Cortical Control of the Fusimotor System in the Tenuissimus Muscle of the Cat

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by

A. ASGARI-KHOZANKALAEI, B.Sc. (Summa Cum Laude), M.Sc.

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Institute of Physiology
Faculty of Medicine
Glasgow University

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IN THE NAME OF *ALLAH*
THE BENEFICIENT, THE MERCIFUL

And certainly **We** created man of an extract of clay.

Then **We** made him a small life-germ in a firm resting-place,
then **We** made the life-germ a clot, then **We** made the clot a lump of flesh, then **We** made (in) the lump of flesh bones, then **We** clothed the bones with flesh, then **We** caused it to grow into another creation, so blessed be ***ALLAH*** , the best of the creators.

Then after that you will most surely die.

Then surely on the day of resurrrection you shall be raised.

And certainly **We** made above you seven heavens; never are **We** heedless of creation.

HOLY QUR'AN

Chapter 23

Verses 13-17

ABSTRACT

Cortical control of the sensory output of muscle spindles was studied in anaesthetized cats in two series of complementary experiments. Gamma motoneurone activity was monitored during electrical stimulation of the sensorimotor cortex: a) by recording from single primary and secondary sensory afferents from the tenuissimus and flexor digitorum longus muscles in dorsal root filaments and b) by visualizing directly the movements of intrafusal muscle fibres in exteriorised muscle spindles of the tenuissimus muscle.

It was found that the state of anaesthesia was crucial in obtaining reproducible results and variation in the state of anaesthesia can alter the fusimotor effect from static to dynamic or even from excitation to inhibition. This is consistent with findings of Vedel and Mouillac-Baudevin (1970). The anaesthetic agent used was also important in determining the magnitude and type of the response to electrical stimulation. The initial burst of the primary afferent in response to passive stretch was by far greater with chloralose than with barbiturate anaesthesia in both tenuissimus and flexor digitorum longus muscles, suggesting that there may be a tonic low-level dynamic gamma excitation in chloralose anaesthesia.

The state of the sensorimotor cortex is important too. Prevention of CO_2 escape from the surface of the cortex in the present experiments by covering the cortex with 1 cm of mineral oil is thought to be the sole factor which made these results different from those obtained by Gladden and McWilliam (1977a,b).

Other new findings were 1) the topographical mapping of the sensorimotor cortex in relation to the type of gamma motoneurones recruited, static or dynamic, and 2) evidence for independent cortical control of different types of static gamma motoneurones:

1) A "dynamic area" was identified from which dynamic effects were clearly elicited during stimulation. The boundaries were the cruciate sulcus (anteriorly), the ansate sulcus (posteriorly) and the sagital longitudinal fissure (medially). Laterally, the area extended half way to the postcruciate dimple. In addition from direct observation of intrafusal fibre movements it was clear that dynamic gamma motoneuroneswere never recruited alone.

2) Static effects were elicited following stimulation of a much wider area across the sensorimotor cortex, the postcruciate dimple being almost at the centre. The sensorimotor cortex was not only capable of controlling static gamma motoneurones independently from dynamic ones, but also capable of simultaneously inhibiting some static gamma motoneurones and exciting others, lending support to the idea (Boyd, 1986) that there is more than one type of static gamma motoneurone.

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I should also take this opportunity to thank my family abroad, for their encouragement and interest in my career throughout my life.

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CHAPTER ONE

INTRODUCTION and LITERATURE REVIEW

SECTION A: INTRODUCTION

The sensory receptors are the gateways through which the outside world enters our mind. They are the structures which define the limits of sensitivity and determine the range of stimuli that can be perceived and acted upon. One peripheral receptor with the unique characteristic of having efferent motor innervation is the muscle spindle. Muscle spindles are peripheral sense organs of the greatest importance. They are as essential for awareness of limb position as they are for the fine control of movements, the finer the muscular control over a joint, the richer is the spindle content of the controlling muscles.

Research on the muscle spindle had been concerned with a wide range of aspects, including morphology, functional properties, central action of spindle afferent neurones and peripheral action of fusimotor neurones and their central control. Although this review focuses on the central control of spindle activities, morphology and functional properties will be discussed briefly because part of the work for this thesis involved direct observation of living spindle activity as well as a histological study of a few spindles.

Structure and innervation of the mammalian muscle spindle

The muscle spindle has three main components: a bundle of specialized muscle fibres, intrafusal muscle fibres; motor nerves, the axons of gamma and beta motoneurones; and sensory nerves, primary and secondary afferents.

History

Kühne was the first to see muscle spindles in mammals and called them, from their shape, MUSKELSPINDELN (muscle spindle), which name has been adopted since then. However they were not recognized as sense organs until Sherrington in late 1890's demonstrated that the spindles were specialized receptor structures. He reported the presence of large myelinated afferents and their termination in those sense organs. Almost simultaneously Ruffini (1898) provided us with his elegant drawings, dividing nerve endings on morphological criteria into three distinct types: primary and secondary afferents and plate endings. However, identification of plate endings by Ruffini was for long unnoticed until 1930's when B.H.C. Matthews demonstrated the effect of fusimotor activity on excitation of spindle afferents by supramaximal stimulation of the motor nerve to their parent muscle. Earlier, Langley (1922) had noticed that myelinated ventral root fibres fell into two groups according to diameter and he suggested that the small motor nerve fibres might "perhaps form the small nerve endings in muscle spindles". O'Leary, Heinbecker and Bishop (1935) felt that the anatomical differentiation of motor nerve fibres would be reflected functionally and that they too suggested that the group of small motor fibres might innervate muscle spindles. However, due to technological inadequacies their experiments were inconclusive. The larger group of fibres soon acquired the prefix "alpha" (Erlanger and Gasser, 1937) while the smaller group of fibres were given the prefix "gamma" by Leksell (1945). In fact, systematic research on the separate fusimotor innervation of these receptors essentially began with Leksell's monograph in 1945.

In the first half of the current century attempts to research the function of muscle spindles were not somehow on the right track as almost every investigator was looking at the spindles through Sherrington's spectacles and that was the involvement of these sense organs, in a linear manner, in simple spinal reflexes as the basis for motor control. In spite of those efforts, it is now clear that muscle spindle afferents do project strongly to the sensorimotor cortex (Amassian and Berlin, 1958; Oscarsson and Rosen, 1963; Landgren and Silfvenius, 1969 and Starr et al., 1981).

It is believed now that more than two thirds of the myelinated nerve fibres in a muscle nerve innervate the muscle spindles (Boyd and Smith, 1984). Although both Ruffini (1898) and Matthews' (1933) investigations vaguely and that of Leksell (1945) essentially indicated that the bulk of the fusimotor innervation of the spindle was mediated by small gamma motoneurones, we now know that a substantial contribution is also made by the mixed skeletofusimotor or beta motoneurones, which in addition innervate extrafusal motor units.

The outer capsule and fluid space

The outer capsule of the spindle is continuous with the perineurium of the nerves which supply the spindle. It presents a significant barrier to the passage of tracer protein and bears some resemblance to the blood-brain barrier (Boyd, 1985). The fluid space which is formed by expansion of the central 2 mm of outer capsule contains a jelly-like substance rich in acid mucopolysaccarides, probably to protect the sensory endings from mechanical interference and to lubricate the system so that the intrafusal fibres slide

easily past each other. It is likely that it provides a controlled chemical environment for the satisfactory functioning of the sensory endings (Fukami, 1986).

Structure of intrafusal fibres

Two types of intrafusal fibres were first recognized in muscle spindles of both cats and humans from light microscopy (Boyd, 1985; Cooper, and Daniel, 1963). Cat muscle spindles usually contain two relatively large "nuclear bag" fibres up to 10 mm long and 25 μm in diameter, so named because of a large accumulation of nuclei at the spindle "equator" underlying the terminals of the primary sensory ending; and three to five smaller "nuclear chain" fibres about 4 mm long and 12 μm in diameter, with a single row of nuclei in the equatorial region.

The two nuclear bag fibres are themselves of two distinct types termed "bag_1 fibre" and "bag_2 fibre" because of the histochemical difference between them, or "dynamic nuclear bag fibre" and "static nuclear bag fibre" because of their differing mechanical properties. Many human spindles contain three or four dynamic bag_1 and static bag_2 fibres and up to ten chain fibres making a total of up to 14 in all, but other human spindles contain the same number of intrafusal fibres as those in the cat.

Sensory innervation

Each spindle contains one primary sensory ending consisting of spiral or annular terminations, each of which encircles an intrafusal fibre. Terminals round all three types of intrafusal fibre, are all connected to the same group Ia afferent axon which has an external

diameter of .7 m to .21 m and conduction velocity from about 55 m/sec to 120 m/sec. Secondary sensory endings in the cat consist of less regular spiral or annular termination round each nuclear chain fibre and some spray-like terminations on the nuclear bag fibres. Group II fibres have an external diameter of between .1 m with conduction velocities of 20 m/sec to 65 m/sec. It is believed that all three types of intrafusal fibres can contribute to the group Ia input, whereas the chain fibres provide most, and in some cases all, of the group II input. Some spindles may have no secondary endings at all, whereas others have up to five such endings, two on one side of the primary ending and three on the other (Boyd, 1962). The most common arrangement, however, is for there to be one primary ending and one secondary ending adjacent to it on each side.

Motor innervation

Historically, Leksell (1945) concluded that the small efferent fibres of the ventral root are most likely the motoneurones innervating intrafusal muscle fibres. He studied the action of these gamma efferents on their own by eliminating the large alpha motor fibres by a pressure block; thus both groups of fibres could be electrically excited in the ventral root, but only the gamma efferent impulses reached the muscle. On their arrival there, they failed to elicit any appreciable contractile tension, but multifibre recordings showed that they increased the afferent discharge from the muscle. These findings were soon refined by Hunt and Kuffler (1951) by using a double single fibre preparation, single gamma motor axons were stimulated in ventral root filaments while recording in dorsal root filaments from the Ia afferents of spindles which the motor axons

innervated. Together these experiments established the gamma efferents as a specific fusimotor system devoted solely to control the muscle spindle.

Spindles receive two distinct types of fusimotor innervation from gamma motoneurones in the spinal cord, dynamic and static, the differences between which being due to the mechanical properties of the intrafusal fibres innervated. Thus dynamic gamma axons innervate the dynamic bag_1 fibre at one or both poles. In about one third of spindles the dynamic bag_1 fibre is also innervated by a dynamic beta axon, which additionally innervates slowly contracting extrafusal fibres, type S. The static bag_2 fibre is innervated by static gamma axons. No beta innervation of this fibre has been identified. In contrast both static gamma and static beta axons innervate the chain fibres in a manner more complex than those two other fibres, summarized by Boyd (1985). Static beta axons also supply fast contracting extrafusal muscle fibres.

In addition to motor innervation selective to each type of intrafusal fibre, most spindles receive at least one non-selective static gamma axon branch innervating the static bag_2 fibre and some chain fibreS. In other words, a single static gamma axon may terminate on the static bag_2 fibre, one or more chain fibres, or both in several spindles it supplies.

The story of beta axons is gaining more and more importance. The evidence that mammalian muscle spindles are supplied by branches of alpha motoneurones was put forward by Bessou, Emonet-Dénand and Laporte (1963, 1965) in their work on the first deep lumbrical muscle of the cat. It was about the same time that skeletofusimotor fibres acquired the alternative name of beta fibres. The prefix beta was

introduced by Boyd and Davey (1959) to indicate the conduction velocity of a group of motor fibres to tenuissimus. Steg (1962) and Kidd (1964) also found beta axons having conduction velocity midway between alpha's and gamma's. However, it was not until the time of the Stockholm symposium (1965) that the prefix beta was being used by Barker to indicate the function of an axon, i.e. that it innervated both intrafusal and extrafusal muscle fibres. Almost simultaneously Brown, Crowe and Matthews (1965) confirmed the existence of dynamic beta axons in the cat during their study on the tibialis posterior muscle. The label appears to have stuck and a beta fibre is now accepted as one of particular function rather than conduction velocity.

Since the innervation of dynamic bag_1 (Db1) fibres and that of static bag_2 (Sb2) and nuclear chain fibres in the cat muscle spindle are largely independent of one another; therefore, it might not be too irrelevant if some people refer to them as dynamic and static intrafusal systems. Although microscopic observation of living spindles has emphasized the specificity of innervation of the bag_1 fibre by either beta or gamma dynamic fusimotor axons, anatomical studies show that in about 15% of cat tenuissimus spindles the bag_1 fibre also receives motor innervation by axons which also innervate chain fibres (Kucera, 1984). Having found non-selective innervation in 50% of bag_1 fibres in lumbrical spindles in monkey, Kucera interpreted it as indicating less selective innervation of intrafusal fibres in monkey as compared to cat. He also found non-selective innervation of human bag_1 fibres, though Gladden, Wallace and Craigen (1985) did not. In rat spindles there also appears to be considerable non-selectivity in the innervation of the bag_1 fibre by static axons (Walro and Kucera,

1985), but in the sample studied by Arbuthnott, Gladden and Sutherland (1989) non-specific innervation of bag_1 fibres occurred only when a single axon innervated an entire spindle pole. We can only be sure, at present, that bag_1 fibres are innervated rather independently, since physiological evidence is not yet available to indicate whether non-selective innervation of bag_1 fibre has any functional importance.

Functional properties of muscle spindles

Stretch of the muscle in which the muscle spindles are embedded gives rise to sensory discharges, as does activation of the intrafusal muscle fibres by fusimotor stimulation.

Afferent discharge during a stretch

Typical responses of primary and secondary endings of a spindle to a ramp stretch and release of the muscle at different velocities were well demonstrated by Cooper, 1961. Characteristically, the primary ending discharges at high frequency during the stretch and falls silent during the release, whereas the secondary ending responds with a smaller overshoot in its discharge and continues to fire during the release phase. Also, the discharge of the primary ending is usually much less regular than the secondary ending. Secondary endings show an almost linear rise in discharge frequency during the stretch which is related to the length of the spindle at any point in time. Primary endings, on the other hand frequently show a non-linear rise in discharge frequency during the stretch (Boyd, 1986). This rise is preceded by a fast rising phase at the start of the stretch and followed by a fast fall at the end of stretch, both of which are much more marked in the group Ia discharge

than in group II discharge. However the increased frequency of primary endings may adapt during the hold-stretch, either when the stretch is applied at long muscle lengths or during dynamic gamma axon stimulation. This is thought to be due to a mechanical phenomenon, "creep", which only happens in dynamic bag_1 fibres.

When a ramp and hold stretch is applied to an isolated spindle, the dynamic bag_1 fibres exhibit "creep" after the completion of stretch (Boyd and Ward, 1969). This appears to be due to "give" in the region of the fibre beyond the end of the fluid space so that it creeps towards the spindle equator, past the other intrafusal fibres, within the fluid space (Boyd and Ward, 1969). Thus the extension of the primary sensory spirals around the fibre when the creep is complete is less than it was at the completion of the ramp stretch, as is the primary afferent discharge (Boyd, Gladden and Ward; 1977). The term "slow decay" is applied to that fall in the primary discharge due to the creep phenomenon. The nuclear chain fibres do not show any creep.

Two further features of the response of the primary ending attract some attention. The first is the "initial burst" of impulses at the start of the stretch, which increases with velocity Boyd (1985). Brown, Goodwin and Matthews (1969) working on soleus muscle of barbiturate-anaesthetized cats with cut ventral roots suggested that the occurrence of an initial burst in their experiments may be attributed to an initial overextension of the central region of the intrafusal fibres relative to their polar regions which are relatively more rigid at the beginning of the stretch. Histologically, central regions of the intrafusal fibres contain very few myofilaments and are also devoid of motor nerve endings. Hunt

and Ottoson (1976) showed that there is a deflection in the generator potential at the beginning of a ramp stretch, indicating that the initial burst is mechanical. Cellularly during the stretch, the bonds break between the actin and myosin filaments which slackens the intrafusal fibres. This "yield" contributes to the sudden drop of sensitivity, which corresponds to the sudden drop in primary afferent discharge following the "initial burst" to the beginning phase of the stretch. Therefore, because of this phenomenon and that of the creep, during a ramp-and-hold stretch the frequency of firing falls in two phases: the first being very fast and the second being approximately exponential with a time constant of about 0.5 msec, the latter due to creep (Crowe and Matthews, 1964).

The second, and unique feature of a primary sensory ending is that its response is very non-linear: the ending may be one-hundred fold more sensitive to small stretches than to large ones (Matthews, and Stein, 1968), which they suggested " indicates that the stretch reflex should be relatively much more effective in resisting small perturbations of the muscle length than could otherwise have been supposed". This is thought to be related to the role of primary afferents in the reflex maintenance of posture. Accordingly, Matthews and Stein (1968) proposed that the primary endings do seem likely to play an important part in reflexly stabilizing the length of a muscle at a constant value, particularly in adjusting for small disturbances.

Effect of fusimotor stimulation on intrafusal fibres and afferent discharges

All three types of fibre respond to repetitive activation of their fusimotor axons with graded contraction in the extracapsular region so that the central sensory region is stretched and its endings are deformed. The behavior is not the same in all three, and the differences are well set out by Boyd (1985).

Selective activation of fusimotor neurones supplying the dynamic bag_1 fibre increases the frequency of Ia afferents, relatively little at constant muscle length, and has almost no effect on secondary endings. However, selective activation of a static bag_2 fibre increases primary discharge usually substantially, but the secondary discharge will only be influenced if the secondary sensory ending has terminals on the Sb_2 fibre, as is the case also with the Db_1 fibre. During tonic contraction of the Sb_2 fibre the peak frequency of the primary afferent discharge is followed by "pronounced adaptation" which seems to arise within the spiral transducer mechanism itself. This very obvious type of receptor adaptation is much less evident in the primary ending discharge during dynamic bag_1 fibre activation. The result of their oscillatory contractions chain fibres can drive primary afferents. A linearly increasing stimulation frequency (0-150 Hz) may drive the primary from 1:1 to 1:4, depending upon the specific gamma axon stimulated and on muscle length. Secondary endings, on the other hand, are always powerfully excited by chain fibres in the same pole as the ending, and less powerfully if the secondary ending lies in the other pole of the contracting chain fibre. Pronounced receptor adaptation is also evident.

In short, the principal action of the dynamic bag_1 fibre is to increase the length sensitivity of the primary sensory ending during the movement; the static bag_2 fibre increases the discharge of the primary sensory ending at any particular length of the muscle, without increasing its sensitivity to either the amplitude or the velocity of any change in length; chain fibres can increase the sensitivity of secondary afferents to length change and can drive the primary afferents. It seems, then, that the central nervous system has at its disposal three distinct intrafusal systems. The possibility exists, therefore, that the central nervous system can not only control the dynamic intrafusal system by way of dynamic fusimotor neurones independently of the static intrafusal system, but also that it can control each of the static systems more or less independently, possibly by way of two types of static fusimotor neurone with morphologically different intrafusal motor terminals (Arbuthnott et al., 1982; Boyd, 1985).

Projection of Muscle Afferents to the Sensorimotor Cortex in Cats

In the 1940's, with the refinement of recording techniques, the detection of a potential wave on the cortical surface in response to a peripheral stimulus became the standard way of showing that an afferent input projected to the cerebral cortex by a reasonably direct pathway. Stimulation of high-threshold muscle afferents (apparently group III) elicited evoked potentials in both SI and SII of the contralateral cortex; however no potential was recorded on stretching the muscle or stimulating the muscle nerves of both fore- and hind-limbs at lower strength, which activated group I or II muscle afferents (Mountcastle, Covian and Harrison, 1952). However,

Gardner and Haddad (1953) found that group II muscle afferents of the hind limb of the cat project to the sensorimotor cortex as well as group III. These negative findings for group I were subsequently confirmed by McIntyre (1953, 1962) with respect to low-threshold muscle afferents (group I of Lloyd, 1943) in hind limb muscle nerves. It was then concluded from previous studies, based on hind limb muscles of cats, that either group III (Mountcastle, Covian and Harrison, 1952) or group II and III muscle afferents (McIntyre, 1953; Gardner and Haddad, 1953) projected to cerebral cortex, but not group I.

On the other hand results obtained on stimulation of forelimb muscle nerves have been contradictory. In spite of the negative finding of Mountcastle, Covian and Harrison (1952), Amassian and Berlin in two brief notes (1958a, 1958b) reported that stimulation of these afferents in contralateral forelimb flexor nerves of the cat evoked surface-positive potentials in the first somatic area after a latency of 6-8 msec. They concluded that the cortical projection of group I afferents was related to slowly-adapting receptors in muscles, as the potential was reduced during a steady pull applied to the corresponding muscle. Woolsey and his colleagues (1947) showed that the potentials evoked from group I afferents occurred only in rostral part of the SI region, largely rostrally of the post-cruciate dimple; and those from cutaneous and high threshold muscle afferent of the forelimb were detected in two separate parts of SI, one rostral to the dimple (R-SI) and one caudal (C-SI). Cortical projection of the group I muscle afferents of the forelimb to the rostral part of the SI was later confirmed by Oscarsson and Rosen

(1963) who reported that cortical responses can be obtained in the cat by electrical and physiological activation of afferents from the stretch receptors of the contralateral forelimb only.

By the year 1969 it was well established that low-threshold muscle afferents from the contralateral forelimb project to the cat's cerebral cortex (Amassian and Berlin, 1958; Oscarsson and Rosen, 1963; Oscarsson, Rosen and Sulg, 1966; Swett and Bourassa, 1967 and Landgren, Silfvenius and Wolsk, 1967).

Several investigators had looked in vain for the equivalent hind limb projections (McIntyre, 1962; Oscarsson and Rosen, 1963; Megirian and Troth, 1964) and thus concluded that group I muscle afferents from the hind limb do not project to the somatosensory cortex of the cat. Norrsell and Wolpow (1966) did, in fact, observe cortical potentials evoked by electrical stimulation of the muscle afferents in the group I range. The potentials were, however, not found in all experiments, and it was assumed that they were not due to stretch receptors in the muscles. A confident observation of a cortical response to stimulation of low-threshold afferents from gastrocnemius muscle was, however, reported by Landgren, Silfvenius and Wolsk (1967). The response was located in the anterior suprasylvian sulcus close to the forelimb group I region, and a later investigation (Silfvenius, 1970) on single cortical neurones in this area confirmed the observation.

Further persistent study by Landgren and Silfvenius (1969) duly demonstrated a hind limb projection on stimulating several of the standard nerves in the chloralose-anaesthetized cats (nerves to quadriceps, posterior biceps-semitendinosus, gastrocnemius-soleus and deep peroneal nerve). They showed that electrical stimulation of

group I afferents from contralateral hind limb muscles evoked responses in two separate areas. One of the areas was located on the dorsal surface of the hemisphere and the other on the medial surface. The dorsal locus was found medial and rostral to the post-cruciate dimple (Pcd). The diameter of this area was 1-4 mm and the point where the amplitude of the evoked group I potentials was maximal (the maximal point) was located 4-5 mm lateral to the midline and 1-3 mm caudal to the cruciate sulcus. It is worth noting that the dorsal group I locus overlapped with the medial border of the projection area of group I muscle afferent from the contralateral forelimb. The distance between the maximum points in the two areas was of the order of 4 mm.

The medial group I locus was situated near the cruciate sulcus on the medial aspect of the postsigmoid gyrus. In some animals a fringe of the area extended on to the dorsal aspect of the gyrus near the midline. The evoked potentials in this region were initially positive potentials when recorded from the surface of the cortex. They changed into negative focal potentials about 0.5 mm below the surface. The negative potentials were maximal in amplitude at depth between 1 and 1.5 mm.

The postcruciate projection area of the group I afferents from the forelimb as well as the two hind limb areas are located at the border of 4y, the cortex containing the giant pyramidal cells of Betz. This area was outlined by Hassler and Muhs-Clement (1964). It covers the pericruciate cortex on both sides of the lateral half of the cruciate sulcus. The group I loci are found in area 3a with some overlap into area 4y in the rostral and into area 3b in the caudal direction.

The use of controlled stretch stimuli strongly suggested that activity from muscle spindle primaries is capable of modulating motor cortex cells (Murphy, Wong and Kwan, 1975). Interestingly, there is electrophysiological evidence for a direct link from area 3a (just rostral to the Pcd in the postsigmoid gyrus) to area 4 in cats (Zarzecki, Shinoda and Asanuma, 1978), and this connection appears to be by way of "specific" U fibres, so-called short arcuate fibres (Grant, Landgren and Silfvenius, 1975).

The Ascending Path of the Group I Muscle Afferents from the Forelimb

In 1963, Oscarsson and Rosen showed that cortical potentials evoked by a volley in group I afferent from extensors disappeared completely after a lesion in the dorsal funiculi and did not decrease in experiments in which the spinal cord at the C3 level was transected, sparing only the dorsal funiculi. Therefore, it seems that the forelimb primary afferent collaterals ascend through the dorsal funiculi. The second-order neurones of the pathway occur in the ventral part of the cuneate nucleus and are excited by afferents from a few forelimb muscles (Rosen, 1969a and 1969b). Following these experiments Rosen and Asanuma (1973) reported that half of the proprioceptive neurones recorded in this region were excited antidromically from the contralateral medial lemniscus.

The third-order neurones are located in a narrow zone of the ventrobasal thalamic complex (Mallart, 1964). Andersson, Landgren and Wolsk (1966) reported that stimulation of group I muscle afferents in contralateral forelimb nerves in barbiturate-anaesthetized cats evoked a response in the nucleus ventralis posterolateralis (VPL) in

the thalamus of the cat. This response was located in the rostral third of the VPL in a narrow zone near the dorsomedial border of the nucleus.

In a series of recordings from thirty cells in the thalamus activated by group I afferents, convergence of excitation was usually observed from group I afferents in more than one of the branches of the deep radial nerve (Andersson, Landgren and Wolsk, 1966). Excitation from cutaneous afferents was also observed in about half of these cells. A micro-electrode study of the projection area (R-SI) demonstrated that many of these neurones were activated by afferents not only from synergists, antagonists and muscles acting at different joints, but also from cutaneous afferents as well (Oscarsson, Rosen and Sulg, 1966). A similar pattern of convergence was encountered by Landgren, Silfvenius and Wolsk (1967). Thus with ascent of the central sensory pathway there appears to be a progressive convergence of inputs from different modalities.

It was suggested that integration of information from synergistic muscles occurs at the thalamic level and that integration of information from muscle groups of more unrelated function occurs at the cortical level (Rosen, 1969b).

The Ascending Path of the Group I Muscle Afferents from the Hind Limb

Lloyd and McIntyre (1950) and McIntyre (1962) have shown that low-threshold muscle afferents from the hind limb enter the dorsal column but do not reach cervical level. This was in full agreement with Landgren and Silfvenius (1969) finding that the cortical potentials evoked by group I afferents from the contralateral hind limb were not affected by transection of the dorsal column at high

cervical levels. It is interesting to note that the group I paths from the forelimb and from the hind limb differ in their spinal course. Landgren and Silfvenius (1969) reported that the evoked responses disappeared after a superficial section in the dorsolateral fascicle at C1 level. The hind limb path, therefore, closely agrees with the location of the dorsal spinocerebellar tract (DSCT). There are thus two alternative possibilities: 1) the spinal component of the path comprises the DSCT neurones of the Clarke's column, and 2) the path utilizes other neurones with ascending axons travelling together with the DSCT.

Lundberg and Winsbury (1960) have in fact shown that group I_a, I_b and II muscle afferents excite the cells in Clarke's column, which is compatible with the first alternative. If DSCT collaterals are involved they must be given off below the cerebellar nuclei, because removal of cerebellum did not change the cortical group I response (Landgren and Silfvenius, 1969). One should bear in mind that the dorsolateral fascicle includes several ascending paths which are independent of the DSCT.

Landgren and Silfvenius (1969) went on further to claim that the group Ib path was largely independent of the Ia path, because a maximal group I volley evoked a response when the Ia path was made refractory by simultaneous stimulation with a maximal Ia volley at 20 per second.

For hind limb group I muscle afferents, the medullary relay in the projection path to the cerebral cortex was located by Landgren and Silfvenius (1971) in the subnucleus Z just rostral to the gracile nucleus and close to the dorsal surface of the medulla.

Mallart (1968) working on chloralose-anaesthetized cats reported that no responses were evoked in the VPL or CM (central median) nuclei of the thalamus by stimulating hind limb muscle nerves, especially that of medial gastrocnemius. [It is worth noting that Hunt (1951) by detailed analysis of afferent fibre diameter-receptor relation clearly demonstrated that all of group I and II muscle fibres of the medial gastrocnemius nerve are connected to muscle stretch receptors, ruling out the possible contribution by afferents from receptors in the connective tissue around the muscle]. However, Grant, Boivie and Silfvenius (1973) convincingly showed that axons of nucleus Z ascend through the midbrain and terminate in a restricted area of the VPL and of the VL (ventrolateralis) nuclei of thalamus.

The external cuneate nucleus (ECN) neurones also receive group I input, but these neurones are known to project to the cerebellum. There is no evidence in the cat that any ECN neurones project to the thalamus.

Do muscle afferents mediate a position sense?

The belief that muscle afferents have no access to consciousness in man was based on the findings of several investigators (Brindley and Merton, 1960; Browne, Lee and Ring 1954; Gelfan and Carter, 1967; Merton, 1964; Provins, 1958). According to this work, mostly done in 1960's, a muscle could be stretched over the whole of its physiological range without producing any clear kinesthetic sensation or any muscle sense in man. Although the spindle endings relay signals concerning the instantaneous value of the length of the parent muscle the signal from the primary endings

appears almost unusable for this purpose because it also depends upon so many other factors. It is non-linear with regard to the amplitude of the movements, it is dependent on the velocity and direction of movement and it is influenced by two separate kinds of fusimotor control system. The secondary ending, however, gives a much simpler signal and one which is fairly directly related to the length of the muscle, and which is relatively unaffected by movement. Moreover, it is influenced by only a single type of fusimotor fibre. In spite of the fact that it could be fairly easy to work out the length of various muscles on the basis of their spindle group II discharges and the knowledge of the amount of static fusimotor firing directed to each one of them, there is no evidence of the presence of a mechanism which might be equipped for this particular purpose.

These various experiments suggested that muscle afferents on their own are unable to mediate position sense, and second that joint afferents are solely responsible. Of course, a possible contribution by cutaneous afferents is not ruled out.

However, it is now known that spindles do contribute to kinesthesia because selective excitation of primary sensory endings by vibration usually results in a large error (up to 40 degrees) in matching the position of the vibrated arm to the other arm in a blindfold subject (Goodwin, McCloskey and Matthews 1972). As was mentioned earlier, the secondary endings by virtue of the regularity of their discharge and modification by a single form of fusimotor outflow, provide a much better length signal than the primary ending. Furthermore, the length sensitivity of the secondary ending under static conditions is often markedly increased by activation of the chain fibres at the spindle pole containing the ending, whereas the

length sensitivity of the primary ending under static conditions can be abolished by driving caused by chain fibre contraction. [The dynamic bag_1 fibre increases the length sensitivity of the primary ending greatly but only under dynamic condition]. Thus an excellent signal of the muscle length is provided in group II afferents during static fusimotor drive to the chain fibres. To obtain an absolute measure of muscle length the brain requires to calibrate the length signal for which it needs a measure of the state of activity of the chain fibres. This calibration signal is exactly the information provided by the primary ending when driven by active chain fibres, for at fusimotor frequencies up to at least 50 Hz the length sensitivity of the primary ending is abolished so that the Ia afferent continually monitors the aggregate static fusimotor outflow to the chain fibres (Boyd, 1985). It is perhaps significant that the static length sensitivity of secondary endings is often at a maximum during activation of chain fibres at 50 Hz, because the physiological frequency of gamma activation is lower than 50 Hz.

Thus the chain fibre intrafusal system is well suited to play a role in kinesthesia. There is as yet no evidence that it is used in this way, but the illustration serves to emphasize that the brain can, and no doubt does, use the intrafusal systems separately, or together, in many different ways (Boyd, 1985).

Observations at the time of early studies on fusimotor activity (1950's) gave birth to the introduction of the "follow-up length servo" hypothesis and the concept of "alpha-gamma linkage". Since it suggested that motor activities, including motor tasks involving the cortex, might be initiated via the gamma loop, it is preferred to discuss them critically and briefly.

The "follow-Up Length Servo" Hypothesis

Hunt (1951), Granit and Kaada (1952) and Merton (1953) reported increased fusimotor activity preceding that of alpha-motoneurones. Experiments on reflexly elicited movements (Eldred and Hagbarth, 1954) and on stimulation of various central nervous system structures (Elder, Granit and Merton, 1953) clearly demonstrated that almost invariably, fusimotor neurones possess lower thresholds than alpha motoneurones. These findings along with the suggestion of Kuffler and Hunt (1952) on an important function of the fusimotor neurones in maintaining a steady afferent discharge from the spindles in spite of shortening of the parent muscle, led Merton (1953) to put forward the hypothesis that the job of the gamma motor fibres was to supply the command signal in a "follow-up length servo" controlling muscular contraction. This hypothesis stated that some fast urgent movements could be produced by impulses from higher centres impinging straight on to the large alpha motoneurones, where as slow ordinary movements could be commanded from supraspinal structures by initially increasing fusimotor activity. Then the fusimotor activity causes contraction of the intrafusal fibres in the muscle spindle. The contraction stretches the primary sensory spirals in the spindle with a resultant increase in discharge of the group Ia fibre. The impulses of the group Ia fibre in turn produce monosynaptic, and probably polysynaptic excitation of its own and synergistic alpha motoneurones. Finally, the alpha motoneurones call forth the extrafusal muscular contraction and a new equilibrium of afferent discharge and extrafusal muscle length will be reached . In this system, therefore, the fusimotor discharge may be looked upon as signaling the demanded length of the muscle which is then produced

over the monosynaptic arc. The reflex was interpreted as a servo loop: muscle length to be the controlled variable, with muscle spindles acting as mis-alignment detectors and their feed back negative.

However, as objections increased, the follow-up length servo became less popular. No one was able to show that the gain of the gamma loop was sufficient to drive reasonably strong muscle contraction. Loop gain was thought to be limited by problems of stability given the relatively long loop delay. Some experiments against the hypothesis were carried out on jaw movements by Taylor and Davey (1968) with lightly anaesthetized cats and by Taylor and Cody (1974) on fully conscious cats, who recorded spindle activity of the jaw closing muscles and found that spindle discharge did not accelerate during active shortening as required by the follow-up length servo hypothesis. Instead, it always decreased. Similarly, Vallbo (1973) in micro-neurographic recordings from human muscle spindle afferents in awake human subjects failed to observe activity leading electromyographic (EMG) activity.

The consequence of these observations was a decline in popularity and also the replacement of the hypothesis with the notion of "servo assistance" of movement introduced by Matthews in collaboration with Stein (Matthews, 1972; Stein, 1974) in which the movements were seen to be initiated not purely by way of the gamma route but by inputs to both gamma and mainly alpha motoneurones. Consequently, there was no need for the gain of the servo loop to be so high, but the advantage of servo control could be retained.

Although the "follow-up length servo" hypothesis did not get much support subsequently, it stimulated considerable interest in the central control of gamma motoneurones.

Alpha-Gamma Linkage or Coactivation?

The concept of "alpha-gamma linkage" was introduced by Granit (1955) from observations made in early studies of fusimotor activity even before the recognition of different fusimotor types. In this concept fusimotor activity was thought to parallel that of alpha motoneurones, thus ensuring that afferent activity continued during muscle shortening. Hunt (1951) observed that alpha and gamma motoneurones (distinguished on the basis of spike sizes) always discharged together during reflex movement. In addition, Hunt and Kuffler (1951) observed that electrical stimulation of the small efferent fibres could partially maintain spindle afferent discharge during active shortening of the muscle. This led Granit (1955) to conceive the role of gamma efferents as maintaining spindle discharge during muscle contraction, and to introduce the phrase "alpha-gamma linkage" in respect of all such parallel discharge of two types of neurone. "Alpha-gamma linkage" does not specify whether this parallel firing of alpha and gamma motoneurones was one possibility or was the inevitable consequence of shared inputs. Moreover, it does not specify if the linkage occurs through some interconnection between the alpha and gamma motoneurones. Furthermore, it failed to specify the role of the two types of fusimotor neurones and did not explain what advantage derived from a separate fusimotor system if it were

always co-activated with alpha motoneurones. Therefore, the term "alpha-gamma co-activation" (Sears, 1964; Granit, 1970) is a better replacement.

In current usage "alpha-gamma coactivation" is a looser term implying some, but not necessarily a tight, coupling between alpha and gamma motoneurones. Coactivation also lies behind the concept of servo assistance, where fusimotor outflow is adjusted so as to compensate for spindle firing at approximate constant level (Matthews, 1972, Stein, 1974).

Coactivation has been described for the following descending systems:

1) The vestibulospinal tract exciting monosynaptically both alpha and gamma motoneurones to extensors (Grillner, Hongo and Lund, 1969). This pathway seems to act on static gamma motoneurones relatively selectively.

2) The medial longitudinal funiculus, originating probably from pontine reticular formation, coactivates predominantly static gamma and alpha motoneurones to flexor (Grillner, Hongo and Lund, 1969; Bergmans and Grillner, 1968).

3) The rubrospinal tract has also been found to act reciprocally on flexor and extensor motoneurones, either by co-exciting (flexors) or by co-inhibiting (extensor) alpha and gamma motoneurones (Hongo, Jankowska and Lundberg, 1969; Appelberg, Jeneskog and Johansson, 1975; Appelberg et al., 1982)

The best evidence for precise coactivation came from natural respiratory movement (Sears, 1964). The afferent discharge increased when the muscle shortened during contraction and decreased during passive lengthening in the relaxation phase. This pattern reversed

after a selective blockade of gamma axons and was therefore attributed to the efferent activation of the muscle spindles in parallel with the extrafusal shortening.

Coactivation of alpha and gamma motoneurones in humans was demonstrated through a series of technically elegant experiments by Vallbo and his colleagues (1970a,b, 1971, 1973, 1974a,b). These experiments in humans shift the balance of evidence away from the idea of servo assistance (Matthews, 1972) and back toward the early suggestion by Kuffler and Hunt (1952) that the main function of the fusimotor fibres is "to maintain the afferent discharge from spindles in spite of a certain amount of muscle shortening" so that their information input could be preserved at all times. It is worth noting that although many experiments done in this field did not confirm the idea of Kuffler and Hunt the results of Vallbo's experiments are directly against the idea of servo assistance.

Vallbo (1971) found that at the onset of a voluntary isometric contraction the excitation of spindle afferents invariably lagged behind the first burst of EMG activity, indicating that, at best, fusimotor neurones were activated at the same time as, but not before, alpha motoneurones were. Note that if the "follow-up length servo" were true, the activation of gamma motoneurones and spindle afferent fibres should precede the onset of EMG activity at the beginning of a voluntary movement.

The function of the fusimotor system must be considered separately for at least two subgroups of gamma motoneurones that govern different parameters of muscle spindle activity. The dynamic gamma motoneurones control the sensitivity of the primary endings to stretches of small amplitudes, and they may

therefore have special significance in situations in which the spindles should react to small perturbations and irregularities. Only static fibres are able to increase the firing of primary and secondary endings during muscle shortening (Lennerstrand and Thoden, 1968). Consequently, if the gamma loop and muscle spindles contribute to the excitation of alpha motoneurones during extrafusal shortening, the central command has to include the static gamma motoneurones. It may be, however, that the most important aspect of the coactivation of static gamma motoneurones with alpha motoneurones is to ensure that the muscle spindle afferents are ready to respond to small perturbations added on a large active muscle shortening in the line with the suggestion by Kuffler and Hunt (1952). Note that static gammas do not sensitize the primary afferent to small perturbations. However, in moderate extrafusal contraction dynamic beta would be active. [Strong contraction would bring in the largest alpha motoneurones and therefore the static beta motoneurones, Henneman's size principle (Henneman, Somjen and Carpenter, 1965)]. On the basis of such general considerations, the central nervous system is expected and does use the available possibility for separate control of static and dynamic gamma motoneurones (Taylor, Stein and Murphy, 1985; Donga et al., 1986 and 1988; Greer and Stein, 1990).

One should bear in mind that although parallel monosynaptic excitatory projections could provide a route for tightly coupled coactivation of alpha and gamma motoneurones, nevertheless even if monosynaptic projections were dominant, they might exist as two functionally separate groups of descending axons, one to the alpha and to the gamma motoneurones. Electrical stimulation in laboratory

preparations might, however, lack the potential to activate these pathways separately; but under physiological conditions intrinsic central circuitry might be capable of doing just that.

Alpha-Gamma Independence

In spite of findings reviewed above, there is considerable evidence to show that the central nervous system might independently influence both alpha and gamma motoneurones. Although, in man there is so far surprisingly little evidence for an independent control of fusimotor activity (Burke, McKeon, and Westerman, 1980; Burke et al., 1980; Burke, Hagbarth and Skuse, 1978, 1979; Vallbo, and Hulliger, 1979; Vallbo, Hagbarth, Torebjork and Wallin, 1979; Vallbo, and Hulliger, 1981). In contrast, findings of various degrees of independence of fusimotor and skeletomotor activity have been described in experimental animals (Appenteng, Morimoto and Taylor, 1980; Koeze, Phillips, and Sheridan, 1968; Loeb and Duysens, 1979; Prochazka and Wand, 1981; Sjostrom and Zangger, 1976). This was demonstrated strikingly by Granit, Holmgren and Merton (1955). They reported that on cooling or ablating the anterior lobe of the cerebellum in the decerebrate cat, the discharge of alpha motoneurones increased while that of gamma motoneurones decreased. So there seems little doubt that alpha and gamma motoneurones can be controlled independently. Furthermore, the pyramidal tract is believed to be a descending system that shows independent control of alpha and gamma motoneurones by the central nervous system, with the former receiving a monosynaptic projection while the latter does not (Clough and Sheridan, 1968; Clough, Phillips and Sheridan, 1971).

In summary, the examples discussed provided reasonable grounds on which it could be assumed that influences on alpha motoneurones from some descending tracts were different from those to gamma motoneurones, allowing the central nervous system the choice to independently influence afferent activity by way of gamma efferents in different motor plans.

Yet with the recognition of dynamic and different types of static gamma motoneurones, the issue had become more complex. One should answer questions like: The extent of coactivation of alphas with static and/or with dynamic gammas...etc? To be more specific one should try to decide if different types of gamma motoneurones are being controlled separately by higher centres in the central nervous system or not and this has of course attracted some attention in recent years.

SECTION B: LITERATURE REVIEW

The CENTRAL CONTROL of FUSIMOTOR NEURONES

Methods of Study

It is worth going briefly over different methods of investigation of fusimotor activity before reviewing any results from Vedel and others who worked on selective control of static and dynamic gamma axons by sensorimotor cortex of the cat.

Activity of fusimotor neurones can be studied by different methods. However, no single method is available that can provide comprehensive information on synaptology and selectivity of a particular pathway and on the strength and type of fusimotor effects elicited. At first, recording of afferent rather than efferent

discharges was chosen for studying fusimotor activity because it is easier to isolate large spindle afferents in the dorsal roots rather than small gamma efferents in the muscle nerve. It can also provide information that is still unobtainable by the apparently more direct recording of efferent discharges. The main advantage of this approach, especially when it is quantitative, is that it permits classification of the fusimotor effects as static and dynamic, relying on the original criteria, whereas in the case of efferent recording, direct functional identification is not possible as no absolute difference is known, for example between the conduction velocities of the two static and dynamic types of fusimotor axons. Moreover, the degree of contamination of one type of action by the other can also be estimated (Appelberg et al. 1981). Further, the measures taken estimate total fusimotor outflow to the spindle at issue, and for functional consideration this may be more relevant than quantitative data from single gamma motoneurones. On the other hand, it has some disadvantages. Unless the EMG is recorded with the highest resolution, gamma action can not be separated from beta action. Moreover, inhibitory effects can only be detected when fusimotor neurones discharge spontaneously. Finally, weak effects on one type of gamma motoneurone may go unnoticed when activity of the other type is dominant. This holds true especially for weak dynamic fusimotor effects when static action prevails.

Intracellular recording from gamma motoneurones is another technique to assess fusimotor activity. Its main limitation for gamma motoneurones is the limited size of the sample, attributable to the technical difficulties in recording from small cells.

Intracellular recordings are further limited, as they do not permit a direct classification of gamma cells as either static or dynamic, and as they tend to be biased towards analysis of short-latency effects.

A recent method adopted by Gladden and McWilliam for the first time in 1977a is to assess the activity of fusimotor neurones through direct observation of exteriorised tenuissimus muscle spindles, and this will be thoroughly discussed later in this section.

Criteria to Distinguish between Recruitment of Different Gamma Populations

The question of how to "distinguish between static and dynamic fusimotor activation" is extensively covered by Matthews and is summarized in his review on muscle receptors and their central control (1972). However, it is worth going briefly over criteria used in interpreting our results. Those are broadly categorized into two fusimotor effects: dynamic and static. The dynamic effects are brought about by dynamic bag contraction which becomes active mechanically if dynamic fusimotor axons are excited with a frequency of more than 15-20 impulses/sec. The main effect of stimulating a dynamic fusimotor axon is on the primary ending although less frequently secondary endings are also weakly affected. As a result of dynamic fusimotor neurone stimulation the discharge frequency of the primary ending rises moderately at constant length and increases dramatically during ramp stretch compared to the passive spindle; and finally it might lessen the slowing of the primary discharge.

One should bear in mind that on central stimulation, both dynamic and static fusimotor axons might be recruited and a mixed effect appears from afferent recordings. In addition,

skeletofusimotor neurones that innervate both extra- and intrafusal fibres and which are categorized into dynamic and static beta fibres, may well get excited and in turn can elicit contraction in dynamic bag_1 and long chain fibres. Therefore, in interpreting the effect of central stimulation using only afferent recording, one should be very cautious not to attribute the effects to a wrong class of neurones which happens without much difficulty.

Stimulation of static fusimotor axons brings about the contraction of static bag_2 and/or chain fires. The impact on secondary sensory endings is more pronounced if chain fibres are innervated. However the typical effect of static fusimotor stimulation on the primary ending is to increase its discharge frequency at constant length and to diminish its dynamic responsiveness during ramp stretch. It also lessens the abrupt slowing of primary discharge to the release of stretch. It is claimed that a paradoxical effect on stimulation of static fusimotor axon is obtainable if it is stimulated with a low frequency which increases the dynamic sensitivity of the primary ending (Baumann, Emonet-Dénand and Hulliger, 1982). This paradoxical effect is not understood but may well be significant physiologically since the discharge rate of static fusimotor neurones is normally well below 75/sec and small perturbations of length often occur.

Therefore, it is convenient, as in the case of Vedel and Mouillac-Baudevin work (1970), to attribute pure dynamic and pure static effects to contraction of dynamic and static fusimotor systems. However, when it comes to interpret the results that are classified somewhere in between the two pure responses, it is difficult and sometimes impossible. Of course, one might postulate;

however, it may well be too far from what exactly happened cellularly at the level of the muscle spindle. Hence, there seems to be a necessity to have an alternative method of looking at the impact of central stimulation on the fusimotor system, not by substituting afferent recording technique, but rather by complementing it.

Effect of Central Stimulation on the Fusimotor System

The central influence on the gamma system was studied for the first time by Granit and Kaada (1952). They found that the discharge of both the gamma axons and the muscle spindle afferents were facilitated or inhibited by stimulation of various parts of the central nervous system, including cerebral cortex. After that Elder, Granit and Merton (1953) proposed two motor pathways, that is, the alpha and the gamma systems, suggesting that, inasmuch as the gamma system is well provided with diffuse central connections, all concepts involving motor activity must be reconsidered from this point of view. In continuing their work, many researchers have dealt with a number of unsolved problems centering around the general question of the scope of the central control of gamma efferents and its significance in the proprioceptive regulation of muscular contraction.

It was unknown to what extent supraspinal gamma control can display itself after cutting the dorsal roots. It has been claimed by Hunt (1951) that in spinal cats spontaneous discharge in gamma efferents ceases after de-afferentating that region of the cord. However, in the decerebrate cat such central effects on the gamma motor neurones may persist virtually unchanged after section of the dorsal roots of the segments of the spinal cord in which the studied

fusimotor neurones lie. They thus appear to depend very little, if at all, upon support from the muscle proprioceptors. Indeed, it is been claimed that it is easy to tell from the behavior of the muscle spindle whether it has been de-efferented or not (Elder, Granit and Merton, 1953); but with regard to de-afferentation, it is almost impossible to tell whether the afferent connections are intact or not. All the signs of gamma activation usually remain: irregular discharges, high spontaneous firing rate (or low threshold if silent) and a brisk reaction to twisting the pinna (Elder, Granit and Merton, 1953).

Regions of the central nervous system where stimulation has been found to have effects on fusimotor neurones include the reticular formation, the motor cortex, the pyramidal tract, the basal ganglia, the thalamus, the red nucleus, the cerebellum, the amygdala, hypothalamus,.....etc.

As so often happens on applying electrical stimulation to a complex structure such as central nervous system the effect produced from a particular site is often far from constant. Sometimes it may even change from static to dynamic or from gamma excitation to gamma inhibition on altering the strength or frequency of stimulation, the depth of anesthesia, or even on simple repetition of the stimulus. Not surprisingly, therefore, no comprehensive scheme has yet been formulated explaining the relation between regions which directly or indirectly control the fusimotor neurones, and in what manner and for what purpose.

