and all of those neurones which respond in addition to pinch. In the present experiments, all of those p.s.d.c. cells excited from the d.l.f. could be excited from the periphery by both light tactile stimuli and noxious pinch. It is unlikely that the collateral link alone would be powerful enough to account for these responses, but clearly it represents one of the polysynaptic afferent pathways mediating hair afferent and high threshold mechanoreceptive input to neurones of the p.s.d.c. system. This arrangement whereby p.s.d.c. neurones receive some of their input via s.c.t. neurones resembles the lamina cascade arrangement suggested by Wall (1967,1969) in which it was proposed that cells in lamina IV excited more ventrally located neurones in lamina V.

Implications for dorsal horn somatotopy and plasticity

S.c.t. cell collaterals that arise from the initial part of the axon in the grey matter distribute their terminal arborizations within 600um of the cell body in the sagittal and transverse planes and most are situated directly under the dendritic tree of the parent neurone (Brown et al., 1977b). If collaterals of this type are responsible for the connections made with p.s.d.c. neurones, as was the case for the example observed by Maxwell and Koerber (1986, D.J. Maxwell - personal communication), then the p.s.d.c. neurones receiving such contacts are likely to be located directly beneath the s.c.t. parent cell and to have a similar receptive field.

Those collaterals that arise from the s.c.t. cell axon as it ascends the d.l.f., re-enter the dorsal horn and arborize in a position corresponding in the sagittal plane with the position of the initial collateral arborizations (Brown et al., 1977b). Therefore, even if this type of collateral also makes contact with p.s.d.c. neurones, the somatotopic organisation of sagittal columns of neurones with overlapping receptive fields would appear to be maintained. It therefore seems unlikely that the collateral connections between neurones of the s.c.t. and p.s.d.c. system could account in any way for the dorsal horn plasticity that some workers claim is revealed by deafferentation (Basbaum & Wall, 1976; Devor & Wall, 1978, 1981; Lisney, 1983).

Excitatory effects from C_1

The results presented in this section also confirm that p.s.d.c. neurones may be excited from the ipsilateral d.l.f. at C_1. Jankowska et al. (1979) showed, by stimulation of the pyramids, that e.p.s.p.'s evoked from the d.l.f. at C_1 originate via the corticospinal tract. There are however, a number of possible mechanisms for the present observations. These include the antidromic activation of the axons of ascending neurones, some of which may have collaterals terminating either directly on p.s.d.c. neurones or on interneurones in the afferent pathways to them. Another possibility is the activation of descending axons in addition to those of the corticospinal tract.

Stimulation of several brainstem sites which give rise to descending spinal pathways with a predominantly inhibitory effect on dorsal horn neurones, have been shown to produce an initial facilitation in a minority of units (McCreery et al., 1979; Haber et al., 1980; Hodge et al., 1981; Mokha et al., 1985).

Although in the present experiments, the facilitation produced from C_1 was always less effective than stimulation of the d.l.f. at C_3, it is most unlikely that these effects could be due to stimulus spread to cells or terminals in the l.c.n. The stimulus strength employed at C_1 is the same as that commonly used as part of the procedure for identification of s.c.t. neurones. If significant stimulus spread to s.c.t. terminals in the l.c.n. occurred, then electrophysiological mapping experiments would be expected to underestimate the number of s.c.t. cells in the lumbosacral enlargement. In fact however, there is excellent agreement between electrophysiological mapping studies and retrograde labelling studies performed in the same animal (Brown et al., 1980a).