Independent Control of Dynamic Gamma and Static Gamma Motoneurones

When it was recognized that there are two subgroups of fusimotor neurones that have preferential actions on the dynamic or static sensitivity of the muscle spindle afferents, the possibility of their independent control also become important. In 1961 a short note by Jansen and Matthews came as the earliest indication of independent control of static and dynamic properties of muscle spindles by anterior lobe of the cerebellum in the decerebrate cats. The findings were reported in full the following year (Jansen and Matthews, 1962) and gained immediate support by observations made by Appelberg (1962) where the red nucleus was being stimulated while recording from primary afferents, and also by Granit and Van der Meulen (1962). Later work on the organization of the fusimotor system has shown that static and dynamic gamma cells have different intrafusal distributions, and when active, produce fundamentally different effects (Barker et al. 1976b; Matthews, 1972).

In 1965, Appelberg and Emonent-Denand, working on medial gastrocnemius muscle of cats anaesthetized with barbiturate and urethane reached the conclusion that central stimulation in appropriate regions may, in a rather selective way, activate different populations of fusimotor fibres having either a dynamic or static effect on the spindles. However, no attempts were made in those experiments to relate effective stimulating regions to histologically defined areas of the brain, although it was suggested, from stereotaxic coordinates, that a central area for control of muscle spindle dynamic sensitivity was situated in the red nucleus area of the mesencephalon.

Vedel and his colleagues provided various examples of a rather selective central activation of either static or dynamic neurones using afferent recording from primary endings in cats under halothane. With regard to the possible existence of higher centers than the red nucleus in the mesencephalon having descending systems which influence fusimotor neurones, the work of Vedel (1965) is of considerable interest. This author obtained contralateral spindle effects very similar to the ones described by Appelberg and Molander (1967) by repetitively stimulating the sensorimotor cortex. He claimed that the pyramidal tract in cats exerts its control exclusively on the dynamic fusimotor neurones. This conclusion was based on the following evidence:

i) Stimulation of the postcruciate area produced an augmentation of the dynamic responsiveness of a primary ending in the soleus muscle to a ramp stretch.

ii) A similar change was observed on stimulating the medullary pyramid.

iii) The effects of cortical stimulation could be eliminated by electrocoagulation confined to the medullary pyramid.

There can be little doubt that these results strongly indicate pyramidal tract control over the dynamic fusimotor neurones. However the question was raised as to whether or not the pyramidal control is exclusively over the dynamic fusimotor neurones. In subsequent work, Vedel and his colleagues found that responses produced by stimulation of the reticular formation in the medulla, pons and mesencephalon tended to be rather labile and at some sites the effect might change from predominantly static to predominantly dynamic on repeated application of the stimulus (Vedel and

Mouillac-Baudevin, 1969a,b). A more thorough investigation of the effects of cortical stimulation showed that on varying the depth of anaesthesia static effects could sometimes be obtained instead of the more usual dynamic effect previously described (Vedel and Mouillac-Baudevin, 1970).

Gladden and McWilliam (1977b) suggested, on the basis of their observations of exteriorised tenuissimus muscle spindle in anaesthetized, decerebrate and spinal cats, that their results were compatible with the conclusion that the central nervous system can control the dynamic bag_1 fibres of muscle spindles entirely independently from the static bag_2 fibres and nuclear chain fibres. Gladden (1981) confirmed the suggestion stated above and reported that firstly contraction of dynamic bag_1 fibre often occurred sequentially with that of other intrafusal muscle fibres. They were the last to become spontaneously active in light anaesthesia and the first to stop during deepening anaesthesia. Secondly intracellular recording from dynamic bag_1 and static bag_2 fibres in the same pole during recruitment of gamma axons in the muscle nerve showed no coupling between the junctional potentials of the two. Therefore, physiological evidence well proves by now that dynamic and static fusimotor neurones are largely independently controlled.

Independent Control of Different Types of Static Gamma Motoneurones

Gladden and McWilliam (1977a,b) developed a new method of observing intrafusal fibre contractions in response to reflex fusimotor activity. Unlike before (e.g. Hunt 1951 in which fusimotor activity was recorded from cut ventral root filaments), it was now possible to visualize contractions of the three types of

intrafusal fibres and from that, to deduce the type of fusimotor neurones that were active. Although this method had the advantage of revealing the type of fusimotor neurones that were influenced by a particular input, it did not present the opportunity of providing quantitative information such as the discharge frequencies of the fusimotor neurones that may have been influenced. However, this method of Gladden and McWilliam (1977a,b) was and still is the most sensitive in providing information about activity in particular sub-groups of the fusimotor system. Criteria had to be set as to what the different intrafusal fibre types looked like under the light microscope. Distinction between nuclear bag and nuclear chain fibres was based on their relative diameters, with the latter having a smaller diameter than the former. Dynamic bag_1 fibres were distinguished from static bag_2 fibres by their greater sensitivity to topically applied acetylcholine (Gladden 1976). A reasonable and important assumption made was that movement of dynamic bag_1 fibres signified that dynamic gamma motoneurones were active, while movement of static bag_2 or nuclear chain fibres signified activity of static gamma motoneurones.

A consistent observation made by the above authors was that static bag_2 fibres were active in the lightly anaesthetized preparations (cats under barbiturate anaesthesia). Sb_2 fibres were also spontaneously active in decerebrates although this decreased with time. In eleven out of sixteen spindles observed, nuclear chain fibres were not as frequently spontaneously active while only three dynamic bag_1 fibres showed spontaneous activity in the lightly anaesthetized preparation and were never found to be spontaneously active in the decerebrate preparation. Clearly, these observations

strongly implied that the central nervous system of reduced preparations was capable of activating fusimotor neurones selectively to one type of intrafusal fibre.

Gladden and McWilliam (1977a and b) and Gladden (1981) also studied recruitment patterns of fusimotor neurones during electrical stimulation of the central nervous system. The structures stimulated were the contralateral cerebral cortex in the region of the postcruciate dimple and a smaller area just anterior to the cruciate sulcus. They reported that as anaesthesia lightened, cortical stimulation usually recruited static bag_2 fibres alone. Stimulation of smaller areas within the area where electrical stimulation was effective resulted in recruitment of nuclear chain fibres, dynamic bagl fibres or extrafusal fibres. It is not so clear what the order of preference of the stimuli in recruiting different intrafusal fibres was. "In only two instances contraction of the static bag_2 fibres could not be separated from contraction of nuclear chain fibres", (Gladden 1981). It appears as though electrical stimulation of the cerebral cortex in the regions described above was generally selective in recruiting static bag_2 fibres independently of the rest. Selective recruitment of nuclear chain fibres independently of static bag_2 was not as common.

Dynamic bag_1 fibres were never found to be individually recruited by electrical stimulation in the pericruciate cortex. In all six muscle spindles in which dynamic bag_1 fibres were recruited, static bag_2 fibres were recruited simultaneously as well. However, it is also reported that it was possible to find cortical areas where stimulation produced greater movement in the dynamic bag_1 fibres as opposed to that in static bag_2 fibres. In any case it was possible to

recruit static bag_2 fibres alone by altering electrode positions in areas from which other fibres may have been simultaneously recruited. Descriptions of extrafusal recruitment patterns in relation to that of any of the intrafusal fibre species were not available due to visual focusing technicalities which did not permit that aspect of central control of motoneurones (both alpha and gamma motoneurones) to be tested.

The importance of the observations of Gladden and McWilliam (1977a,b) and Gladden (1981) is that they were the first direct evidence from which it was concluded that, not only was the central nervous system capable of independently controlling dynamic fusimotor neurones from static (Jansen and Matthews, 1962; Appelberg and Emonet-Dénand, 1965; Appelberg and Molander, 1967; Appelberg and Jeneskog, 1969; Yokota and Voorhoeve, 1969; Vedel and Mouillac-Baudevin, 1969a,b and 1970; Jeneskog 1974; Jeneskog and Johansson 1977; Appelberg, 1981) but that it was also capable of independently influencing those innervating static bag_2 fibres from those innervating nuclear chain fibres. However, Gladden's work (1981) is limited to a cortical area from which static bag_2 fibres could be selectively recruited.

As already pointed out, the method of Gladden and McWilliam (1977a and b) remains as possibly the most sensitive way of discerning influence of a given central structure on different intrafusal fibres. However, its limitation is that it is probably the most difficult method to adopt and at present none other than Gladden's group are using it.

Although Gladden and McWilliam obtained interesting results; they did not cover the cerebral cortex with a sufficient depth of paraffin to prevent CO_2 escape from the cortex. During the course of cortical stimulation which might have taken 2-3 hours or even more, CO_2 escape would cause deterioration in the cerebral blood flow. It is well known that vascular resistance in the brain is locally modulated by extracellular pH (Betz and Heuser, 1967; Betz and Kozak, 1967 and Raichle et al., 1970) and that this mechanism contributes to a homeostasis of intracerebral pH. CO_2 is a volatile acid itself and can determine strongly the pH of a medium, Kuschinsky et al. (1972) demonstrated that there is a correlation between periarteriolar pH and the vessel diameter at a physiological concentration of potassium. Furthermore, a dependency exists between total cerebral blood flow and pH measured on the cortical surface (Betz and Heuser, 1967 and Betz and Kozak, 1967). As a result of any deterioration of the blood supply one might expect alterations in the behaviour of neurones of interest within that area and ultimately change the nature of effects in periphery. Therefore, in brief, had the cortex been deeply covered with mineral oil in the direct observation experiments of Gladden and McWilliam (1977a,b), different results might have been obtained.

One limitation of this technique and also of afferent discharge recording is that neither of the techniques can reveal any slight activation of bag fibres. Boyd (1976) claimed that because there are no action potentials in bag fibres, if they are stimulated below 10-15 impulses per second, they do not contract. If by any means (e.g. cortical stimulation) fusimotor neurones become slightly active (i.e. with frequency of less than 15), neither afferent discharge

recording nor direct observation techniques can reveal it. However, there is one technique to go round this problem and that is intracellular recording from bag fibres through capillary micro-electrodes penetrating into the bag fibres. One problem with this technique is that it depends on reading junctional potentials which decay with distance from the motor end plate, for junctional potentials do not propagate. Therefore, to claim positively that bag fibre(s), become active in both poles, one requires to record from one microelectrode implanted in each pole of the bag fibre.

It was known from the work of Barker et al. (1973), Bessou and Pages (1975) and Boyd et al. (1977) that static gamma axons may innervate chain fibres, Sb_2 fibres or both together. However at first it appeared that static gamma axons did not selectively innervate one type of fibre, Sb_2 or chains, in all the spindles which were innervated. However, Gladden and McWilliam (1977a,b) and Gladden (1981) suggested that since Sb_2 fibres were frequently active without any chain fibre activity in anaesthetized or decerebrate cats there might be a group of static gamma axons which innervate Sb_2 fibres predominantly. In 1986 Boyd on the basis of physiological tests, divided static gamma motoneurones into two groups one innervated predominantly static bag_2 fibres in all spindles supplies, with some chain fibres occasionally in addition. Another group of static gamma supplying predominantly chain fibres with some Sb_2 fibre involvement. Boyd suggested also that the static gamma axons supplying predominantly chain fibres had type m_c endings on the chain fibres. Arbuthnott et al. (1982) had earlier divided endings on chain fibres

into types m_c and m_a. Boyd thought that the type m_a endings on chain fibres were the terminations of the other type of static gamma axon which predominantly innervated Sb_2 fibres.

Gladden and Sutherland (1989) in their histological approach traced the axons to their endings on chain fibres through serial sections of tenuissimus muscles by combined light and electron microscopy. They proposed that static gamma axons with type m_c endings on chain fibres constitute a discrete entity, because these axons had no endings on Sb_2 fibres. Also, some axons with type m_a endings on several chain fibres did not innervate Sb_2 fibres. Gladden and Sutherland (1989), therefore, proposed that there are three types of static gamma axons: one innervating predominantly static bag_2 fibres with some chains having m_a endings; a second group innervating chain fibres mainly with m_a ending and the third group specifically innervating chains, with m_c endings.

The purpose of the present work was firstly to investigate whether the specific types of intrafusal fibre can be recruited reproducibly from the same areas in the pericruciate cortex in different cats. Secondly, to find out whether different types of fusimotor neurones can be independently recruited from specific areas within the sensorimotor cortex of the cat. Thirdly, to find out if two or three types of static gamma motoneurones can be controlled independently by the sensorimotor cortex to any degree. The final objective was to map the sensorimotor cortex topographically.

CHAPTER TWO

MATERIALS and METHODS

The aim of the preparation was to record from muscle spindle afferents of the tenuissimus muscle of the cat's hind limb while stimulating sensorimotor cortex to assess the nature of their central control through gamma motoneurones.Therefore, procedures which were carried out will be discussed in the following consecutive order:

A. Surgical Procedures: First stage

B. Experimental Set-up

C. Experimental Procedure: Dorsal roots

D. Surgical Procedure: Second stage

E. Experimental Procedure: Sensorimotor cortex stimulation

Twenty three cats of either sex in the weight range of 2.0 to 3.8 Kg were used for the present investigation.

A. SURGICAL PROCEDURES: First Stage

The following surgical techniques were common to all experiments and are given in chronological order.

Anaesthesia

Chloralose (40 mg/kg) was used in the first and the last two experiments. Induction of anaesthesia was done by intramuscular injection of a combination of Vetalar (Ketamine Hydrochloride, 22 mg/kg) dose and Rompun (Xylazine, 1.1 mg/kg) dose which anaesthetized the animal deeply enough for just under an hour, time quite sufficient to cannulate the superficial vein in the forelimb

and inject the chloralose , the temperature of which was 40°C while perfusing it into the body. Subsequent experiments were performed under barbiturate anaesthetic.

Induction of anaesthesia by barbiturates was by intra-peritoneal injection of 45 mg/kg of sodium pentobarbitone (Sagatal, May and Baker). Additional supplements (usually ≤0.1 ml) were given via the intravenous cannula, cautiously. Supplements of anaesthetic were not usually necessary for the whole period while carrying out surgical procedures. After this period the animals were treated cautiously because it was of crucial importance to maintain a satisfactory level of anaesthesia - not too light for the animal to suffer and not too deep to silence the gamma motoneurones' spontaneous activity.

Shaving

Once anaesthetized, the cat was prepared for surgery by shaving the forelimb, hind limbs (both medial and lateral aspects), back, throat region and top of the head with fur clippers.

Tracheostomy

A pretracheal midline incision was made through the skin from the suprasternal notch to the hyoid bone. The skin was retracted and the superficial muscles covering the trachea were separated by blunt dissection to expose the trachea. Any overlying connective tissue and the sides of the trachea was cleared by blunt dissection. A linen thread was passed round the trachea using an aneurysm needle. The thread was then tied in a half knot round the trachea. The trachea was lifted by the thread and a cut made half way through it

between two cartilaginous rings cranial to the thread. A small longitudinal cut was given to the caudal ring in order to ease insertion of cannula into the trachea. The caudal edge of the incision was gripped with Spencer-Wells forceps and a glass cannula of appropriate size was then slipped into the trachea and tied in position with the thread. The incision was then closed with Michel suture clips.

Intravenous Cannulation

An intravenous cannula was inserted into a superficial branch of the cephalic vein of the right forelimb. Three way taps were attached to the end of the cannula to allow syringes to be connected. This allowed the infusion of supplementary doses of anaesthetic when required. Any nutritive solution (Dextran or a mixture of D-Glucose and sodium bicarbonate- 10 - 20 ml.) was given through the same means as well.

Hind limb Denervation: Femoral and Obturator Nerves

With the animal still in the supine position it was appropriate to carry out denervation of the medial aspect of the left thigh at this stage. An incision, about 4 cm long, was made from the ileopectineal arch along the line of the femoral neurovascular bundle. The femoral nerve was exposed. A thin cotton roll soaked in Lidocaine (2%) was looped round the femoral where it emerges from the dorsal ileopectineal arch, to minimize any possible central effect through afferents when cutting the nerve. The cotton roll was removed after a minute and femoral nerve was cut.

The obturator nerve gives off a superficial branch called the gracilis nerve which lies in between two adductors namely femoris and brevis before becoming superficial. It ultimately supplies the gracilis muscle. Following this nerve centrally, by retracting the muscles surrounding it, enables one to approach the deep branches of the obturator nerve which lie next to the pubis. When the superficial and the three deep branches of the obturator nerve had been exposed, they were sectioned taking care not to cut any major blood vessels at the same time. The incision was then closed with sutures, rather than clips which might occlude the femoral artery by pressure during the course of the experiment.

The same procedure was carried out to denervate the right hind limb as well, in case the left hip denervation did not go well. This avoided having to turn the animal back to the supine position to cut the femoral and obturator nerves.

Cannulation of the Right Femoral Artery

The right femoral artery was cannulated by separating it from the femoral nerve and vein over the upper half of the thigh. Two pieces of linen thread were passed under the artery each one at the upper and lower ends of the freed artery. The lower end thread was then ligated and the upper one half tied. A pair of Spencer-Wells forceps were clamped on the artery just above the upper ligature. The artery was opened between the ligatures and a white (or red)-luer nylon cannula (Portex) was inserted. The upper ligature was made firm but not tight around the cannula, and the Spencer-Wells forceps removed. The cannula was passed up the artery until the tip

was estimated to be at or near the bifurcation of the aorta. The upper ligature was then made secure. The skin incision was sutured and the animal was turned over to lie prone on the operating table.

The next three procedures were followed in experiments in which muscle spindles were isolated.

Isolation of Muscle Spindles in Tenuissimus Muscle

In a series of experiments in which the spindles of tenuissimus muscle were to be directly visualized, uncovering of muscle spindles had to be performed. The long process of uncovering of muscle spindles was carried out by Dr. Gladden. Although I learnt to locate muscle spindles in the tenuissimus muscle, these experiments require extensive microdissection to uncover the spindles sufficiently to identify the intrafusal fibres and record their movements while avoiding damage to their nerve supply. this required considerable experience. The cats in this series of experiments did not undergo the preceding surgical procedure (e.i., laminectomy or extensive hind limb denervation).

Once the procedures mentioned above were carried out, the cat was turned over to the prone position. An incision was made from just below the base of the tail over the posterior aspect of the thigh to the popliteal fossa. The lateral edge of biceps femoris was freed along its edge by blunt dissection. The biceps femoris was reflected medially to expose the sciatic nerve and tenuissimus muscle. The muscle was dissected free from surrounding tissue and reflected into a glass bottomed bath containing Krebs solution (in mM): NaCl, 119; KCl, 4.7; KH_2PO_4, 1.2; $NaHCO_3$, 24.8; $CaCl_2$, 2.5;

$MgSO_4$, 1.2 and glucose, 1 g/l; equilibrated with a 95% O_2, 5% CO_2 gas mixture. The sciatic nerve was severed below the tenuissimus nerve, and it was also necessary to cut the nerves to biceps femoris, semitendinosus and semimembranous to free the muscle with the sciatic nerve pedicle so that it could be exteriorised. The bath was mounted on a microscope stage and the muscle was illuminated from below.

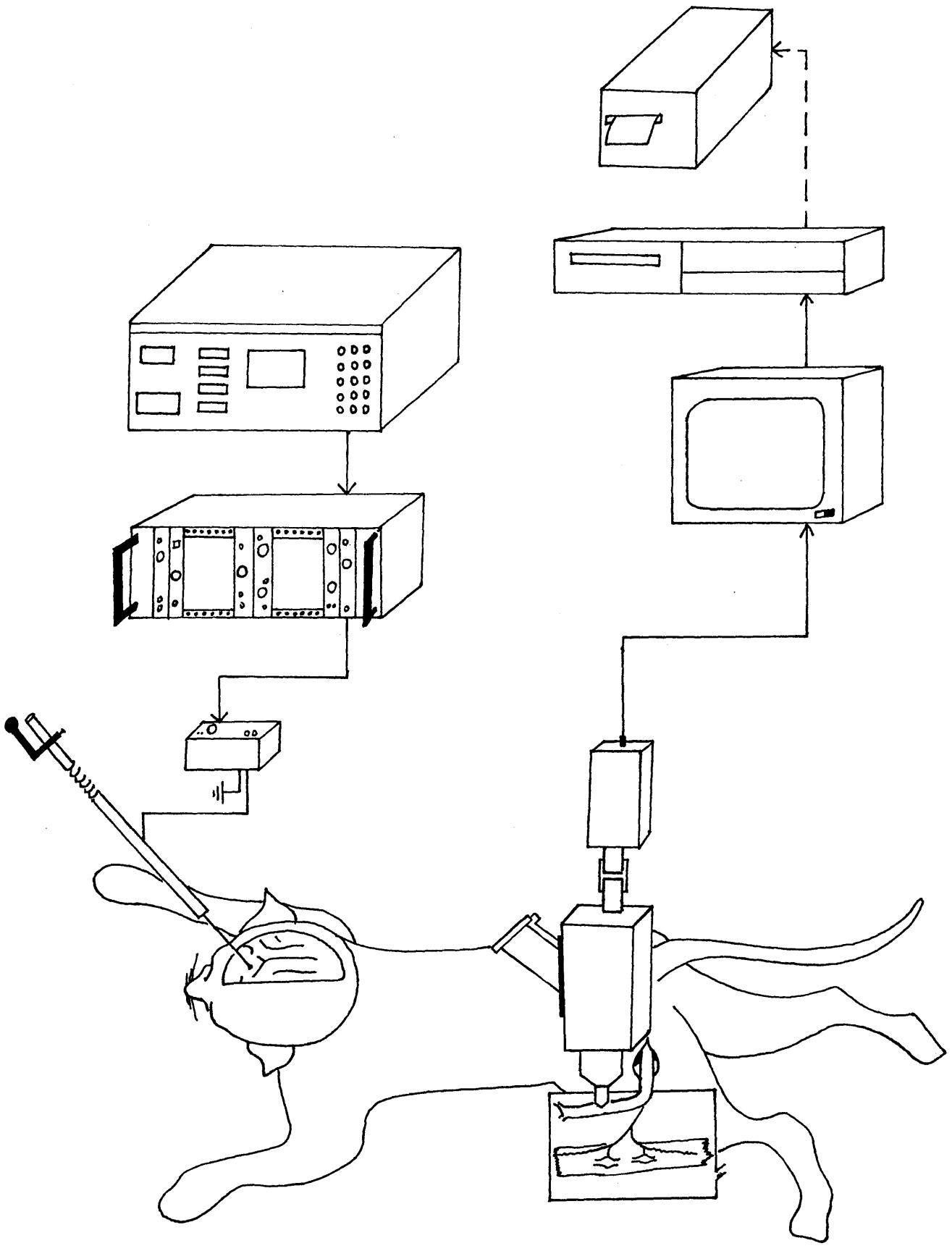
The tenuissimus muscle normally receives its blood supply from branches of the gluteal, deep femoral and popliteal arteries. Where the muscle was dissected free and reflected into the bath these vascular supplies were severed. However, a certain amount of vascular re-routing usually took place and the small blood vessels serving the sciatic nerve and the tenuissimus muscle nerve provided an adequate blood supply to the portion of muscle in the bath.

Once the tenuissimus muscle was in the bath, a spindle fluid space was located under a binocular dissecting microscope (Wild-Heerbrugg). In most tenuissimus muscles the fluid spaces could not be seen at this stage. The extrafusal fibres of the tenuissimus muscle were removed until the fluid spaces of muscle spindles became clearly visible and the intrafusal fibres could then be directly observed using a high power light microscope or/and could be displayed on a TV monitor (Phillips) and at the same time recorded on videotape (videocassette recorder, UVCSR, model CR-8200E; width of the videocassette tapes 19 mm (3/4) or VHS Fergusson Videorecorder)-fig 1. Usually three muscle spindles were dissected.

Fig 1. Diagram of the set-up used for isolated muscle spindle experiments. A. Devices from top to bottom are: Digitimer, Neurolog set, Isolated Stimulator and Stimulating Monopolar Electrode. B. Devices are: Video Copy Processor, Videocassette Player, Monitor, Videocamera, Light Microscope and the Muscle Bath.

A. Stimulus Control

B. Video Recording and Processing



Identification of Intrafusal Fibres

Nuclear chain fibres could easily be distinguished from nuclear bag fibres by their smaller diameter. It was sometimes possible to distinguish between Db_1 and Sb_2 fibres by their mechanical behaviour (Boyd, Gladden and Ward, 1977). If this was not possible during the experiment, the bag fibres had to be identified histologically after the experiment was finished.

According to Barker et al. (1976a) the Db_1 fibre is characteristically dissociated from Sb_2 and chain fibres in the equatorial region. Indeed, each of the Db_1 and Sb_2 fibres was separated from the chain fibres in individual compartments of the inner capsule. However, the Db_1 fibre is said to be consistently non-aligned with the chain and Sb_2 fibres throughout the equatorial and juxta-equatorial regions (Barker et al., 1976). It is worth noting that differences in the diameters of the Db_1 and Sb_2 fibres can not be a reliable difference, for it is too inconsistent. However, Gladden (1976) showed that the elastic tissue round Sb_2 fibre is considerably more in the polar regions compared to that around the Db_1 fibre, which provides another alternative way to distinguish between the two nuclear bag fibres (see figures 48 and 49).

Histological Procedure

Four tenuissimus muscles were excised and the whole muscles were fixed without further dissection for 12 hours at room temperature. Specimens were then postfixed with osmium tetroxide (pH 7.4), dehydrated in ethanol and flat-embeded in Araldite resin. Transverse 1-2 μm thick serial sections were cut from approximately

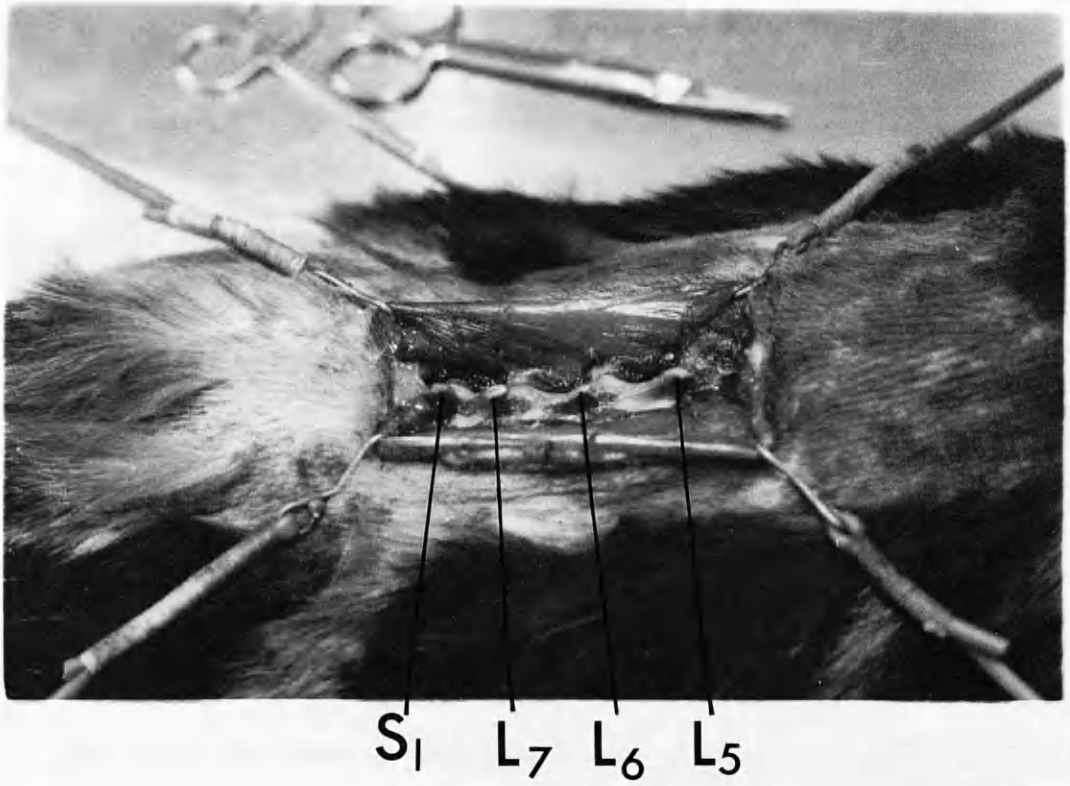
one pole of the muscle spindle to the other using a Reichert-Jung ultratome (model 2050). The sections were then stained with 1% toluidine blue, and studied using a light microscope with X40 and X100 oil objectives.

Laminectomy

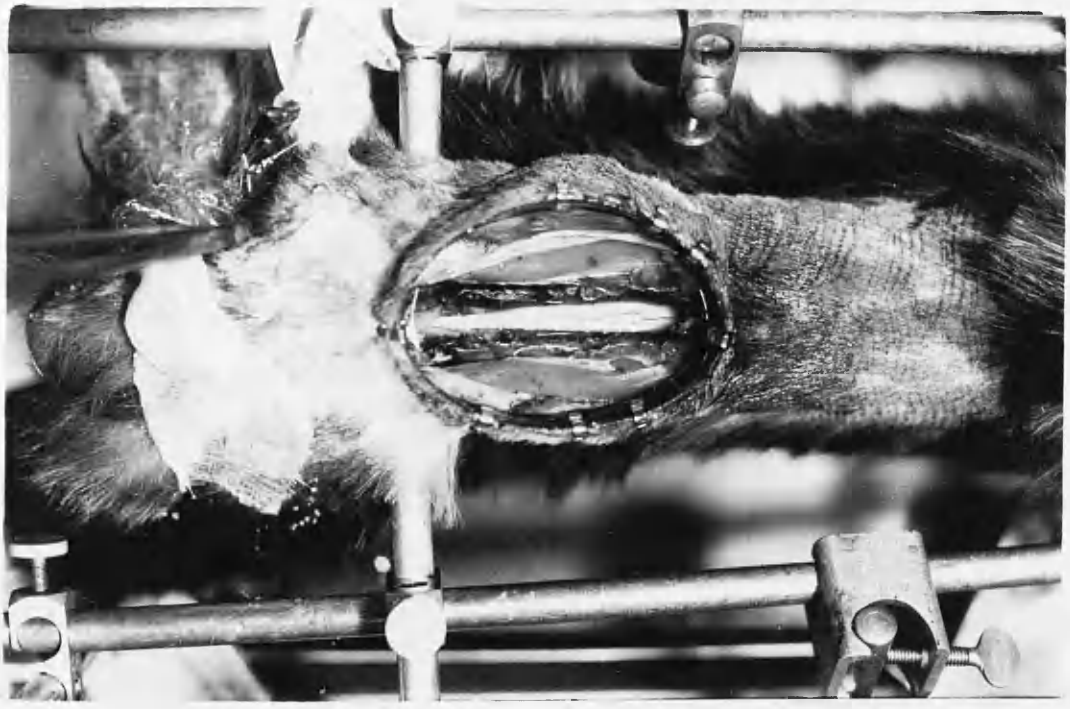
The purpose of the laminectomy was to expose the spinal cord and its roots without damaging them and with the minimum loss of blood. A midline skin incision was made along the vertebral column from L4 to the sacrum. The skin on both sides was freed from the underlying fascia by blunt dissection. With the skin flaps pulled back, cutaneous nerves emerging from the body wall and running to the skin on the left and right sides of the animal were located and cut. Two parallel incisions of the same length as the skin incision were made on either side of the dorsal processes of the lumbar vertebrae. The longissimus dorsi muscles on both sides were separated from lumbar multifidus muscles of the vertebral column, and held aside by retracting hooks (fig 2,A). The multifidus muscles were then cleared from the vertebral column and removed and the longissimus dorsi muscles were denervated. To begin the laminectomy, the joint between S1 and L7 was opened by gripping the L7 spinous process in Spencer-Wells forceps and lifting the vertebral column as much as possible. Lifting the vertebral column encouraged the spinal cord to remain on the floor of the vertebral canal, out of the way of the bone nibblers. One jaw of a large pair of nibblers was inserted into the joint and the bone forming the wall of L7 was cut away which exposed the dorsal longitudinal ligament. Cutting the dorsal longitudinal ligament by using a pointed pair of scissors allowed the

Fig 2. A. The exposed vertebral column from the right side. The spinous processes of vertebrae L5, L6, L7 and S1 respectively are visible from right to left. B. The exposed spinal cord, after completion of the laminectomy, in paraffin pool.

A



B



use of a small bone nibblers to remove the rest of the vertebra. Each vertebra from L7 to L5 was removed in a similar fashion (fig 2,B). Any jagged edges of bone were trimmed with a small pair of bone nibblers. The cord was then covered with a moist swab (or cotton roll) and the incision closed with Michel suture clips. Note that unlike the three previous procedures the following surgical procedures were carried out on cats undergoing the dorsal root-recording experiment.

Hind limb Denervation: Sciatic Nerve

With the cat in the prone position an incision was made from just below the base of the tail over the posterior aspect of the left thigh to 2 cm below popliteal fossa. By blunt dissection with scissors, the lateral edge of biceps femoris was freed along its length and the muscle was reflected medially to expose the thick sciatic nerve. At this point it was usually possible to see the thin tenuissimus muscle as it crossed the fat pad in the popliteal region. The sciatic nerve was exposed by blunt dissection between gluteus maximus and biceps femoris. The gluteal muscles were lifted using forceps to expose the sciatic nerve as much centrally as possible. It was then the time when the tenuissimus could best be seen. Tenuissimus (abductor cruris caudalis) muscle originates from the tip of the transverse process of the second caudal vertebra and inserts with biceps femoris into rather more than one third of the dorsal border of the tibia along its lateral margin. It acts as a weak abductor and extensor of the thigh and as a weak flexor of the shank. It is innervated by a branch of the sciatic nerve and sometimes a

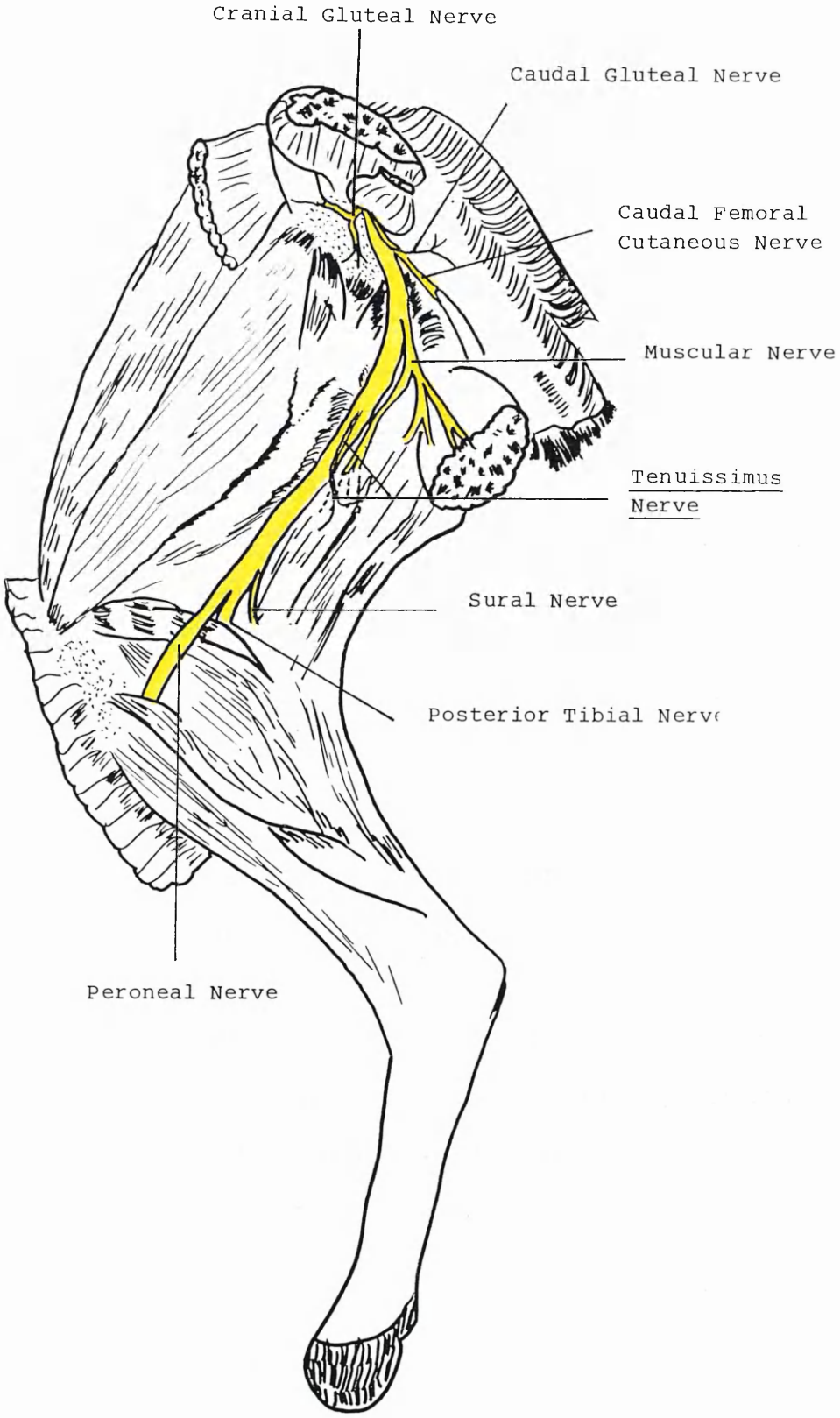
second nerve higher up in the sciatic and receives its arterial supply from branches of the caudal gluteal, deep femoral and popliteal arteries.

The first nerves cut were those so-called caudal and cranial gluteal nerves which branch off the sciatic trunk even before it comes out of great sciatic notch (fig 3). The next nerves cut were caudal femoral cutaneous, caudofemoralis and gemelli nerves, the last two supplying caudofemoralis and gemelli muscles respectively. Then, the muscular branch going to the semimembranous/semitendinosus and biceps femoris group of muscle was cut (fig 3).

Tenuissimus nerve was then identified and the sciatic was cut 2 cm below the point of tenuissimus branching. Local anaesthetic, Lidocaine (2%), was applied to the sciatic nerve before cutting to prevent any possible effect on cardiovascular and pulmonary systems.

As a final check, the laminectomy incision was opened and the L7 and S1 ventral roots stimulated. A successful denervation would result in only the tenuissimus muscle twitching. Occasionally some tail and upper hip muscles twitched as well as tenuissimus and so attempts were made to cut these intact nerves to give as an extensive limb denervation as possible, leaving only the nerve to tenuissimus muscle intact. The caudal end of the tenuissimus was freed and a thread was tied to it as caudal as possible in order to attach the muscle to the puller later on. The skin incision was closed with Michel suture clips.

Fig 3. Diagram of the lateral aspect of the hind limb of the cat showing branches of sciatic nerve severed in preparation for dorsal root recording experiments.


Cranial Gluteal Nerve
Caudal Gluteal Nerve
Caudal Femoral Cutaneous Nerve
Muscular Nerve
Tenuissimus Nerve
Sural Nerve
Posterior Tibial Nerve
Peroneal Nerve

Fixing the Cat to the Experimental Frame

Before removing the cats from the operating table to the experimental frame, a knitting needle was inserted between interspinous ligament 5 cm craniad to the laminectomy. A second needle was passed underneath the pelvic bone, through the body cavity to support the hip bone in frame. After surgery, the animal was transferred to the frame (fig 4).

Cats were mounted in a conventional stereotaxic frame (Narishige). This involved the insertion of ear bars as far as the middle ear, two bars positioned on the lower orbits and one bar positioning between the canine teeth supporting the maxilla to ensure that the head does not move (or roll) when attempts are taken to remove the bone from the skull.

B. EXPERIMENTAL SET-UP

Temperature and Blood Pressure Control

It was necessary to prevent a steady fall in the body temperature of the animal by supplying heat, from above, by two infrared lamps mounted on a frame, one of which was a thermostatically controlled lamp which would have been automatically switched off if the temperature was about normal (36±1°C) or higher. The temperature was monitored throughout the experiment with a rectal thermistor.

Fig 4. Animal in the experimental frame showing spinal pool, skull pool and the position of different electrodes.

The cannula in the right femoral artery was flushed with heparinized saline and then connected to a pressure transducer (Elcomatic EM752) which was in turn connected to a pressure monitor. The alarm of the pressure monitor device was also set to the minimum of 70 mmHg.

Hind limb Arrangement

The hind limb had to be arranged to allow easy access to the tenuissimus muscle so that stimulating electrodes, and, later on the muscle puller could be used. A surgical forceps was attached to the free edge of the biceps femoris. The forceps was then taped to surrounding apparatus.

A flexible flat plastic tape bearing two tiny recording wires on its surface was passed underneath the tenuissimus muscle in a way that it would not disturb the muscle in any way whatsoever. In other words the tenuissimus muscle was laying on it freely. The purpose of it was to record EMG during the course of cortical stimulation. It could also be moved to a different part of the muscle as desired.

Construction of the Spinal Pool

The laminectomy incision was re-opened. An oval-shaped pool was formed by attaching a strip of X-ray film to the skin flaps of the laminectomy incision by Michel suture clips (fig 2,B). Liquid paraffin at 37°C was then poured into this pool, so covering the spinal cord. The thermistor was sometimes placed in the pool instead of the rectum, to maintain the temperature of this pool at about 37°C.

Retraction of the Dura and Exposure of the Spinal Cord

With the aid of a dissecting microscope, an incision was made in the dura and extended along the full length of the exposed spinal cord, care being taken not to rupture any of the small blood vessels overlying the spinal cord. The left hand flap of the incised dura was then retracted and cut transversely in 2-3 places along its length to facilitate exposure of the dorsal roots.

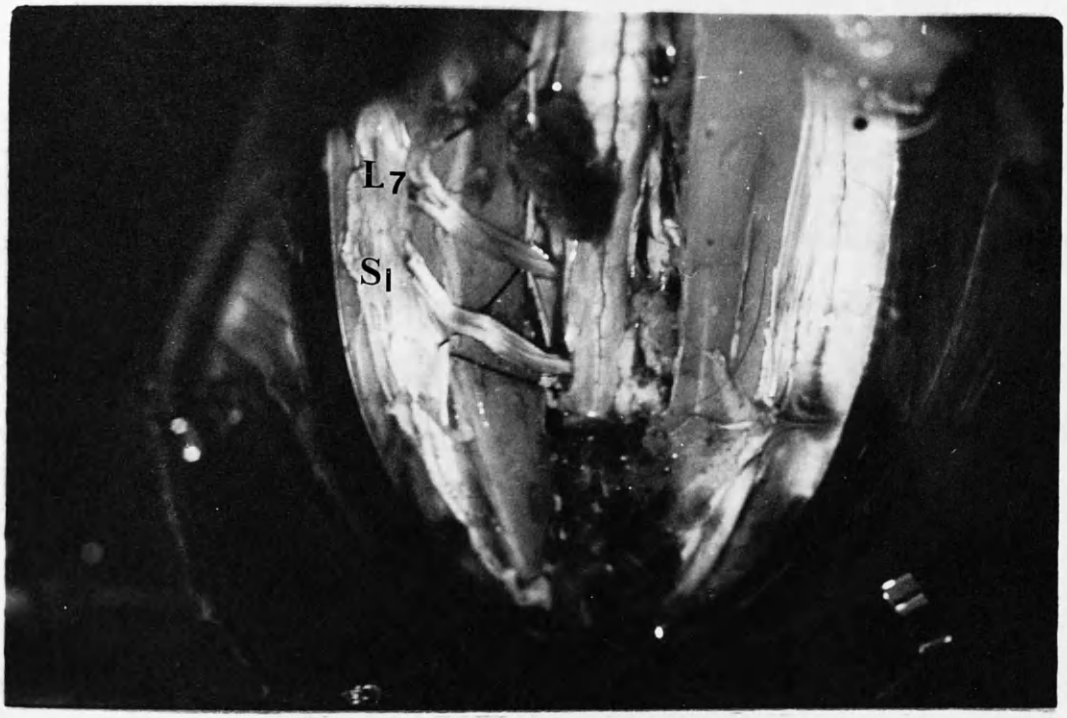
C. EXPERIMENTAL PROCEDURE: Dorsal Roots

The first stage involved cutting the dorsal roots L7 and S1 as close to their entry into the spinal cord as possible (fig 5). L6 was also cut to prevent any reflex activity taking place. It was of course essential to keep the ventral roots intact.

A single pair of silver electrodes were lowered into the spinal pool and a pair of stimulating electrodes were placed on the nerve to tenuissimus muscle. A stimulus pulse (usually of 0.02 msec duration) was generated through an isolated stimulator (Devices Sales) which was controlled by a digitimer (D4030 Device Sales) The digitimer also provided trigger and gated pulses for the muscle puller, Neurolog pulse generator and also trigger pulse for the oscilloscope (Tektronix).

The nerve to the muscle being studied was stimulated directly and evoked action potentials were sought for in all naturally occurring filaments of L7 and S1 dorsal roots. Individual natural rootlets of the dorsal roots were teased free and placed in turn on bipolar recording electrodes in the spinal pool. The electrical activity of each rootlet was amplified (1000 times using a

Fig 5. The completed paraffin pool with left spinal roots L7 and S1 severed from the cord.


L7
S1

pre-amplifier) and displayed on one beam of the Tektronix 502A oscilloscope. The digitimer triggered the oscilloscope every 500 msec, 1 msec before the stimulus was applied to the muscle nerve. The oscilloscope sweep speed was set initially to 1 msec/division and rootlets which showed regular evoked potentials 1 to 5 msec following the muscle nerve shock were isolated. These rootlets were then subdivided to give filaments which contained only active afferents from tenuissimus muscle. Occasionally some of these "single fibre" filaments contained other active fibres which were "separated" from the I_a fibre by use of the window discriminator. When a "single fibre" filament was isolated, a tiny piece of coloured silk was tied to the end of it to act as a marker.

Afferent fibres from tenuissimus primary sensory endings were distinguished from other afferent fibres on the basis of having conduction velocities over 75 m/sec. The conduction velocity of each fibre studied was calculated from the time delay between the moment of stimulating the muscle nerve and the start of the rising phase of the action potential recorded from the spinal root filament, with no allowance made for the utilization time of the fibre. A rough estimate of the conduction velocity of a fibre could be made during the experiment knowing that the conduction distance from the spinal roots to tenuissimus was approximately 12±1 cm.