Inhibitory effects

Results presented in this section have shown that p.s.d.c. neurones are profoundly inhibited by stimulation of the ipsilateral d.l.f. at C_3 and C_1. Since similar inhibitory effects were evoked from both C_3 and C_1, it is unlikely that they were elicited either via the s.c.t. or by the system of descending axons originating in the

l.c.n. (Svensson et al., 1985). Results presented in Section 2 show that the modality and receptive field characteristics of p.s.d.c. neurones can be profoundly modified by descending inhibitory mechanisms and it seems most likely that a set of descending axons were being stimulated in the present experiments. Several descending systems including the raphe spinal and reticulospinal systems are known to have axons which descend in the dorsolateral funiculus (Martin et al., 1978; Basbaum et al., 1978; Abols & Basbaum, 1981). Nishikawa et al. (1983) have provided some evidence for a direct serotoninergic innervation of p.s.d.c. cells, and it is possible that this may be responsible for some of the inhibitory actions observed. On the other hand, Jankowska et al. (1979) did not report evoking i.p.s.p.'s in p.s.d.c. neurones following electrical stimulation of the d.l.f. at various segmental levels. The inhibition elicited in the present experiments had a time course of about 300ms which is similar to that of presynaptic inhibitory action in the spinal cord (Eccles et al., 1962; Eccles et al., 1963).

GENERAL DISCUSSION

Anatomical studies have established that the p.s.d.c. system forms a substantial ascending projection to the d.c.n. (Rustioni, 1973,1974; Enevoldson, 1982; Bennett et al., 1983; Gordon & Grant, 1982), suggesting that potentially it may exert considerable influence on the processing of activity within these nuclei. The following discussion concerns the relationship between neurones of the p.s.d.c. projection and cells on which they terminate in the d.c.n. The extent to which the response properties and receptive fields of cells in the d.c.n. reflect input from p.s.d.c. neurones is considered and the possible contributions of this input to the modulation and relay of impulses through the d.c.n. are discussed. Finally, a speculative discussion of the possible functions of the p.s.d.c. projection is presented.

A comparison of the characteristics of neurones forming the p.s.d.c. projection and the d.c.n.

Anatomical and physiological studies of the d.c.n. (Kuypers & Tuerk, 1964; Gordon & Jukes, 1964) suggests that they consist of two main regions; a central core, containing clusters of cells, surrounded by a reticular region (Hand, 1961) composed of the base and rostral zones of the nuclei.

Cells of the clusters region are unlikely to

receive direct input from the p.s.d.c. projection: their major input is from cutaneous primary afferent fibres (Hand, 1966; Keller & Hand, 1970; Nyberg & Blomqvist, 1984) and their receptive fields tend to be located on the distal limb, to respond to one or sometimes two sensitive cutaneous receptor types and to have surround inhibition (Gordon and Paine, 1960; Perl, Whitlock and Gentry, 1962, Gordon & Jukes, 1964).

In contrast, cells of the reticular region receive a diverse input from primary afferent fibres of both cutaneous and muscle origin (Hand, 1966; Keller & Hand, 1970; Nyberg & Blomqvist, 1984) and in addition from non-primary afferent fibres ascending both the dorsal and dorsolateral funiculi (Rustioni, 1973,1974; Rustioni & Molenaar, 1975; Gordon & Grant, 1982). The electrophysiological characteristics of cells in the reticular regions reflect these different inputs: these cells tend to have larger receptive fields on proximal skin and to receive a convergence of input from a number of cutaneous receptor types (Gordon & Paine, 1960; Perl et al., 1962; Gordon & Jukes, 1964). Responses to stimuli of a noxious intensity have rarely been investigated but cells responding to noxious pinch (Dart & Gordon, 1975; Angaut-Petit, 1975b) and to noxious radiant heat (Angaut-Petit, 1975b) have been described, both in animals with intact spinal cord and in animals with either lesions of the dorsal columns (Dart & Gordon, 1975) or dorsolateral funiculi (Angaut-Petit, 1975b).

Neurones in the rostral region, particularly those responding to pressure, have been shown either by electrical stimulation of peripheral nerves not directly exciting the unit (Gordon & Paine, 1960) or by electrical stimulation of skin beyond the receptive field (Perl et al., 1962; Gordon & Jukes, 1964) to have facilitatory surrounds.