Primary afferents from flexor digitorum longus (FDL) muscle spindles were distinguished from I_b tendon organ afferents by inducing a twitch in the parental muscle, FDL. It was easier to recognize I_a's from I_b's by vibration of the FDL tendon with 100 Hz which increased the I_a firing without any alteration in the I_b

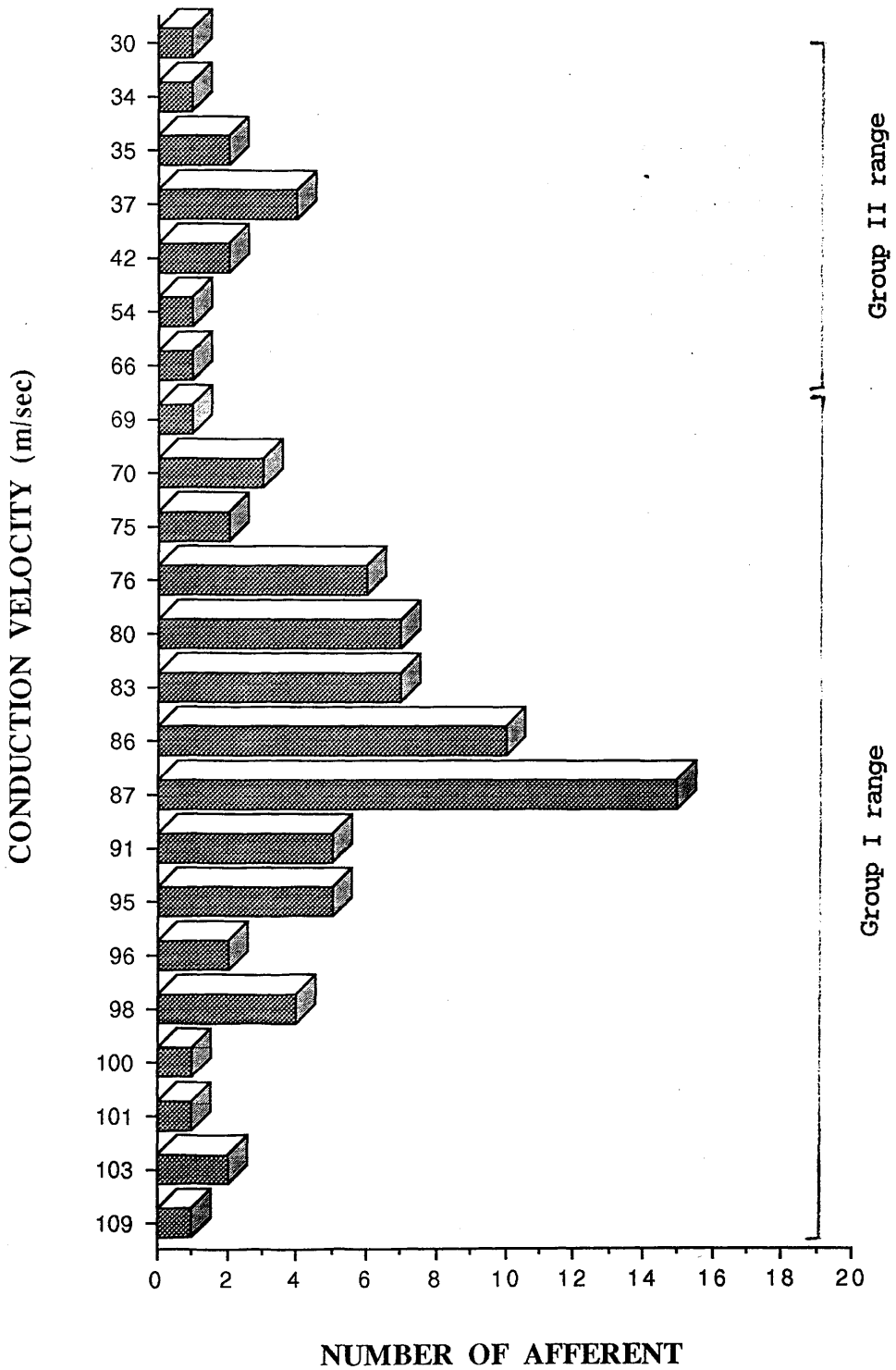
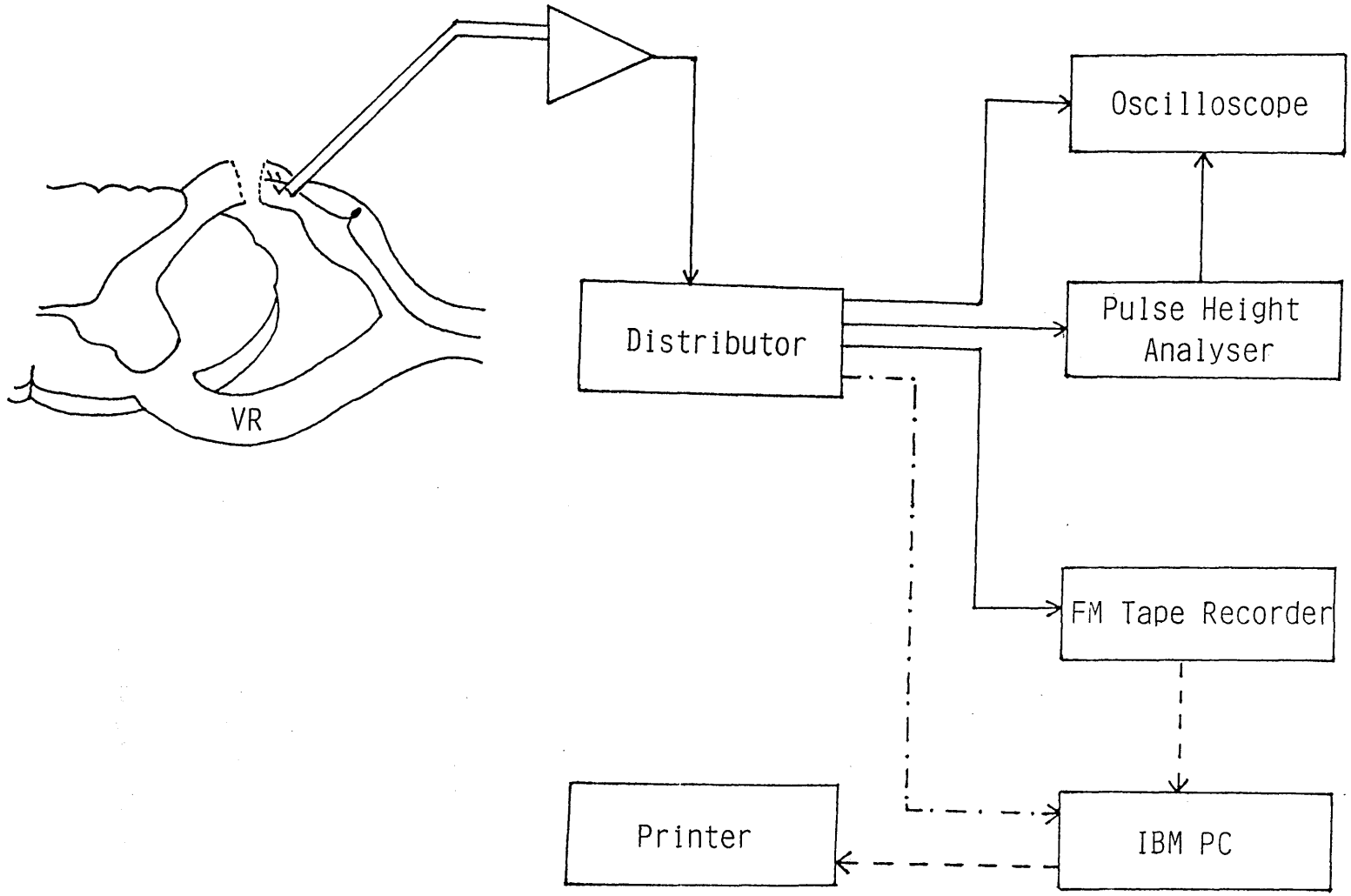

CONDUCTION VELOCITY (m/sec)
30
34
35
37
42
54
66
69
70
75
76
80
83
86
87
91
95
96
98
100
101
103
109
0
2
4
6
8
10
12
14
16
18
20
NUMBER OF AFFERENT
Group II range
Group I range

Fig 6. Diagram of the experimental set-up used in dorsal root recording experiments.


VR
Distributor
Oscilloscope
Pulse Height Analyser
FM Tape Recorder
Printer
IBM PC

Right sensorimotor cortex was usually exposed and stimulated. Points of stimulation were marked with numbers in order to make communication easier. It was reported previously (Mortimer and Akert, 1961) that the tenuissimus extrafusal muscle fibres are more likely to be recruited (with or without intrafusal fibres) if any point in orbital gyrus (anterior to cruciate sulcus) is stimulated. Therefore, exposure of the cerebrum was carried out to an extent just enough to have access to only 3-4 mm of orbital gyrus, and not further forward. Posteriorly, enough was removed to stimulate the anterior part of the suprasylvian and marginal gyri.

Construction of the Head Pool

A metal loop of 10 cm diameter was mounted on the body frame on top of the skull. The retracted skin was tied round the metal loop using surgical thread. Liquid paraffin at 37°C was introduced to this pool before any attempts were made to remove the dura.

A slightly-bent syringe needle was used to lift the dura to avoid any possible harm to the surface of the cortex. The cut dura was then retracted and pia-covered sensorimotor cortex exposed completely (fig 7).

E. EXPERIMENTAL PROCEDURES: Sensorimotor Cortex

Figure 8 shows most of the devices used during the dorsal root recording experiments.

Fig 7. The completed paraffin pool of the skull showing the pericruciate cortex and the spring-mounted stimulating electrode.

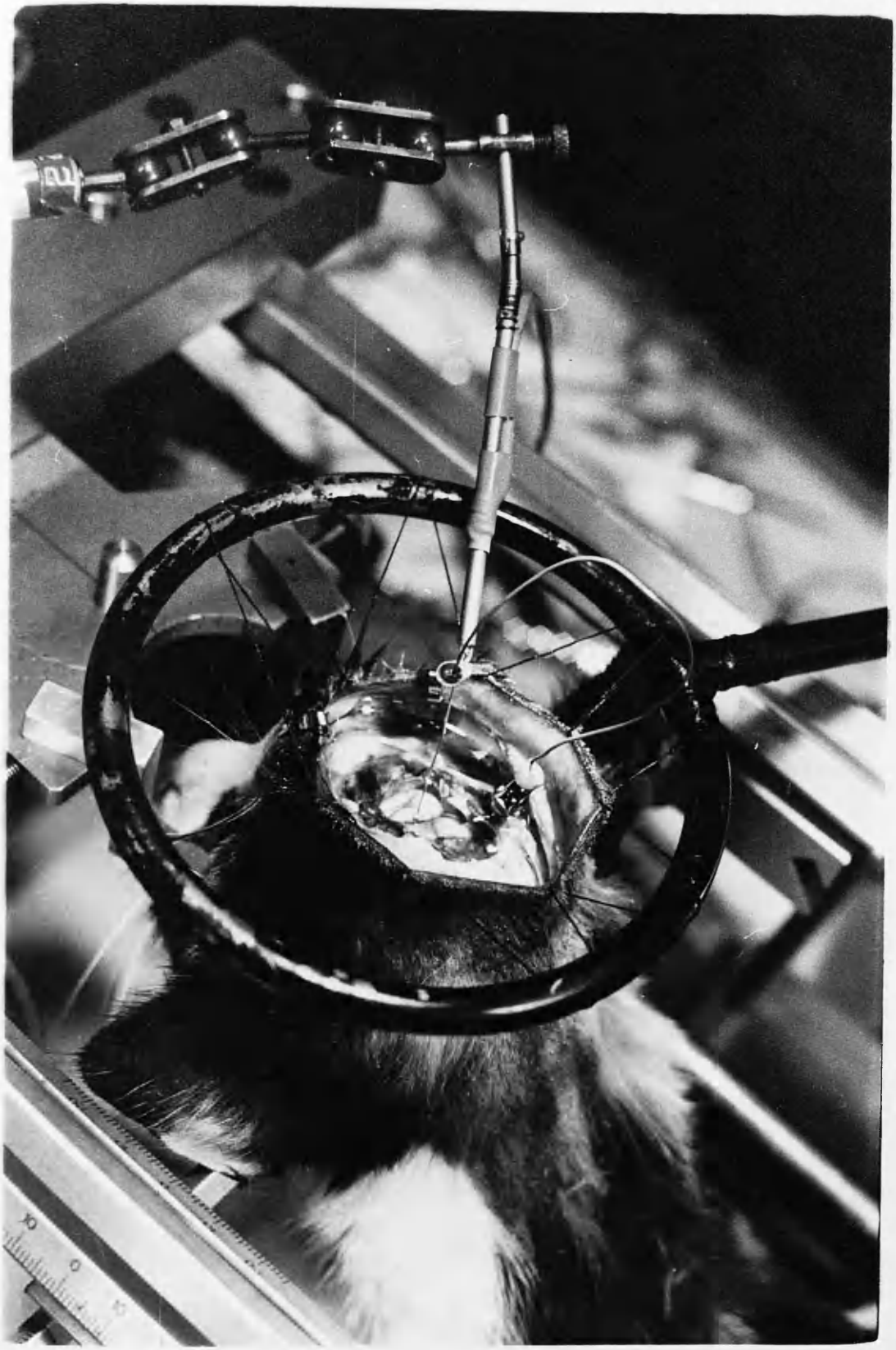
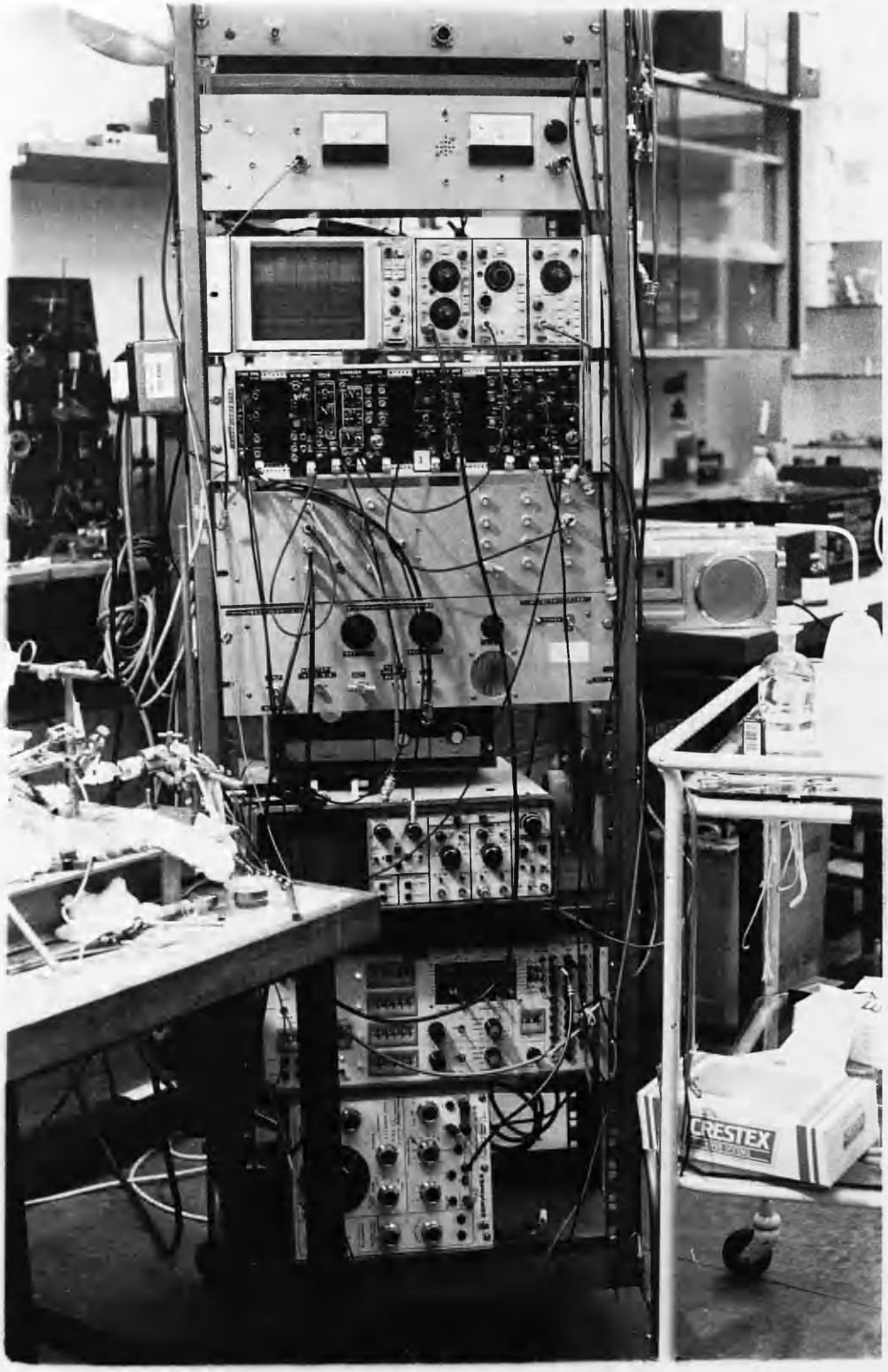


Fig 8. Devices used during dorsal root recording experiments. From top to bottom: Temperature and Blood Pressure Recording Device, Oscilloscope, Neurolog set, Distributor, Pulse-Height Analyzer, Digital Oscilloscope, Digitimer and a Power Oscillator at the very bottom.


CRESTEX

Setting-Up the Puller

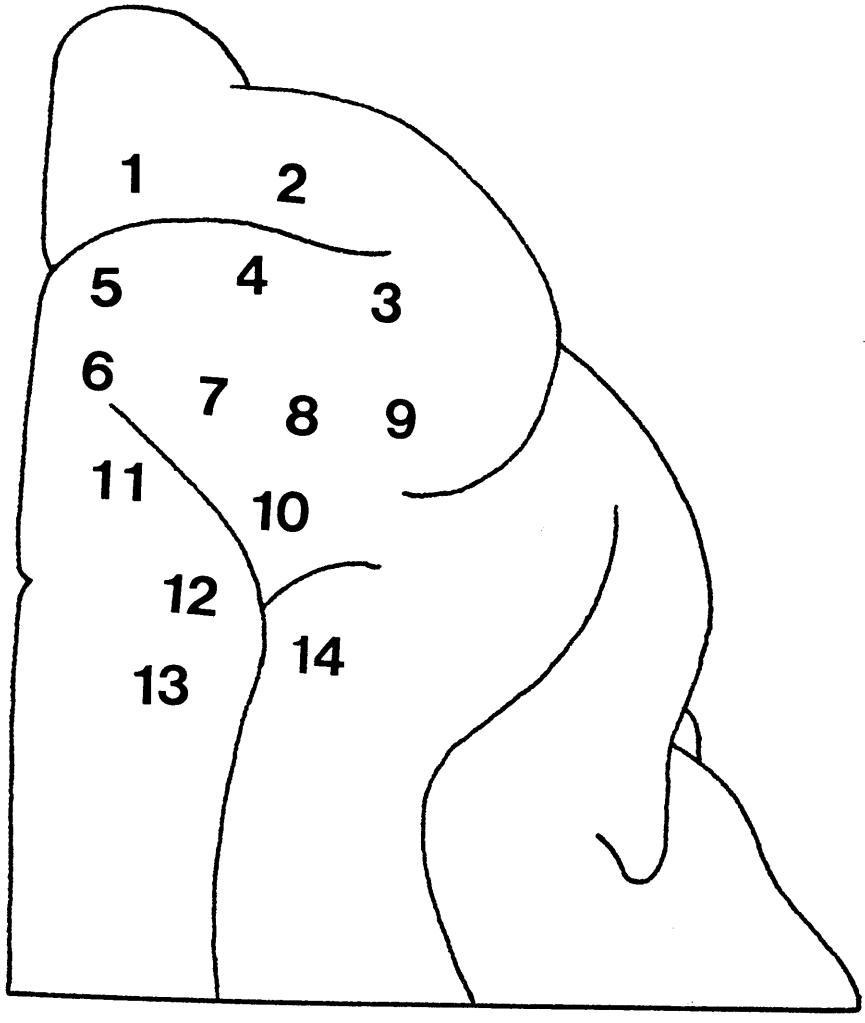
The thread on the distal end of the tenuissimus muscle was tightly connected to the puller which was driven by a power oscillator (TPO, 25) which itself was controlled externally by a gated triggering pulse originally from the digitimer and modulated by a wave-form generator (Servomex Control).

Cortical Stimulation

Figure 9 displays points of stimulation by their numbers. Fourteen points were chosen conventionally, the first two of which were located on the orbital gyrus, 1 mm forward to cruciate sulcus and 2 mm apart from one another. Point 3 was 1 mm posterior to where usually the cruciate sulcus terminates laterally. Point 5, at the same level coronally, but very close to midline. Point 4 somewhere in the middle of points 3 and 5. Postcruciate dimple (Pcd) was numbered 8 and points 9, 7 and 10 lay lateral, medial and posterior to the dimple respectively. Point 6 is 1 mm anterior to the termination point of ansate sulcus which also is 2 mm posterior to point 5. Three locations on the marginal gyrus were numbered 11, 12 and 13 caudally and the last point, 14, was located on anterior edge of suprasylvian gyrus.

The cortex underlying points 12-14 is less likely to have any role in fusimotor control, for it rarely evoked any fusimotor responses, if at all. Therefore, it seems reasonable to grossly locate the boundary of sensorimotor cortex which has influence on the fusimotor system somewhere on ansate sulcus, or at most 1 mm beyond it posteriorly.

Fig 9. Diagram of the right frontal cortex of the cat. The numbers show the main points of stimulation. Cruciate sulcus lies behind points 1 and 2 and ansate sulcus almost ends at point 6. Point 8 represents postcruciate dimple (Pcd).


1
2
5
4
3
6
7
8
9
11
10
12
14
13

The stimulating pulses were derived from a Neurolog stimulator supplying a stimulus isolation unit with a constant current output, which provides automatic compensation for changes in tissue resistance at the electrode tips. The Neurolog stimulator was itself controlled by the digitimer in order to provide a gated stimulating pulse, usually between seconds 3-8 of the 12-sec cycle period.

Surface stimulus current of 0.3-3 mA and rarely up to 4mA was applied through the platinum ball electrode (tip diameter of 0.6 mm) both cathodally and anodally starting from a low current (fig 7). The other pole of stimulating electrode was attached to the bulk of the cut temporalis muscle using a pair of crocodile clips.

It was experienced in the early experiments and also reported in previous works (Gladden and McWilliam, 1977a,b) that it is less likely to get a fusimotor response if the cat is too deep in anaesthesia. Usually, attempts were made to stimulate the cortex when the cat was light enough to respond weakly to a fairly strong pressure applied to the forepaw pad. On the other hand if the withdrawal reflex of the forepaw was too strong, then supplementary doses of anaesthesia were given, in order to prevent any suffering. Therefore, under barbiturate anaesthesia one can only stimulate the cortex properly in a short window of time, averaging about 10-15 minutes.

Stimulus parameters were chosen carefully to be in the most effective range, according to the experiences of other workers (Jansen and Matthews, 1962; Koeze, 1968; Grigg and Preston, 1971; Vedel and Mouillac-Baudevin, 1970; Koeze, 1973; Gladden and McWilliam, 1977a). Frequency and pulse width were changed within a

range of 100-250 Hz and 0.2-0.3 msec respectively in some experiments; however, since changing the parameters had no obvious effect, then frequency of 200 Hz and pulse width of 0.2 msec were chosen to be the routine stimulus parameter.

A low stimulus current was chosen at the very beginning and increased if no fusimotor activity could be recruited. Most of the animals were responsive to a current of 2.0 mA. It was necessary rarely to increase the current to a level above 3.0 mA and usually no responses were obtained below 0.5 mA.

Surface positive (anodal) and surface negative (cathodal) stimuli were applied to the cortex. It was found that most of the time, anodal pulses were more effective and did not need to be increased beyond a certain level, whereas in the case of cathodal stimulation, the same response could only be obtained with a higher current.

Not all the afferents studied contributed to the results. Some of the afferents were not affected by cortical stimulation at all. Fig 10 demonstrate that 20 out of 73 afferents remained unaffected by cortical stimulation.

Cortical Recording

In a few experiments tenuissimus and flexor digitorum longus (FDL) nerves were stimulated at two stimulus levels: one at slightly above group I afferent threshold and the other at X4 threshold. Cortical evoked potentials in a boundary shown in fig 11,A were recorded by means of a unipolar silver ball electrode. The emphasis was on the positions of hind limb group I afferent projection areas introduced by Landgren and Silfvenius on 1969 (fig 11,B).

Fig 10. Diagram of the total number of tenuissimus afferents in each experiment and also the ones that were not responding to stimulation of the pericruciate cortex. Number of experiments is given in chronological order. The cats in experiments 21 and 23 were chloralose-anaesthetized.

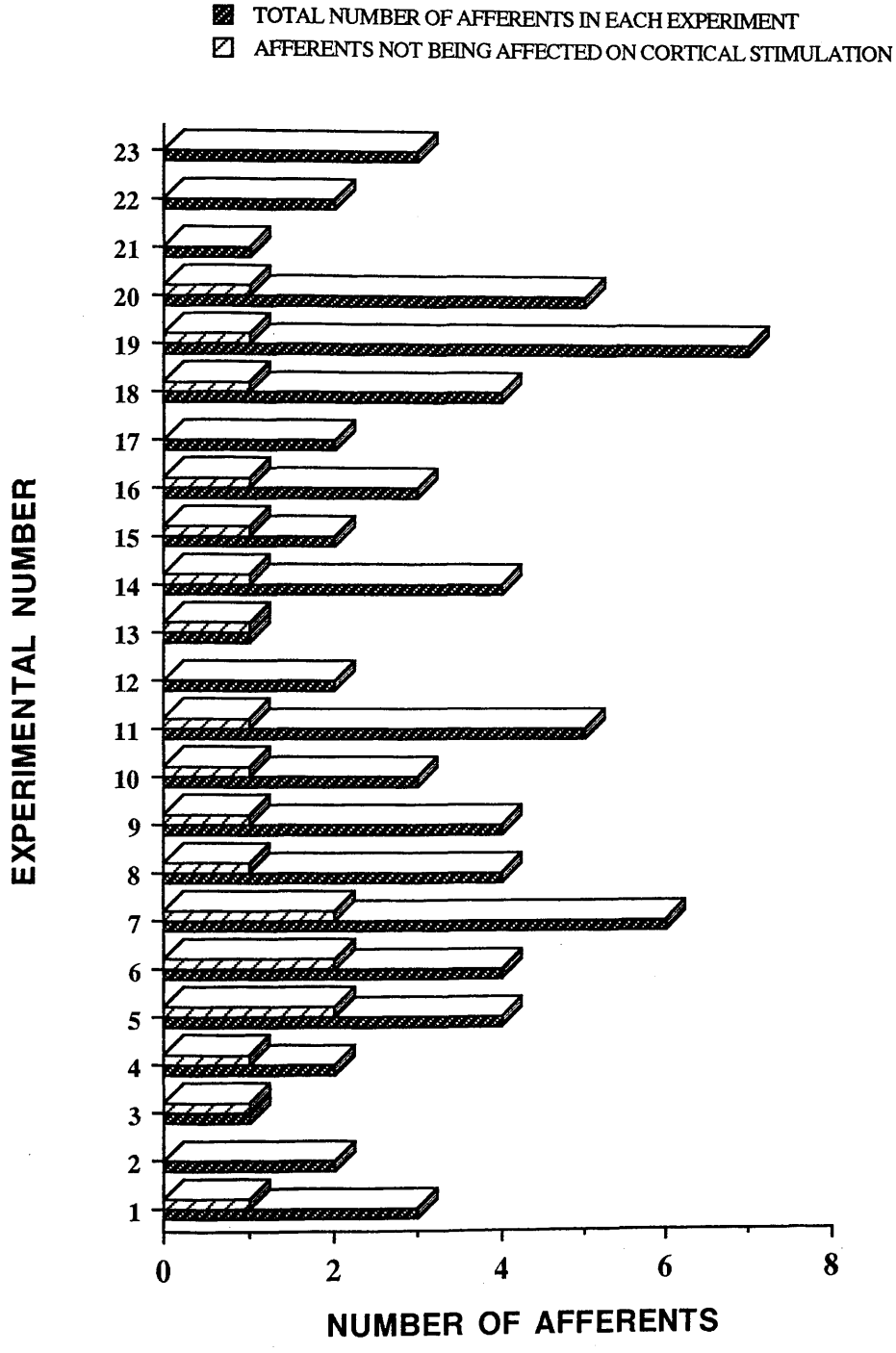
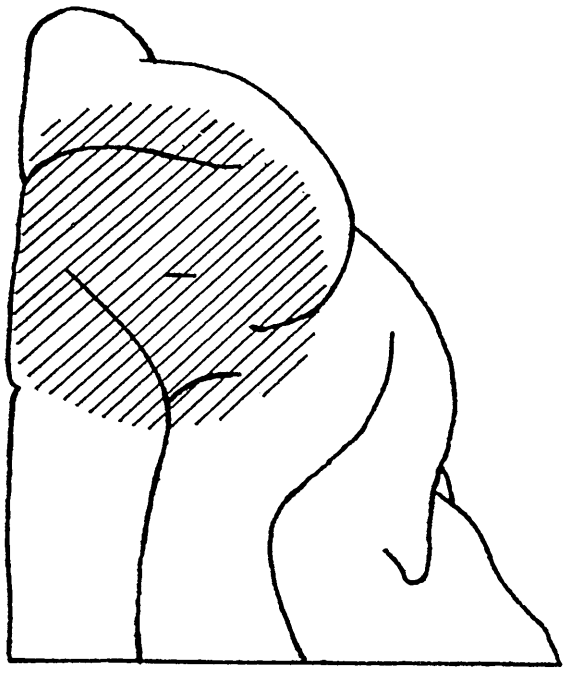
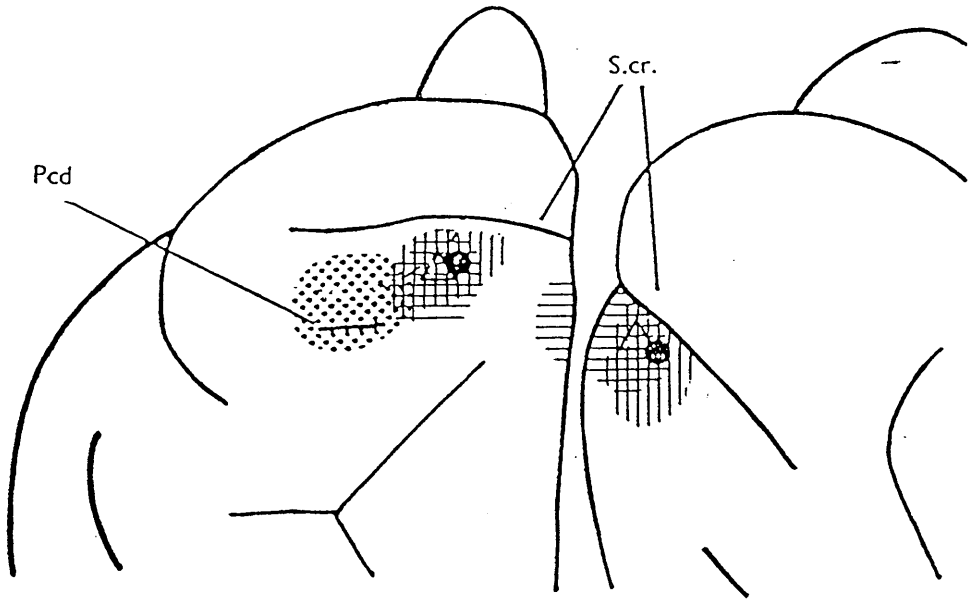

TOTAL NUMBER OF AFFERENTS IN EACH EXPERIMENT
AFFERENTS NOT BEING AFFECTED ON CORTICAL STIMULATION
EXPERIMENTAL NUMBER
23
22
21
20
19
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
2
4
6
8
NUMBER OF AFFERENTS

Fig 11. A. Area of the right cortex where attempts were made to record surface evoked potentials. B. Diagram of the dorsal and medial aspects of the rostral pole of a cerebral hemisphere. The location of the projection areas of the group I muscle afferents from the contralateral forelimb are shown stippled and from the hind limb hatched. Horizontal hatching: area of quadriceps. Vertical hatching: area of posterior biceps-semitendinosus. S.cr., cruciate sulcus (B taken from Landgren and Silfvenius, 1969).

A



B



Data Storage

A 4-channel FM tape recorder (3960 instrumentation recorder, Hewlett, Packard) was used to store the data for further analysis (fig 6). The first two channels usually had the afferents' inputs while the third channel belonged to the RAMP signal and the forth to synchronizing pulse. It was crucial to have synchronizing pulse on one of the channels stored, for it was necessary in further analysis of the data.

In the case of isolated muscle spindle experiments, an Umatic or a VHS videorecorder was used to store pictures of movements and replayed later for careful (frame to frame) observations.

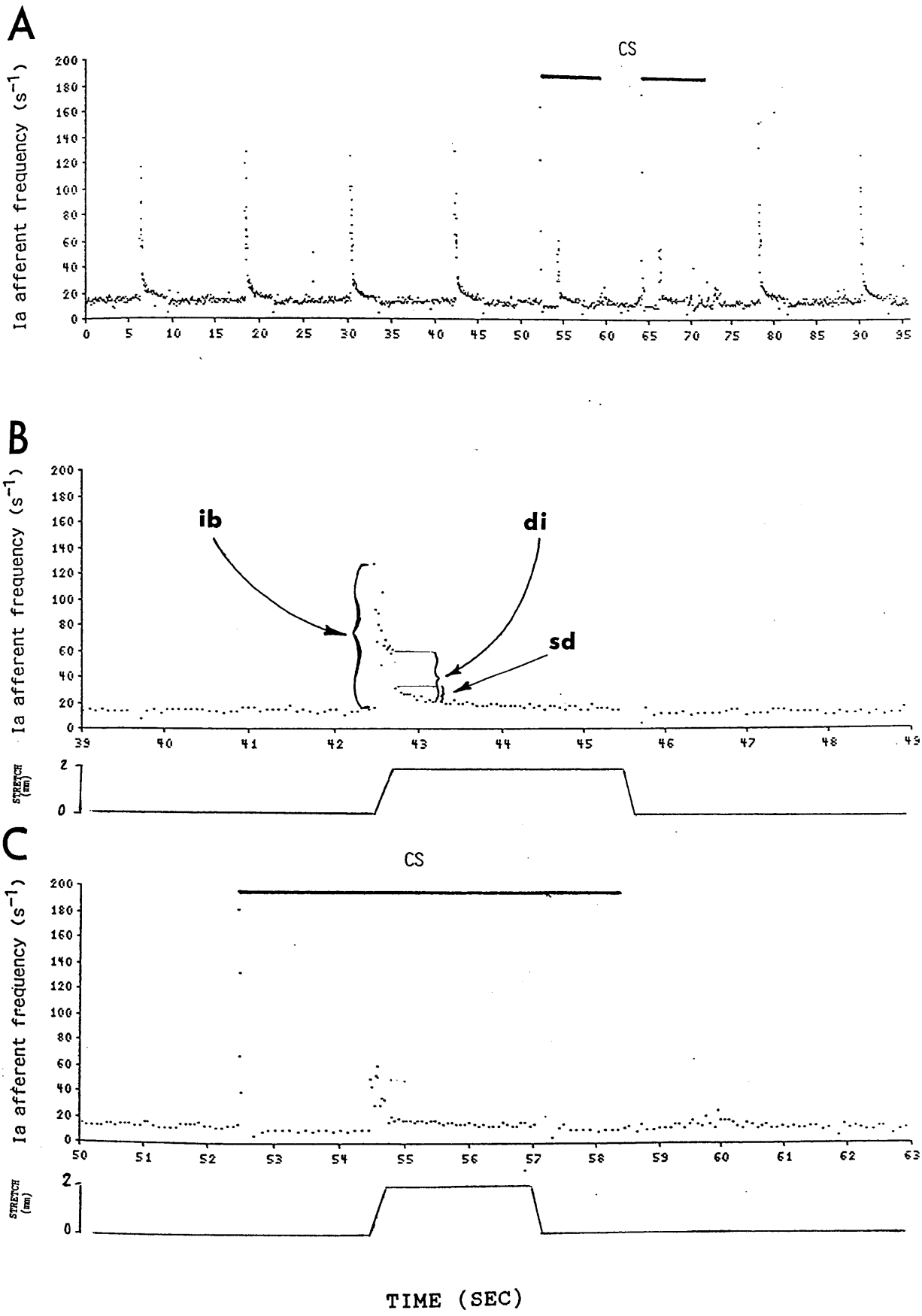
Analysis of Data

An IBM Personal Computer fitted with a digital input/output interface card was used to collect the data (fig 6). The spike-trains to be analyzed were fed into Neurolog Spike-Trigger units (at the time of experiment or later) and the gate pulses from these units were fed into the digital interface card. The time of occurrence of each spike was recorded and stored in a file on the computer's disk for analysis and graph prints.

Each computer file consists of a response of an afferent to stimulation of a specific point on the sensorimotor cortex and the preceding and subsequent responses to stretches for comparison. To determine the character of an intrafusal effect (excitatory or inhibitory and if excitatory, whether dynamic or static) elicited by cortical stimulation, it was necessary to measure the "initial burst", "dynamic index" and "slow decay" of the afferent response (on

a ramp-hold stretch) before, during and after cortical stimulation. In order to measure them precisely, it was necessary to display each response to a ramp and hold stretch with an extended time scale. One example of such work is illustrated in fig 12, where the time base for a stimulating cycle and the preceding cycle is displayed on an extended time scale. The values presented were measured by hand using a square set. Where there was more than one interval in a given time, the average value would have been calculated and used. Of course results would have been more reliable statistically if one could average the responses of the spindle afferents to stretch prior and during cortical stimulation. However, because the afferent responses to cortical stimulation seemed not to be similar in two or more consecutive cycles of stimulation, it was not possible to do so.

Fig 12. A. Display of a computer digitized file whose time axis is partially extended in B and C in order to make measurements of the dynamic index, slow decay and initial burst possible. The middle trace illustrates how the initial burst (ib), the dynamic index (di) and slow decay (sd) were measured.


A
CS
Ia afferent frequency (s^{-1})
B
ib
di
sd
Ia afferent frequency (s^{-1})
STRETCH (mm)
C
CS
Ia afferent frequency (s^{-1})
STRETCH (mm)
TIME (SEC)

CHAPTER THREE

RESULTS

Results obtained will be introduced in three different sections: dorsal root recording, direct visualization of exteriorised tenuissimus muscle spindles and lastly the cortical areas for tenuissimus and flexor digitorum longus (FDL) muscle afferent projection.

Chloralose was our first choice of anaesthetic agent at earlier stages of experiments. However, we did not find intrafusal effects in dorsal root experiments, neither did we have any spontaneous activity or intrafusal recruitment in exteriorised muscle spindles when the cortex was stimulated. Therefore, we felt obliged to switch to barbiturates, and as soon as we did we got satisfactory results. Surprisingly, on using chloralose again, intrafusal effects were obtained (on cortical stimulation), and the reason of earlier failure is yet unknown to us.

Section A: Dorsal Root Recording

Most of the results were obtained from tenuissimus muscle afferents (primaries and secondaries) under barbiturate anaesthesia. However, in the last three experiments where chloralose was used as an anaesthetic agent in order to increase the chances of recording surface cortical evoked potentials on stimulation of nerves supplying tenuissimus and FDL muscles, recordings were obtained from primaries on cortical stimulation as well. Therefore, in the end, a set of results from tenuissimus primary endings of three cats were obtained under chloralose anaesthesia, reasonable enough to compare with the bulk of results under barbiturate anaesthesia.

On cortical stimulation, both anodal and cathodal stimuli were applied. Anodal pulses proved to be more effective most of the time. Fig 13 is an example of anodal (A) and cathodal (B) stimulation in a cat under barbiturate anaesthesia. Fusimotor responses in fig 13 were obtained by stimulation of a point just anterior to the Pcd. Anodal stimulation was followed by cathodal stimulation at the same anaesthetic level. The current was 1.6 mA in both cases. It is worth noting that an increase of 0.3 mA in cathodal stimulation did not bring about any fusimotor response.

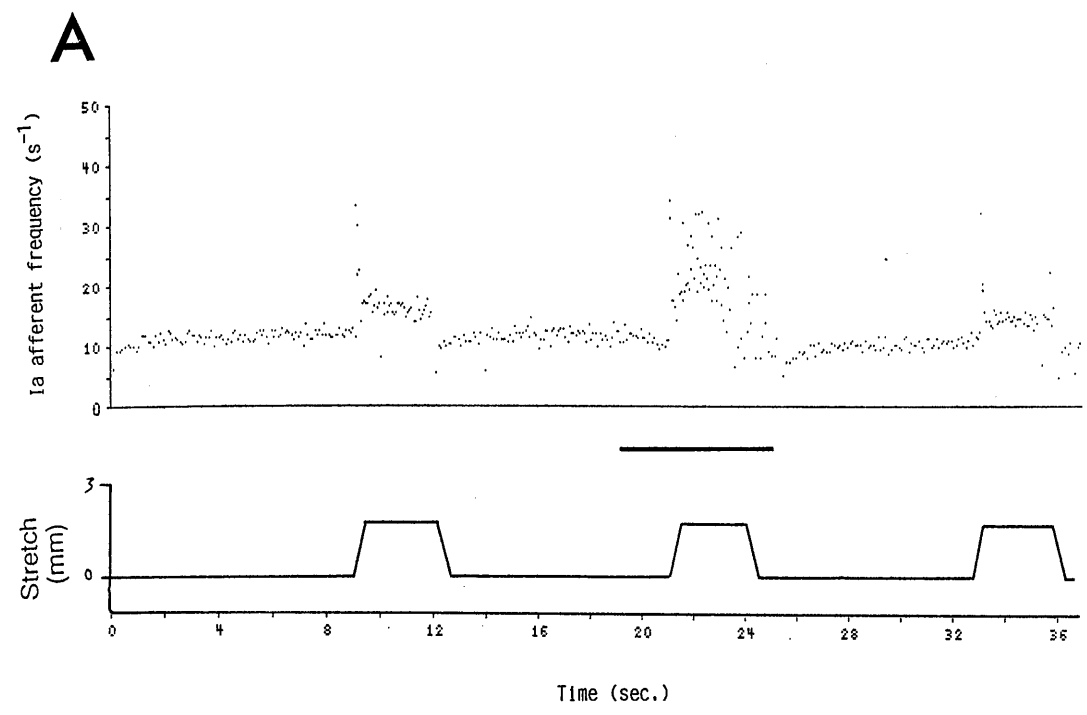
Unfortunately, the results obtained were not reasonable enough quantitatively to compare the strength of cathodal and anodal stimulus on producing a similar fusimotor response.

I. Effect of Cortical Stimulation on Tenuissimus Primary Afferents

Primary afferents from the tenuissimus muscle were mostly found in L7 and to a lesser degree in S1. They were identified from other groups of afferents by their fast conduction velocities. If the tenuissimus nerve is stimulated just caudad to its emergence from sciatic nerve, spikes are picked up in dorsal root filaments within a latency of 1.2-1.8 msec depending much on the distance between emergence of tenuissimus nerve from sciatic nerve and the spinal cord, which gets longer if tenuissimus nerve emerges out low and vice versa. However, the mean latency value was around 1.4 msec for an average distance of 12 cm between the two stimulating and recording electrodes, which gives an average conduction velocity of 86 m/sec.

In earlier stages of experiments when the intrafusal effects were being only displayed on the oscilloscope, a dynamic and a static effect was attained as shown on fig 14. Traces A and B are discharges

Fig 13. The effect of anodal (A) and cathodal (B) cortical stimulation on the response of a single tenuissimus primary afferent to ramp stretch. Point of stimulation was 1 mm anterior to Pcd. Tenuissimus stretched 2 mm. Cortical stimulation shown as a solid bar.


A
Ia afferent frequency (s^{-1})
50
40
30
20
10
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

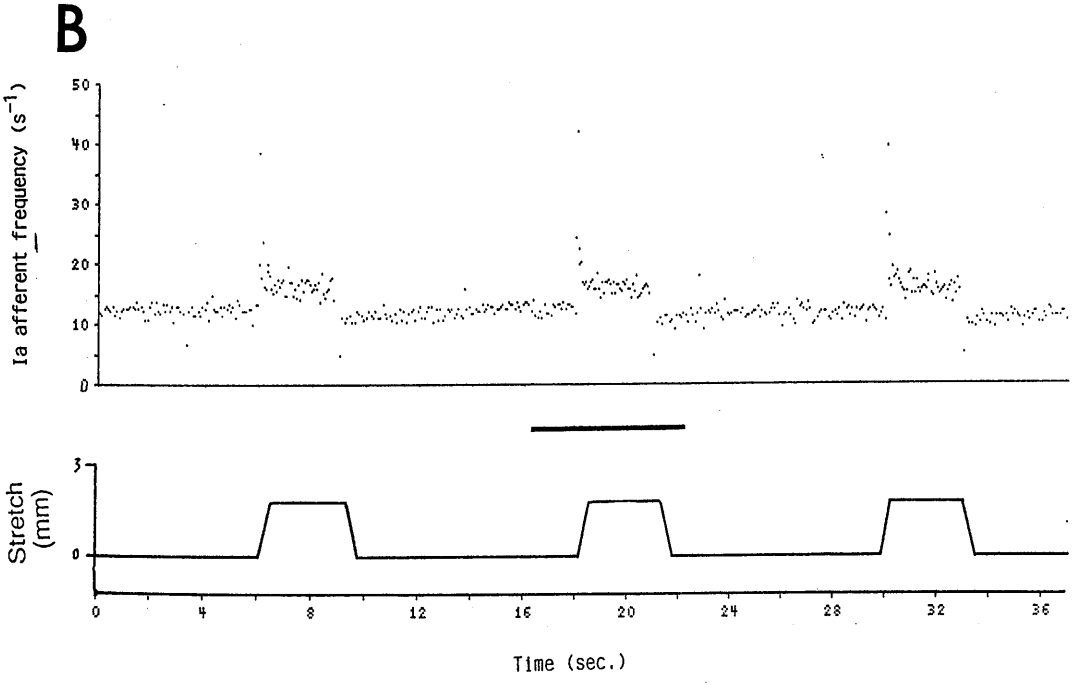
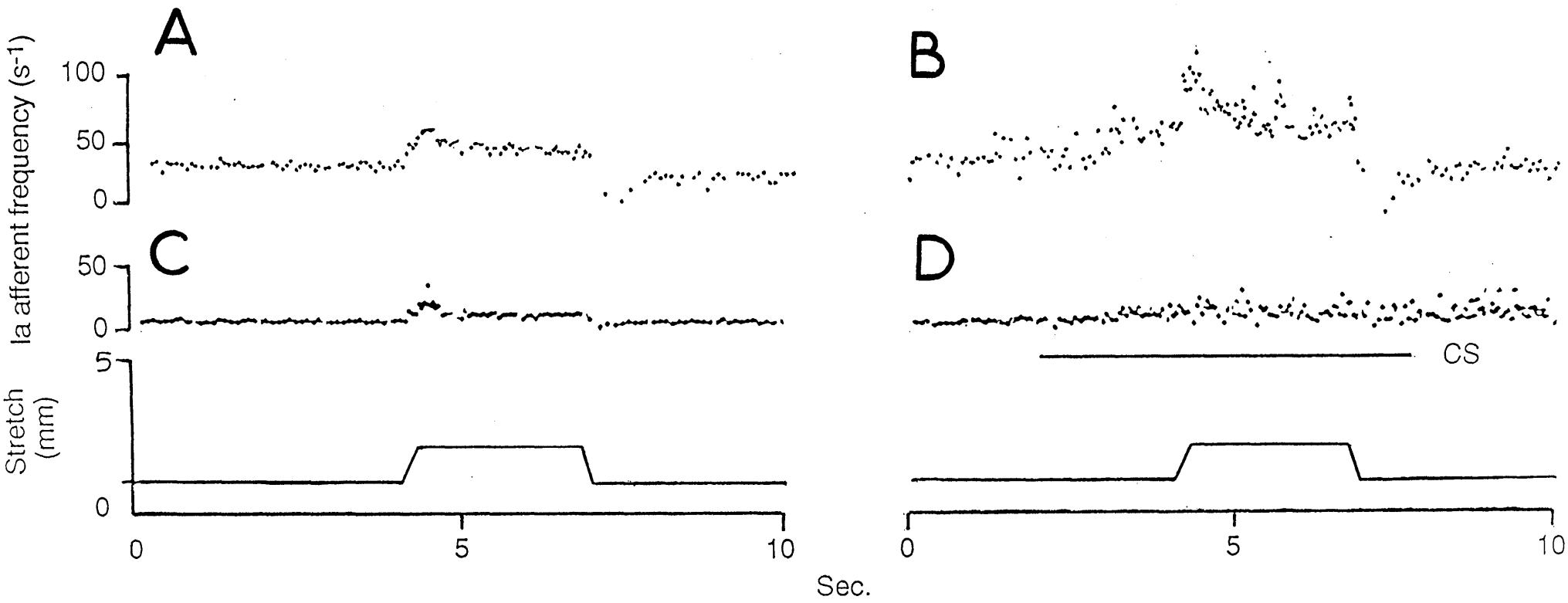

B
Ia afferent frequency (s^{-1})
50
40
30
20
10
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

Fig 14. The effect of anodal cortical stimulation on a tenuissimus primary afferent discharge. Upper traces are the responses of the primary afferent to ramp stretch with (B) and without (A) cortical stimulation of point 5. Middle traces are the response of another tenuissimus primary afferent to ramp stretch with (D) and without (C) cortical stimulation of Pcd. Lower traces showing the tenuissimus muscle was stretched 2 mm. Cs, cortical stimulation.


A
B
C
D
100
50
0
Ia afferent frequency (s-1)
50
0
5
0
Stretch (mm)
CS
0
5
10
Sec.

of the same afferent with and without cortical stimulation. The same is true for traces C and D. Trace B illustrates a dynamic response of primary afferent to a ramp hold stretch during cortical stimulation of point 5. The static response in trace D, characterized by abolition of the ramp response, was obtained on cortical stimulation of the Pcd. With these preliminary results, emphasis was put on finding out whether they were reproducible from stimulation of the same points and the points nearby, and also on finding a separating line between the dynamic and static area within the pericruciate cortex. With the completion of a digitizing program, subsequent results were digitized and the following figures will be presented in a style of computer output.

A. Intrafusal Recruitment alone: Dynamic Effects

A classic dynamic effect is characterized by a rise in static firing at the beginning of stimulation followed by an increase in both dynamic responsiveness to ramp stretch and dynamic index. However, not all afferents show all these criteria collectively and at the same time it would be possible for Db_1 contraction to occur but contraction of other intrafusal fibres simultaneously would mask the effect. In other words, depending on the degree of activation of static (bag_2 and nuclear chain) fibres, one or even two criteria might be masked. It is necessary to take into account that in the exteriorised experiments, where intrafusal fibres are under direct observation, the Db_1 was not recruited on its own, not even in one single case (results of the exteriorised muscle experiments will be fully presented in section B). Stimulation of the "dynamic area" of the contralateral cortex corresponding to our marked points 4, 5 and 6,

with anterior and medial borders being the ansate sulcus and longitudinal fissure respectively, gave rise to dynamic effects. No dynamic effect was attained on stimulation of other areas within the sensorimotor cortex except in one case which will be represented in fig 21. For instance, in fig 15, the dynamic index did not increase; however, the dynamic decay in afferent firing during the first half of a second on ramp hold is remarkably increased. Since this decay could only have happened if the Db_1 fibre was active a dynamic gamma motoneurone must have been recruited.

Fig 15 shows that cortical stimulation of a point just lateral to point 5 almost doubled the static firing level, from 18 ips to 36 ips. The initial burst to the ramp was also increased from 80 ips to 155 ips. Although the dynamic index did not seem to change much from 32 ips to 35 ips, the decay increased remarkably from 7 ips to 23 ips. The response to hold stretch became more irregular and the firing of the afferent did not stop during the ramp release.

Point 5 was stimulated in fig 16 by a surface positive (S+) current of 1.7 mA. It gradually increased the static firing level after a latency of about 300 msec. The initial burst to the ramp increased on stimulation from 78 ips in the preceding cycle to 130 ips; so did the dynamic index, from 18 ips to 30 ips, and the slow decay from 6 ips to 10 ips. Looking at the response of the afferent to ramp hold, it seems that the effect on gamma motoneurones is building up during the course of stimulation. Moreover, the increase in static firing seems to interrupt the slow decay which might suggest recruitment of Sb_2 fibre on cortical stimulation as well.

Fig 15. Response of a tenuissimus primary afferent to cortical stimulation at an area 1 mm lateral to point 5. A dynamic gamma motoneurone(s) was thought to be recruited (see text). Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as a solid bar.

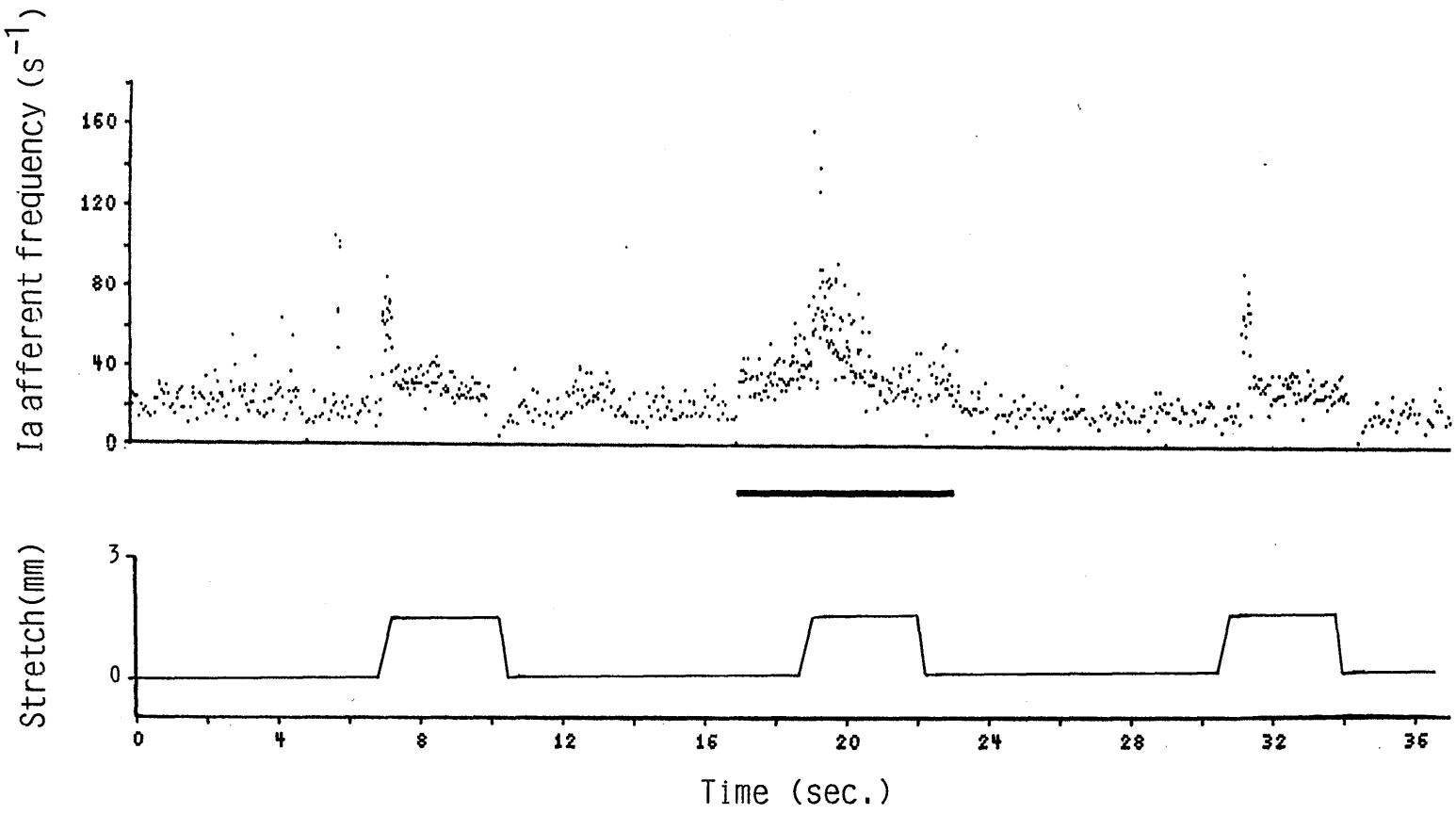
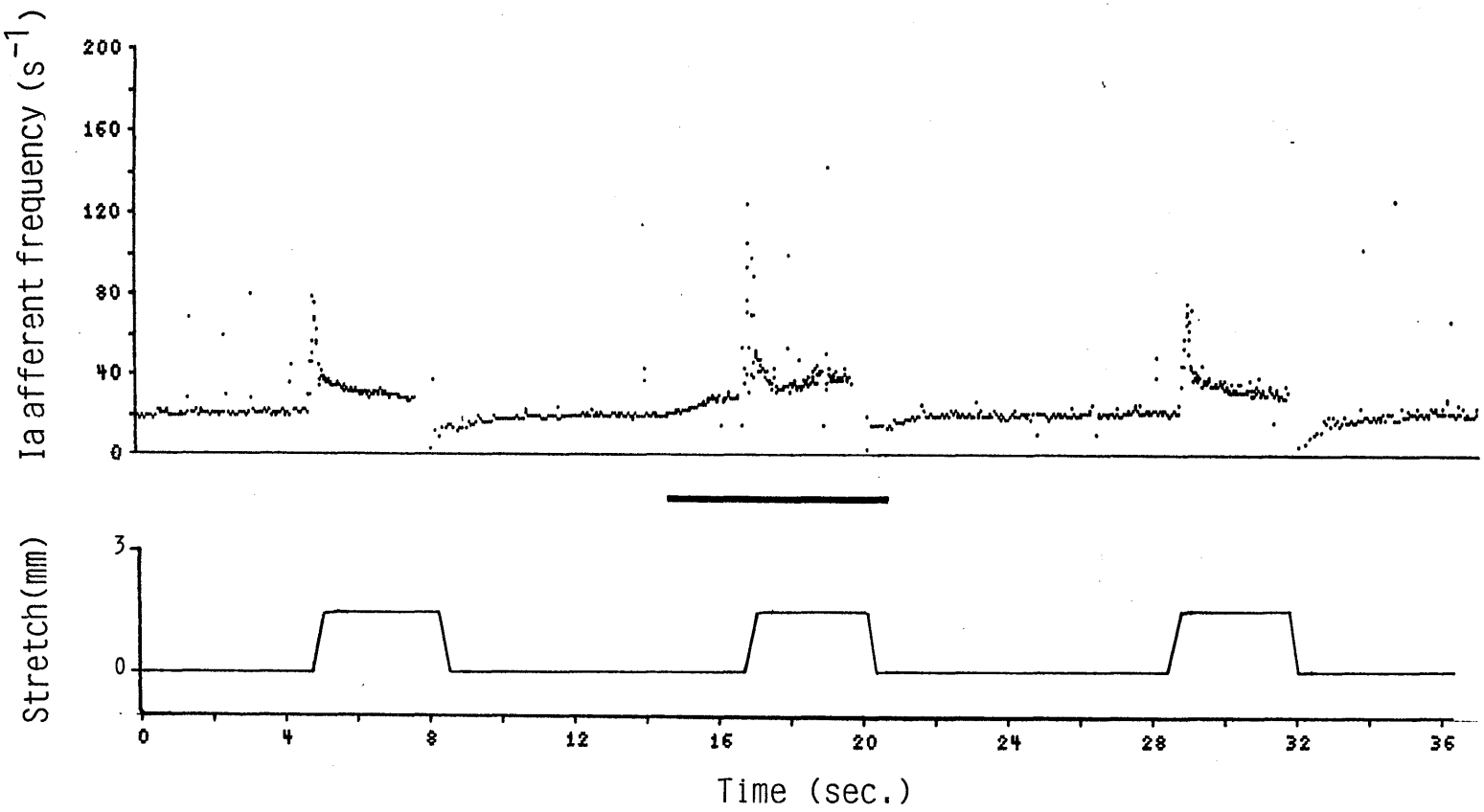

Ia afferent frequency (s^{-1})
160
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

Fig 16. Response of a tenuissimus primary afferent to cortical stimulation at point 5. A dynamic gamma motoneurones was thought to be recruited (see text). Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as a solid bar.


Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

However, if that was so, it should have been a rather weak contraction of the Sb_2 fibre because of the regularity of the response during cortical stimulation.

A similar dynamic effect was obtained on another primary afferent on stimulation of the cortex posterior to point 4 with an increase in dynamic index of 24 ips: from 11 ips to 35 ips (fig 17). However, it differs from the effect seen on fig 15 in two respects. First, it lacks the initial rise in the static firing of the afferent; instead the firing gradually rises and at the same time gets more irregular. Secondly, the afferent stops firing on the release of the ramp.

In fig 18 a slight dynamic response was visible during stimulation of points 6 (18,A) and 5 (18,B). The dynamic index had risen by 5 and 13 ips in both A and B respectively. The initial bursts to ramp stretch and the decay were also increased. What is noticeable is the regular bursts of spontaneous activity in gamma motoneurones giving rise to miniature bursts in the afferent firing of the primary in fig 18,B. The spontaneous bursting activity seems to have been added to the slow decay, and their frequency increased even after stimulation had stopped. The shift to an increased bursting activity happened in less than 10 seconds, and that could not have occurred because of a change in anaesthetic level.

The stimulus intensity of 3.2 mA was applied to point 5 in fig 19. It illustrates a different pattern of response, a weak dynamic effect compared with previous examples. The irregularity of static firing increased although the mean frequency did not seem to change significantly. The latency of the effect was about 350 msec. The response to ramp stretch progressively declined over time. The

Fig 17. The effect of cortical stimulation at an area just posterior to point 4 on tenuissimus primary afferent discharge. The effect is of dynamic type. Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as a solid bar.

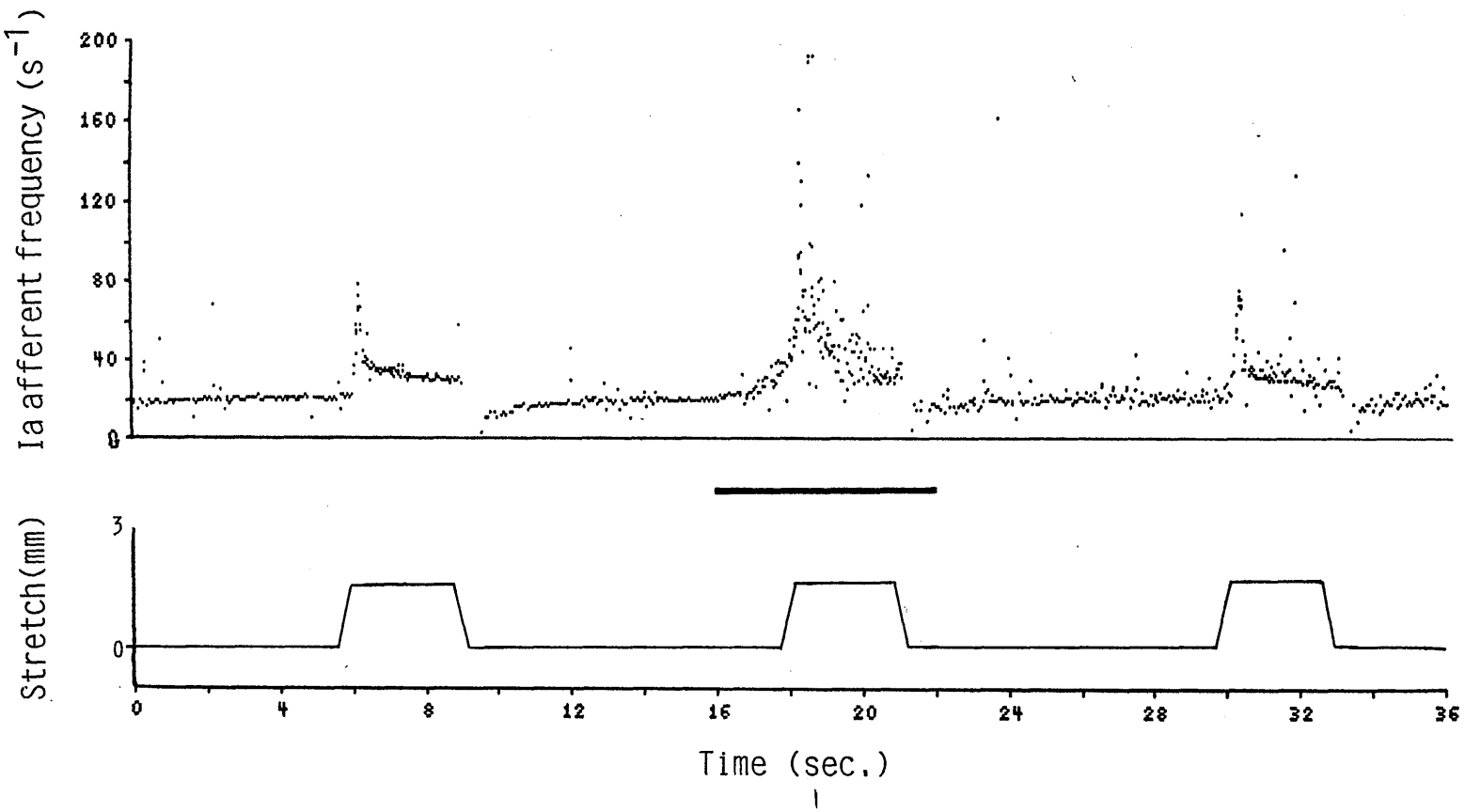
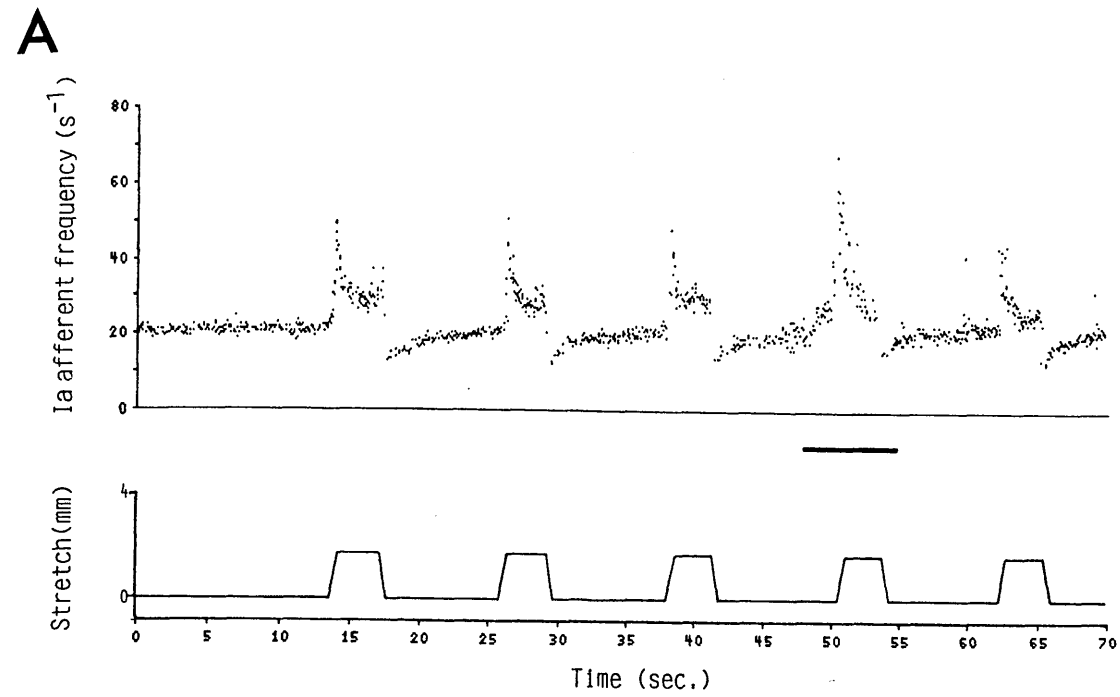

Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

Fig 18. A slight dynamic response of a tenuissimus primary afferent to cortical stimulation at points 6 (A) and 5 (B). Tenuissimus stretched 2 mm. Notice how the frequency of spontaneous regular bursting activity of the primary afferent in B increased due to cortical stimulation (shown as solid bars).


A
Ia afferent frequency (s^{-1})
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
Time (sec.)

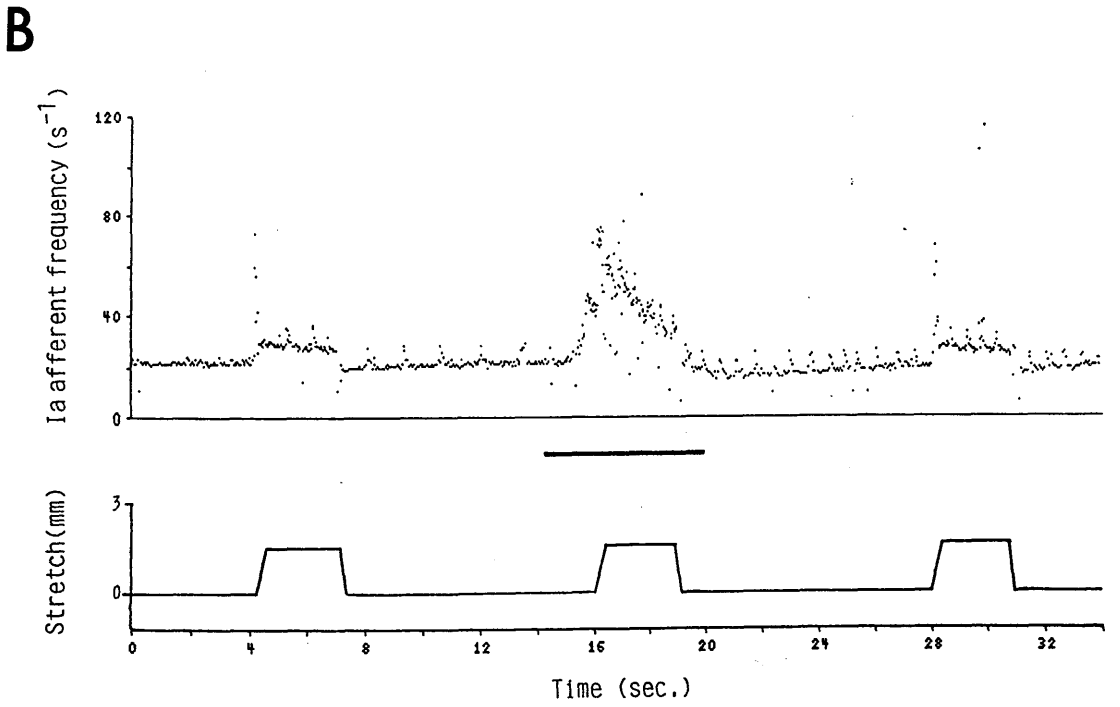
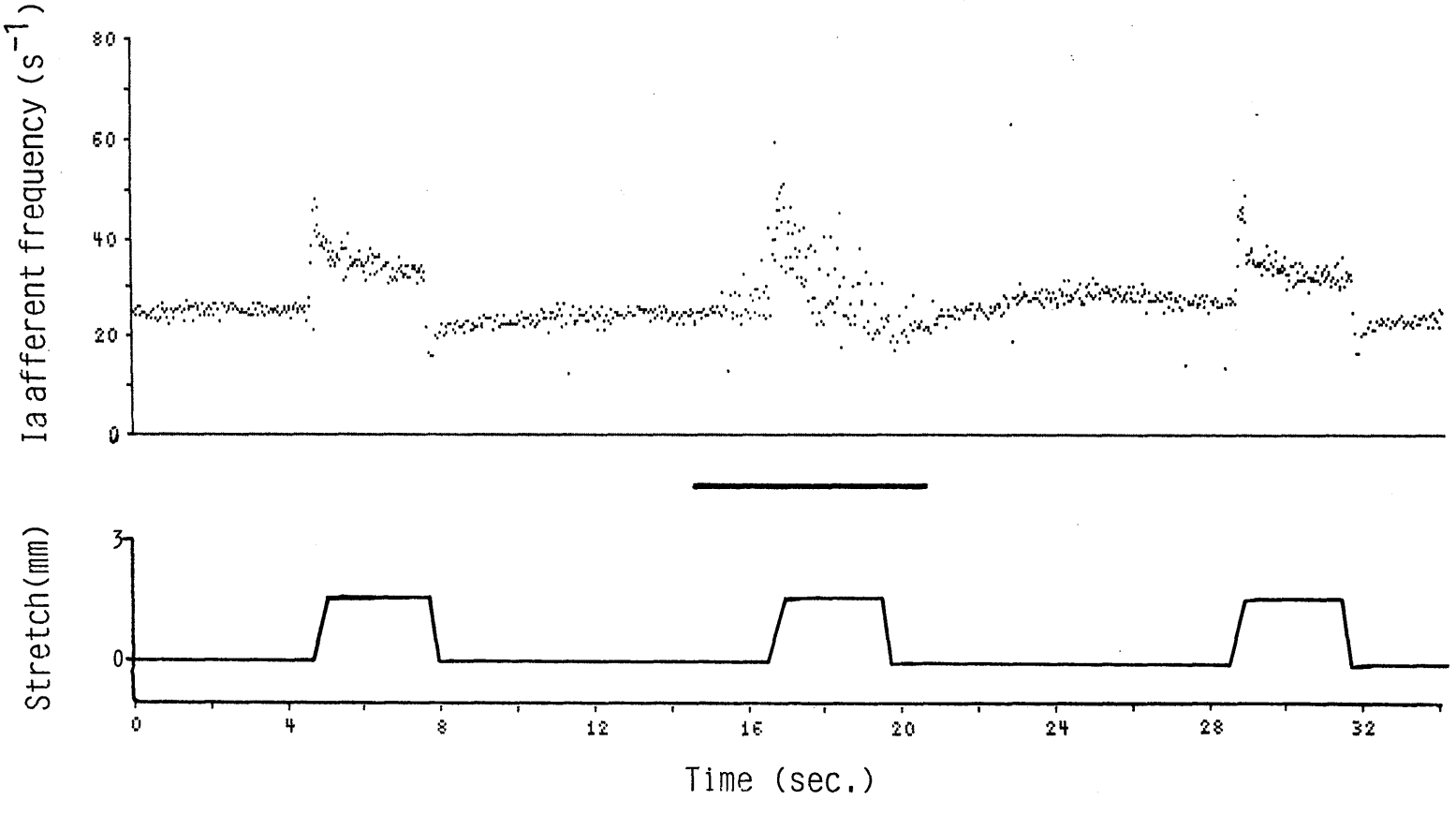

B
Ia afferent frequency (s^{-1})
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec.)

Fig 19. The effect of cortical stimulation at point 5 with a high stimulus strength (3.2 mA) on a tenuissimus primary afferent discharge. Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as a solid bar.


Ia afferent frequency (s^{-1})
80
60
40
20
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec.)

silent period of the primary afferent which usually happens at the ramp release was abolished here. The initial burst and the decay were increased. Note that there was a gradual rise in the static firing of the afferent at the initial length after stoppage of the stimulus, but this vanished after the following stretch.

Another pattern of dynamic effect is illustrated by fig 20, where the rise in initial burst (from 72 ips to 100 ips) and dynamic index (from 10 ips to 18 ips) is obvious with no apparent change in the slow decay. A slight increase in relative irregularity of afferent firing on the ramp hold in this case and at the same time the silent period on the ramp release are things to take into account in interpreting the results. Point 5 was stimulated with a low stimulus current of 0.6 mA in this illustration.

Quite unusually and only once a dynamic effect was obtained from the same afferent represented in fig 17, when the cortex was stimulated at the Pcd and this response is shown in fig 21. A similar (but weaker) effect to that in fig 17 is seen in the first cycle and an effect remarkably different in the second cycle of stimulation (fig 21). In the second cycle, afferent firing increased sharply with a latency of just over 100 msec which declines within 1 sec. Note, the response to the ramp stretch after stimulation was quite comparable to that previous to stimulation in both of the last figures, suggesting that cortical stimulation at that level did not have any sustained effect on cortical gamma motoneurones.

In the later experiments, where cats were anaesthetized with chloralose, the static firing rate of the primary afferents was as low as in barbiturate anaesthesia; however, the initial burst of the afferent to the ramp stretch was by far greater. In fig 22 point 5

Fig 20. The effect of anodal cortical stimulation at point 5 on a tenuissimus primary afferent discharge. Stimulus strength was 0.6 mA. Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as a solid bar.

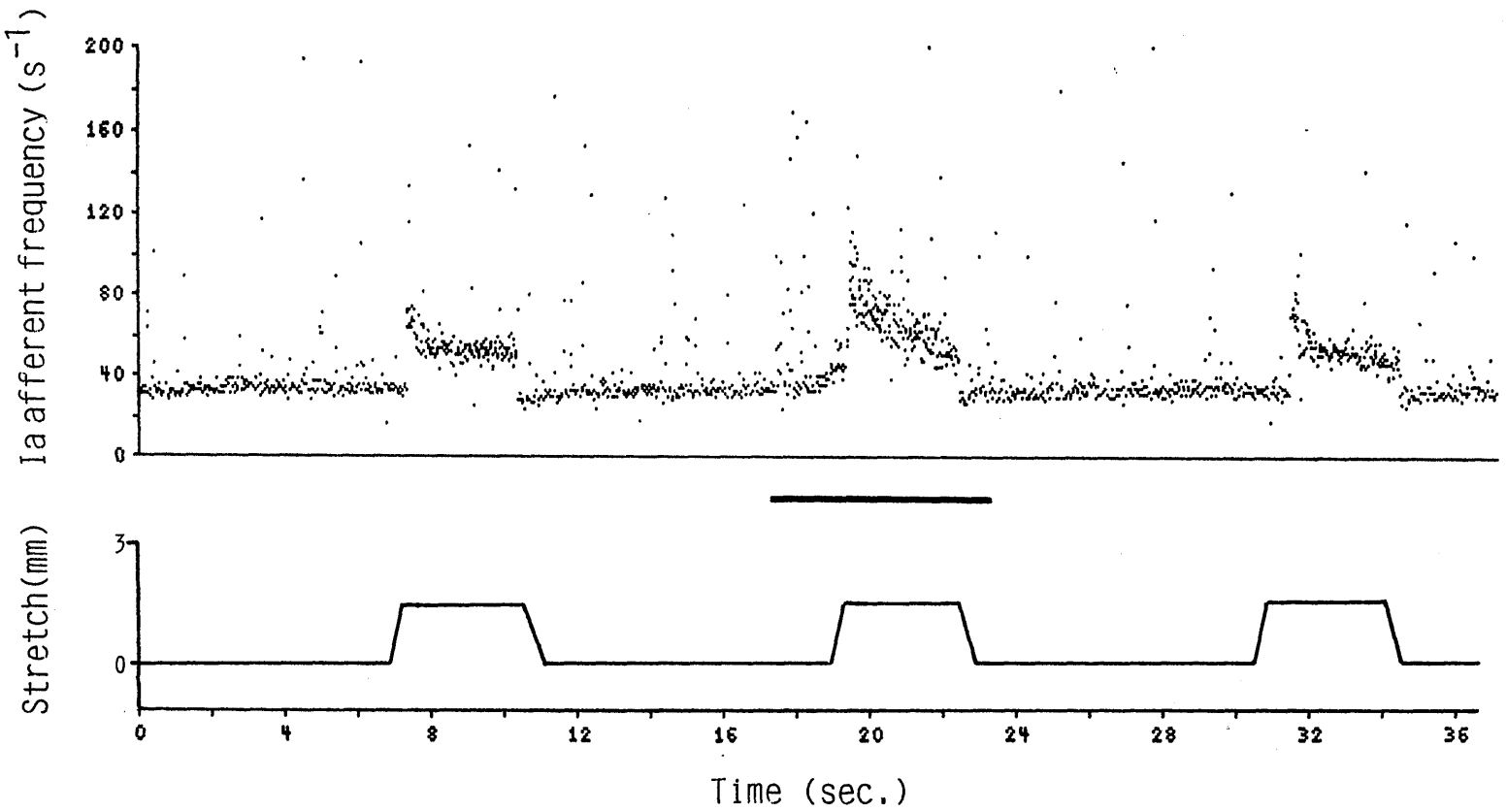

Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

Fig 21. The effect of two consecutive cycles of cortical stimulation at Pcd on a tenuissimus primary afferent discharge. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

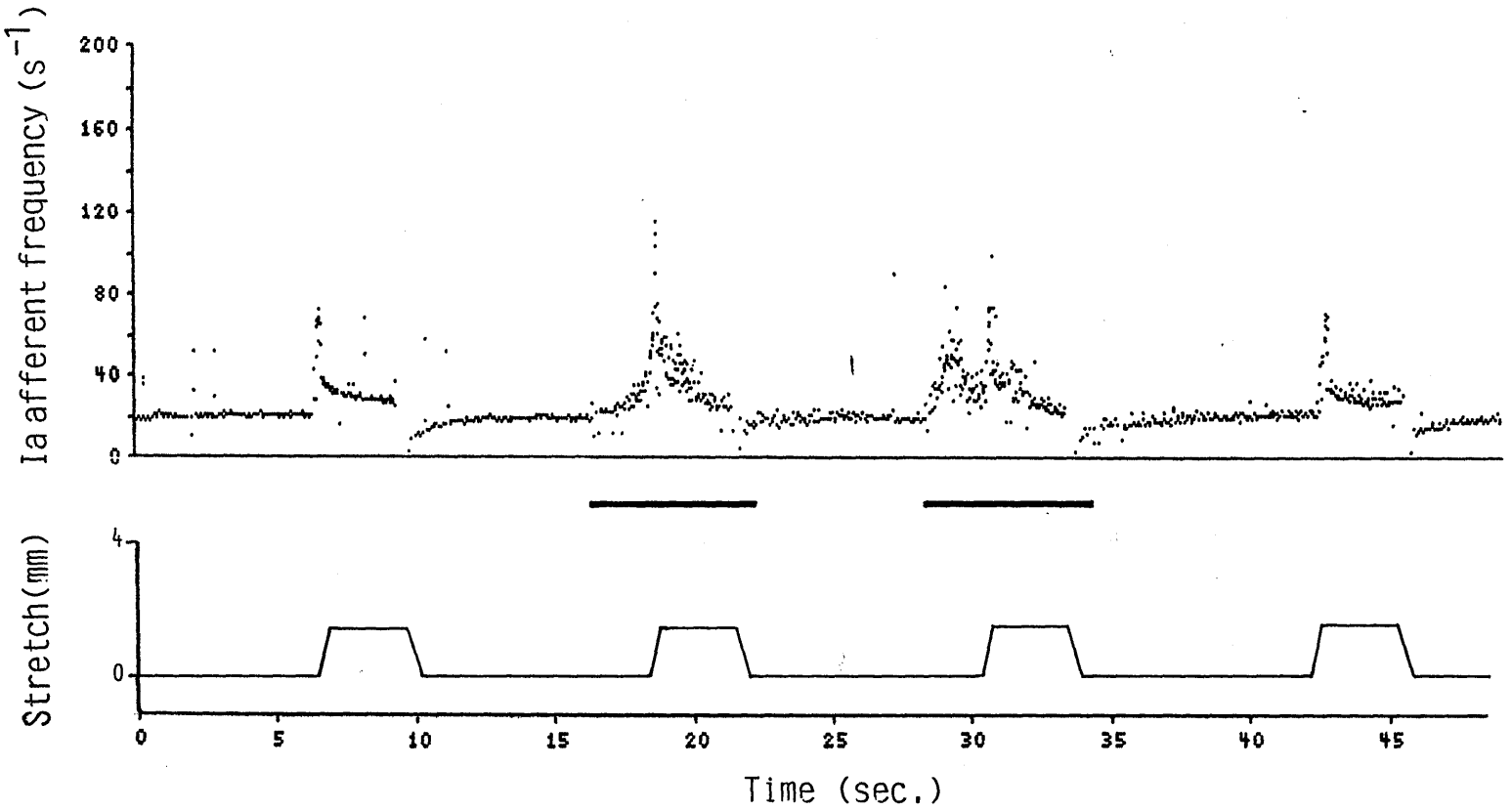
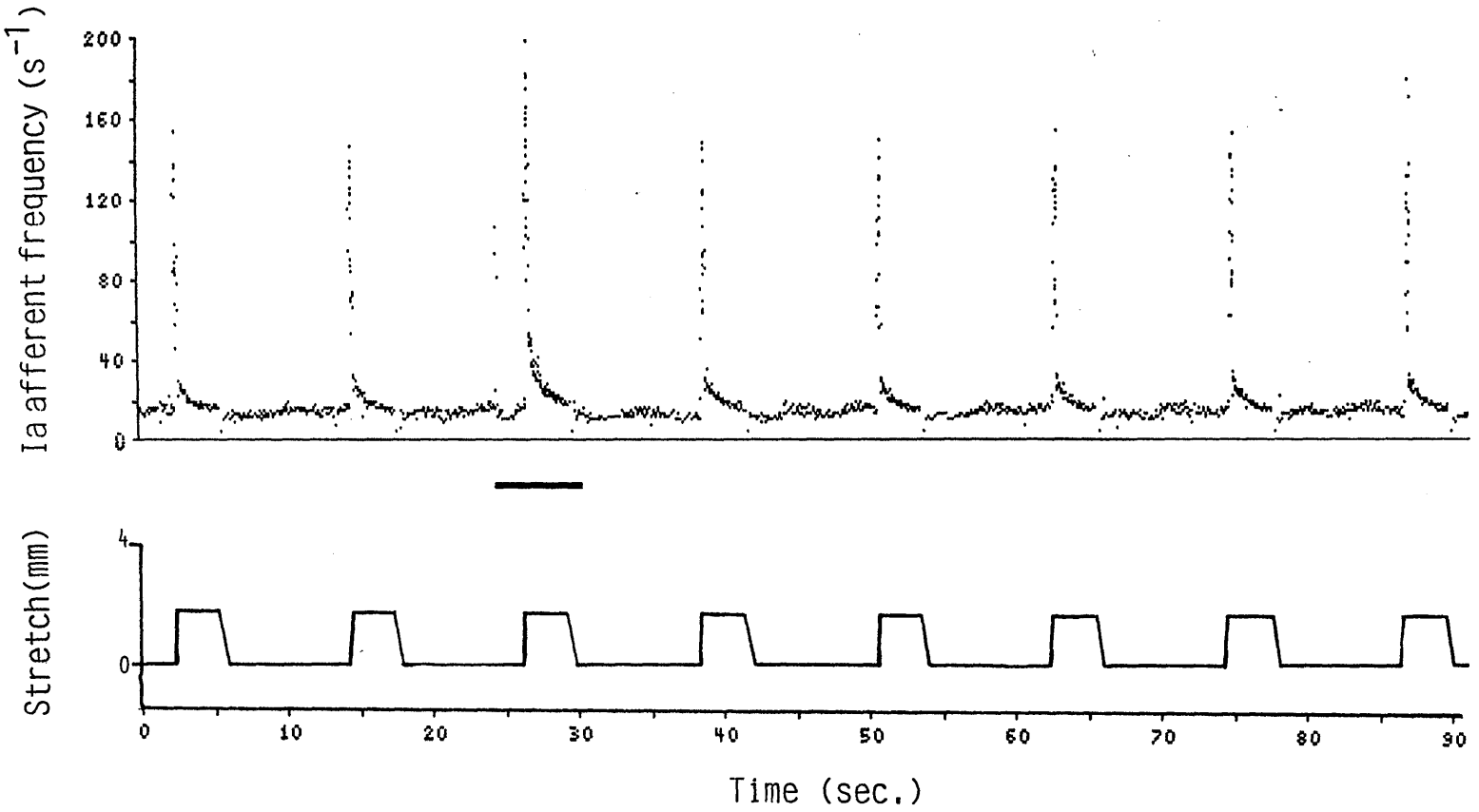

Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

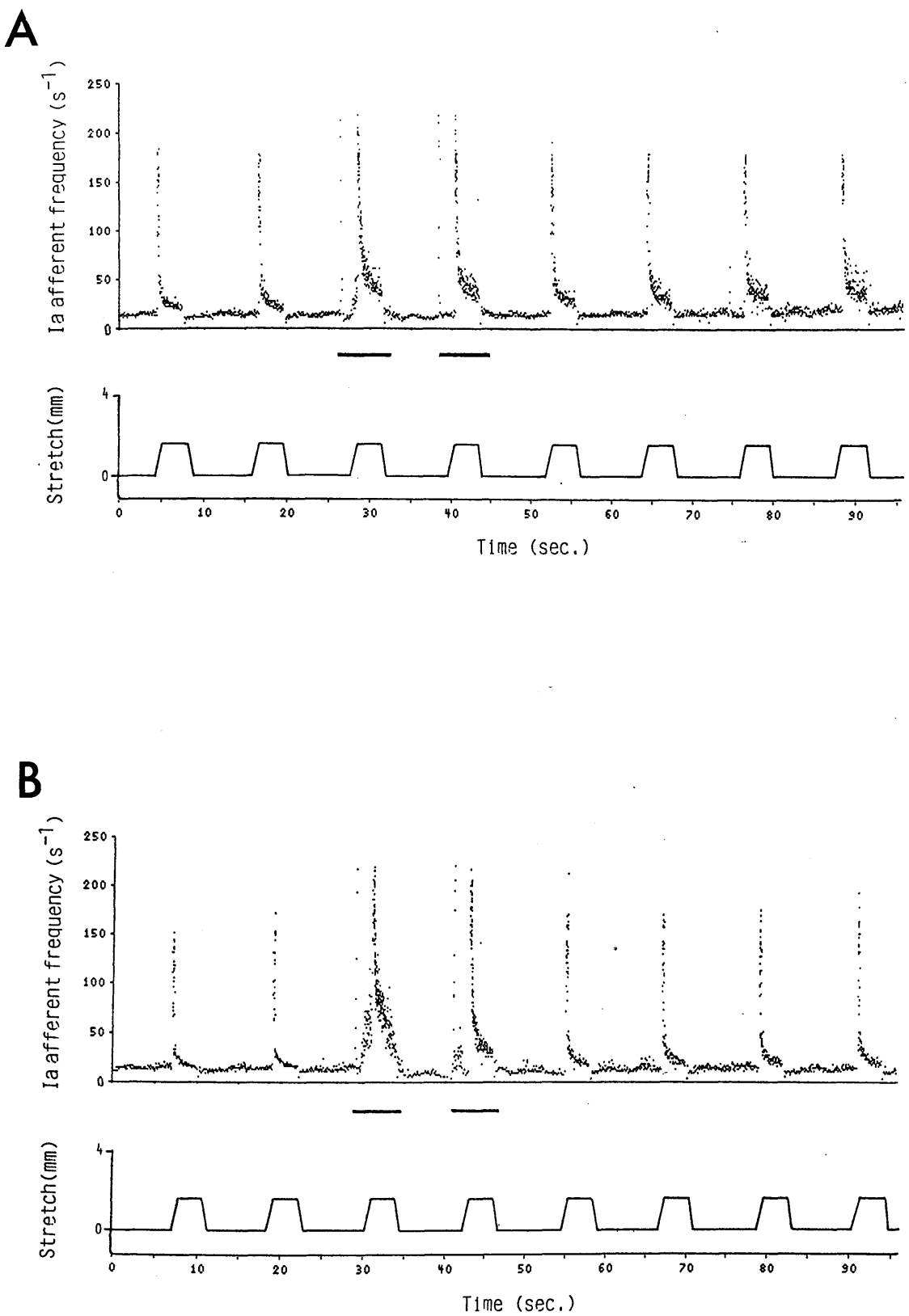
Fig 22. The effect of cortical stimulation on a tenuissimus primary afferent having a very good dynamic response to the ramp stretch. The cat was anaesthetized with chloralose in this case. The point of stimulation was at 5 and the stimulus strength was about 3.0 mA. Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as a solid bar.


Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
Time (sec.)

was stimulated with a current of 3.0 mA (S+). The latency of response was between 200-300 msec and started with a very sharp but transient increase, like an initial burst, followed by a small drop in static firing of the primary afferent with more regular discharge which might suggest an inhibition of spontaneous activity. Both initial burst to ramp stretch and dynamic index were increased (from initial values of 155 ips and 48 ips to 200 ips and 73 ips respectively). The decay was also increased from 7 ips to 25 ips in half a second. The EMG electrodes located under the distal part of the muscle did not record any potential which implies that it was unlikely that the reduced frequency was due to unloading by extrafusal contraction.

Similar to the cats anaesthetized with barbiturates repeated cortical stimulation (figures 23 and 24) revealed that the fusimotor system did not respond identically to the same stimuli in consecutive cycles of stimulation. During anodal stimulation at point 4 with 2.8 and 3.0 mA (A and B, fig 23) the primary afferent showed a transient burst of firing with almost no latency, dying off within the matter of milliseconds, and this is suspected to be the stimulus artifact. In the case of the stronger stimulus (fig 23,B), the transient was followed almost immediately by a sharp rise in the firing (to about 70 ips) even before the beginning of the ramp. The initial burst to the ramp increased from 165 ips to 220 ips in the first cycle and 215 ips in the second. The dynamic index rose by 38 ips from 53 to 91 ips in the first cycle and 92 ips in the second. The dynamic decay rose, but to lesser extent, from 9 ips to 32 ips and 62 ips. The silent period of the afferent due to the ramp release was absent in the first cycle, but clearly visible during the second period of stimulation.

Fig 23. The effect of two consecutive cycles of anodal stimulation at point 4 on a tenuissimus primary afferent discharge from a chloralose-anaesthetized cat with 2.4 (A) and 3.0 (B) mA strength. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
250
200
150
100
50
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
Time (sec.)
B
Ia afferent frequency (s^{-1})
250
200
150
100
50
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
Time (sec.)

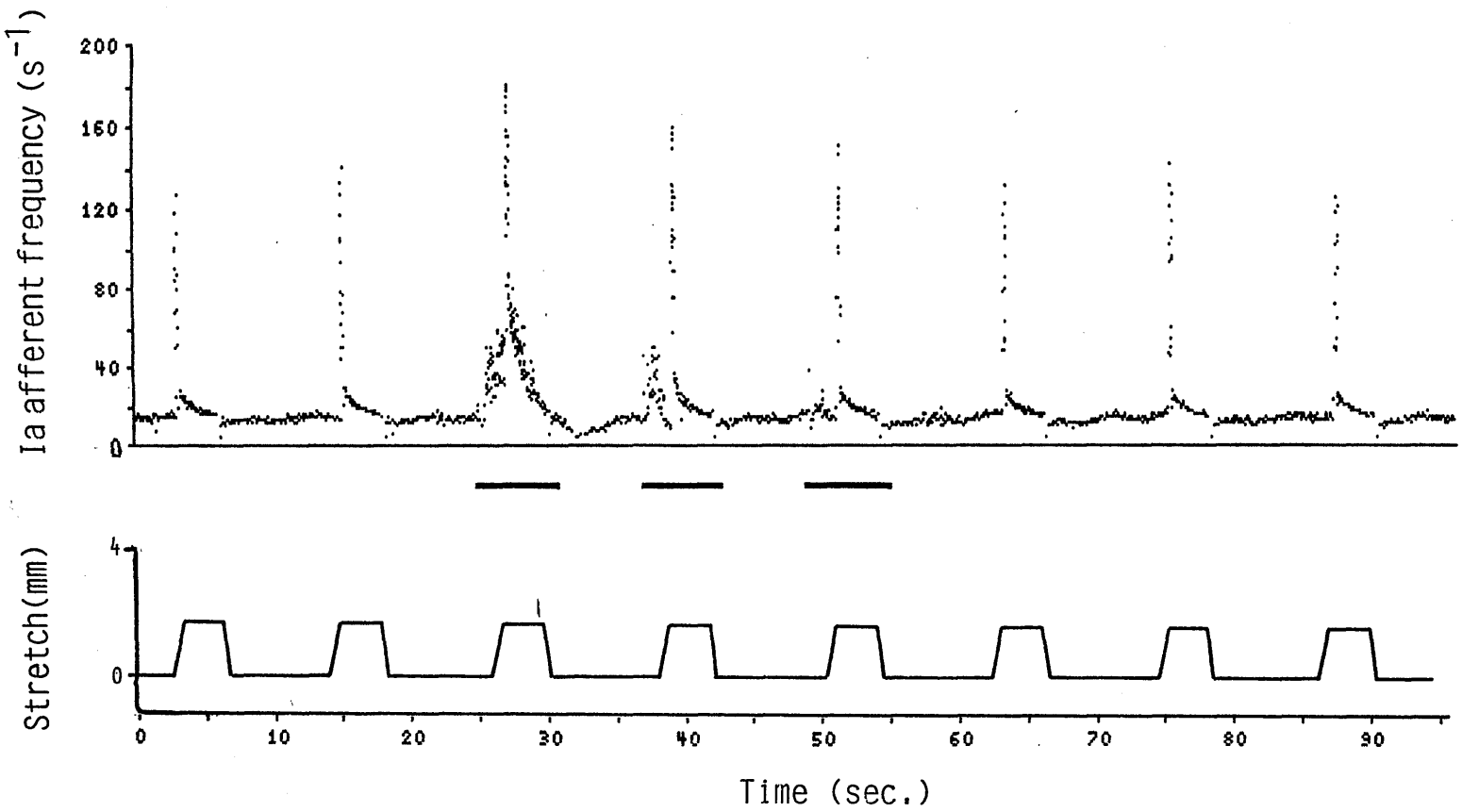
A weaker stimulus gave the same pattern of response (fig 23,A) except that the effect on the afferent before the ramp was less pronounced, but the changes brought about during the ramp are of the same value (i.e. dynamic index rose to 78 ips and 65 ips from the initial value of 30 ips; the dynamic decay from 24 ips to 33 ips and 28 ips). Fig 24 shows the response of the same afferent to anodal stimulation of point 1, forward from the cruciate sulcus, with 2.0 mA. It lacks the fast transient rise at the beginning of the stimulation that was obvious in the previous figure. However, it shows the reduction in responsiveness to stimuli in successive stimulating cycles. The initial burst to ramp stretch increased from 140 ips to 185, 160 and 150 ips, so did the dynamic index: from 42 ips to 71, 61 and 50 ips, and the dynamic decay: from 7 ips to 22, 17 and 8 ips.

The latency of the response (not the very transient rise at the beginning) in both figures 23 and 24 is over 0.5sec; however, that of fig 22 is just over 200 msec.

B. Intrafusal Recruitment alone: Static Effects

Static fusimotor effects can be brought about by contraction of static bag_2 fibre alone, nuclear chain fibre(s) alone or contraction of both. They are well characterized by an increase in mean frequency with reduction or even loss of length sensitivity of the primary ending. There may be an increase in the irregularity of the primary discharge to some degree depending on the recruitment of

Fig 24. The effect of three consecutive cycles of cortical stimulation on the same tenuissimus primary afferent (shown in fig 23) from a chloralose-anaesthetized cat. Point of stimulation was on cruciate sulcus anterior to point 5. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
Time (sec.)

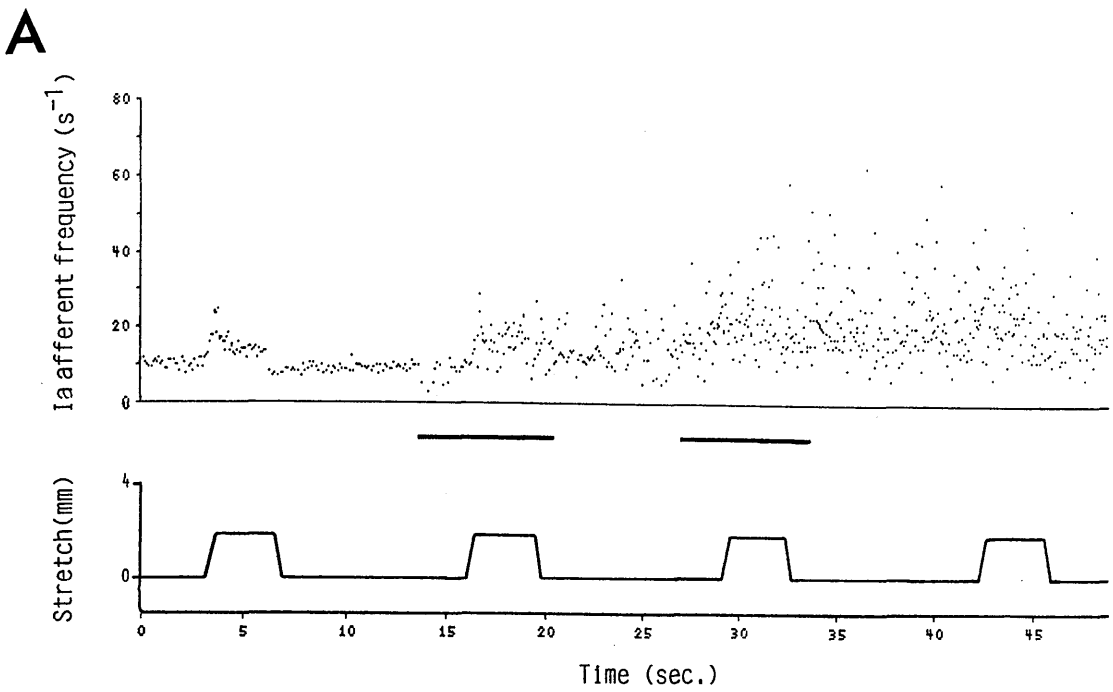
different types of intrafusal fibres. A high frequency scattery response is expected if Sb_2 fibre and nuclear chain fibres are recruited together.

Stimulation of almost all points (1-14) gave rise to static effects, even the points within the dynamic area, depending on the state of anaesthesia. The results generally confirm the findings of Gladden and McWilliam (1977) who stated that the areas from which these effects were produced were reduced with increasing depth of anaesthesia. In fact, it was sometimes confined to an area within 2 mm of postcruciate dimple. The results also show that no driving at constant frequency was seen at any time.

It was clearly visible in the direct visualization of exteriorised muscle spindles that on some occasions gamma motoneurones, and in turn intrafusal fibres, become active as a consequence of a course of stimulation. Fig 25 shows how the two primary afferents were not even responding to the ramp during the stimulation. Note that the abolition of the length sensitivity is accompanied by a scattery response of the afferent and an obvious increase in the mean frequency.