It is clear from the work presented earlier that the properties of d.c.n. cells in reticular regions could be conferred in part by a direct afferent input from the p.s.d.c. system. It has been emphasised that the majority of p.s.d.c. units respond to both light tactile and noxious mechanical stimuli and may respond also to noxious radiant heat. It has also been demonstrated that some at least receive subthreshold excitatory inputs from wide areas of skin which are revealed by the removal of tonic descending influences. It is surprising however, in view of the extensive nature of the inhibitory fields of some p.s.d.c. neurones, that inhibitory effects in the dorsal column nuclei are reported to be less prevalent in rostral areas (Gordon & Paine, 1960; Gordon & Jukes, 1964). Cells in the gracile nucleus which are inhibited by light tactile stimulation of widespread parts of the ipsilateral body surface have occasionally been reported (Gordon & Paine, 1960). It is possible that the p.s.d.c. system is responsible for this type of inhibition and that technical difficulties and the use of barbiturate anaesthetics have prevented its more frequent detection.

Possible contributions of the p.s.d.c. system to activity relayed through the d.c.n.

Thalamic projections

Although the main population of retrogradely labelled cells following injection into the ventroposterolateral (VPL) nucleus of the thalamus are grouped in the dorsal middle zones of the d.c.n. (Blomqvist & Westman, 1975; Blomqvist, 1980; Ellis & Rustioni, 1981) there are nevertheless considerable projections to the VPL and adjacent thalamic zones from the reticular regions. Neurones in the ventral middle region project to the VPL/ventrolateral nuclei border (Berkley, Budell, Blomqvist & Bull, 1986) and neurones in the rostral region to the zona incerta (Boivie, 1971; Hand & Van Winkle, 1977; Berkley & Hand, 1978; Berkley, 1983). Most neurones in the gracile nucleus that project through the medial lemniscus, and many lemniscal axons, have small receptive fields responding to one or two sensitive cutaneous receptor types and have surround inhibitory fields (Gordon & Jukes, 1964; Brown, Gordon & Kay, 1974; Cooper & Dostrovsky, 1985); these are therefore unlikely to be directly influenced by p.s.d.c. neurones. Some, however, have larger receptive fields and receive convergent input from different receptor types. A number of such cells receive input from hairy and glabrous skin and may have discontinuous receptive fields (Brown et al., 1974). These resemble the p.s.d.c.

units with distally located receptive fields (glabrous skin units) described earlier in this thesis.

Certainly there is evidence that non-primary afferent fibres terminating in the d.c.n. may exert an excitatory action on the transmission of light tactile input to the cortex. Dart & Gordon (1973) found that 30% of cells synaptically activated from the d.l.f. after section of the d.c.'s were relay cells projecting in the medial lemniscus and some of these could be activated from the periphery by light tactile cutaneous stimuli. Furthermore, Kleider (1974) showed that light tactile stimuli applied to a limb evoked small mass potentials in the limb area of the contralateral sensorimotor cortex after section of the dorsal columns and hemisection of the contralateral medulla. These responses could be abolished by lesions of the d.c.n. or of the ipsilateral d.l.f.

Cerebellar and mesencephalic projections

There is also a substantial projection from reticular regions to the cerebellum (Cheek, Rustioni & Trevino, 1975; Hayes & Rustioni, 1979; Somana & Walberg, 1980) and to various mesencephalic structures. These include the pretectum (Berkley & Mash, 1978; Bull & Berkley, 1984; Wiberg & Blomqvist, 1984), the tectum (Balaydier & Mauguiere, 1978; Blomqvist, Flink, Bowsher, Griph & Westman, 1978; Haring, 1984), the olive (Berkley, 1975; Molinari, 1984, 1985), the red nucleus (Hand & Van Winkle, 1977; Wiberg & Bolqvist, 1984; Molinari, 1985)