In an attempt to examine the pattern of response to two consecutive cycles of stimulation, the Pcd was stimulated. Figure 26 demonstrates that the afferent response to the ramp was abolished in the second cycle of stimulation. In the first cycle, however, the ramp response was not abolished although it is obviously seen that the length sensitivity was drastically decreased during the pull. Increased length sensitivity after the first cycle of stimulation had stopped can be looked upon as an after-effect which will separately be introduced. The latency of response in the first cycle was over 1

Fig 25. The effect of consecutive cycles of cortical stimulation on the responses of two tenuissimus primary afferents to ramp stretch. A. The response to ramp stretch is completely abolished after one second past the onset of stimulation at point 14. B. The ramp response is completely abolished following cortical stimulation at point 4. Tenuissimus muscle stretched 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

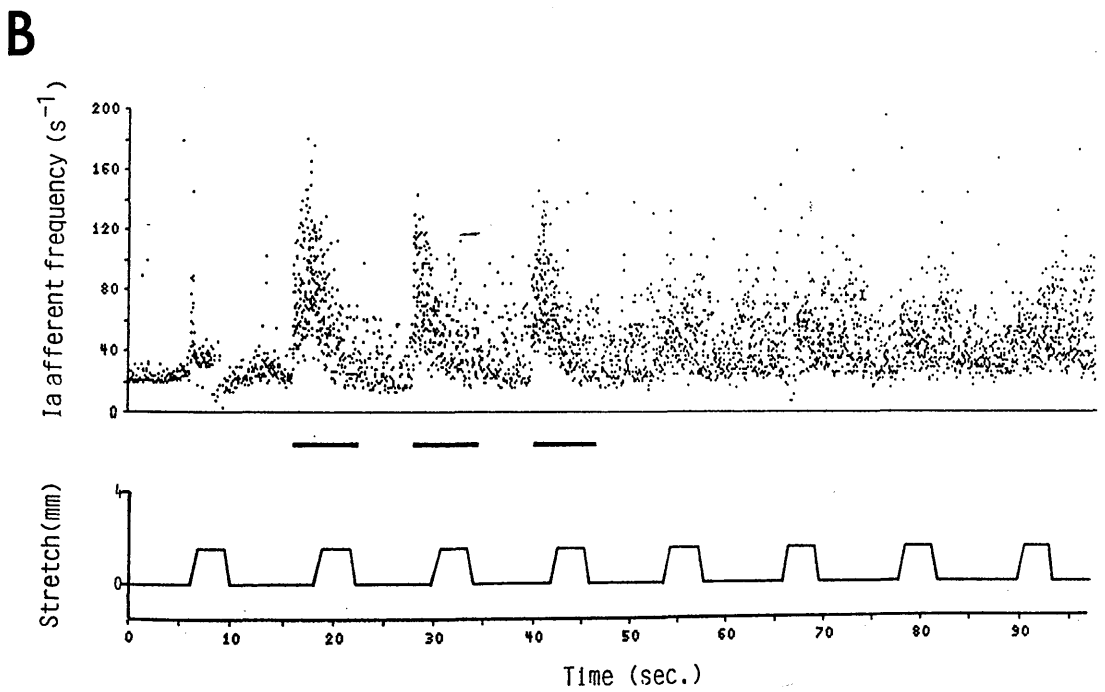
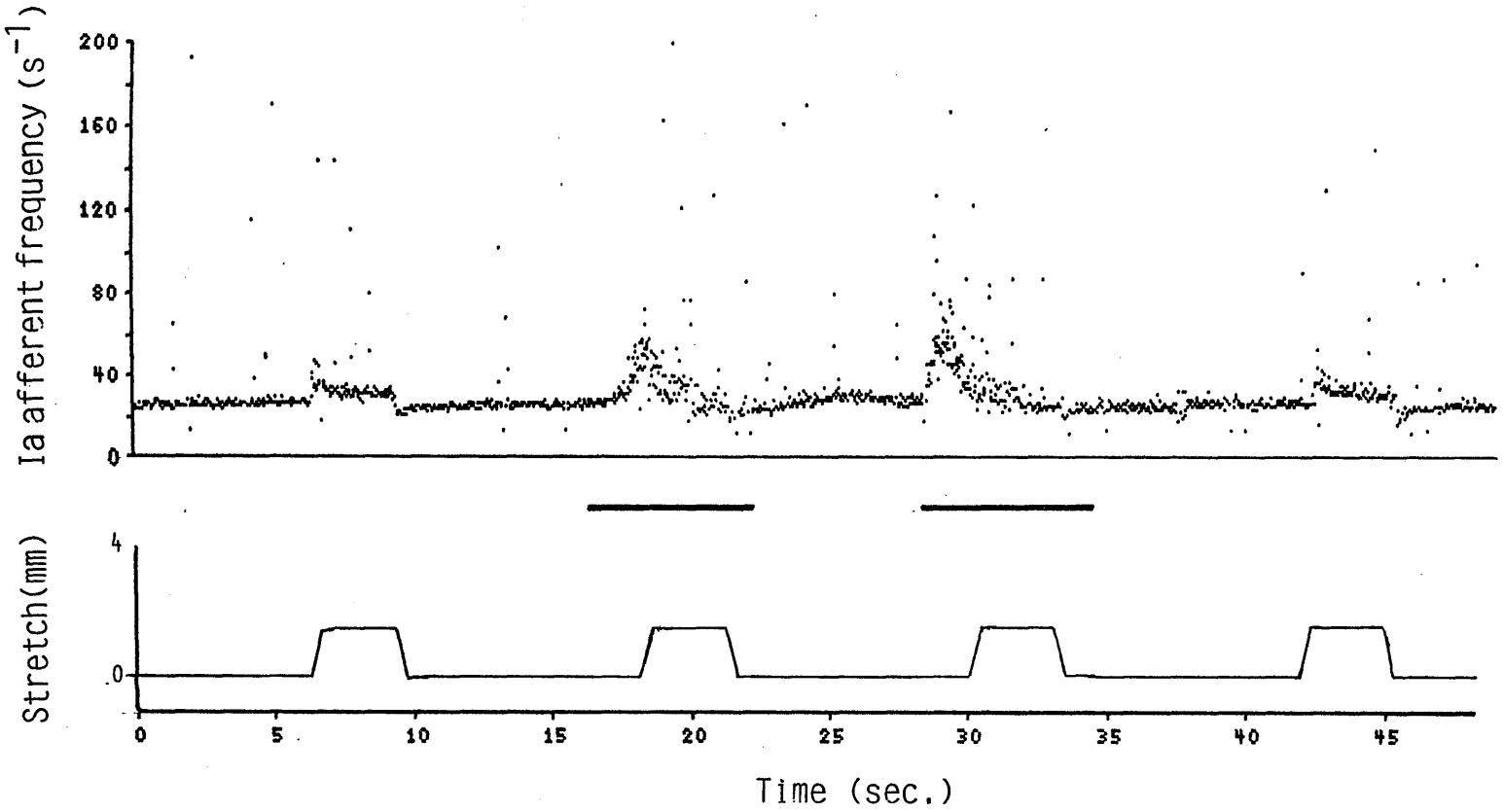

B
Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
Time (sec.)

Fig 26. The effect of two consecutive cycles of cortical stimulation at Pcd on the response of a tenuissimus primary afferent to the ramp stretch with stimulus strength of 2.1 mA. The ramp response is abolished in the second cycle of stimulation. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

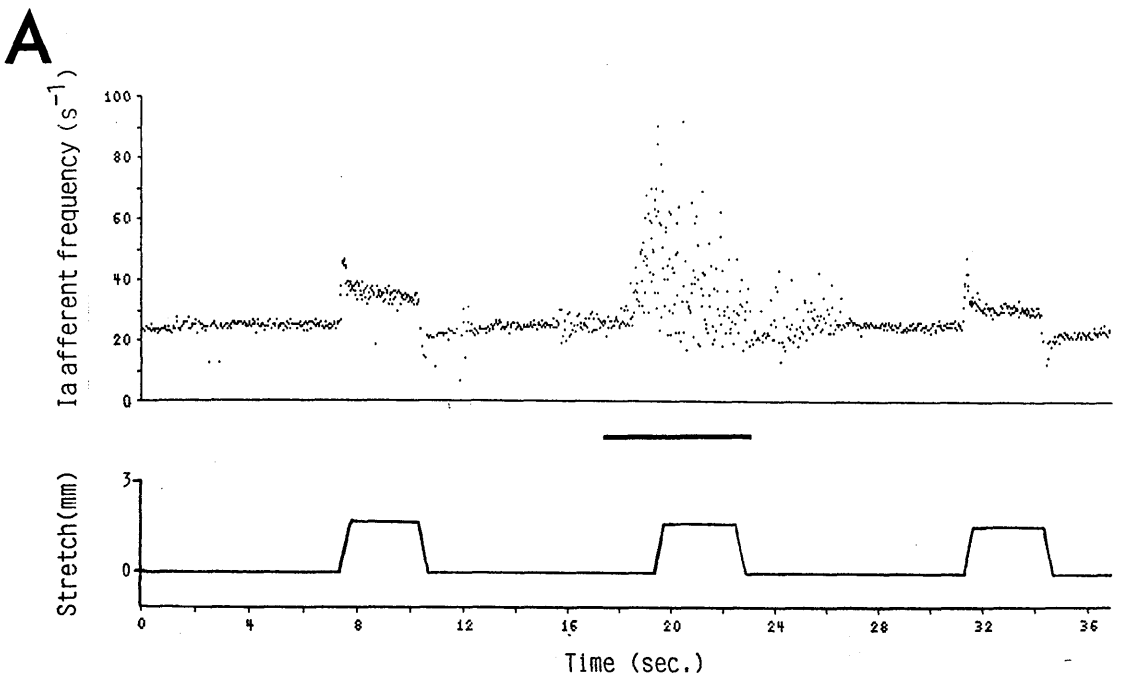

Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

sec but it was just over 100 msec in the second cycle. The amplitude of the rise in frequency of the afferent is slightly greater in the second cycle too. All this suggests that the stimulus effect was building up and had a sustained effect on the gamma motoneurones which lasted at least up to a few seconds.

Sometimes stimulation of a point increased the scatter of the response such that the response to the ramp was almost abolished. An example of this pattern is given in fig 27. It displays responses of another tenuissimus primary afferent to anodal stimulation applied to two nearby points on the cortex with different intensities in a cat anaesthetized with barbiturate. Note that the excitation in this pattern of response in comparison with figure 25 is transient and it was reproducible in many experiments. The latencies of these effects are different, mostly dependent upon the intensity in this case.

Point 5 was stimulated anodally when fig 27,A was obtained; and the current applied was 3.5 mA, slightly higher than in fig 27,B. It not only shows the scattery firing of the afferent, but also the fact that cortical stimulation desensitized the spindle to length changes throughout the course of stimulus. It seems that there was some habituation to the stimulus at some level, for the afferent discharge declined progressively throughout the course of stimulation, and even returned back to the previous static firing level during the very last second of stimulation. Scattery firing of the afferent after the stoppage of stimulus might be considered as a rebound activity of a yet non-specific intrafusal fibre which was possibly inhibited during the course of stimulation.

Fig 27. The effect of cortical stimulation at point 5 (A) and 6 (B) on the same tenuissimus primary afferent discharge during a ramp stretch. The stimulus strength was 3.5 and 2.0 mA respectively. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
100
80
60
40
20
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

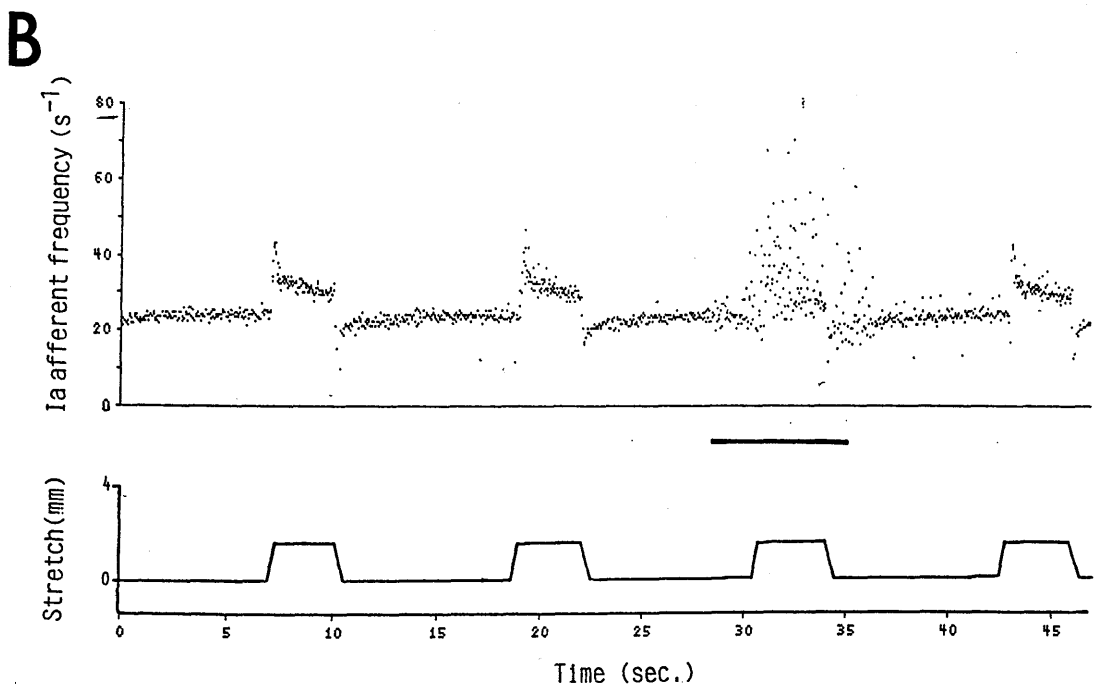

B
Ia afferent frequency (s^{-1})
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

Fig 27,B shows the response of the same afferent to a stimulus current of 2.0 mA applied at point 6. The firing became scattery and even more, when the cortical stimulation was accompanied by ramp stretch. The cortical stimulation could not abolish length sensitivity of the primary as one can still see the rise in frequency at the beginning of the ramp and the silent period on the release of the ramp. Also there is some condensation of points around 50 Hz during the second half of the hold phase. The effect of stimulation wears off sometime after stopping the stimulation.

Sometimes the effect of cortical stimulation on the fusimotor system was apparent only when the muscle length was increased. Figures 28 and 29 both demonstrate this phenomenon. One millimeter anterior to Pcd was the target point in stimulating the cortex in fig 28. A stimulus of 1.2 mA (S+) was not strong enough to recruit the gamma motoneurones before the ramp. However, it seems that the stimulus increased the scattering of the response at the longer length but not the sensitivity, because the mean frequency during the ramp hold did not change, suggesting a very weak recruitment of one or more intrafusal fibre.

In fig 29 the situation is a little bit different in the sense that there is an increased scatter before the pull, but it had become more scattery in response to ramp stretch. Although fig 29,A is a good example of increased scatter affected by the length change in the muscle, there is also a clear reduction in static length sensitivity during the second half of the pull, a drop of 10 ips as compared to the preceding cycle with no stimulation. In fig 29,B the condition is more or less the same with less pronounced reduction in length sensitivity at the end of the pull. The afferent discharge,

Fig 28. The effect of cortical stimulation (1 mm anterior to Pcd) on the response of a tenuissimus primary afferent to ramp stretch. Tenuissimus stretched 2 mm. Cortical stimulation shown as a solid bar.

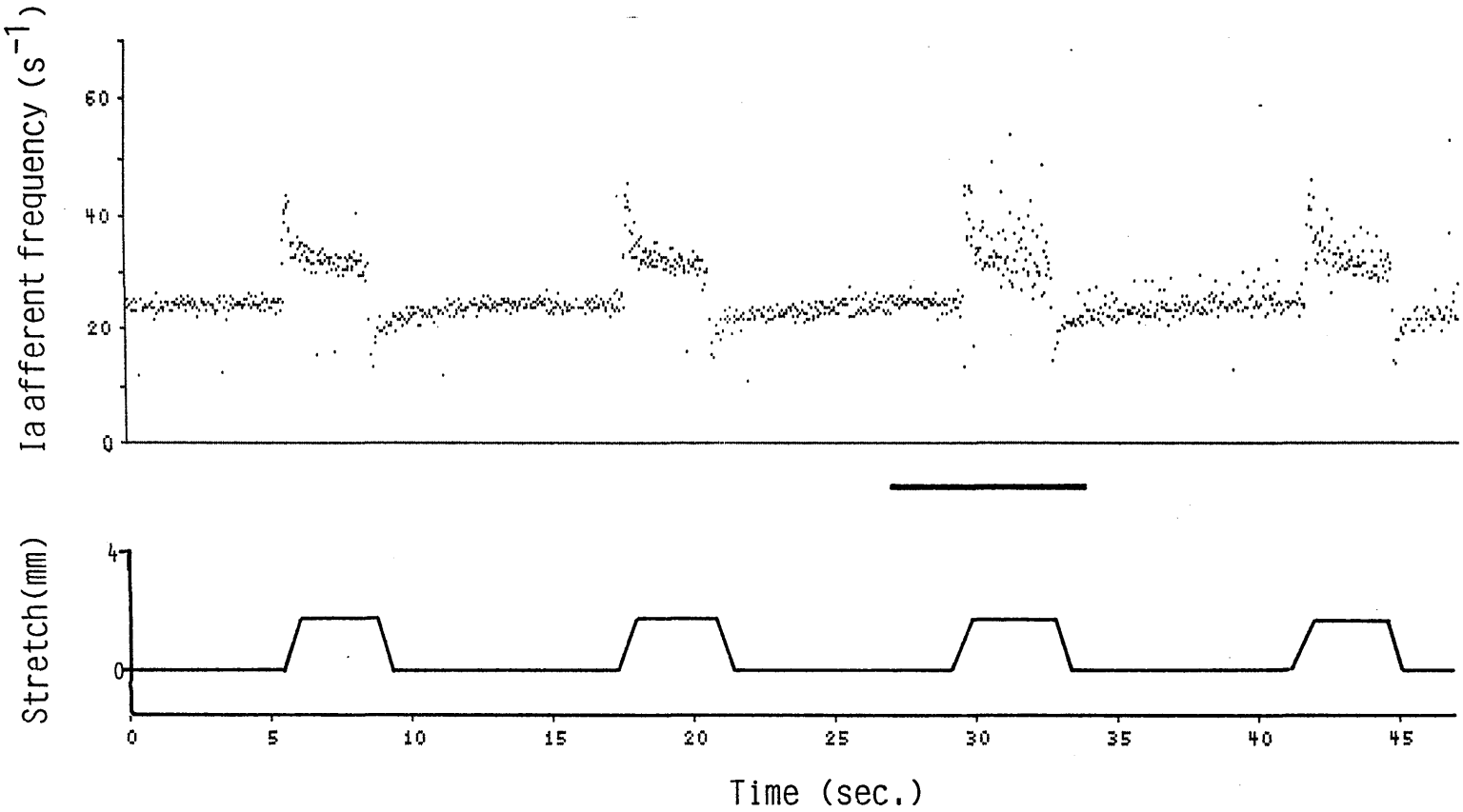
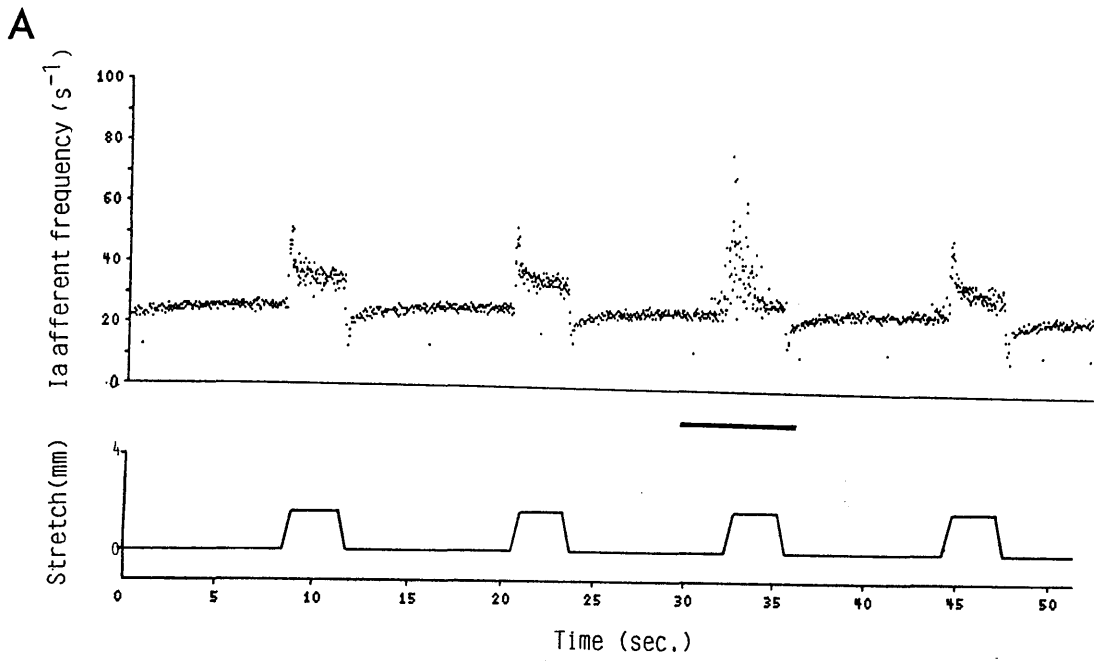
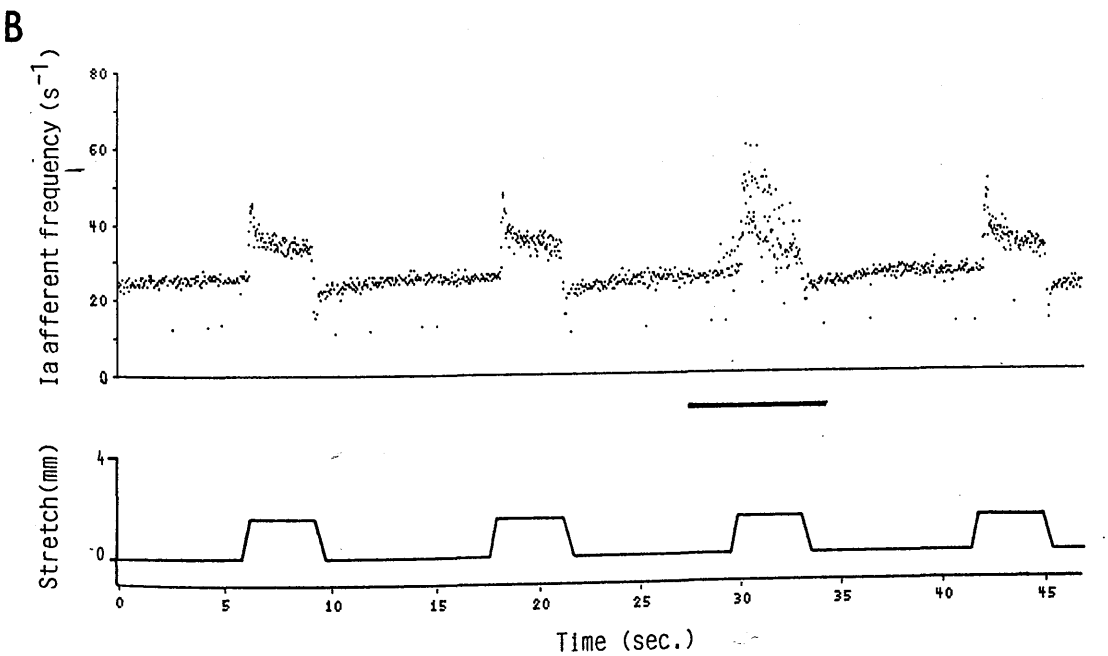

Ia afferent frequency (s^{-1})
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

Fig 29. The effect of cortical stimulation on the response of a tenuissimus primary afferent to ramp stretch. Pcd (A) and point 5 (B) were stimulated. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
100
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
50
Time (sec.)


B
Ia afferent frequency (s^{-1})
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

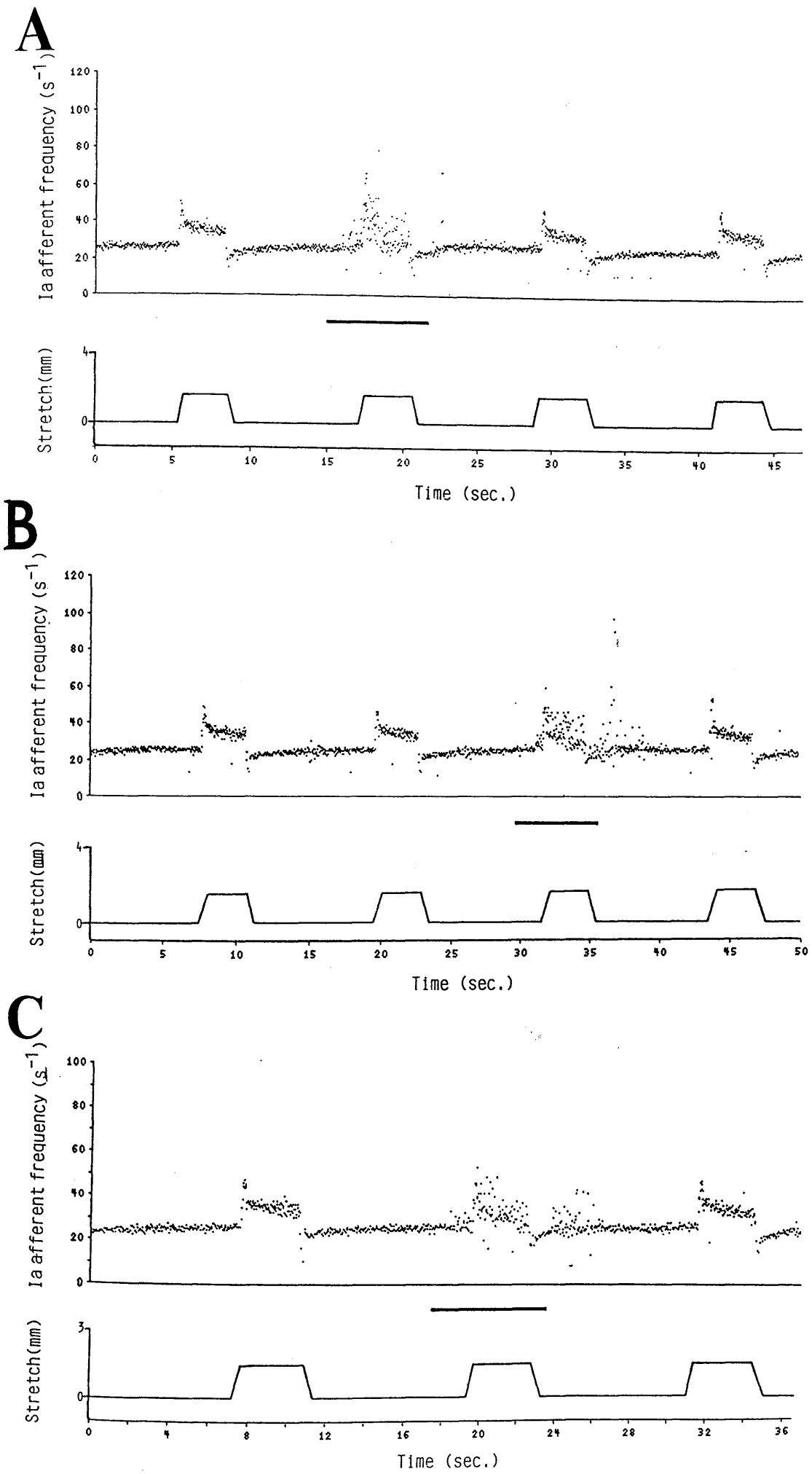
however, is not much different at the initial length meaning that the primary ending could pick up the previous static firing before the next pull. Note that in fig 29,A the Pcd was stimulated with 2 mA and in fig 29,B point 5 with 3 mA, both sites being stimulated anodally.

Fig 30 was obtained on stimulation of point 5 with very closely similar intensities (3.0, 3.0 and 3.2 mA respectively) but different anaesthetic levels. The interval between the time of recording of the 30,A and 30,B is 6-8 minutes and between 30,B and 30,C about 12-15 minutes. Therefore, apart from a slight change in the intensity of stimulus, the anaesthetic level seems to be the only factor that is variable in the three cases.

In fig 30,A there is a rise in the initial burst to the ramp due to cortical stimulation which is followed by a slight rise in the static firing. However, the dynamic index did not change significantly. The firing level stayed scattery during the period of ramp hold with a lower mean frequency as compared with the preceding cycle, and the ramp release silenced the afferent. A slight rise in static firing following the stimulus was abolished by the next stretch.

The mean frequency of the afferent in the case of fig 30,B did not change but the initial burst (from 46 ips to 60 ips) and the dynamic decay (from 3 ips to 7 ips) were increased. However, the pattern of firing is very scattery and similar to the top and bottom records.

Fig 30. The effect of cortical stimulation at point 5 on the response of a single tenuissimus primary afferent with different intensities, 3.0 (A), 3.0 (B) and 3.2 (C) mA respectively. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
120
100
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)
B
Ia afferent frequency (s^{-1})
120
100
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
50
Time (sec.)
C
Ia afferent frequency (s^{-1})
100
80
60
40
20
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

In fig 30,C neither the initial burst to the ramp nor the dynamic index increased on stimulation. However, the afferent did not go silent during the ramp release. It is almost definite that the Db_1 was not recruited.

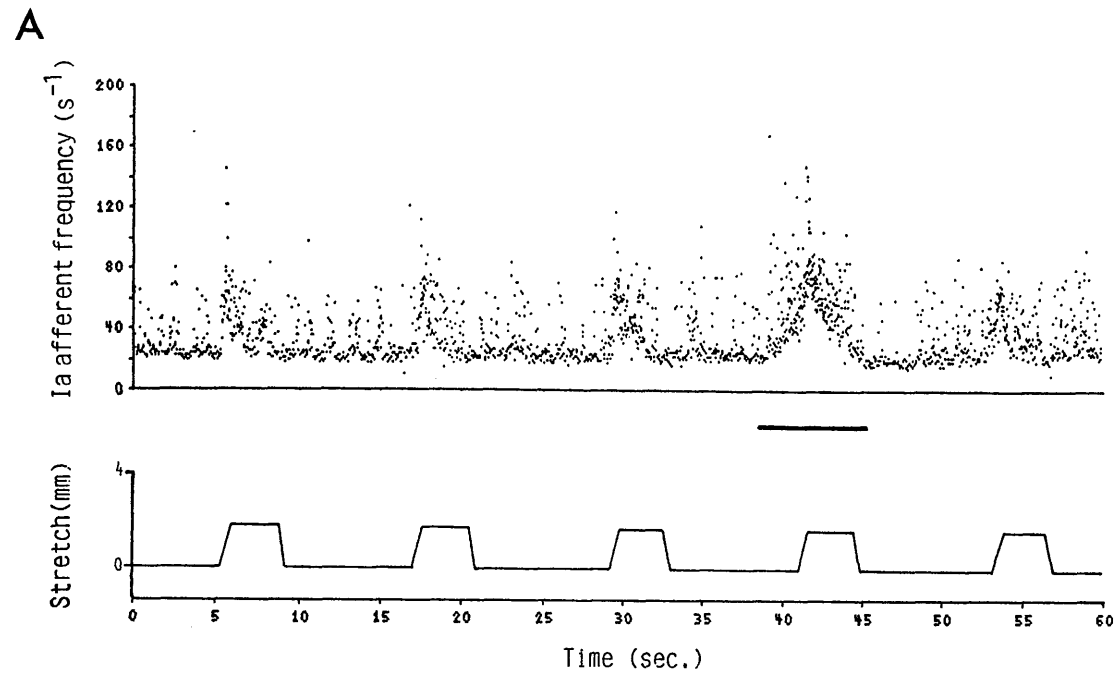
Note that there is rebound activity in all three examples. In fig 30,A there is only a transient burst after cessation of stimulation. The rebound activity is clearest in fig 30,C because the static firing had become regular by the end of the period of stimulation. The response then became irregular in less than a second after the termination of stimulation. It is worth noting that this pattern of results was reproducible in the same cat over and over again and was also seen in other cats.

It seems as though the intrafusal fibres are put on alert with the onset of stimulation but will do nothing to change the firing frequency of the primary ending. As soon as an external signal such as a ramp comes along, it works as a trigger to drive those already alert intrafusal fibres into activity.

C. Mixed Intra and Extrafusal Recruitment

Figures 31, 32 and 33 represent recruitment of extrafusal fibres along with intrafusal fibres on cortical stimulation at various points. The tenuissimus muscle EMG was picked up during these occasions and some deep back muscles were sometimes contracting too. The occurrence of this pattern of response was not confined to a particular area of the sensorimotor cortex as it was reproducible almost from all the points. Common characteristics of these responses were their similar short latencies (≥200 msec), shape and abolishment of the response to the ramp. It seems that the responses

Fig 31. The effect of cortical stimulation on the response of two tenuissimus primary afferents from 2 different cats to ramp stretch. Pcd was stimulated in both cases with 0.2 (A) and 1.7 (B) mA. Tenuissimus stretch 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
50
55
60
Time (sec.)

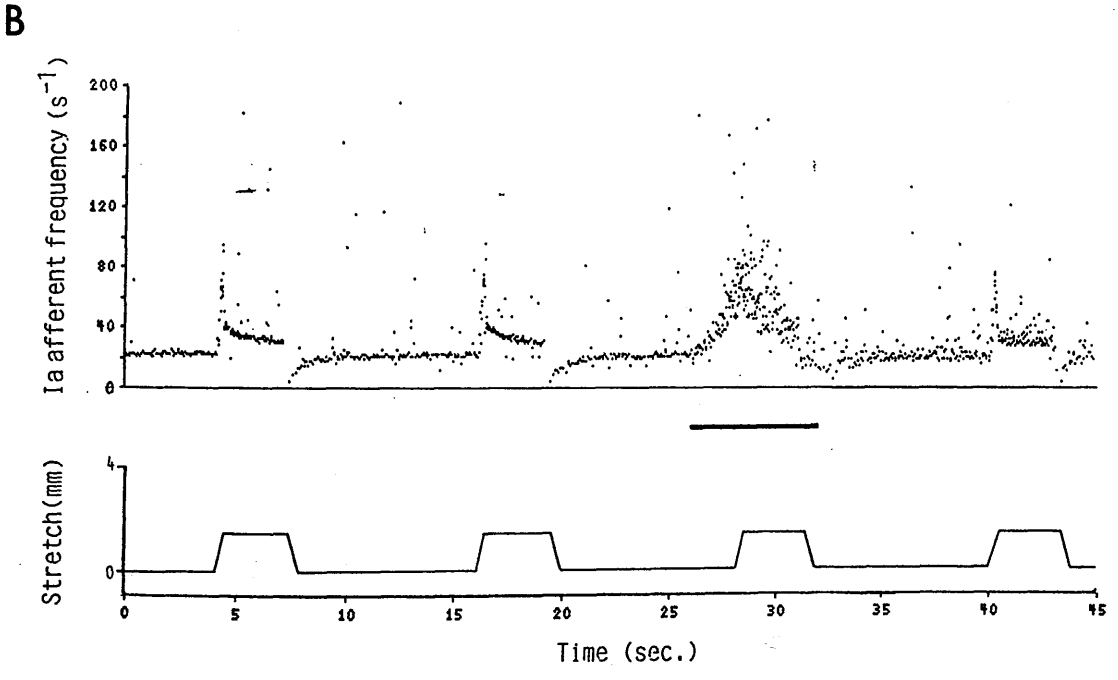
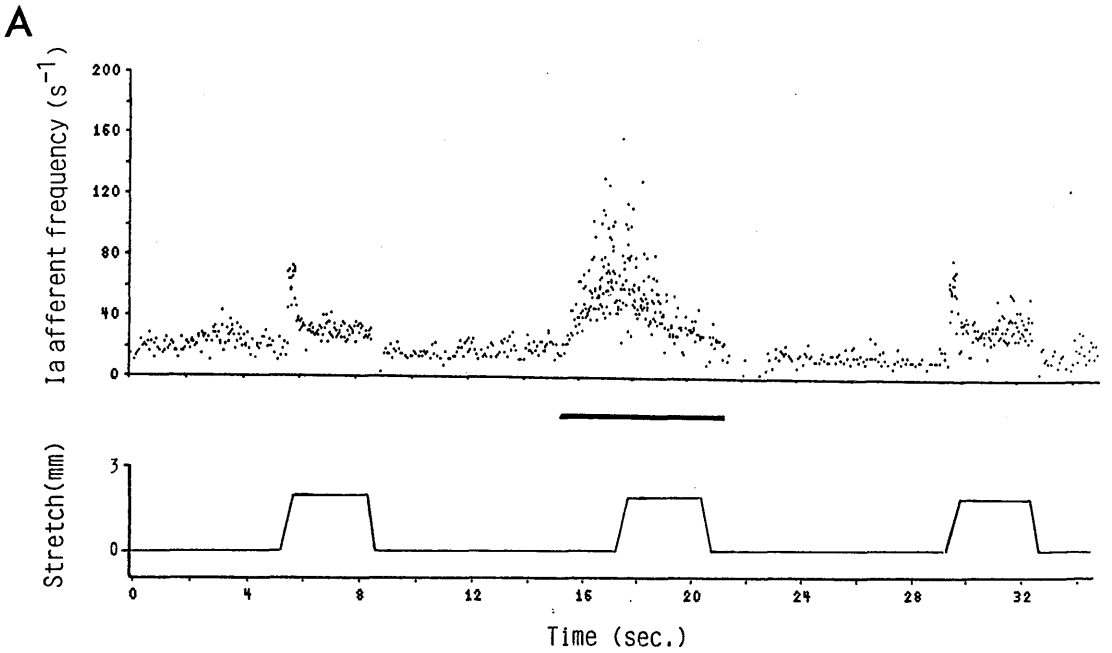

B
Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

Fig 32. The effect of cortical stimulation at points 4 (A) and 9 (B) on the response of two different tenuissimus primary afferents to ramp stretch. Stimulus strengths were 1.6 and 0.2 mA respectively. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


A
Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec.)

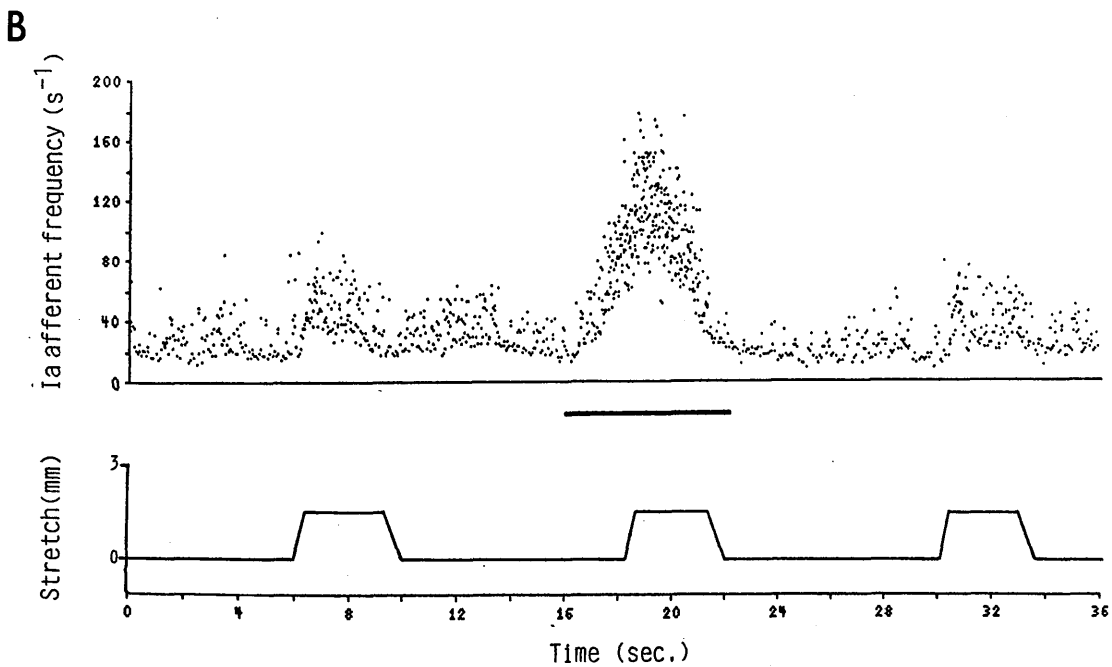
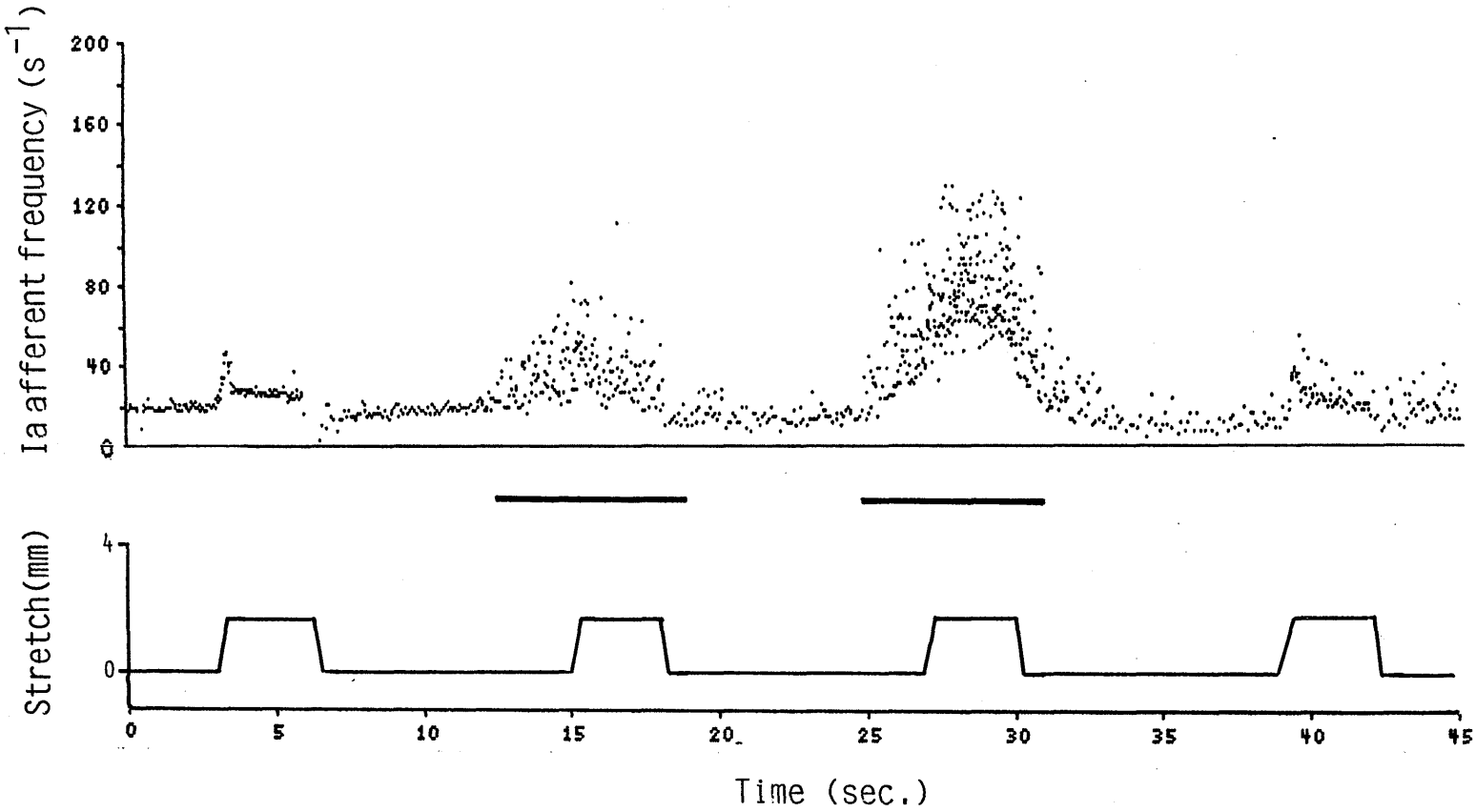

B
Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec.)

Fig 33. The effect of two consecutive cycles of cortical stimulation at point 4 on the response of a tenuissimus primary afferent to ramp stretch with intensity of 0.8 mA. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


Ia afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

saturated at some point, with a maximum mean frequency of around 120-140 ips (fig 32,B). It is more likely that descending neurones synapsing with gamma motoneurones (directly or indirectly) in the spinal cord were involved, since gamma motoneurone stimulation in isolated muscle spindles can increase the primary afferent discharge to over 200 Hz (Boyd, 1986). The frequency reached a maximum in about 3 seconds, but it dropped significantly over several seconds towards the end of the stimulation.

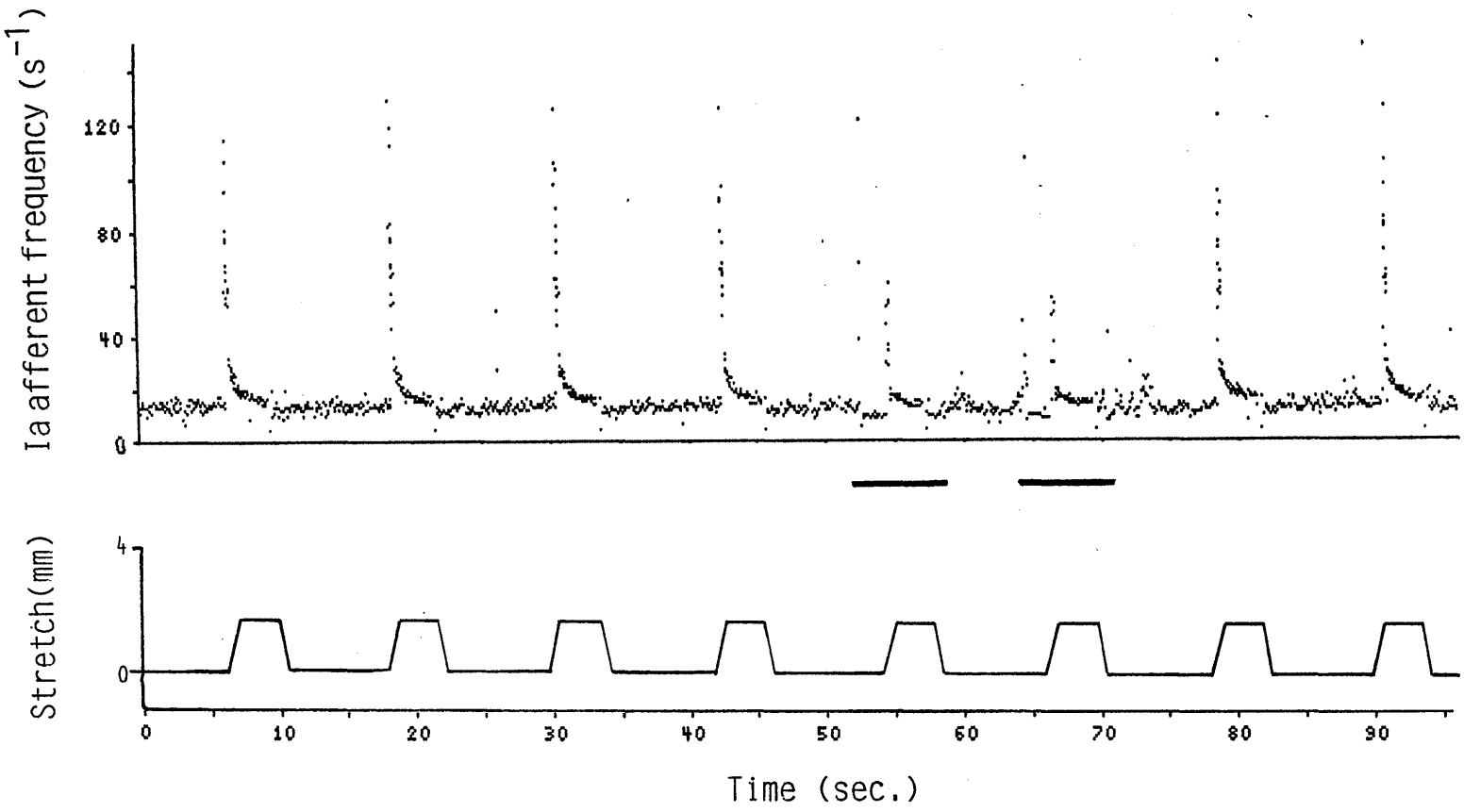
These responses not only could be obtained with currents of about 2.0 mA (31,B) but also with currents as low as 0.2 mA (31,A and 32,B) they were easily induced only when spontaneous intrafusal activity caused the afferent firing to be very scattery.

Figure 33 shows the effect of applying a current, 0.8 mA (S+), to point 4 in two consecutive cycles. Again, as in previous examples, the sustained effect of the first stimulus on the fusimotor neurones increased the amplitude of the response to the second. Even on stopping the stimulus, the afferent did not respond as regularly to the ramp as before, suggesting an increase in fusimotor activity at least for the next few cycles (although only one cycle is included in the figure). The results generally suggest that the lighter the cats became, the easier it was to get extrafusal contraction during cortical stimulation.

D. Inhibition of Intrafusal Muscle Fibres

Inhibition occurred in only one chloralose-anaesthetized cat. The cortex was anodally stimulated at point 4 in two consecutive cycles with 1.4 mA (fig 34). Afferent static firing dropped and the

Fig 34. The effect of consecutive cycles of cortical stimulation at point 4 on the response of a tenuissimus primary afferent from a chloralose-anaesthetized cat to ramp stretch. Note the good dynamic response of the afferent to the ramp stretch before and after the stimulation. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.


Ia afferent frequency (s^{-1})
120
80
40
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
Time (sec.)

initial burst to the ramp stretch was reduced remarkably, from 135 ips in preceding cycle to 60 ips and 52 ips. Dynamic indices were reduced from 38 ips to 14 and 13 ips respectively. The dynamic decay was also reduced from 13 ips to 2 ips in both cycles. In the absence of stimuli in the following cycle(s), the response to the ramp was as good as before. Note the rebound activity of the afferent on the "off" of the stimulus in both cycles. Since EMG electrodes did not pick up anything during the period of stimulation, it seems that some intrafusal fibres were inhibited and the reduced static firing did not occur as a result of unloading of the muscle spindle.

II. Effect of Cortical Stimulation on FDL Primary Afferents

Six FDL primary afferents, four from two cats anaesthetized with barbiturates and two from a cat anaesthetized with chloralose, were studied. Fig 35 illustrates the responses of two afferents of a cat anaesthetized with barbiturates. In both cases the slope of the slow decay increased, so did the dynamic index but to a lesser extent. The activity of the afferent on the "off" of the stimulus also increased. However, effect in 35,B is of rebound type suggesting a possible inhibition during the course of stimulation. Again, in both cases, afferent firing did not alter previous to involvement of the ramp stretch.

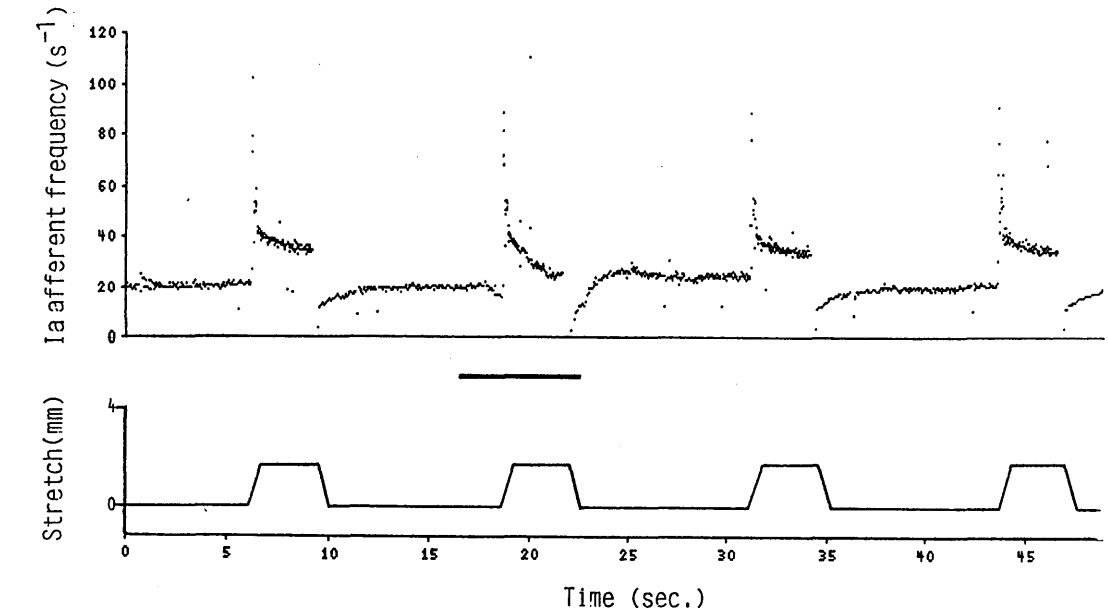
In fig 36, where the cat was chloralose-anaesthetized, the dynamic response is more of the classical type: a rise in both static firing of the afferent and dynamic index. In addition, the initial burst to the ramp stretch is considerably increased. The static

Table showing the occurrence of dynamic and static effects in responsive primary afferents of both tenuissimus and FDL muscles.

Points of Stimulation	Tenuissimus (53 responsive I_a afferents)		FDL (6 I_a afferents)	
	Dynamic	Static	Dynamic	Static
1		14/53		NS
2		19/53		NS
3		48/53		3/6
4	31/53	40/53	6/6	4/6
5	39/53	35/53	5/6	3/6
6	28/53	47/53	4/6	3/6
7		50/53		5/6
8	1/53	53/53		5/6
9		42/53		4/6
10		31/53		NS
11		8/53		NS
12		3/53		NS
13		2/53		NS
14		4/53		NS

NS: cortex not stimulated at that point.

Fig 35. The effect of cortical stimulation at points 4 and 5 on the response of two different FDL primary afferents of a cat, anaesthetized with barbiturates, to ramp stretch. FDL stretched 2 mm. Cortical stimulation shown as solid bar.


A
Ia afferent frequency (s^{-1})
120
100
80
60
40
20
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec.)

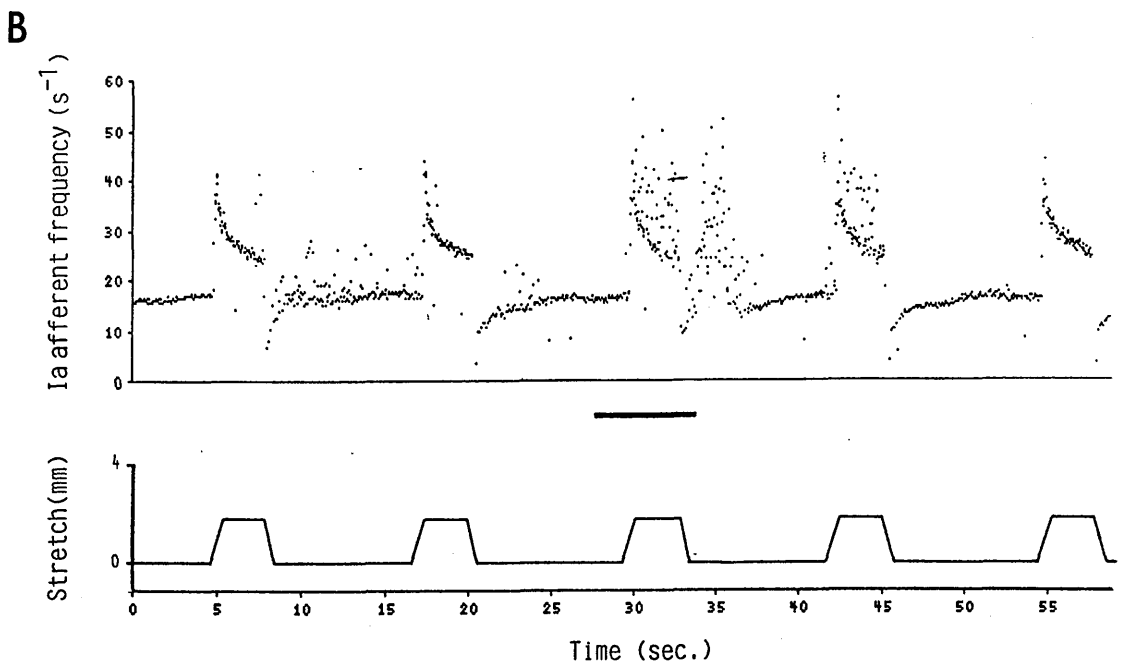
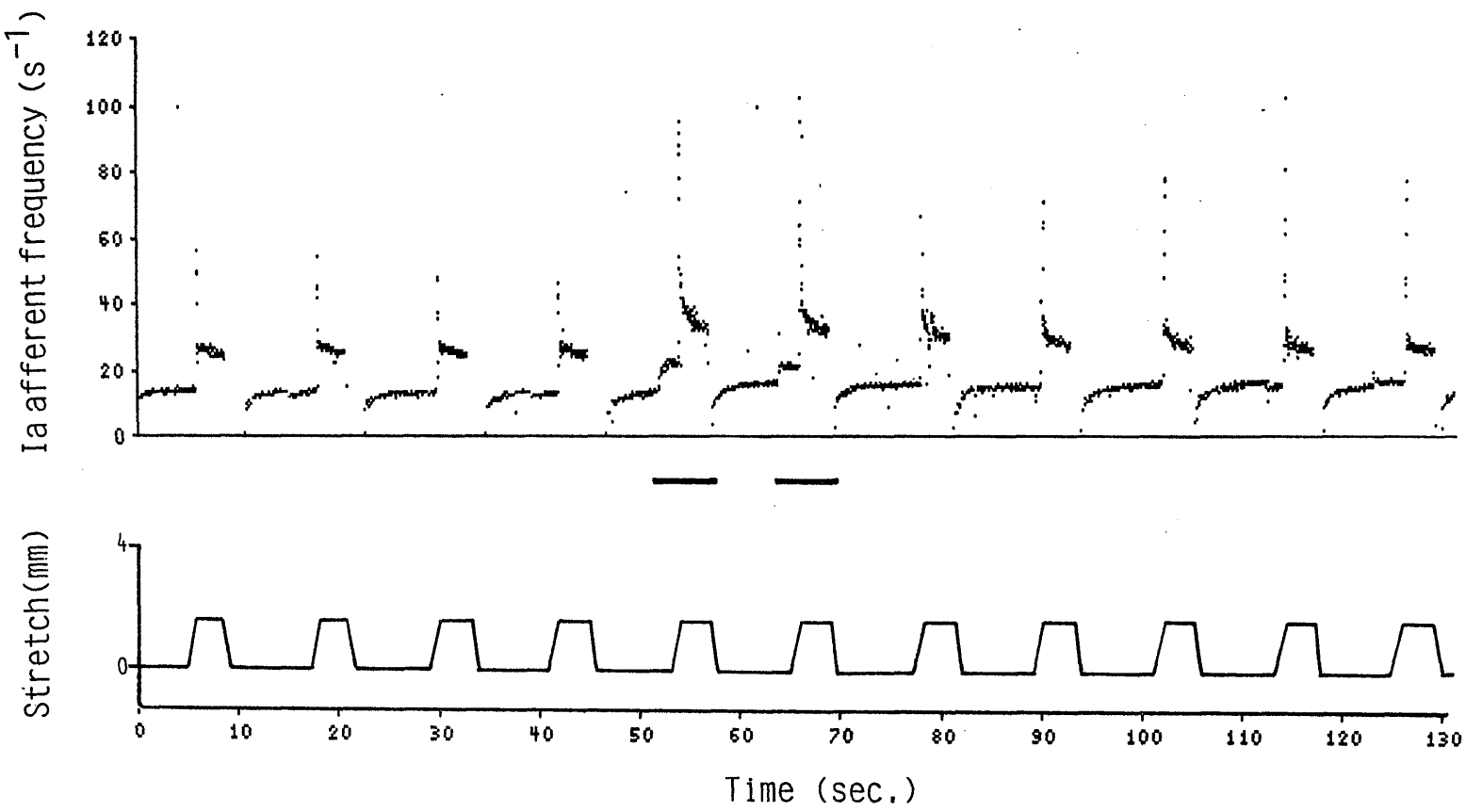

B
Ia afferent frequency (s^{-1})
60
50
40
30
20
10
0
Stretch(mm)
4
0
0
5
10
15
20
25
30
35
40
45
50
55
Time (sec.)

Fig 36. A typical dynamic response obtained from a chloralose-anaesthetized cat's FDL primary afferent on cortical stimulation at an area 1 mm medial to point 5. FDL stretched 2 mm. Cortical stimulation shown as solid bar.


Ia afferent frequency (s^{-1})
120
100
80
60
40
20
0
Stretch(mm)
4
0
0
10
20
30
40
50
60
70
80
90
100
110
120
130
Time (sec.)

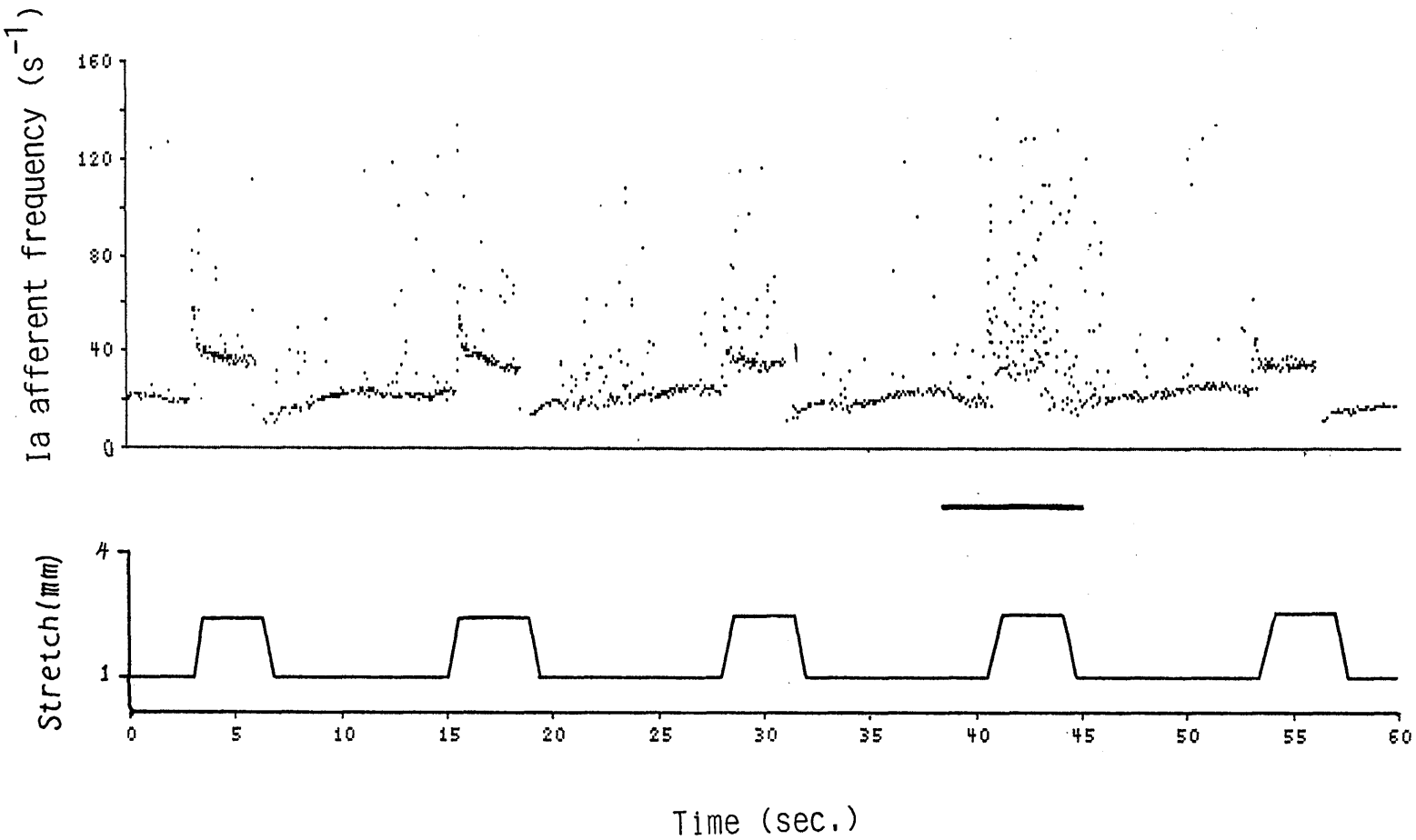
firing level stayed high (by 5 ips) in the following cycles. The latency of the response was about 200 msec. The point of stimulation was 1 mm medial to point 5 with 1.9 mA (surface positive).

A static fusimotor effect on FDL primary afferents is illustrated in fig 37, where a point 1 mm anterolateral to the Pcd was stimulated anodally with 2.2 mA. The scattered firing of the afferent before cortical stimulation as well as fluctuations in the static firing of the primary suggest that the cat was in light anaesthesia having good spontaneous intrafusal activity. On the other hand, the spread of irregularity on the ramp stretch and also abolition of the silence on the release of the stretch all suggest that a static fusimotor axon(s) was recruited on cortical stimulation. The drop in the afferent discharge at the beginning of the cortical stimulation might not exclusively represent an inhibition of any intrafusal fibre(s), rather it may be the spontaneous fluctuation of the gamma axons only happening at the time of stimulation. The decrease in static firing at the time of 0-2 sec and 10-13 sec in the figure favors that idea. It is reckoned that nuclear chain fibres were responsible for the scatter of the response before the stimulation and even during the course of stimulation.

III. Effect of Cortical Stimulation on Tenuissimus Secondary Afferents

Since the secondary afferents are mostly affected by nuclear chain contraction, and only to a minor degree by Sb_2 and Db_1 fibres, one might not find an extensive range of diverse effects on secondaries due to cortical stimulation.

Fig 37. The effect of cortical stimulation on a FDL primary afferent response to ramp stretch, from a cat anaesthetized with barbiturates. FDL stretched 2 mm. Cortical stimulation shown as solid bars.


Ia afferent frequency (s^{-1})
160
120
80
40
0
Stretch(mm)
4
1
0
5
10
15
20
25
30
35
40
45
50
55
60
Time (sec.)

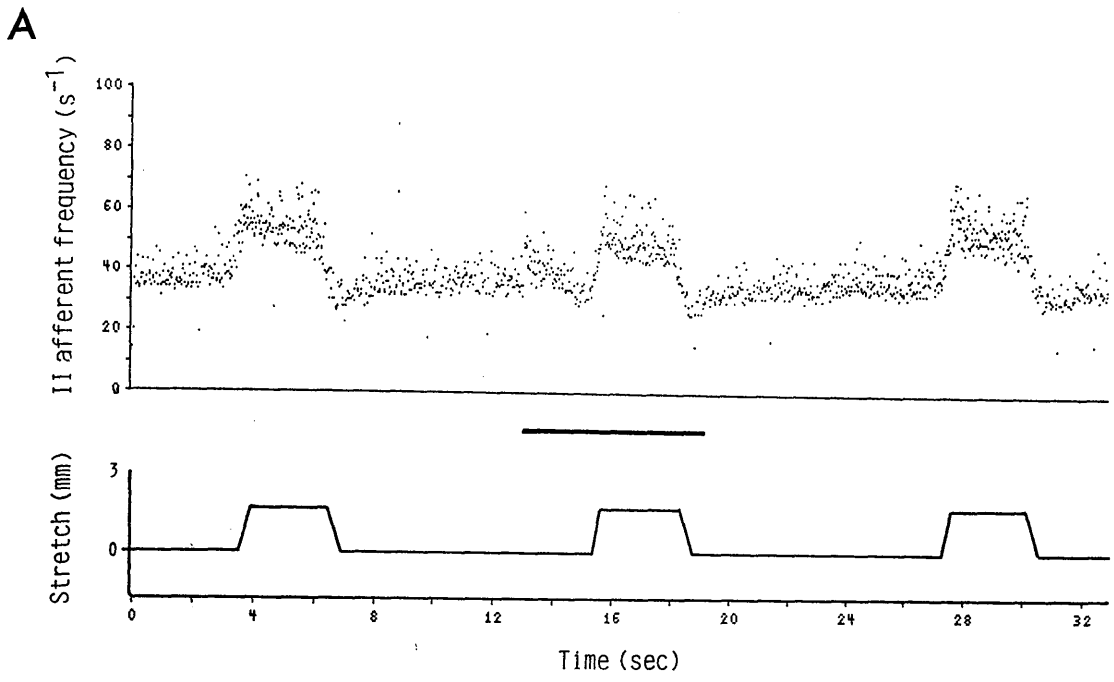
Out of 12 tenuissimus secondaries studied during the experiments, 3 were not responding to cortical stimulation at all. These were the ones which were firing at a static level of above 50 Hz. The pattern of responses obtained from secondaries was not in fact as diverse as those from primaries and were of 4-5 types.

Fig 38 illustrates a graded response of a secondary afferent to a slight increase in stimulus intensity from 0.9 mA in (A) to 1.0 mA in (B). In both cases the stimulus was applied to point 4 on the cortex. The latency of response was around 200-300 msec. Apart from the initial sharp rise in the firing of the secondary which died off in about two seconds, the mean amplitude of the response during ramp hold period was slightly decreased (4-5 ips) in A and increased in B (by 10 ips). Note that the splay of the scatter did not alter, suggesting that likely whichever intrafusal fibre(s) was responsible for the increase in static firing above the passive level, it was the same fibre(s) that was recruited during the course of stimulation. On the other hand, the scatter could be due to a mechanism involving the sensory terminals and there need not be any ongoing static gamma activity. Even so, an intrafusal fibre(s) was recruited on cortical stimulation which increased the length sensitivity of the secondary in fig 38,B.

One other point to notice in fig 38,A is the regularity of the afferent firing during changes in length compared to that in ramp responses before and after. This pattern of response was reproducible from an extensive area within the sensorimotor cortex, even from point 2, anterior to cruciate sulcus, where it is more likely to recruit extrafusal fibres at most of the times.

Fig 38. The effect of cortical stimulation at the same point, but with different intensities (see text) on the response of a tenuissimus secondary afferent to ramp stretch. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

(Conduction velocity of the fibre : 48 m/sec)


A
II afferent frequency (s^{-1})
100
80
60
40
20
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec)

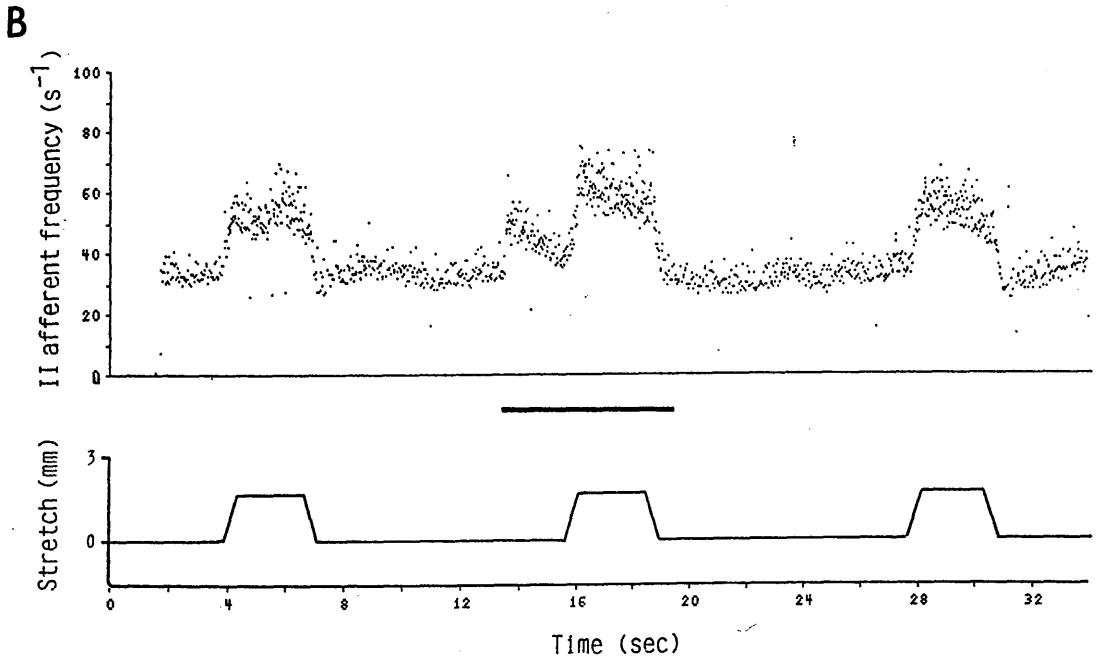

B
II afferent frequency (s^{-1})
100
80
60
40
20
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec)

Fig 39 represents the responses of a secondary afferent to anodal stimulation of a point 1 mm lateral to the Pcd (above) and point 2 (below). The response of the secondary afferent in fig 39,A was a weak transient effect similar to the response in fig 38,A. However, in fig 39,B although static firing and the splay of the scatter were increased, the length sensitivity was not increased.

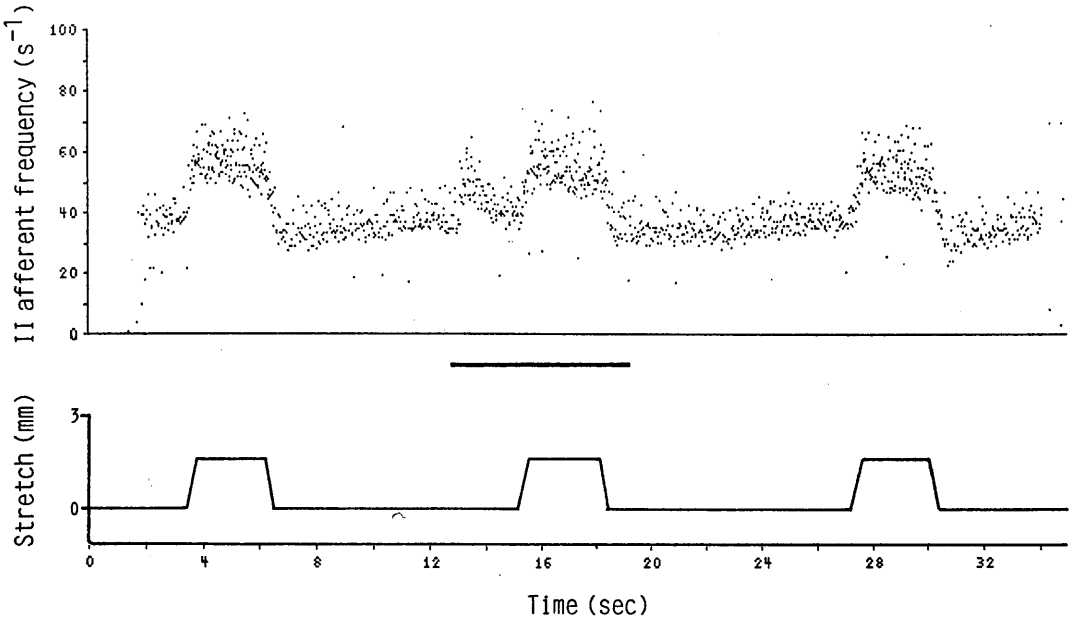
Sometimes, as in the case of primaries, cortical stimulation abolished the afferent response to the ramp. Fig 40 demonstrates that phenomenon. Point 5 (A) and 4 (B and C) were stimulated anodally with 1.15, 0.8 and 1.1 mA current respectively. In fig 40,A the effect was long-lasting, for the response to the ramp was also depressed in the next cycle even without cortical stimulation. Additive effects of stimulation were present in fig 40,B where the current was even lower. The length sensitivity was abolished in both cycles of stimulation*. The reduced length sensitivity of the secondary afferent is obvious in the next pull, suggesting again a long-lasting effect of stimulation. The pattern of response was almost the same in fig 40,C except that there seemed to be some length sensitivity, yet, during the stimulation and also rebound activity in the intrafusal fibres, suggesting that although the pattern appeared to be very similar, the intrafusal mechanism underlying the changes in afferent discharge might not in fact be similar. The latency of the effect was about 200-300 msec for the three records in fig 40. Fig 41 demonstrates a pattern of secondary response to cortical stimulation where the sensitivity to length changes may actually have been increased, but it is very difficult to

* (Strong contraction of Sb_2 fibre in the same pole can reduce the length sensitivity of a secondary afferent.)

Fig 39. The effect of cortical stimulation of different points (see text) on the response of a tenuissimus secondary afferent to ramp stretch. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

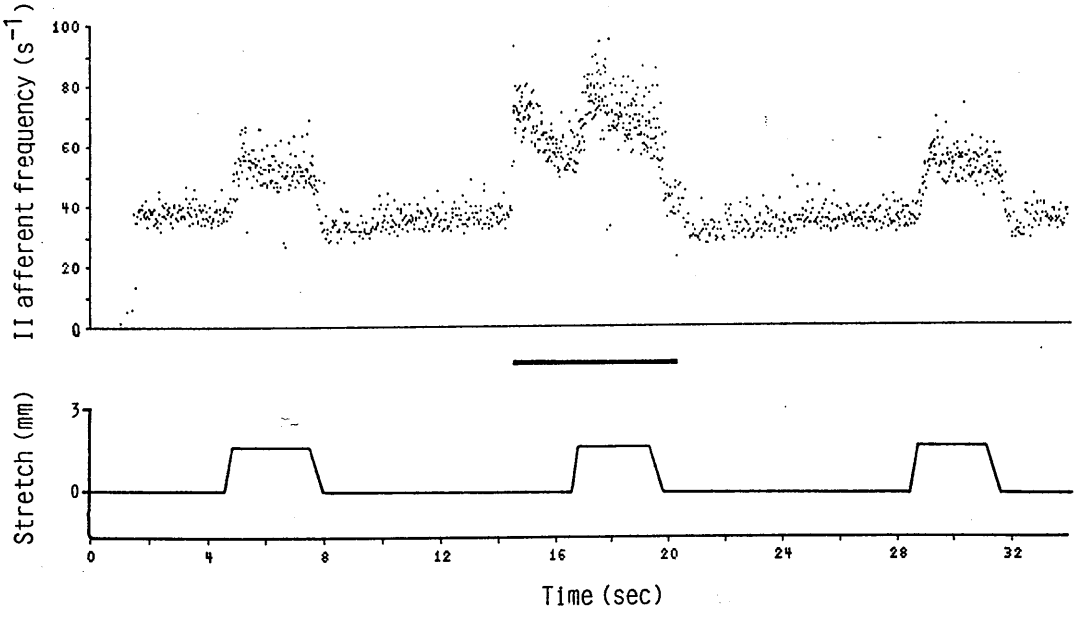
(Conduction velocity of the fibre : 39 m/sec)

A


II afferent frequency (s^{-1})
100
80
60
40
20
0

Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec)

B


II afferent frequency (s^{-1})
100
80
60
40
20
0

Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec)

Fig 40. The abolishment of the response to ramp stretch of tenuissimus secondary afferents due to cortical stimulation of points 5 (A) and 4 (B and C) with 1.15, 0.8 and 1.1 mA. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

(Conduction velocity of the fibre A, B; 37 m/sec)

(Conduction velocity of the fibre C: 30 m/sec)

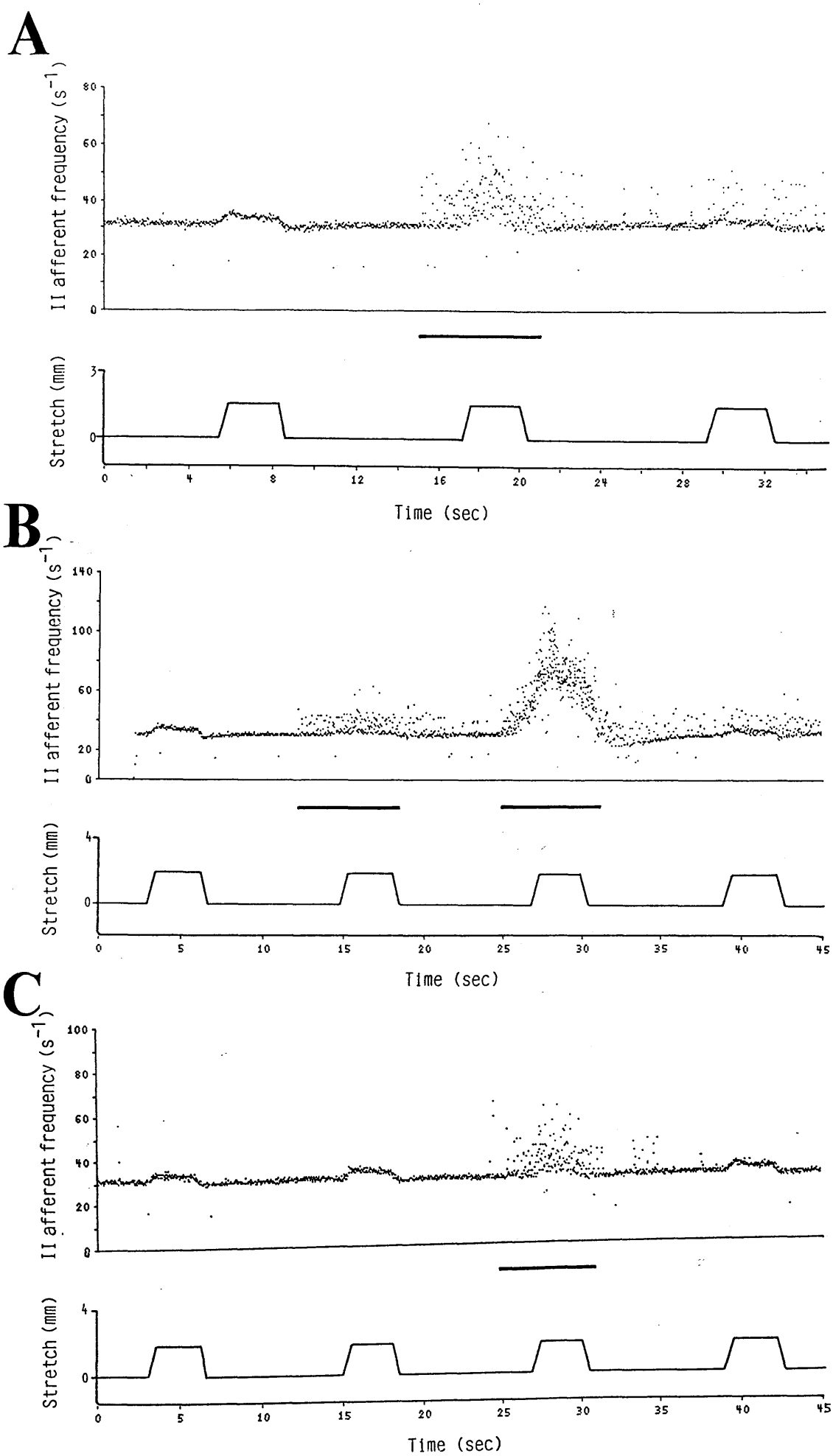
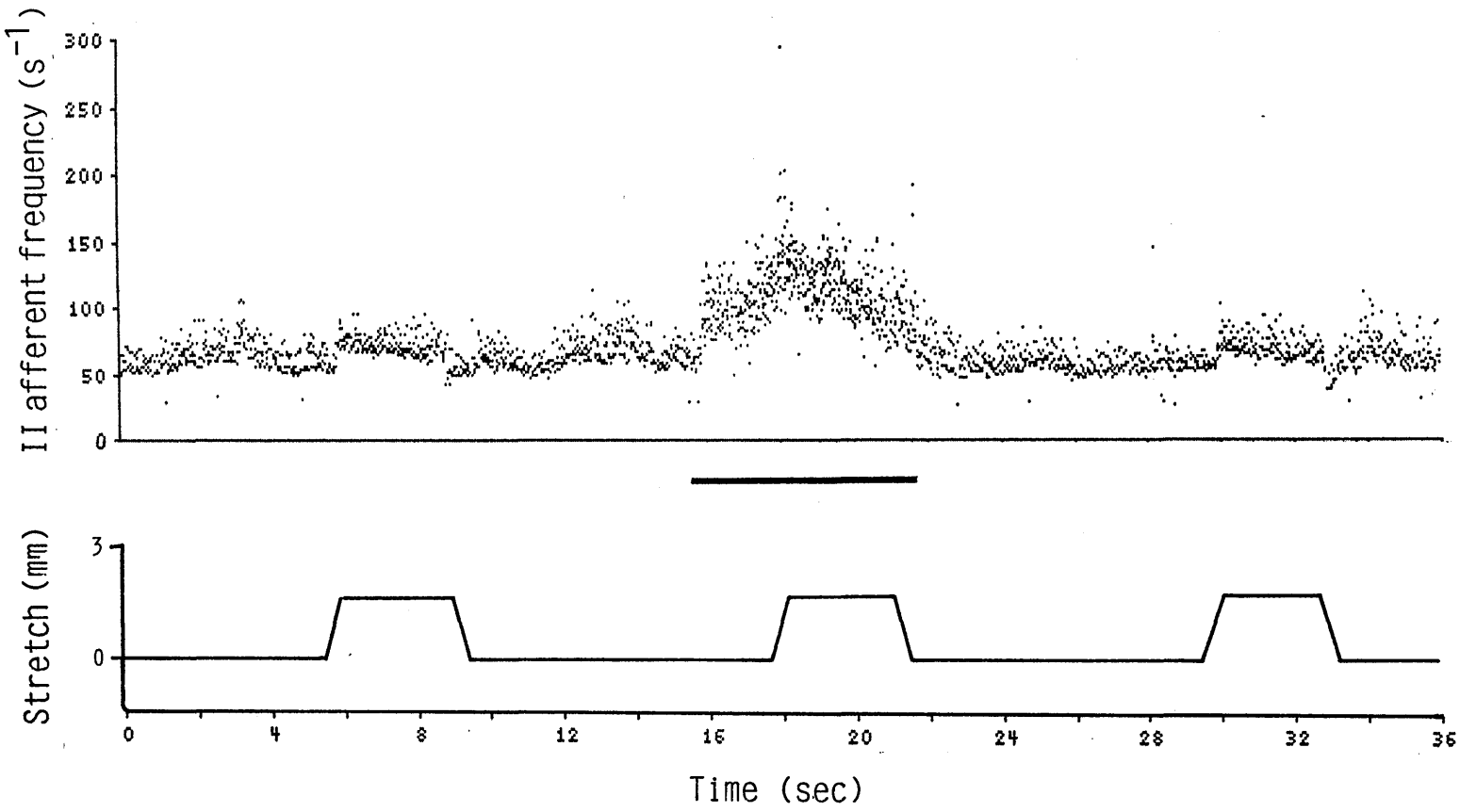

A
II afferent frequency (s^{-1})
80
60
40
20
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec)
B
II afferent frequency (s^{-1})
140
100
60
20
0
Stretch (mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec)
C
II afferent frequency (s^{-1})
100
80
60
40
20
0
Stretch (mm)
4
0
0
5
10
15
20
25
30
35
40
45
Time (sec)

Fig 41. The effect of cortical stimulation at point 9 on the response of a tenuissimus secondary afferent to ramp stretch. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

(Conduction velocity of the fibre : 54 m/sec)


II afferent frequency (s^{-1})
300
250
200
150
100
50
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec)

ascertain because of the increased scatter. However, the secondary reached its maximum firing during the ramp stretch which suggests that the response to the pull was certainly not completely abolished.

Yet another response pattern is shown in fig 42 where the afferent frequency increased to around 200 ips, but it was rather short lasting and did not extend throughout stimulus period. Stimulation had absolutely no effect on response to length change. In fig 42 the responses were attained on cortical stimulation of points 5 (above) and 4 (below). Current of stimuli applied was 1.4 mA in both cases.

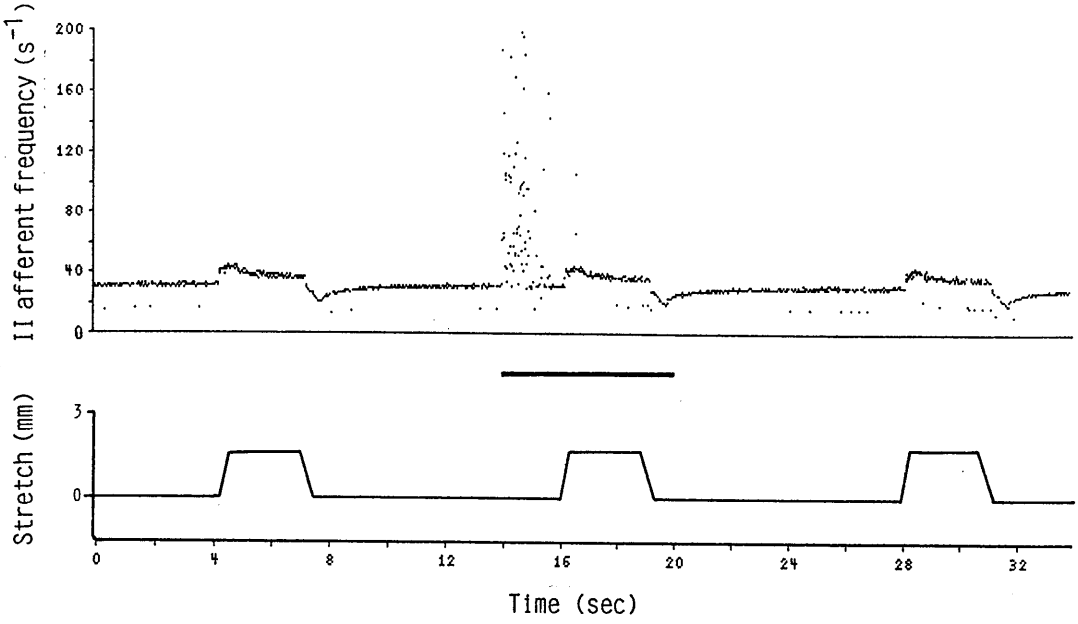
IV. Latencies of Intrafusal Effects

The latency of intrafusal effects, either excitatory or inhibitory, in primary afferents of both muscles and tenuissimus secondary afferents varied extensively within a range of 100 msec to about 2 sec. The mean latency for dynamic responses in barbiturate-anaesthetized cats was about 300 msec and it was 350 msec in chloralosed anaesthetized cats. The mean latency, however, for static fusimotor effects was about 650 msec in barbiturate-anaesthetized cats and 250 msec in chloralosed anaesthetized cats. The big variation in latencies suggest that they do not necessarily represent latencies dependent on different physical characteristics of the descending pathways: different axonal diameters, myelinated or not myelinated axons.....etc. What could positively be said, however, is that the different stimulus intensity applied to the cortex accounts for a great proportion of this variation. This suggest that much of the time is taken up in bringing neurones to their threshold.

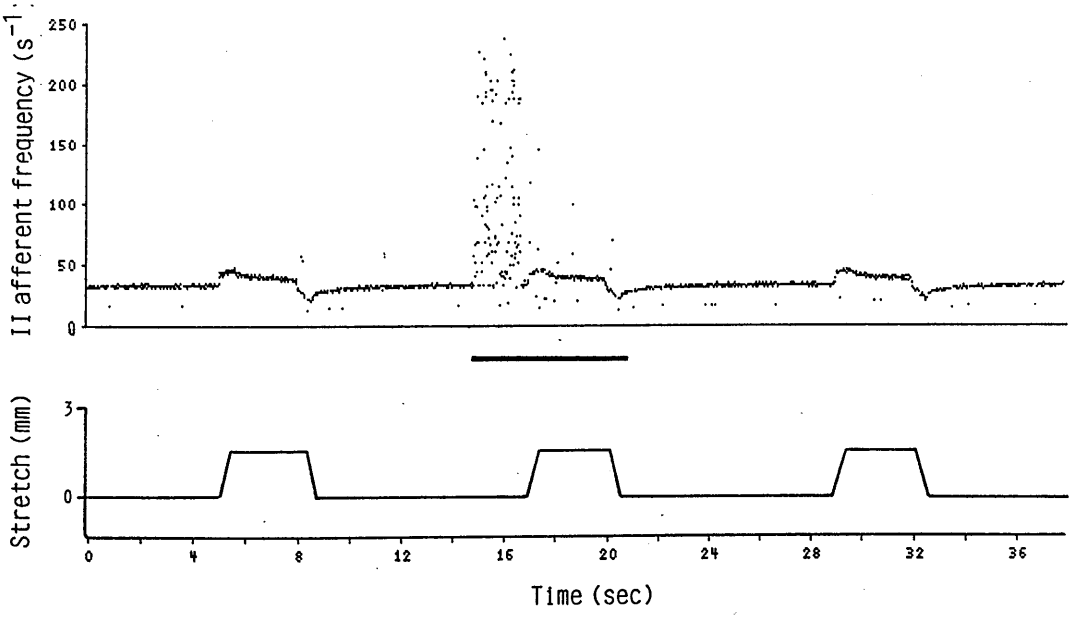
Fig 42. The effect of cortical stimulation at points 5 (A) and 4 (B) on the response of a tenuissimus secondary afferent to ramp stretch. Tenuissimus stretched 2 mm. Cortical stimulation shown as solid bars.

(Conduction velocity of the fibre : 34 m/sec)

A


II afferent frequency (s^{-1})
200
160
120
80
40
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
Time (sec)

B


II afferent frequency (s^{-1})
250
200
150
100
50
0
Stretch (mm)
3
0
0
4
8
12
16
20
24
28
32
36
Time (sec)

SECTION B: Exteriorised Muscle Spindle Experiments.

I. Without Dorsal Root recording

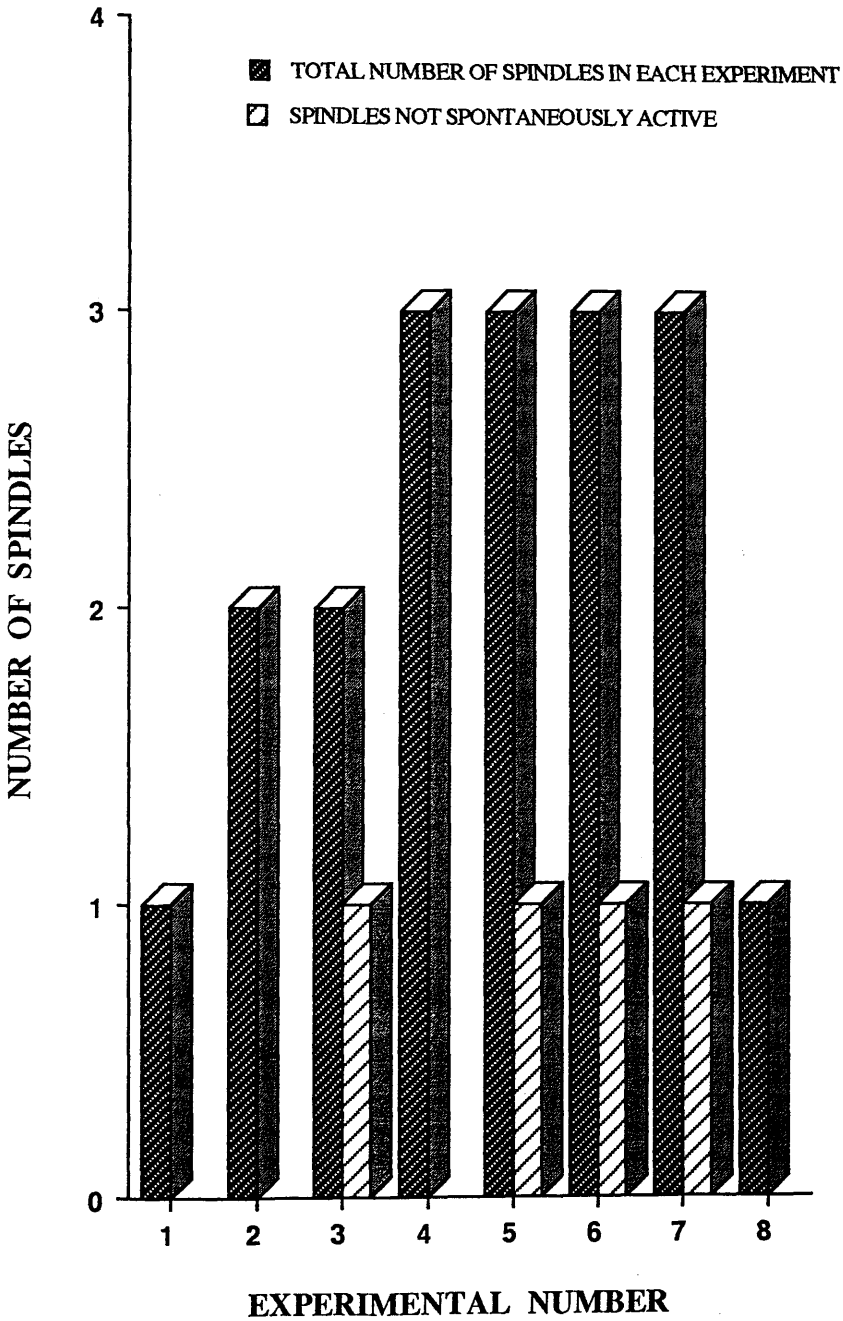
Eight tenuissimus muscles were examined in this series of experiments and in these seventeen spindles altogether were carefully uncovered by Dr. Gladden. Some of these spindles are illustrated in the Appendix in addition to those described in this section.

A. Spontaneous activity of intrafusal fibres

When cats were fairly lightly anesthetized (under barbiturates), it was unusual not to have any spontaneous activity. In fact there was always spontaneous activity in at least one of the spindles isolated. If a cat showed a withdrawal reflex on squeezing the forepaw pad, it was believed to be fairly light. The half-opened pupil of the cat was another sign of the cat being fairly light. Some silent spindles were driven to act spontaneously by pressing the forepaw pad strongly. Most of the time it worked. However, four out of seventeen spindles did not show any spontaneous activity throughout the whole experiment no matter what the anaesthetic level was (fig 43). Even stimulation of sensorimotor cortex failed to initiate contraction in the intrafusal fibres.

Spontaneous activity was most commonly seen in nuclear chain and static bag_2 fibres, the former being active in more spindles. Only in one experiment was a Sb_2 fibre spontaneously active without any nuclear chain fibre activity. Spontaneous activity of both

Fig 43. Histogram showing the total number of spindles in each experiments in direct visualizing series and the number of spindles with neither spontaneous activity nor recruitment from the cortical stimulation.


TOTAL NUMBER OF SPINDLES IN EACH EXPERIMENT
SPINDLES NOT SPONTANEOUSLY ACTIVE
NUMBER OF SPINDLES
0
1
2
3
4
1
2
3
4
5
6
7
8
EXPERIMENTAL NUMBER

nuclear chains and static bag fibres was also observed frequently in seven out of thirteen active spindles. Spontaneous activity of different spindles are summarized in table 1.

The dynamic bag$_1$ fibre was spontaneously active only in three spindles; and that was usually the time when the cat was about to receive a supplementary dose of anaesthetic.

An unusual spontaneous activity was observed in a spindle shown in the Appendix, upper photograph (A). The unique pulsar activity of this spindle was in the left pole and the whole spindle was pulled to the left in a frequency of about 50/min (the arterial pulse rate was about 100 at the time). It seemed that the origin of the activity was lying somewhere in the secondary sensory ending.

B. Innervation and identification of intrafusal fibres

One way of assessing what the innervation of a spindle might be is by both looking at its spontaneous activity and the pattern of recruitment of intrafusal fibres. In spindles in which it was clear which bag was dynamic and which static, no further histological sectioning was done. Fig 46 gives some examples of spindles whose innervation was postulated from their spontaneous activity and the pattern of intrafusal recruitment. Figures 44 and 45 show the pattern of innervation of intrafusal fibres in a pole of two spindles which were reconstructed from serial sections.