and the pontine grey (Swenson, Kosinski & Castro, 1984); several of which may have close functional interactions (Berman, 1977; Itoh, Takada, Yasui, Kudo & Mizuno, 1983; Molinari, 1984; Swenson et al., 1984). The electrophysiology of these projections has not yet been studied in detail, but cells in the gracile nuclei antidromically activated from the cerebellum tend to have light tactile receptive fields on the hind limb which are larger than average for cells in the rostral region (Gordon & Seed, 1961). Cuneocerebellar tract neurones in the main cuneate nucleus receive di- and polysynaptic excitation from cutaneous afferents and most receive additional excitation from high threshold muscle afferents. When investigated with natural stimuli, most respond to tactile stimulation of the skin but some only to pressure on glabrous skin (Holmqvist, Oscarsson & Rosen, 1963; Cooke, Larson, Oscarsson & Sjolund, 1971). Cooper and Dostrovsky (1985) have recently investigated d.c.n. neurones projecting to mesencephalic areas. Receptive fields of these units were generally larger than those of neurones antidromically activated from the diencephalon and many were located on proximal limb and trunk. Most responded with rapidly adapting discharges to low intensity mechanical stimulation of the skin although responses to stimuli of a noxious intensity were not tested. The presence of these projections from the rostral regions of the d.c.n. to the cerebellum and mesencephalic areas concerned with motor control,

suggests that afferent input from the p.s.d.c. system might contribute to the modulation of motor activity.

Spinal projection

Neurones in the dorsal column nuclei have also been shown to give rise to axonal projections to the spinal cord (Dart, 1971). The majority of neurones retrogradely labelled from the cord lie outside the clusters region, the densest distribution being at the base of the nuclei and in the area between them (Burton & Loewy, 1977; Armstrong, Blesovsky, Corsiglia & Gordon, 1979; Enevoldson & Gordon, 1984). Although the main concentration of cells is therefore in a more caudal area than the major region of termination of non-primary afferents, there is some overlap in their distributions and furthermore most descending cells have extensive stellate dendritic fields (Enevoldson & Gordon, 1984); it seems almost certain therefore, that they will receive input from the p.s.d.c. projection. Descending neurones have been shown, by electrical stimulation of the d.l.f. caudal to a d.c. lesion, to receive both excitatory and inhibitory input from non-primary afferent fibres (Kleider, 1974); although their general lack of responsiveness to natural cutaneous stimuli in d.c. lesioned animals suggests that a substantial part of their input is derived from fibres ascending the d.c.'s. A full characterisation of their receptive fields has not yet been achieved, but some have rapidly adapting and others slowly adapting responses to low threshold

cutaneous stimuli (Bromberg, Burham & Towe, 1981; Cole, Gordon & Sanders, 1984) and most appear to have large receptive fields on proximal limbs and trunk (Cole et al., 1984, but see Bromberg et al., 1981). In addition, they have been shown to receive an excitatory drive from the cortex (Kleider, 1974; Bromberg et al., 1981; Cole et al., 1984). The axons of spinally projecting cells descend in either the ipsilateral d.l.f. or d.c.'s (Burton & Loewy, 1977; Enevoldson & Gordon, 1984) and probably terminate in lamina IV-V of the cervical cord (Burton & Loewy, 1977). Some at least, also have an ascending branch projecting initially through the medial lemniscus though not to the VPL (Bromberg et al., 1981; Cole et al., 1984). Assuming that the terminal distribution of these spinally projecting neurones is confirmed in the cervical cord and demonstrated also in the lumbosacral cord, then clearly this system has the potential to influence transmission through both reflex and ascending spinal pathways. The s.c.t., p.s.d.c. and d.l.f. - d.c.n. pathways may be included in this action. Indeed if, as seems almost certain, non-primary afferent systems provide some of the input to these descending cells, then they could provide a feedback modulatory control, the gain of which might be set by descending cortical influences.

Transmission of nociceptive activity through the d.c.n.

As work in this thesis clearly indicates, a large proportion of p.s.d.c. neurones respond to noxious

mechanical and thermal stimuli, particularly in the absence of inhibitory influences descending from the brain. None of the efferent systems of the d.c.n. discussed above have so far been shown to be excited by stimuli of a noxious intensity; although it should be stressed that stimuli of a noxious intensity have rarely been employed during studies of the output from the d.c.n. However, impulses generated in p.s.d.c. neurones as a result of noxious stimuli may not necessarily have to be reliably relayed through the d.c.n. to higher centres in order to provide useful information about the nature of a noxious stimulus. Such information might equally well be derived from the modulatory effect of noxious stimuli on the transmission of other inputs through the nuclei or from the activity required in descending pathways to suppress such effects. The extent to which the p.s.d.c. system has an ascending somatosensory role in the transmission of nociceptive information therefore remains to be determined.

Modulation of transmission through the d.c.n.

Whilst the extent to which the d.c.n. relays nociceptive input remains unknown, there is clear evidence that noxious peripheral stimuli may exert an inhibitory influence on transmission through the d.c.n. These effects appear to originate from widespread areas of the body and to be mediated by non-primary afferent pathways.

The mass response in the medial lemniscus to cutaneous electrical stimulation of the forepaw has been found to be reduced by conditioning stimuli applied to widespread areas including the contralateral and hindlimbs (Jabbur & Banna, 1968, 1970; Anderson, Etholm & Gordon, 1970). Similar effects have been demonstrated while recording from single neurones in the cuneate nucleus, some of which relayed through the medial lemniscus (Jabbur & Banna, 1970; Davidson & Smith, 1970). Dart & Gordon (1970, 1973, 1975) found that some cells in the rostral gracile nucleus, which could be synaptically excited by electrical stimulation of the d.l.f. below a d.c. lesion, had nociceptive cutaneous and subcutaneous receptive fields. These fields were often widespread and occupied varying combinations of ipsilateral and contralateral limbs. It was suggested that these might be inhibitory interneurones since another group of neurones, which included relay cells, were inhibited by the d.l.f. stimulus. The background activity of these units could be inhibited by noxious pinch, but not by light mechanical stimuli, and the inhibitory receptive fields involved widespread areas of the body.

Speculation on the function of the p.s.d.c. projection

It could be speculated that the p.s.d.c. system, with its high proportion of cells which are activated by noxious stimuli, might mediate similar modulatory effects to those described above. If so, then noxious stimuli

would be expected to produce a widespread inhibition of the transmission of light tactile information through the nuclei which would be sustained if damage resulted. The function of such a mechanism might be to focus the attention of an animal on the presence of an injury. However, it is conceivable that at the same time this action could sharpen the transmission of tactile input through the d.c.n. since activity resulting from a stimulus to the skin area around the injury would be transmitted against a background of generalised inhibition. Perhaps such a mechanism could help the animal to avoid bringing the injury into contact with other objects.

There may however, be situations in which a general suppression of tactile input is a disadvantageous response to injury: when further danger must be avoided, full access of tactile input to the brain may be a more pressing requirement. Under these circumstances descending systems might be expected to suppress the modulatory effect of nociceptive activity on the d.c.n. and the tonic descending inhibition of p.s.d.c. neurones observed in the present preparation could represent such an action. Similarly, if p.s.d.c. neurones are inhibited by electrical stimulation of brain stem sites, then the suppression of such a mechanism could provide an explanation for reports that stimulation produced analgesia in conscious animals is accompanied by hyperreactivity to light tactile stimuli (Mayer, Wolfle,

Akil, Carder & Liebeskind, 1971; Oliveras, Redjemi, Guilbaud & Besson, 1975; Oliveras, Guilbaud & Besson, 1979).