In four spindles, it was not possible to tell for sure which bag was dynamic. Therefore, they were fixed post-experimentally and sectioned serially for histology. Fig 47 and fig 48 shows how dynamic bag fibres were distinguished from static bag fibres in polar and equatorial regions respectively. Fig 47 demonstrate two spindles,

Fig 44. The pattern of innervation of the left pole of the spindle 8 (table 1) from analysis of serial histological sections.

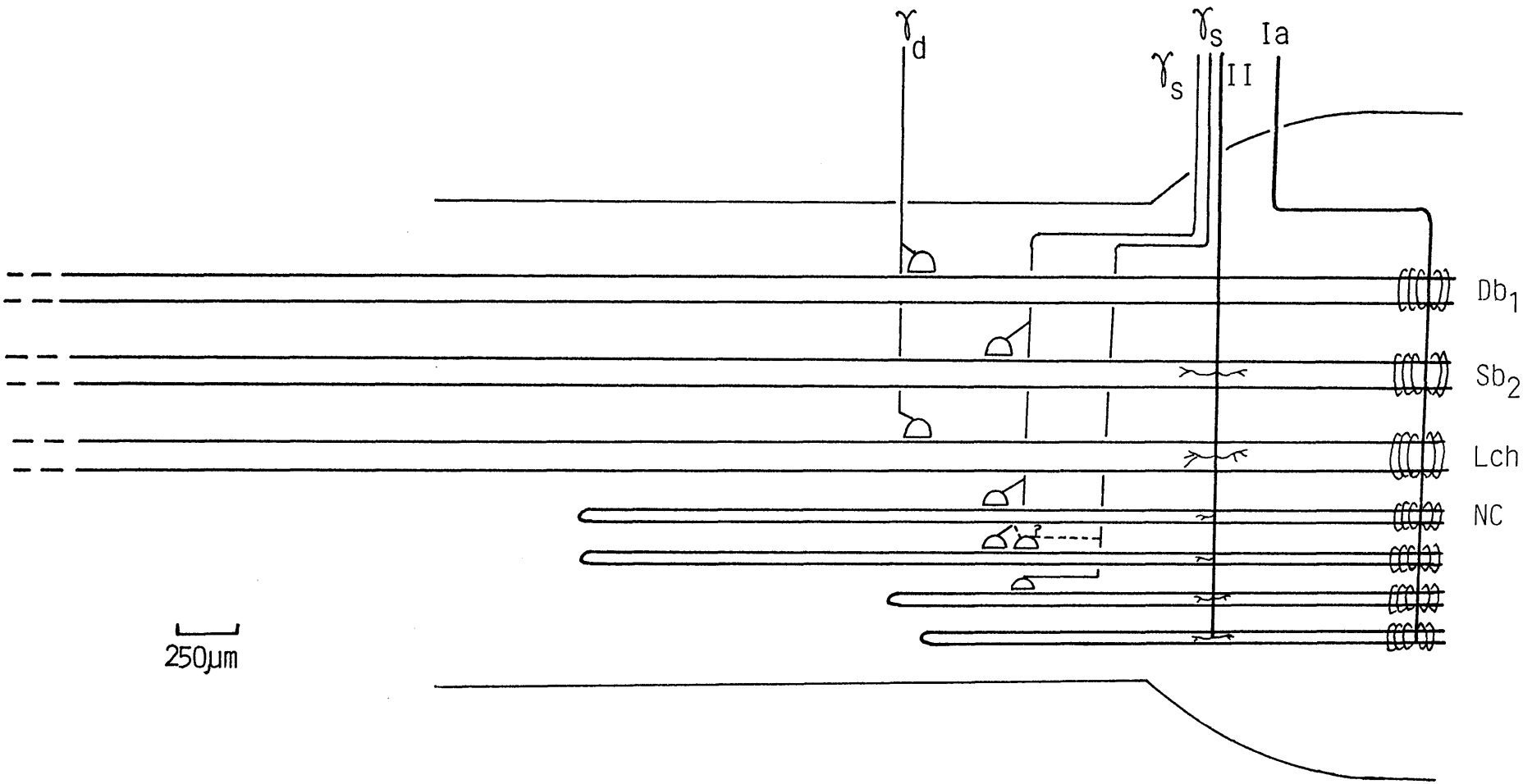

γd
γs
γs
II
Ia
Db1
Sb2
Lch
NC
250μm

Fig 45. The pattern of innervation of the right pole of the spindle 11 (table 1) from analysis of serial histological sections.

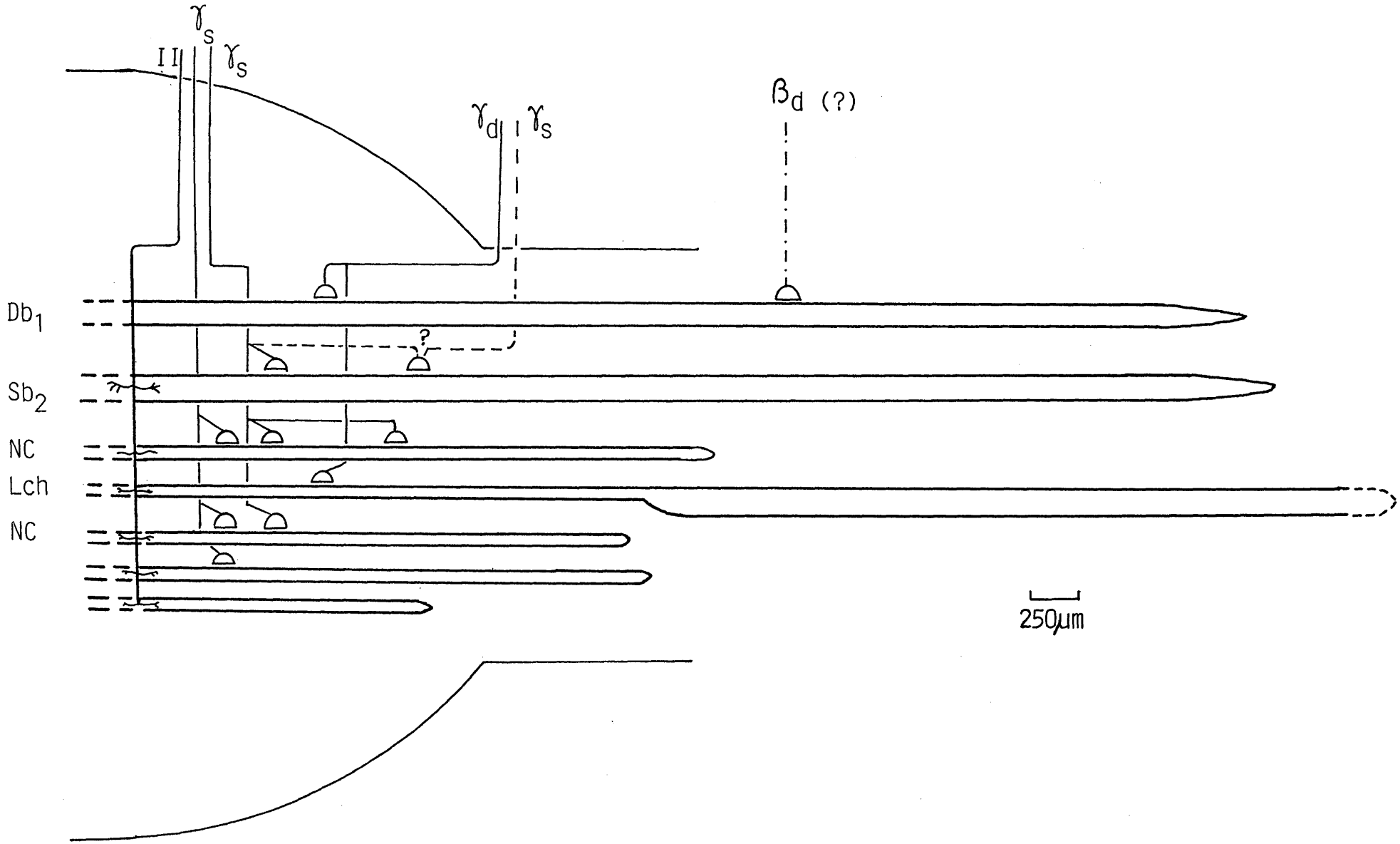
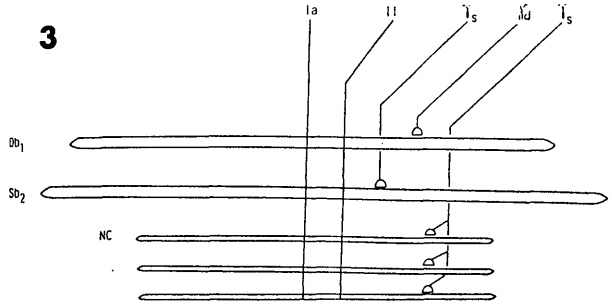
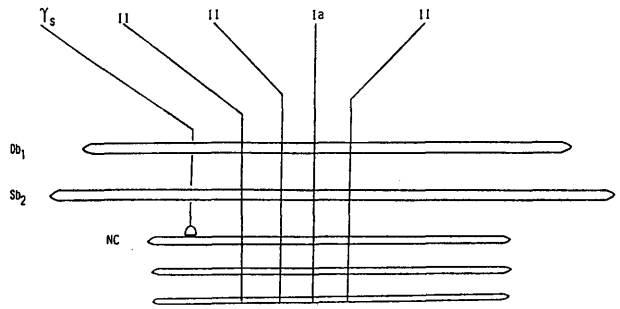

γs
γs
II
γd
γs
βd (?)
Db1
?
Sb2
NC
Lch
NC
250μm

Fig 46. Circuit diagrams showing the pattern of innervation of 7 spindles (numbers correspond to those in table 1) postulated from their spontaneous activity and pattern of cortical recruitment in direct visualizing experiments. Interrupted lines indicate connections in which there is some uncertainty.

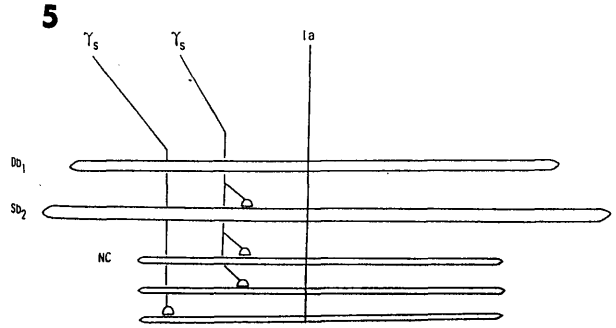
3


Ia
II
γ_s
γ_d
γ_s
Db_1
Sb_2
NC

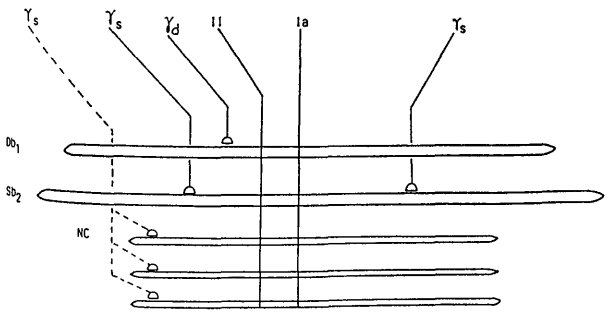
4


γ_s
II
II
Ia
II
Db_1
Sb_2
NC

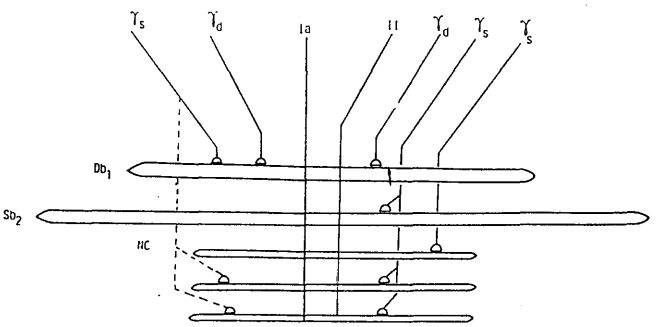
5


γ_s
γ_s
Ia
Db_1
Sb_2
NC

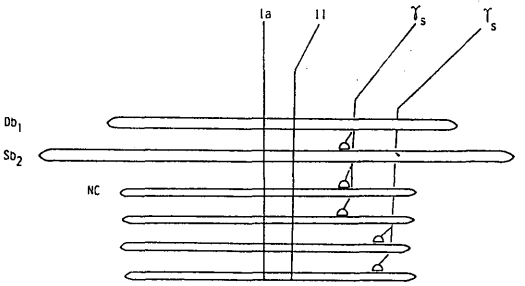
6


γ_s
γ_s
γ_d
II
Ia
γ_s
Db_1
Sb_2
NC

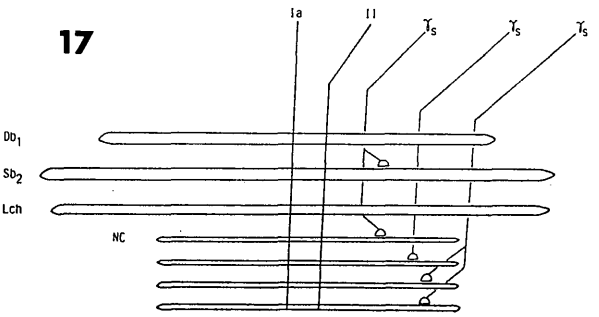
15


γ_s
γ_d
Ia
II
γ_d
γ_s
γ_s
Db_1
Sb_2
NC

16


Ia
II
γ_s
γ_s
Db_1
Sb_2
NC

17


Ia
II
γ_s
γ_s
γ_s
Db_1
Sb_2
Lch
NC

cross sectioned at poles, one having two bag fibres (A) and the other one two bag fibres and one long chain fibre (B). It is very obvious that the elastic tissue round the Db_1 fibre is considerably less than the Sb_2 fibre and even long chain fibre.

To work out which bag fibre was which between the living spindle and the sectioned material, it was necessary to have a landmark in the specimen at the time of observation of sections. For example, in the case of fig 49 where two spindles (number 8 and 9 in table 1) were separated by an artery, the distant bag fibres from the artery were the dynamic bag_1 fibres, the top bag fibre of the upper spindle and the lower bag fibre of the bottom one. It is worth noting that the video picture of these two spindles can be seen in fig 51.

Figure 48 is meant to demonstrate another criterion to distinguish between the bags and that is the separation of dynamic bag_1 fibre from the rest of intrafusal fibres in equatorial region of the two spindles. Fig 50 shows the recruitment of different types of intrafusal fibres of 10 exteriorised spindles on stimulation of different locations within the sensorimotor cortex of the cat in each case.

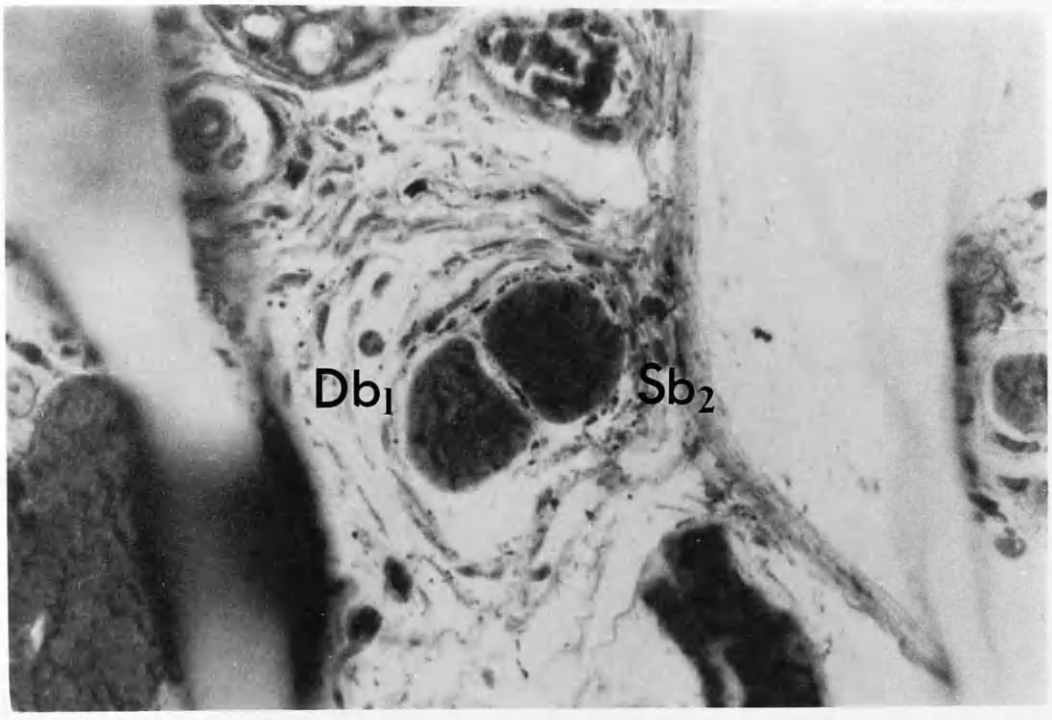
C. Recruitment of static intrafusal fibres

Most of the time, nuclear chains were easily recruited from almost all points on the sensorimotor cortex (tables 1 and 2).

One thing to note is that almost always the fusimotor neurones innervating the Sb_2 fibre and the nuclear chain fibres were recruited first with a shorter latency on stimulation of the sensorimotor cortex compared to those innervating Db_1 fibres, suggesting that they have a lower threshold.

Fig 47. Cross section of spindle 9 (A) and 8 (B) at poles showing almost no elastic fibres around dynamic bag$_1$ fibre. An elastic fibre is indicated by the arrow.

A



0.1 mm

B

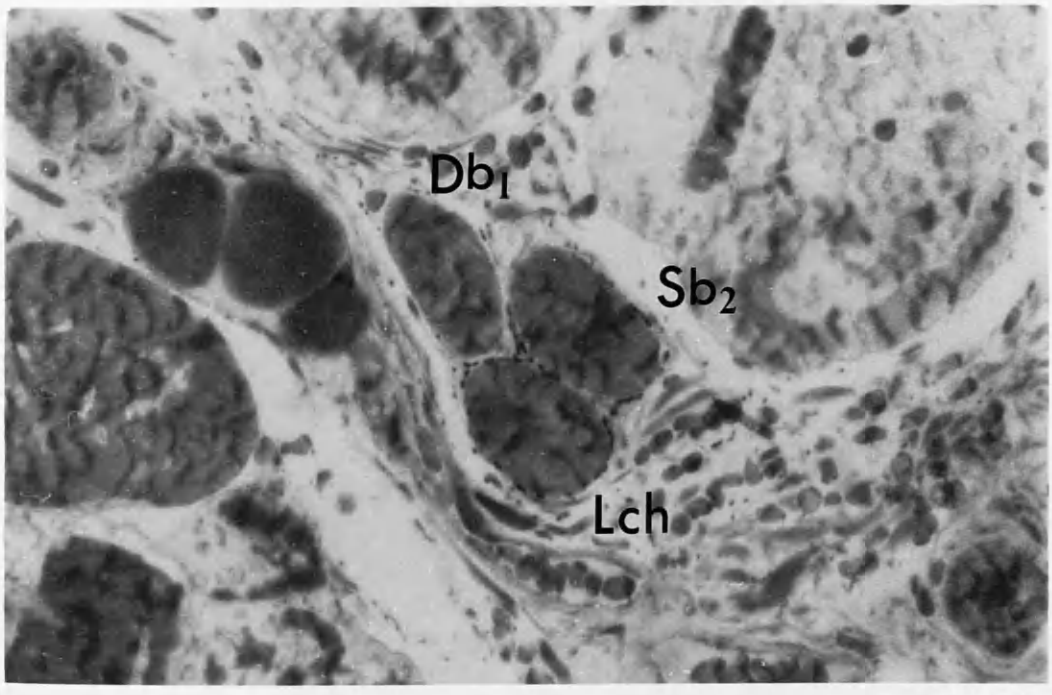
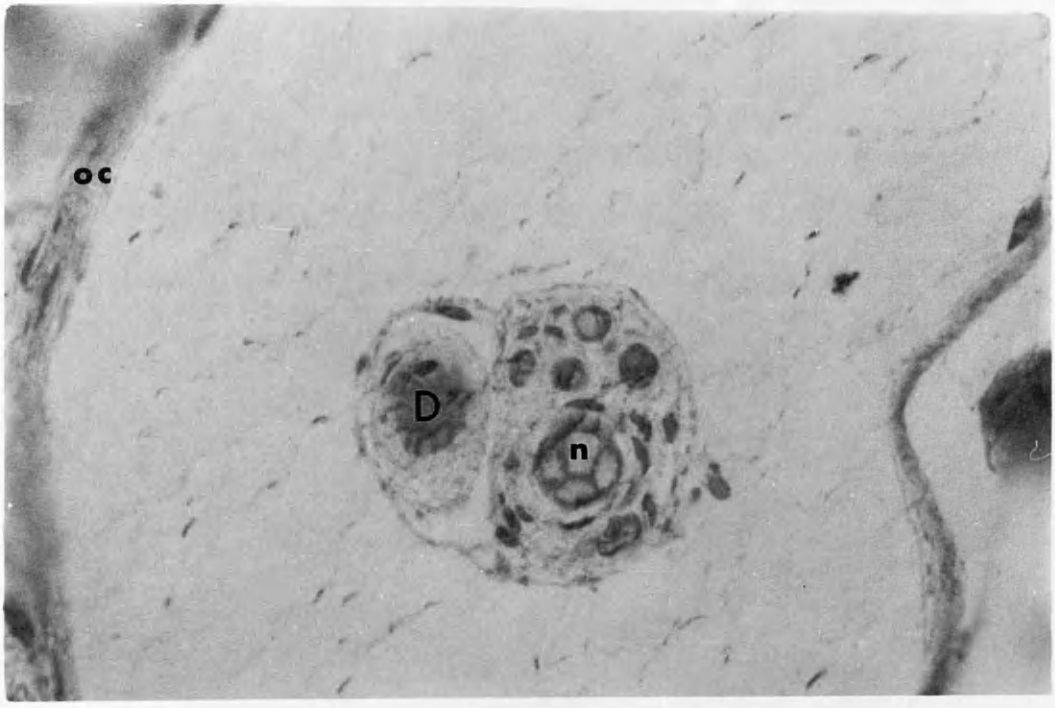


Fig 48. Cross section of spindle 10 (A) and 8 (B) at the equator region showing a clear separation of the dynamic bag_1 fibre from the static intrafusal fibres. The nuclei of the static bag_2 fibres (n) are visible in the upper spindle. L, long chain fibre; C, nuclear chain fibre; OC, outer capsule, D, dynamic bag_1 fibre; S, static bag_2 fibre.

A



0.1 mm

B

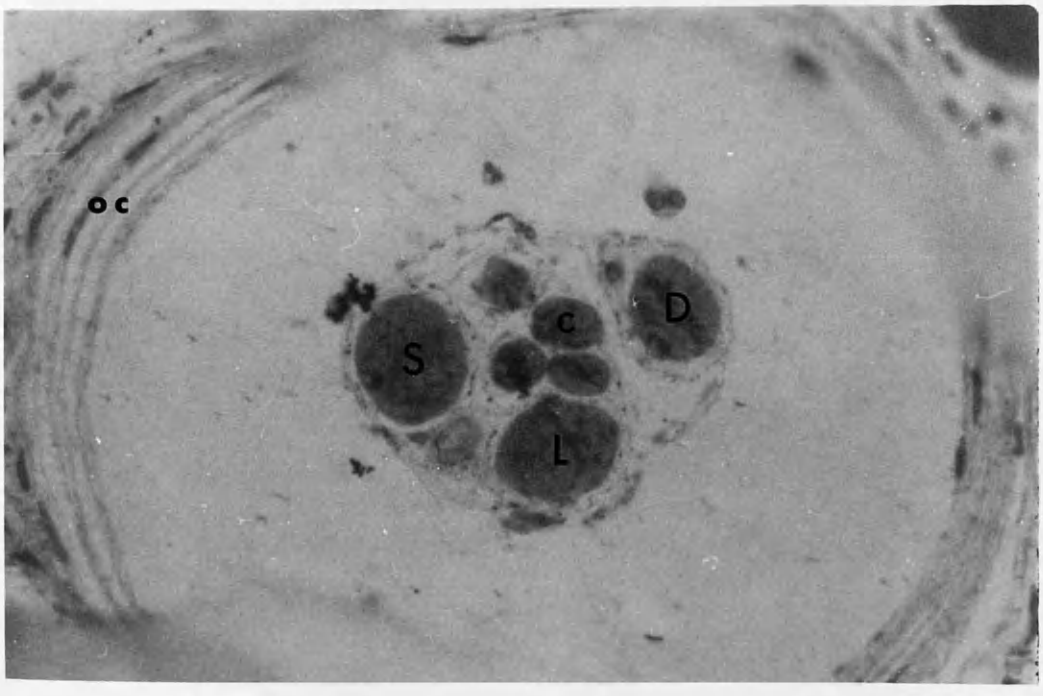


Fig 49. Cross section of spindles 9 (above) and 10 (below) separated by an artery (A). The two bag fibres closer to the artery are static bag_2 fibres. Video pictures of these two spindles is shown in fig 51. D, dynamic bag_1 fibre; S, static bag_2 fibre.

0.05 mm

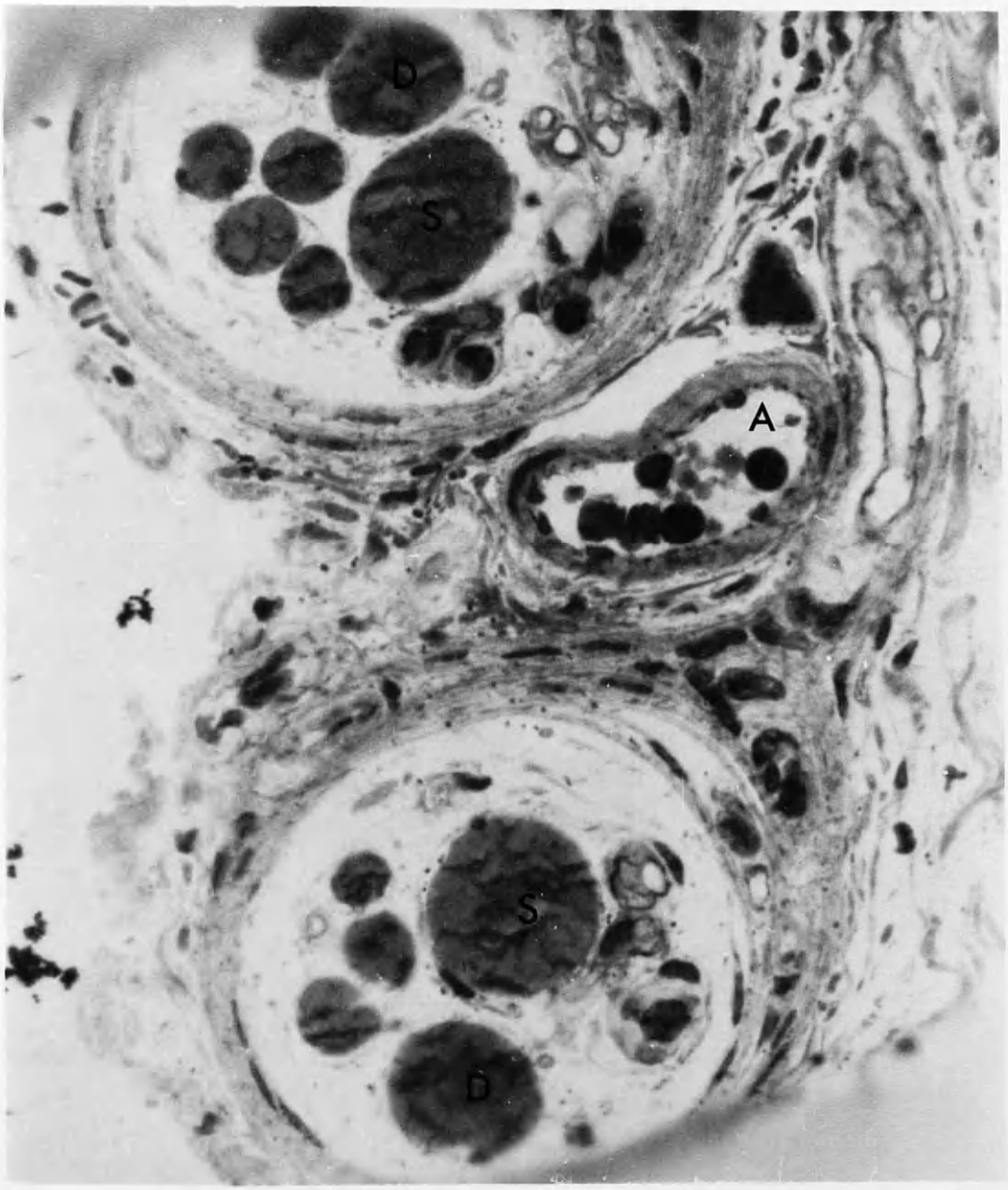


Fig 50. Diagram indicating the points within the sensorimotor cortex from where the activity of intrafusal fibres could be affected on stimulation in direct visualizing experiments. Numbers correspond to those in table 1.

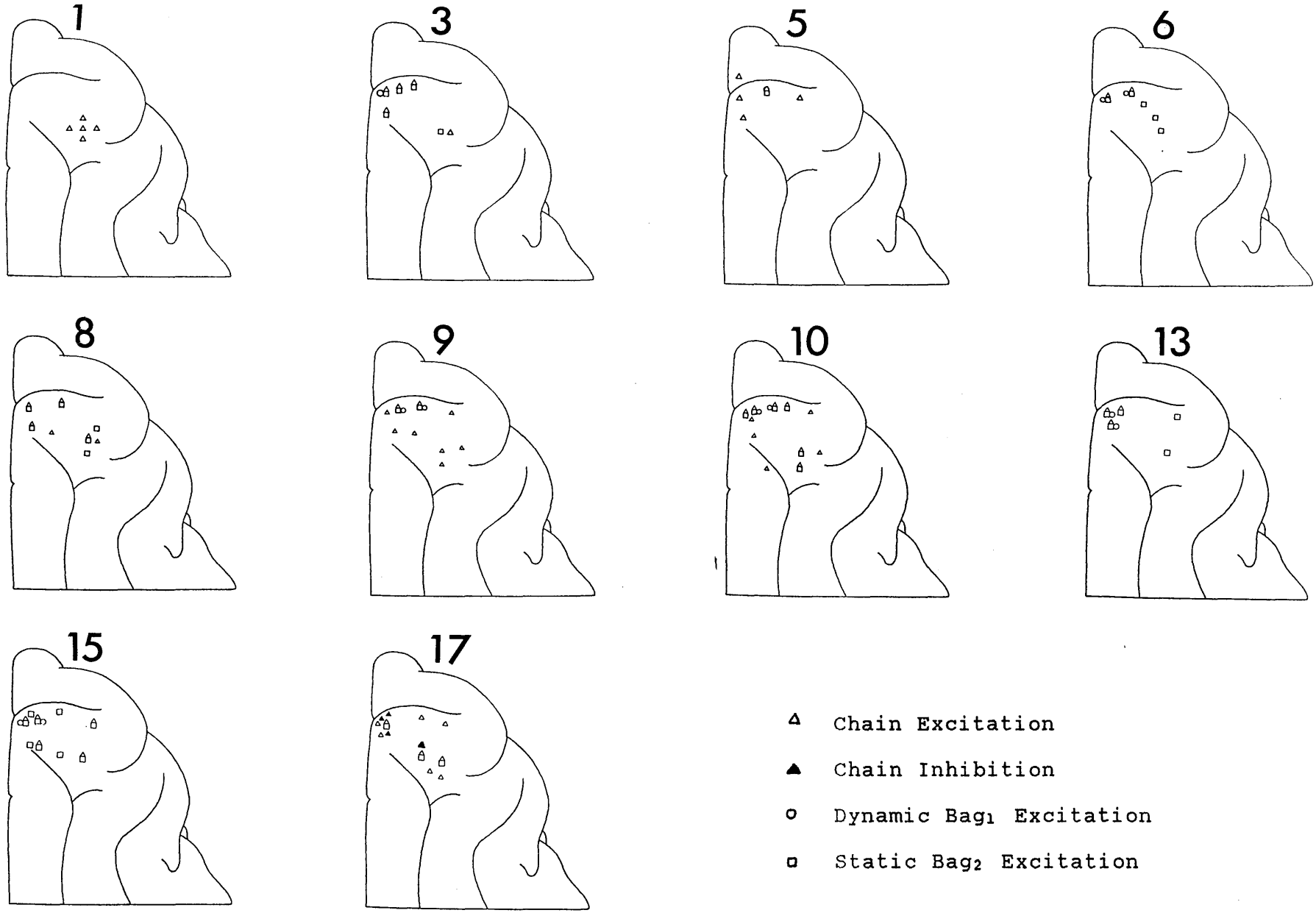

1
3
5
6
8
9
10
13
15
17
Chain Excitation
Chain Inhibition
Dynamic Bag1 Excitation
Static Bag2 Excitation

TABLE 1

Spontaneous activity and recruitment of intrafusal fibres on cortical stimulation of each spindle isolated from tenuissimus muscle of the cats under barbiturate anaesthesia.

Spindle Number	Spontaneous Activity				Recruitment of Intrafusal Fibres on Cortical Stimulation			
	Sb_2	NCs	Sb_2 +NCs	Sb_2 +Db_1 +NCs	Sb_2	NCs	Sb_2 +NCs	Sb_2 +Db_1 +NCs
1		+				+		
2	n	n	n	n	n	n	n	n
3	+	+	+	+	+	+	+	+
4	+		+	+	n	n	n	n
5		+	+		+	+		
6	+			+	+			+
7	n	n	n	n	n	n	n	n
8		+	+		+	+	+	
9		+				+		+
10		+				+	+	+
11rp	+		+		+		+	
11lp	+				+			
12	n	n	n	n	n	n	n	n
13	+			+*	+			+**
15			+	+	+		+	+
16		+	+			+	+	
17		+			?	±	+	

Abbreviations: rp, right pole; lp, left pole; n, no activity.

*, **, On only one occasion the two static and dynamic bag fibres were spontaneous active and recruited on cortical stimulation (no chains).

TABLE 2

The spontaneous activity and cortical recruitment of the three types of intrafusal fibres in muscle spindles isolated in the tenuissimus muscle of the cat under barbiturate anaesthesia.

	Sb_2	NCs	Db_1
Spontaneous Activity	9	12	5
Recruitment on Cortical Stimulation	11	10	7

The kinks in the nuclear chain fibres when the spindle was shortened made it simpler to distinguish if the stimulus could recruit them or not, for it straightened out the kinks to some degree, depending mostly on the strength of stimulus applied.

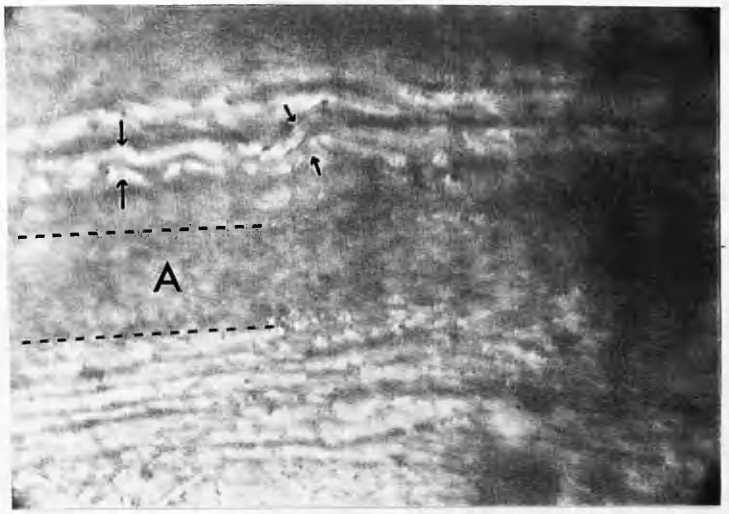
Fig 51 shows two spindles above and below an artery, running in the middle of the picture. Focusing on the right pole of the spindle on top, the kinked chain fibres were straightened out with anodal stimulation (surface positive) of 1.6 mA applied to postcruciate dimple (Pcd) filled circle. A similar response could be obtained repeatedly by stimulation of the same point and other points shown by open-circles with the same stimulus parameters.

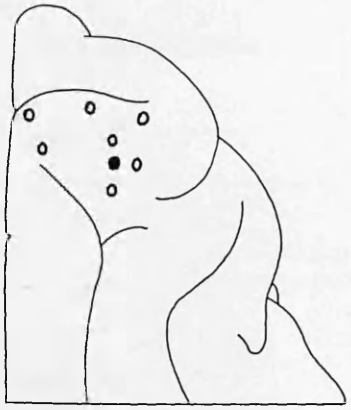
The intrafusal fibres in the lower spindle were recruited with the same stimulus, however, this is not clear in the illustration. Note, the movement of the chain fibres in the upper spindle was towards the right (right pole of the spindle in the picture), whereas the lower spindle had its equator to the right of the picture and the fibres were pulled towards the motor endings on the left. Detailed circuit diagrams of these two spindles are shown in fig 52.

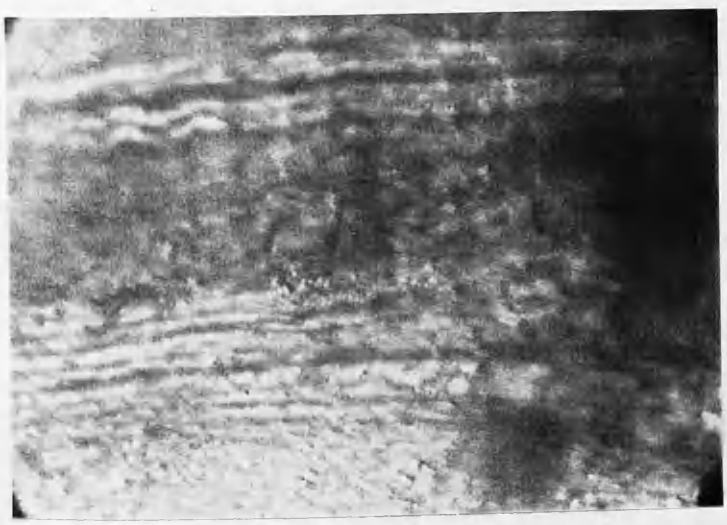
The Sb_2 fibre on its own or along with nuclear chain fibres was not recruited in the top spindle (fig 51), as it usually was in the lower one. That does not mean that the Sb_2 fibre in the top spindle was not recruited at all, for at some stage, Db_1, Sb_2 and nuclear chain fibres were recruited altogether on stimulation of points 4 and 5 with 1.6 mA (S+). Unfortunately, the video picture was not too good to frame the movement as a figure.

Fig 53 shows graded straightening of a nuclear chain fibre by increasing the current from initial level of 0.8 mA to 1.2 mA at the very bottom picture. Again, the point of stimulation is marked with

Fig 51. The effect of cortical stimulation of Pcd (filled circle) on intrafusal movements of spindle 9 and 10 above and below the artery (A). Cortical stimulation of other points (open circles) could produce the same response. The primary region of the top spindle is to the left and that of bottom spindle is to the right side of the picture. The arrows indicate a pair of kinked nuclear chain fibres in the spindle 9 (above the artery) at two locations in the top plate.







0.8 mm

Fig 52. Pattern of innervation of the right pole of spindle 9 (above) and the left pole of spindle 10 (below).

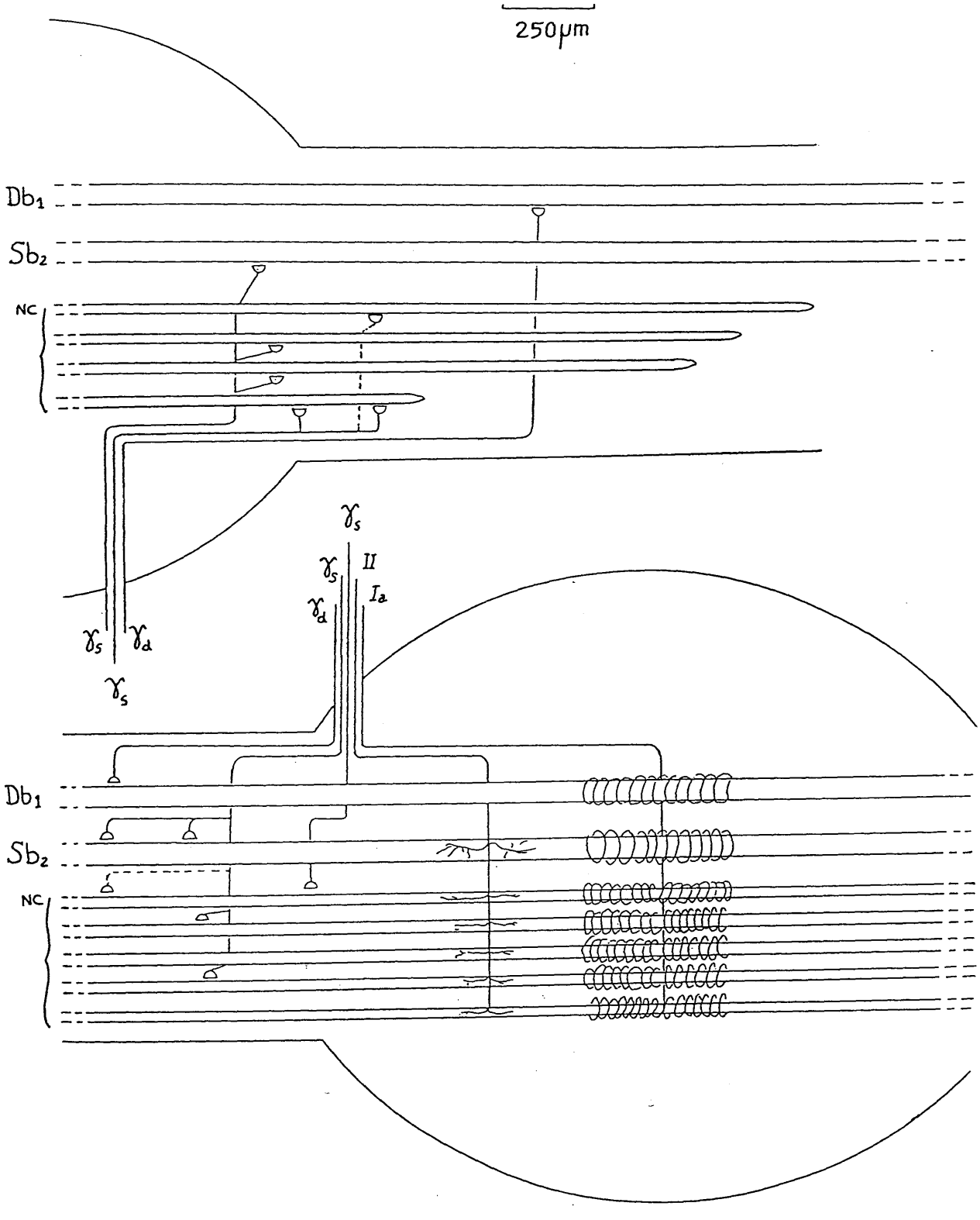
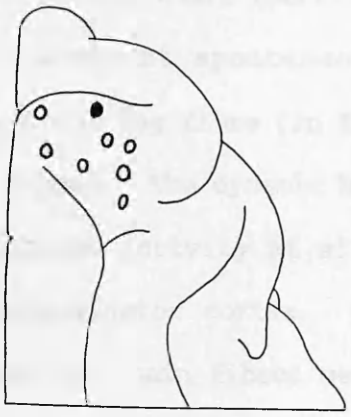

250μm
Db1
Sb2
NC
γs
γs
II
γd
Ia
γs
γd
γs
Db1
Sb2
NC

Fig 53. The effect of cortical stimulation of point 4 (filled circle) and other points (open circles) on intrafusal movements of the right pole of the spindle 3. Note the graded straightening of the nuclear chain fibres from above downward. The arrows indicate a kinked nuclear chain fibre in the top plate prior to stimulation.



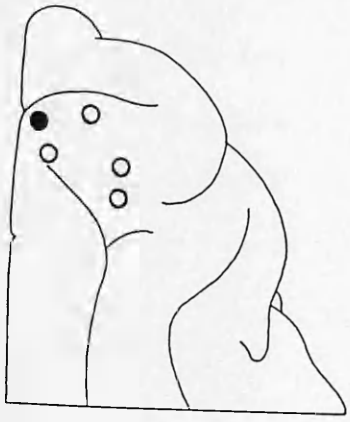
0.2 mm

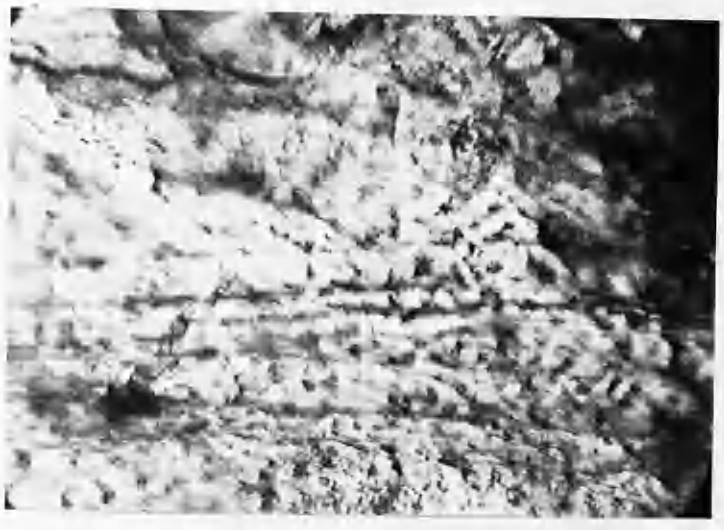
a filled-circle (point 4). Similar results were repetitively obtained from anodal stimulation of the open-circle points. The two bag fibres overlapped one another and underlay the nuclear chain fibre.

Figure 54 is another spindle with a dominant spontaneous activity of nuclear chain fibres compared to static bag fibre (in the middle) or the long chain fibre (upper thick fibre). The dynamic bag fibre (lower fibre) did not show any spontaneous activity at all, neither was it recruited on stimulation of sensorimotor cortex. On anodal stimulation of point 5 with 2.5 mA, nuclear chain fibres were recruited along with the static bag fibre. The response was reproducible. Although the polar side of the spindle is obvious on the illustration (left), however, the movement of the intrafusal fibres were towards right hand side, suggesting that the motor innervated parts of the fibres were somewhere along the fibre to the right.

Figure 55 shows recruitment of at least two gamma motoneurones on stimulation of the Pcd. The spindle consisted of two bag fibres (overlapping) and at least three nuclear chain fibres. The two lower nuclear chain fibres had the same rhythm of spontaneous movement, suggesting strongly a shared innervation by a single static gamma motoneurone. The third nuclear chain- closer to the bag fibres- was innervated independently of the other two chains. It was either individually innervated or shared the static gamma axon innervating Sb_2, for they moved together on stimulation. The stronger the stimulus, the more kinked chain fibres were straightened out. In this case, the static gamma motoneurone innervating the two chain fibres was affected with a shorter latency compared to the one innervating both the Sb_2 fibre and the other chain fibre.

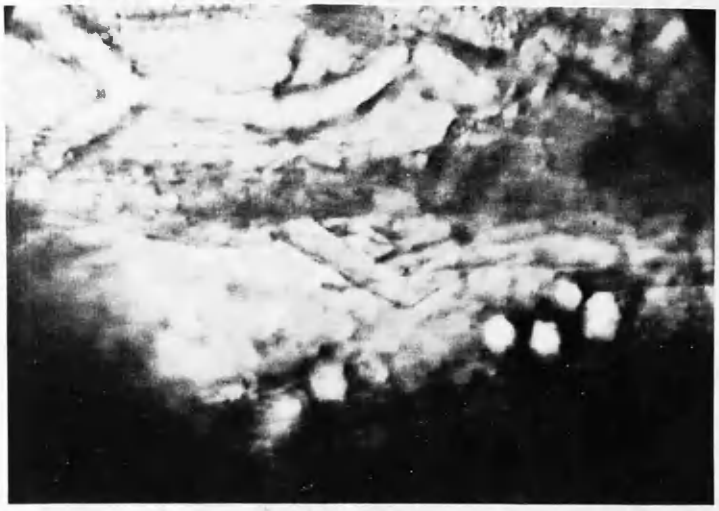
Fig 54. The effect of cortical stimulation at point 5 (filled circle) and other points (open circles) on intrafusal movements of the left pole of the spindle 16 (see text). The arrows indicate a pair of kinked nuclear chain fibres in the top plate prior to cortical stimulation.

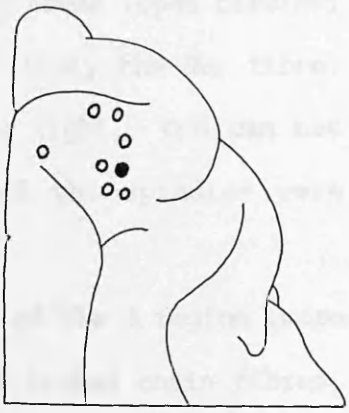


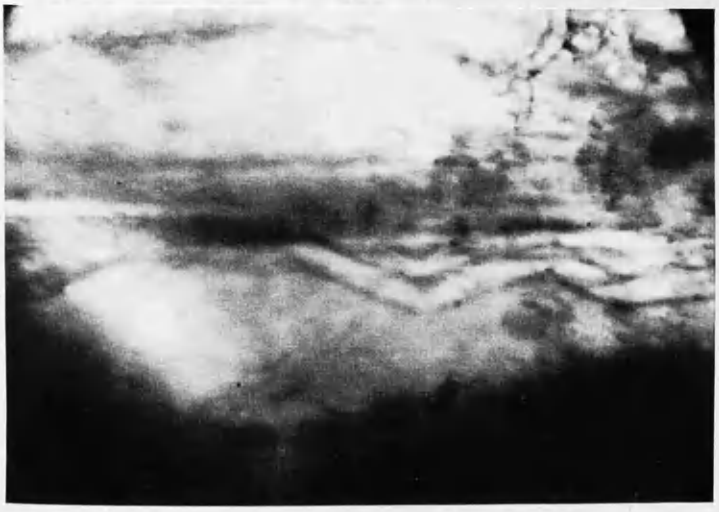


0.2 mm

Fig 55. The effect of cortical stimulation of Pcd (filled circle) and other points (open circles) on intrafusal movements of the right pole of the spindle 17. Schematic diagram of the intrafusal fibres of spindle 17 is shown in fig 58.