In addition to ascending somatosensory functions, the p.s.d.c. system must also have local segmental actions since the great majority of p.s.d.c. axons give off axon collaterals close to the cell body (Brown & Fyffe, 1981; Enevoldson, 1982; Bennett et al., 1984). Between one and three collaterals may arise and usually they arborize ventral to the parent cell body over a wider mediolateral extent than the cells' dendritic tree, although their full extent has not yet been determined. It has been pointed out (Brown, 1981) that s.c.t. cells are unlikely to be a target for these collaterals since neurones of the s.c.t. do not receive input from slowly adapting type I receptors or rapidly adapting mechanoreceptors in glabrous skin. However, the possibility connot be totally excluded since not all p.s.d.c. neurones receive such afferent input and the effects of the link might in any case be subliminal; this and the possibility of recurrent effects upon p.s.d.c. neurones remain to be investigated.

It seems most likely, however, that neurones receiving input from the p.s.d.c. system are on spinal reflex pathways. Those neurones in the present study, which received input from the glabrous skin of the pads seem particularly suited to a role in locomotion. Engberg (1964a, b) has described a reflex involving

muscles in the leg and foot which he has called the toe extensor reflex. In spinal cats, a brisk tap or gentle pressure on the plantar cushion produces a plantar flexion of the toes (Engberg, 1964a, b; Egger & Wall, 1971). In most animals the pressure required is similar to that which occurs when the animal is standing on the leg and it has been suggested that this reflex activation of the foot musculature might function to stabilize the foot during standing or during the stance phase of locomotion. The reflex was found to reach a maximum with application of moderate pressure to the plantar cushion but when the intensity of the pinch was further increased into the noxious range the general flexion reflex involving withdrawal of the whole limb was evoked (Sherrington, 1900, 1910). In the present experiments glabrous skin units were commonly excited by low threshold stimulation of the plantar cushion and some of these units were inhibited when the stimulus was increased to a noxious intensity. For those units inhibited by a noxious pinch it was often difficult to determine whether the low threshold excitatory response involved a slowly adapting component; however, for at least one unit, pinch of the plantar cushion produced an excitatory response while noxious radiant heat produced inhibition. Units with these response properties would seem ideally suited to mediate the toe extensor reflex; their excitatory response to gentle stimuli could drive the reflex whilst their inhibitory response to noxious

stimuli could suppress the reflex and allow the general flexion reflex to come into operation.

Engberg (1964a, b) found that the toe extensor reflex was markedly depressed in the decerebrate state. The present experiments have shown that p.s.d.c. neurones may be subject to powerful descending influences which appear to suppress both the inhibitory and excitatory responses of glabrous skin units to noxious stimuli. If p.s.d.c. neurones do, in part, mediate the toe extensor reflex then descending systems would appear to be able to raise the threshold at which a noxious stimulus to the foot 'switches off' the toe extensor reflex and 'switches on' the withdrawal reflex. Such a mechanism might be expected to operate in circumstances where locomotion is of overriding importance to the animal even when this may potentially result in injury to the feet.

Whether or not p.s.d.c. neurones are directly involved in reflex pathways, the diverse inputs by which they may be influenced (including cutaneous receptors in both hairy and glabrous skin, receptors in muscles and joints and neurones of other ascending tracts) suggests that this system is well organised to monitor activity in the dorsal horn consequent upon movement. This, together with the termination of the p.s.d.c. system in an area of the d.c.n. from which there are substantial projections to the cerebellum and brain areas concerned with the regulation of motor activity (see above), suggests that a major function of the p.s.d.c. system may

be to transmit to the brain information contributing to the control of muscles during locomotor and, in primates particularly, exploratory movements of the limbs.

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APPENDIX

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Inhibitory fields in the post-synaptic dorsal column system of the chloralose-anaesthetized cat

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In a recent electrophysiological investigation of post-synaptic dorsal column (PSDC) neurones, about 40 % were found to have inhibitory fields (Brown, Brown, Fyffe & Pubols, 1983). These were divided into two main types: either small and within or adjacent to the excitatory field, or large and separated from or adjacent to the excitatory field. A further series of experiments has confirmed and extended these observations.

Experiments were carried out on cats anaesthetized with chloralose (70 mg/kg) and paralysed intermittently with gallamine triethiodide. The dorsal columns were lesioned at C2 and bipolar Ag–AgCl ball electrodes were used to apply search stimuli to the dorsal columns at C3 (3–4 V, 100 μs). Glass capillary micro-electrodes filled with 4 M-NaCl (15–20 MΩ) were used to record from axons of PSDC neurones in the dorsal columns at L4–5. The receptive fields of these units were investigated using natural stimuli such as brushing, tapping and pinch applied by a clip.

A total of 28 PSDC units were analysed, 18 of which were found to have areas of skin from which both background activity and the slowly adapting response to pinch could be inhibited. Of 21 units with excitatory receptive fields restricted to hairy skin, 13 had extensive light-tactile inhibitory fields, adjacent to and often overlapping the excitatory field. None, however, could be inhibited by application of a sustained pinch.

Of 7 units with excitatory fields including glabrous skin, 5 had inhibitory fields; 3 of these units could be inhibited by both light tactile stimuli and sustained pinch to the glabrous skin, 1 unit could be inhibited only by sustained pinch, while the remaining unit could only be inhibited by light tactile stimuli.

The results from this sample confirm that in the chloralose-anaesthetized cat a large proportion of PSDC neurones have inhibitory fields. Furthermore, whilst those units with input from glabrous skin are inhibited by both pinch and light tactile stimulation, those with excitatory fields restricted to hairy skin are inhibited only by light tactile stimuli.

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Effects of descending influences on the high-threshold excitatory fields of post-synaptic dorsal column neurones in the chloralose-anaesthetized cat

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Neurones of the post-synaptic dorsal column (p.s.d.c.) system may be excited by noxious mechanical and thermal stimuli applied to the skin (Angaut-Petit, 1975). We have investigated the influence of descending projections in the spinal cord on (1) the responsiveness of these cells to noxious stimuli and (2) the size of the high-threshold receptive fields.

Experiments were carried out on cats anaesthetized with chloralose (70 mg/kg) and intermittently paralysed with gallamine triethiodide. The dorsal columns were sectioned at C_{1-2} and bipolar Ag–AgCl ball electrodes were used to apply search stimuli to the dorsal columns at C_2 (3–4 V, 100 μs). Glass capillary micro-electrodes filled with 4 M-NaCl (15–20 MΩ) were used to record extracellularly from axons of p.s.d.c. neurones in the dorsal columns at L_{4-5}. The receptive fields of these units were investigated using natural stimuli both before and after reversible spinalization produced by cold block of the spinal cord at Th_{13} (Brown, 1971).

A total of 18 units, all of which had light tactile receptive fields which did not expand during cold block of the cord, were adequately analysed. Sixteen of these units also responded with a slowly adapting discharge to a sustained pinch, and during cold block responded more vigorously to the same clip applied to the same skin position. Seven units also responded from areas of skin outside the previously responsive area, indicating an expansion of the high-threshold receptive field; for three of these units, the field expanded to include glabrous skin. One unit which had not previously responded to a sustained pinch did so in the cold-blocked state.

Ten of the above units were also investigated for their response to noxious radiant heat. Before cold block only five units, all of which responded to pinch, could be excited. During cold block three of these units responded from a wider area of skin and all of those units previously unresponsive (five) were now excited by noxious heat.

These results show that (1) the responsiveness of p.s.d.c. cells to noxious stimuli and (2) the area of skin from which such stimuli effectively excite these neurones are both influenced by pathways descending in the spinal cord. These pathways are tonically active in the present preparation.

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