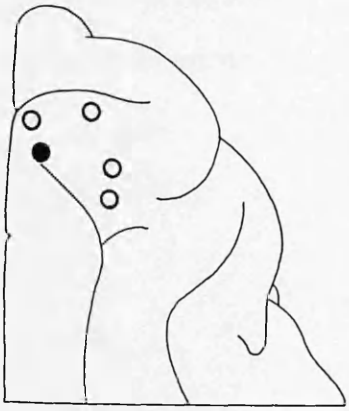
0.2 mm

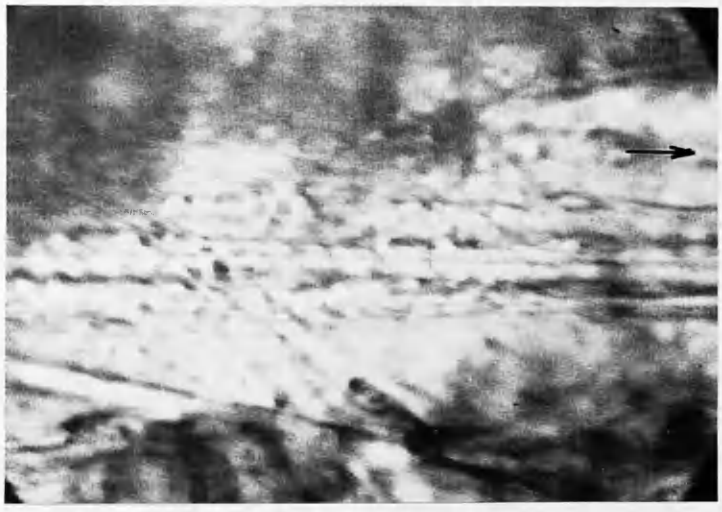
Figure 56 shows the primary region of a spindle. Sensory spirals on bag fibres are clear in the middle of the picture. Anodal stimulation of point 6 (filled circle) and other areas (open circles) activated the right pole of the spindle, more likely the Sb_2 fibre. As a result the whole spindle was pulled to the right. One can not recognize if any chains-in the lower part of the spindle- were activated on stimulation or not.

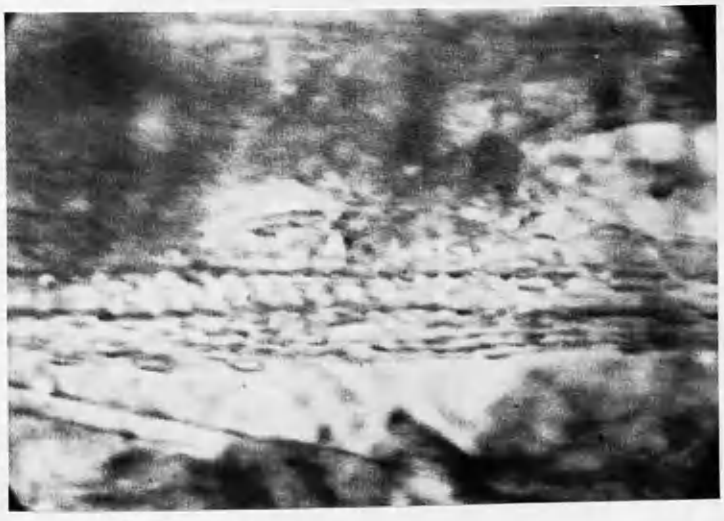
It would have been nice to have a picture of the S region (more likely S_2 or S_3, Boyd, 1962) of a spindle with kinked chain fibres, where if Sb_2 alone could be recruited on cortical stimulation which would have increased the kinks in the nuclear chain fibres. However, that was not achieved. What was achieved is shown on fig 57, where the bag fibres are visible in the background with a secondary axon lying on top of them. Anodal stimulation of the Pcd caused contraction of the Sb_2 fibre to the left hand side, and as a consequence, the kink on the secondary axon straightened out a bit. Nuclear chain fibres were located at the bottom of the spindle and could be recruited on cortical stimulation, rather weakly, with poor visibility.

Another ideal situation would be if there was a kink in a bag fibre somewhere in the sleeve region which was either straightened out by contraction of the fibre or more kinked if the nuclear chains adjacent to it are selectively but strongly contracted. There was one instance where the bag fibre was kinked (Sb_2); however, it was not recruited on cortical stimulation, nor it had spontaneous activity (Appendix, lower photograph-B).

Fig 56. The effect of cortical stimulation of point 6 (filled circle) and other points (open circles) on intrafusal movements of spindle 3 at the primary region. The whole spindle moved to the right hand side as a result of recruitment. The arrows in the middle plate indicate the direction of movement of the intrafusal fibres during cortical stimulation.

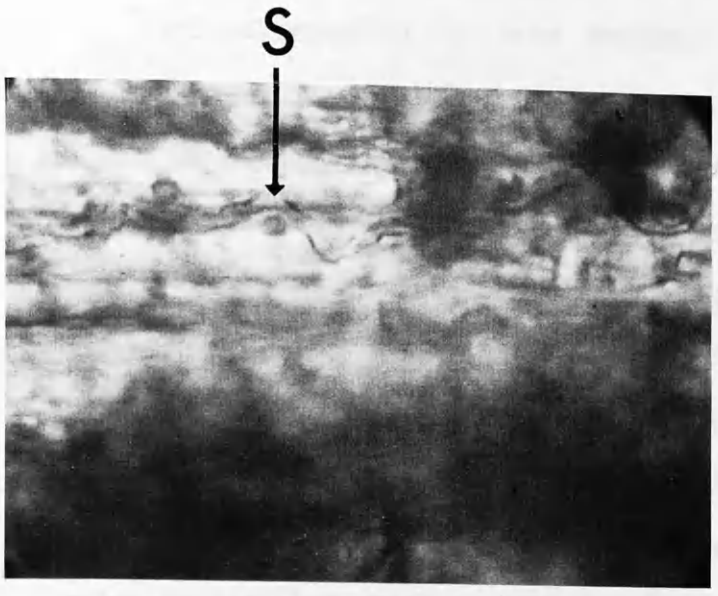


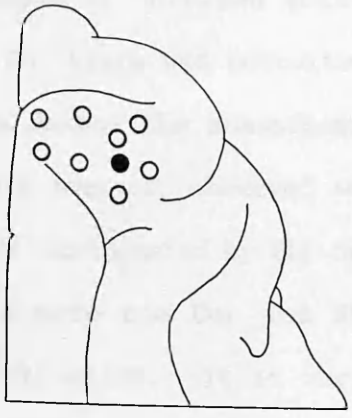




0.2 mm

Fig 57. The effect of cortical stimulation at Pcd on intrafusal fibres of the left pole of the spindle 3. The secondary sensory axon(s) is visible lying on top of the bag fibres.





0.2 mm

D. Recruitment of dynamic bag_1 fibre

Stimulation of an area bounded by points 4,5 and 6 was effective in activating the Db_1 fibre in eight of thirteen active spindles (table 2). In most cases where the Db_1 fibre was recruited, the cats were light and it was necessary to deepen the anaesthesia only a few minutes afterwards. One thing that was not observed was recruitment of Db_1 fibre alone. It was always accompanied by Sb_2 and nuclear chain fibres. Only in one spindle were the Db_1 and Sb_2 fibres recruited without any nuclear chain activation. It is worth noting that nuclear chains were not spontaneously active in that experiment prior to stimulus which recruited only the bag fibres. The response was not reproducible either.

One other point to remember is that the Db_1 fibre never became active prior to other intrafusal fibres, i.e. Sb_2 or nuclear chains fibres, on cortical stimulation. That might suggest that the threshold of dynamic gamma motoneurones may be different from that of static gamma motoneurones in barbiturate anaesthetised cats.

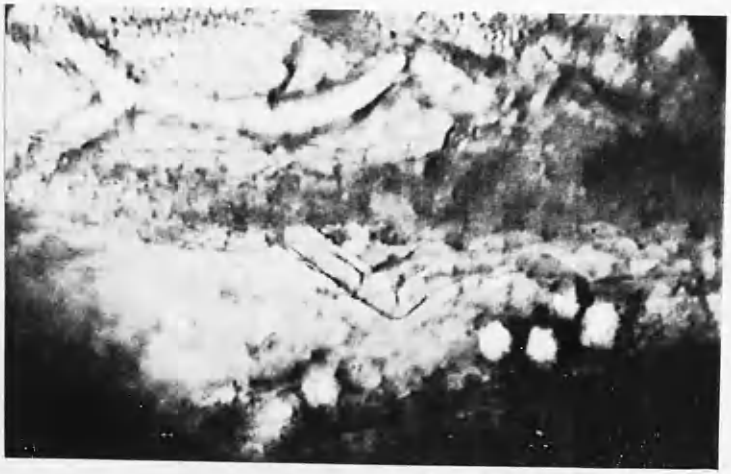
E. Inhibition of intrafusal fibres

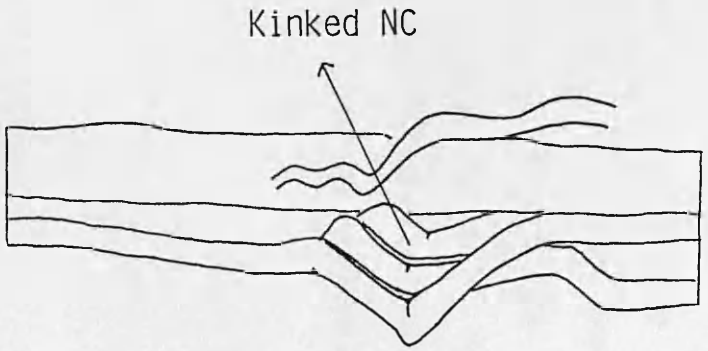
In the spindle where two chains on one hand and a chain and a Sb_2 on the other were innervated by at least two different static gamma motoneurones (fig 55), the two nuclear chains could be inhibited while the Sb_2 and one chain fibre were activated on cortical stimulation of point 5 with a respectable strength of 1.0 mA (S+). The response was reproducible even with lower and also with higher currents, but only from the same confined area. Fig 58 shows the spindle before (A) and during stimulation (B). Points where the

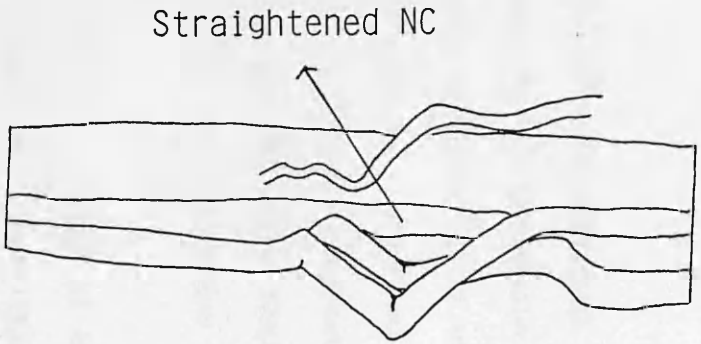
Fig 58. The inhibitory effect of cortical stimulation at point 5 (filled circle) on spontaneous activity of the two lower chain fibres of the spindle 17. The illustration does not actually show the inhibition, it only shows the recruitment of one chain fibre. The static bag_2 fibre above the chain moved to the right as well, but it is not possible to see this in the still photographs.

A

B







0.2 mm

result could be produced is also shown on the cortical map. Rebound activity on two bottom nuclear chains, which were inhibited was vigorous after stoppage of the stimulus.

On stimulation of other points, however, the response was activation of both static gamma axons, for all the nuclear chains were pulled to the right hand side.

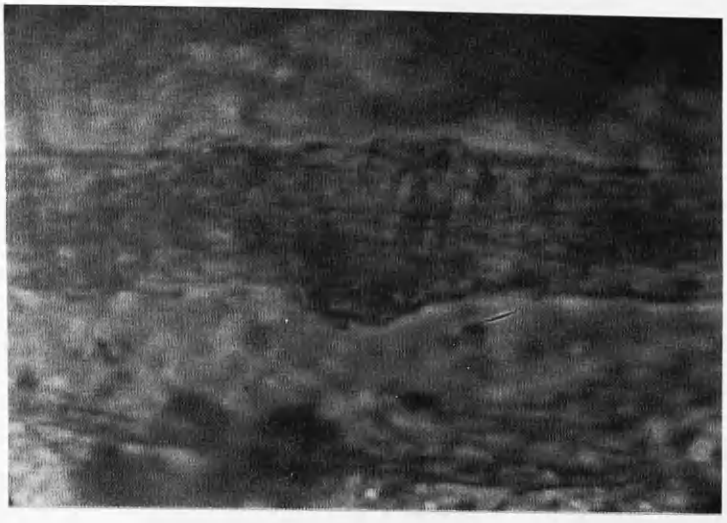
II. Exteriorised Muscle Spindle with Afferent Recording

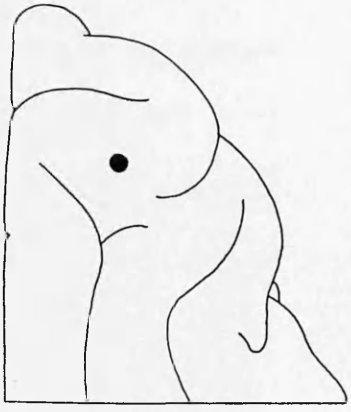
In a single cat experiment where one of the muscle spindles was uncovered, the corresponding primary afferent in L7 was found and recorded simultaneously. The spindle could be recruited centrally on cortical stimulation of 1-2 mA stimulus strength. Unfortunately, the intrafusal fibres were so densely intermingled so that it was not easy at all to distinguish movements of nuclear chains from that of the nuclear bags clearly.

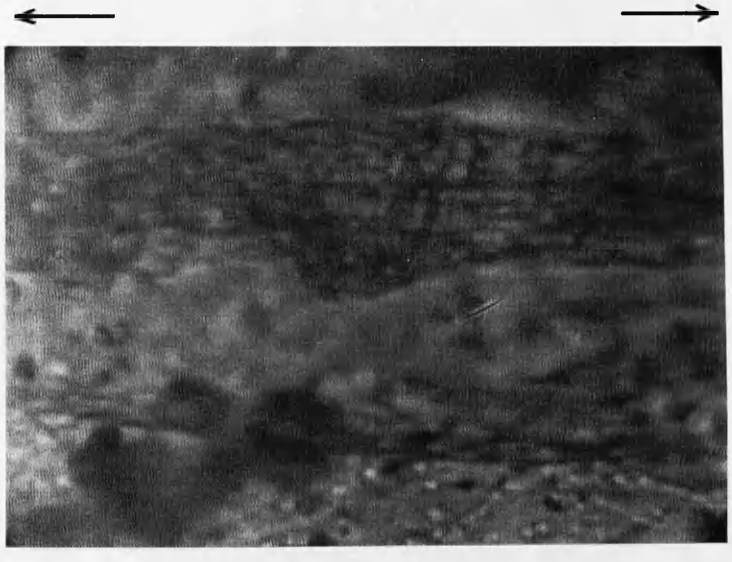
Different points were stimulated and at most of the times the static effect was elicited. It seemed most likely that the static bag_2 fibre was the only intrafusal fibre that could be recruited. Movements were also confined to the left pole of the spindle.

Fig 59 shows the spindle prior and during the cortical stimulation of Pcd, with 1.8 mA (S+). Fig 60,A demonstrates the corresponding rise in afferent firing of the spindle. Fig 60,B is the rise in afferent firing with a similar but weaker movement of the intrafusal fibres in the spindle obtained on stimulation of point 5. It was more likely that static bag fibre was dominantly responsible for the movement.

Fig 59. The effect of cortical stimulation at Pcd on intrafusal movements of the spindle in which the activity of its primary afferent was being recorded simultaneously. (corresponding changes in afferent firing are shown in fig 60, A). Above, the spindle prior to stimulation; below, the spindle during stimulation. The arrows indicate the directions of movement of the intrafusal fibres during cortical stimulation.

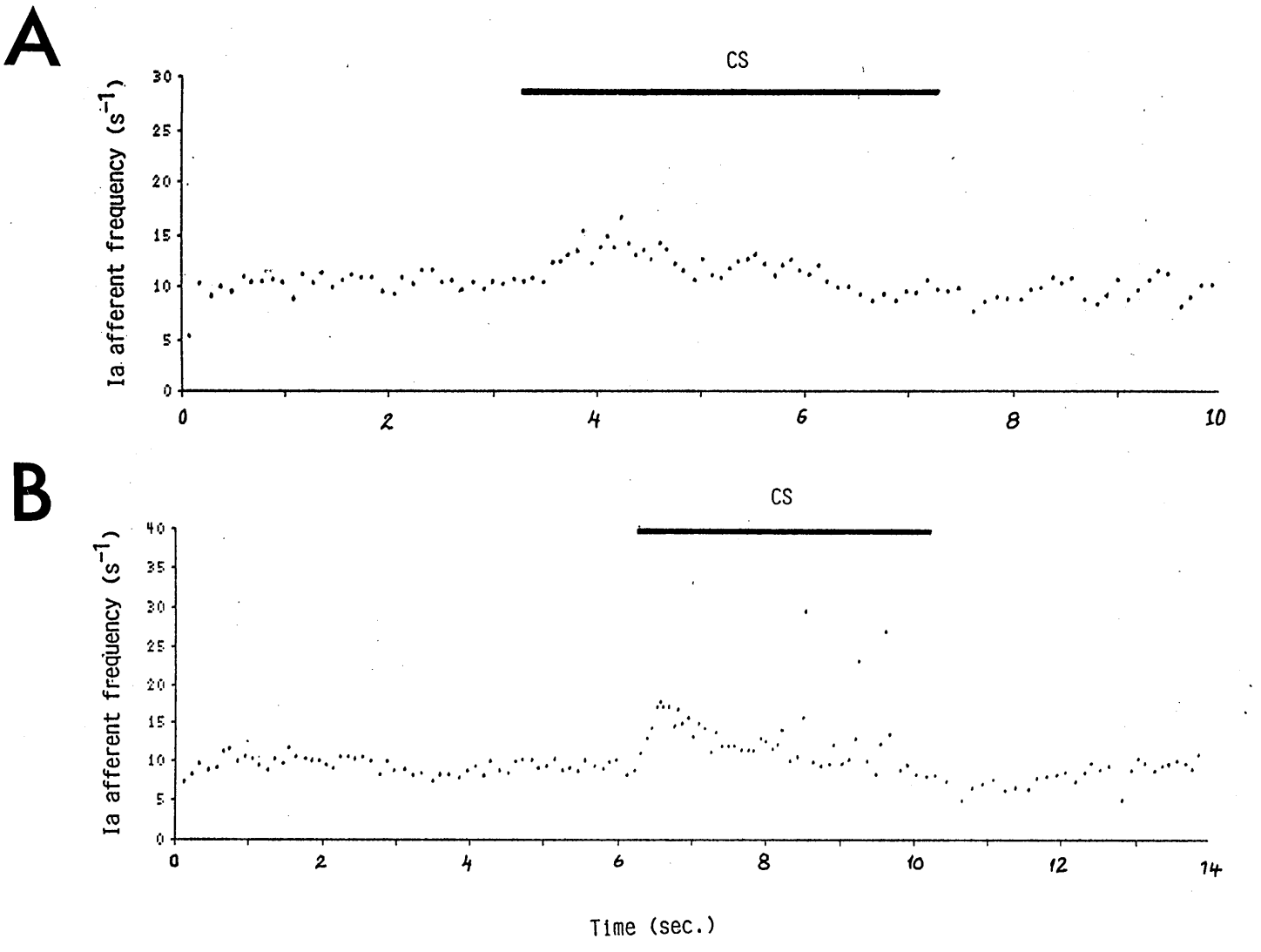






0.2 mm

Fig 60. Changes in primary afferent discharge of a tenuissimus muscle spindle on cortical stimulation of Pcd (A) and point 5 (B). The primary afferent originates from the spindle in fig 59.


A
CS
Ia afferent frequency (s^{-1})
30
25
20
15
10
5
0
0
2
4
6
8
10
B
CS
Ia afferent frequency (s^{-1})
40
35
30
25
20
15
10
5
0
0
2
4
6
8
10
12
14
Time (sec.)

What was remarkable about this particular primary afferent was that its firing did not stop on unloading the muscle spindle which happened due to extrafusal contraction on cortical stimulation of point 7 (environs of post-cruciate dimple). The stimulus strength was about 1.8mA (S+) which apparently could first recruit intrafusal fibres followed by extrafusal contraction. Fig 61,B displays the spindle, Fig 61,C shows it unloaded and 61,A demonstrates the afferent firing before, during and after cortical stimulation.

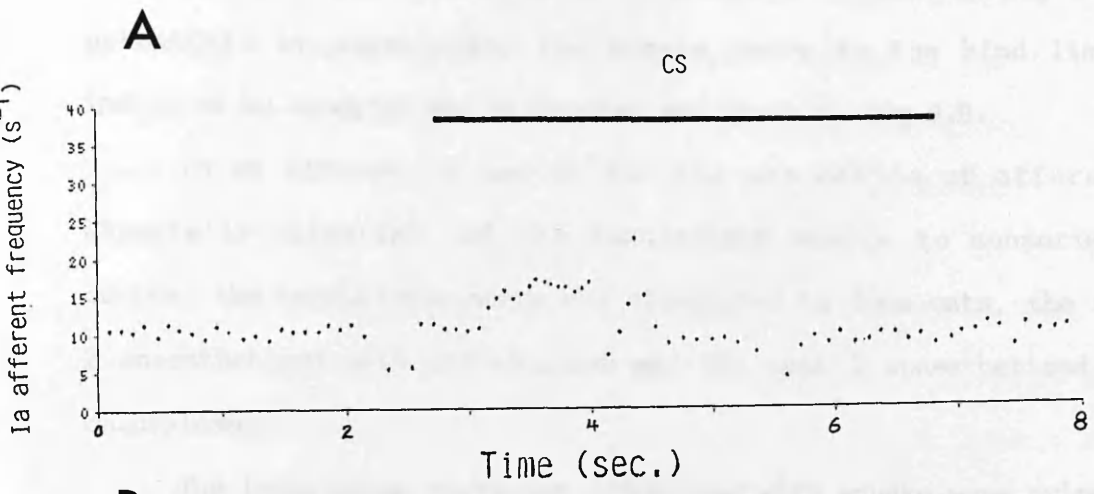
Section C: Afferent Projection to Sensorimotor Cortex

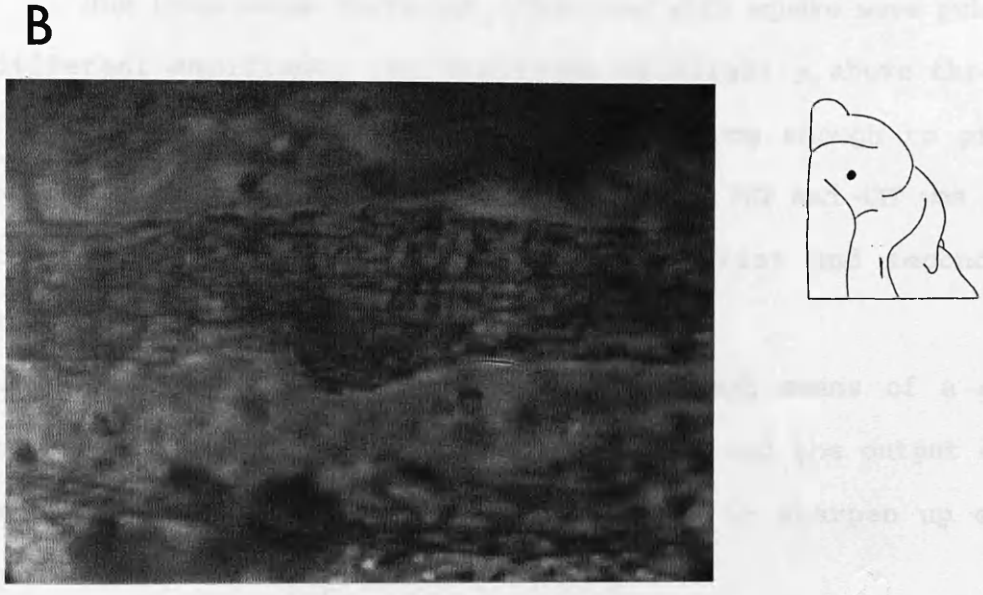
Under barbiturate anaesthesia it was not possible to pick up any surface evoked potential by stimulation of tenuissimus nerve. Dr. Proske (personal communication) suggested the use of chloralose because is believed not to depress neurones in central nervous systems. Unfortunately, in spite of using chloralose, no success was achieved in picking up surface evoked potentials. Dr. Proske also mentioned that if one does not pick up any surface potentials, one is not likely to get anything by even going 1 mm deep into the cortical layers. Note that emphasis was put on the areas of sensorimotor cortex pointed out by Landgren and Silfvenius (1969)- fig 9B.

I. Tenuissimus Muscle

Work has been done to illustrate afferent projection areas in monkeys and cats. It is well known by now that hind limb muscle afferents, both I_a's and I_b's, project to the sensorimotor cortex of

Fig 61. The effect of cortical stimulation of point 7 on tenuissimus muscle spindle intrafusal movements (B and C) and corresponding primary afferent discharge (A). C is the picture of the spindle when weakly unloaded. (An illustration of the unloaded spindle, during maximal extrafusal contraction, could not be shown because the spindle went completely out of focus.


A
CS
Ia afferent frequency (s^{-1})
40
35
30
25
20
15
10
5
0
0
2
4
6
8
Time (sec.)


B


C
0.2 mm

the cat. The areas that one is more likely to pick up any evoked potentials by stimulating the muscle nerve in the hind limb is indicated by Landgren and Silfvenius and shown in fig 9,B.

In an attempt to search for the projection of afferents, especially primaries, of the tenuissimus muscle to sensorimotor cortex, the tenuissimus nerve was stimulated in four cats, the first 2 anaesthetized with barbiturates and the last 2 anaesthetized with chloralose.

The tenuissimus nerve was stimulated with square wave pulses of different amplitude. An amplitude of slightly above threshold (threshold being the level of stimulus strong enough to pick up primary action potentials in dorsal root) and 2XT and 4XT was chosen to recruit only primaries and both primaries and secondaries respectively.

Cortical recording was achieved through means of a silver ball-pointed electrode (0.5 mm in diameter) and the output of the amplifier was passed through an averager to sharpen up evoked potentials.

Unfortunately, no success was reached on stimulation of tenuissimus nerve, no matter how high the stimulus strength might be.

II. FDL Muscle

The nerve to the FDL muscle was stimulated in three cats. In this case, evoked potentials were easily picked up in two cats with the same parameters of stimulus used to stimulate tenuissimus nerve. Note, in the case of tenuissimus there was no I_b afferent present in the nerve; however, in this case, I_b's were stimulated along with I_a's and the whole group 1 afferent projection area could be mapped.

The maximum point, where the amplitude of the evoked surface positive potentials was the greatest, fell in the region of the Pcd and a region anterior to the cranial tip of the ansate sulcus.

Both areas coincide with areas pointed out by Landgren and Silfvenius (1969). However, on one occasion the evoked potential in the medial maximal point (Pcd being the lateral) was surface negative with every parameter similar to those obtained before. The amplitude of the surface positive potentials was about 150 μV and the latency to the peak of the response was just under 30 msec.

CHAPTER FOUR

DISCUSSION

Before discussing the results described in the previous chapter, there are some questions that might occur to the reader which need to be answered. These questions are about the choice of anaesthetic used, the muscles studied, parameters of stimuli applied to the cortex and the condition of the cortex during the course of experiments.

Choice of anaesthetic agent

An ideal anaesthetic agent would produce unconsciousness, analgesia and muscle relaxation suitable for all surgical purposes. Although no single agent is without disadvantages it should be chosen in a way to suit these requirements on one hand and the conditions of the experiment on the other.

Looking back into the literature, three anaesthetic agents have been most popular for use in neurophysiological studies: chloralose, barbiturates and halothane. Halothane, an inhalation anaesthetic, was ruled out to be used in our experiments, because of its depressant action on the cardiovascular system in long experiments. It tends to reduce blood pressure. Respiratory problems, profound hypotension and cardiac arrest might arise with high doses of halothane. To reduce halothane's toxic effects, one might give less anaesthetic (less than 2%) which, on the other hand, might not be enough to produce sufficient sedation for surgical procedures to be carried out. Vedel and Mouillac-Baudevin (1970) used fluothane (a brand of halothane) as an anaesthetic agent. They reported

"persistently light EMG activity in neck and shoulder muscles" during the course of their experiments, which might be an indication of underusage of the anaesthetic agent.

Chloralose, our second choice, as a widely used anaesthetic agent in neurophysiology, produces a unique pattern of anaesthesia characterized by both an excitant (spontaneous myoclonic jerks in response to stimulation such as noise, touch, ...etc) and depressant (sedation and anaesthesia) action. The mechanism of action remains yet to be disclosed. Winters and Spooner (1966) added to the evidence confirming a dual action on chloralose in their neurophysiological studies. But they went further to conclude that chloralose does not meet the criteria necessary to be classified as an anaesthetic. Rather, they postulated that chloralose hyperexcites certain brain areas and that the responses of chloralosed-treated animals more closely mimic an epileptoid state rather than anaesthesia.

In contradiction to the suggestion of Winters and Spooner (1966) that chloralose may be epileptogenic, Dudley, Nelson and Samson (1982) suggested that chloralose is not an epileptogen, and its anaesthetic action appears to result from a depression of regions of gray matter. Dudley, Nelson and Samson, adapting a glucose utilization technique, also reported that chloralose appears to act as a general depressant except in certain gray areas of the midbrain and lower brain stem. Their conclusion was based on their estimates of the rate of cortical glucose use which showed that the average cortical activity is reduced. Therefore, chloralose may not be an epileptogen, as generally accepted, especially in our experiments which involved the cortex.

Ketamine, on the other hand, is believed to be an epileptogen, according to a similar study by Nelson et al. (1980). However, it was used in the present work only as a single intramuscular injection to cause sedation for less than an hour to allow introduction of a venous cannula at the beginning of the experiment.

Barbiturates are famous for their depressant effect on the central nervous system. Sokoloff et al. (1977), working on rats anaesthetized with barbiturates confirmed the idea and added that barbiturates markedly depress the rates of glucose utilization throughout the brain, particularly in gray matter, and the metabolic rate throughout gray matter becomes more uniform at a lower level.

Therefore, comparing chloralose and barbiturates, sodium pentobarbitone was used in the majority of experiments because firstly, it was used in previous work (Gladden and McWilliam, 1977a,b) and we needed to use the same anaesthetic if comparison between results were desirable. Secondly, according to evidence given above, both anaesthetic agents induce a depressant action on the cerebrum and chloralose has no advantage on barbiturates in this respect. Thirdly and finally, it was simply easier to use.

Choice of muscles

The tenuissimus muscle was used in the majority of experiments because it was easier to uncover its spindles. In addition, the literature on this muscle, in contrast to its almost non-significant function on underlying joints, is by far greater than other muscles. No other muscle was available to search for independent control of different populations of static fusimotor neurones, since the

presence of those fusimotor neurones in muscles other than tenuissimus has not been proven yet, neither histologically nor physiologically.

Flexor digitorum longus (FDL) was chosen not as a physiologic antagonist for tenuissimus muscle, as it surely is not, but to test the effect of cortical stimulation on the fusimotor system of a second hind limb muscle. FDL is a physiologic flexor of the hind limb digits whereas tenuissimus acts on different joints, namely hip and knee. Therefore, there is no similarity between these studies and that of Vedel and Mouillac-Baudevin's (1970), where true physiologic antagonists were tested: soleus and tibialis anterior muscles - both functioning on the ankle joint. Another reason why FDL was chosen was its use by our colleague Michael Dickson in the same laboratory working on the influence of brain stem nuclei on the fusimotor system.

Stimulus parameters

It was preferred to use "current" as the variable of intensity rather than voltage which was used by Vedel and Mouillac-Baudevin (1970). In recent literature, it is usually the current that has been preferably used. It directly presents the current that is passed through a network of resistances: stimulating electrode, pia-covered cortex, some depth of cortical tissue all the way back to the indifferent electrode itself. The overall impedance is assumed to be constant; therefore, any change in current will directly be applied to the cortex.

Surface positive (anodal) pulses were mostly used in our experiments, although in some experiments both surface negative and positive pulses were applied to the cortex. The advantage of using surface positive stimulation is the lower threshold of the cortical neurones compared to cathodal (surface negative) stimulation. The fact that anodal thresholds are lower than cathodal was first discovered in the dog by Fritsch and Hitzig (1870). Working on alpha-motoneurones, Livingston and Phillips (1957) also reported a lower anodal threshold for flick movements of the contralateral forelimb of the cat. The lowest - threshold focus for motor responses from the cat's cortex is near the lateral end of the cruciate sulcus; at this focus a large population of "Betz" cells is usually to be found on the convexity of the lateral part of the anterior sigmoid gyrus where it is continuous with the coronal gyrus (Livingston and Phillips, 1957). They claimed that surface anodal threshold was usually, but not always, lower than the surface cathodal.

It was assumed that it is the same considering fusimotor neurones and our results confirm that most of the time, the threshold for fusimotor neurones in the sensorimotor cortex is lower for anodal stimulation than cathodal (fig 13).

State of the sensorimotor cortex

In experiments carried out in mid 70's (Gladden and McWilliam, 1977a,b), the cortex was simply kept moist while it was stimulated and at the same time they were not getting consistent fusimotor effects from the same cortical areas in different cats. It is believed that CO_2 escape from the surface of the pia-covered cortex

lowers the extracellular concentration of pCO_2 which elicits autoregulatory responses. Autoregulation, in turn, will be reflected as a reduction in the diameter of local arteries and finally deterioration of the cerebral blood flow. Therefore, it seems crucial to prevent CO_2 escape from the cortex. Kuschinsky et al. (1972) covered the cortex with a reasonable amount of warm mineral oil and demonstrated that it could stop much of the CO_2 escape. With that simple technique, one can be fairly sure that the blood flow of the cerebrum stays reasonably good throughout the experiment. In fact the technique has been used as a routine method in all pial vessel experiments in veterinary school of Glasgow University since then.

Topographical Mapping of the Sensorimotor Cortex

One of the objectives of the present study was to find a topographical map of the sensorimotor cortex for fusimotor control. The fusimotor effects given in the results were obtained exclusively from the contralateral cortex in order to define the cortical regions particularly involved in the production of changes in fusimotor system of both the tenuissimus and FDL. It seems that points 4, 5 and 6 fall in an area, from where the dynamic bag_1 fibre can be recruited. Therefore the area might be referred to as the "dynamic area". It is worth noting that in only one cat out of 23 (fig 20), an excitation of the dynamic bag_1 fibre was obtained on stimulation of a point away from the dynamic area.

One thing to notice is the small size of the dynamic area compared to the whole area of the sensorimotor cortex from which fusimotor effects can be elicited. Excitatory static effects, on the other hand, can be attained from almost all over the sensorimotor

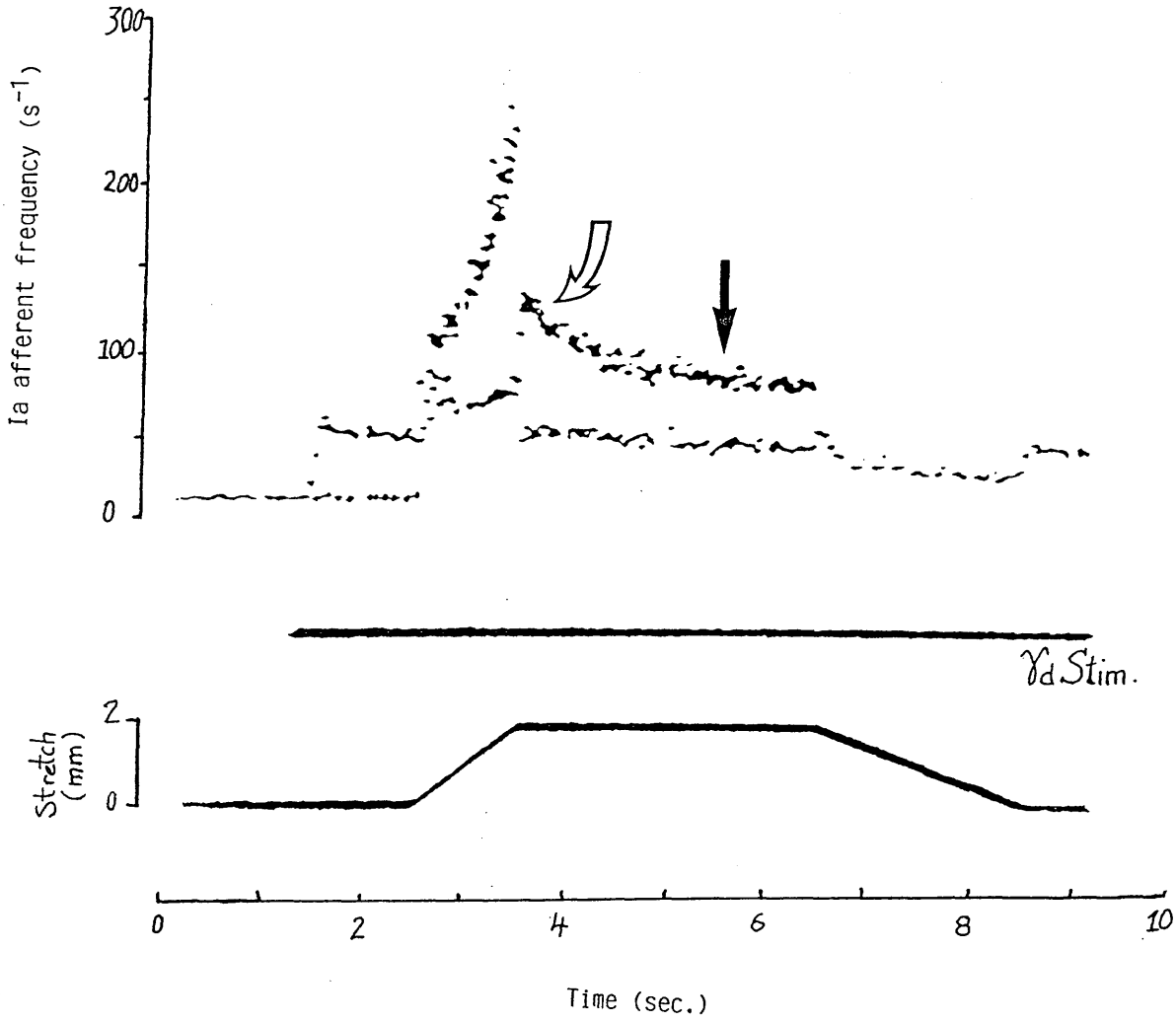
area! There are several reasons for this. One, simply is the number of dynamic gamma axons innervating Db_1 fibres compared to a larger number of static gamma axons innervating other intrafusal fibres. The ratio of dynamic gamma axons over statics is said to be 1 to 3 or 4.

Muscle receptors as well as joint and skin receptors are capable of producing a sense of kinesthesia. The cortex is one of the structures that is believed to have access to both incoming information from primary and secondary afferents, relaying information about the instantaneous length of the muscle, and the ability to adjust spindle afferent sensitivity via outgoing impulses through gamma motoneurones to intrafusal fibres. However, it is much more complicated to use information from primary afferents rather than secondaries because firstly primary afferents' discharges originate from all intrafusal fibres which are under the influence of at least two main gamma populations, static and dynamic. Secondly, it is dependent on the velocity and the direction of movement. Thirdly and more importantly, is the fact that the primary afferent discharge is a nonlinear response to length changes. On the other hand secondaries give a much simpler signal to the brain and this has two advantages: firstly that it is much less affected by movement and secondly it is influenced only by static gamma axons. Moreover, it is established by now that the nuclear chain fibres are most effective in providing a large positive bias to the discharge of both primary and secondary endings. Therefore, having information about the ongoing activity of static gamma axons (innervating nuclear chain fibres) and secondaries' discharges of a muscle, it is fairly easy to work out the length of the muscle (which is the sense of kinesthesia). Although no particular structure in the central nervous

system is known to do so, the role of the sensorimotor cortex may not be ruled out. On the other hand, recalling the idea of nuclear chain fibres being the most important intrafusal fibres in producing a good gateway for the sense of kinesthesia, since they are capable of increasing the length sensitivity of secondaries, one can not see any logical reason for having an extensive area devoted to axons innervating Db_1 fibres.

It has been shown that dynamic and static gamma axons affect different components of the primary and the secondary responses to stretch (Boyd, Murphy and Moss, 1985; Boyd, 1985). It is believed that static gamma axon stimulation increases length sensitivity of the secondary ending (Jami and Petit, 1978) while dynamic gamma axon stimulation can increase that of the primaries. A recent collaborating work between Glasgow and Paris (unpublished) shows the same phenomenon on the primary afferent discharge in tenuissimus muscle of the cat (fig 62). Note that the increase in the length sensitivity of the primary afferent did not last to the end of the dynamic gamma stimulation, apparently due to the adaptation. If the matter of adjusting sensitivity to length changes is being taken care of at the level of spinal cord (in spinal reflexes) one can not imagine why would there be in the sensorimotor cortex a necessity for an exact duplication rather than dedicate more sophisticated functions to higher central nervous system (i.e. cerebrum). What could be then the role of the cortex in motor control? Is it capable of over-riding gamma motoneurone activity in the spinal cord or can it only adjust the fusimotor balance as the cerebellum does for alpha motoneurones? Some of the results support the former idea and some the latter. For instance, on occasions where there was only

Fig 62. Upper trace: the effect of stimulating a dynamic axon in the ventral roots on the response of a tenuissimus primary afferent to ramp stretch. Lower trace: the response to passive ramp stretch only. Open arrow indicates increased length sensitivity due to stimulation; filled arrow indicates no increase in length sensitivity even in the presence of gamma dynamic stimulation. (courtesy of Dr. Gladden, Dr. Emonet-Denand and Michael Dixon).


Ia afferent frequency (s^{-1})
300
200
100
0
γ_d Stim.
Stretch (mm)
2
0
0
2
4
6
8
10
Time (sec.)

facilitation of the response to the peripheral stimulus (e.g. ramp hold stretch) and also a simultaneous increase in static firing level of spindle primary afferents, the cortex is rather adjusting the activity of spinal gamma motoneurones. However, when the usual response to the peripheral stimulus is abolished (the physiological importance of which in unknown to me), then the cortex is revealing its ability to over-ride the ongoing activity of spinal gamma motoneurones. With above examples it seems that the cortex might be able to do both. However, the above statements can be criticized in that "in physiological conditions are the cortical neurones subject to as strong a stimulus as we applied during the cortical stimulation: 200 Hz and an average current of about 2.0 mV while at the same time the spinal gamma motoneurones are firing at a low level, with an average primary afferent frequency of about 25 Hz? " Whatever the real answer is, one can assume that with the presence of at least three types of gamma motoneurones in the spinal cord there should certainly be a centre to "balance" the activity of the three, since an over-activity of any of them would bias wrongly the ascending information to higher central nervous system. Why could the centre not be the sensorimotor cortex since it seems to be able to have influence on spinal gamma motoneurones and at the same time receives information from muscle spindle afferents?

It was not possible to sharply map the areas of the sensorimotor cortex, from where different static gamma axons could be recruited. However, in a broad sense, taking also results of direct observation of intrafusal fibres into account, the static bag_2 fibre could be recruited from the whole area while nuclear chains could either be recruited from the same area or from a more confined area

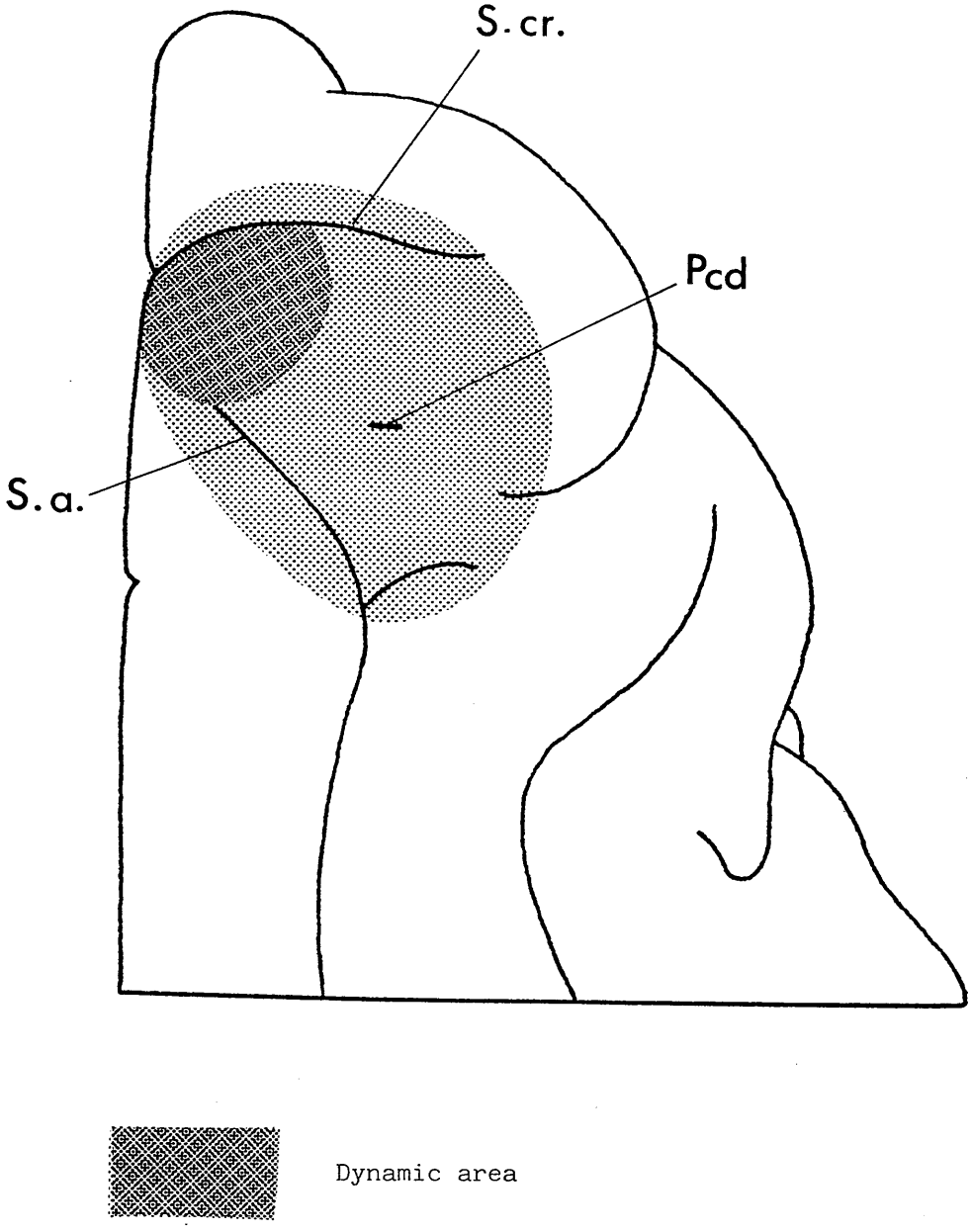
within it (fig 63). Although Vedel and Mouillac-Baudevin (1970) did not give details about their points of stimulation on obtaining excitatory dynamic effects, going only by their graphs, the area seems to be coinciding exactly to our "dynamic area". So does the cortical area of Gladden's experiments on 1982 (personal communication). Unfortunately, the area where different populations of static gamma axons could be selectively recruited could not be mapped with our results.

Exteriorised Muscle Experiments

The analysis of results obtained from direct visualization of intrafusal fibres of tenuissimus muscle spindles on cortical stimulation involved the assumption that movement of the dynamic bag_1 fibre signified that dynamic gamma axons were active and movement of the static bag_2 fibres or nuclear chain fibres signified activity of static gamma axons. This assumption followed from the microscopic observations of living spindles during stimulation of single static gamma axons, and dynamic gamma or beta axons (Boyd et al. 1975, Boyd et al., 1977; Bessou and Pagés 1975). Both groups in Britain and Paris respectively apparently agreed that movement of dynamic bag_1 fibres occurred only during stimulation of dynamic gamma and beta axons, and stimulation of static gamma axons caused movement of static fibres only.

Unlike Gladden and McWilliam (1977a,b) and Gladden (1981) who reported spontaneous activity of Sb_2 fibre in all 16 uncovered muscle spindles studied (in light anaesthesia or in decerebrate cats), our results show that Sb_2 fibres were not always spontaneously active.

Fig 63. Diagram showing the dynamic (dark stippled) and the area from where static fusimotor axons could be recruited (light stippled). S.cr., cruciate sulcus; S.a., ansate sulcus.


S.cr.
Pcd
S.a.
Dynamic area

They were active in 9 out of 14 active spindles (table 2). In fact, nuclear chain fibres were active in more spindles, 11 out of 14. However, they reported that nuclear chain fibres were not so likely to be spontaneously active as static bag_2 fibres in light anaesthesia or decerebrate animals.

Dynamic bag_1 fibres were seen to be spontaneously active in light anaesthesia in 5 out of 14 active spindles in five different cats. Again, this is a higher incidence of spontaneous dynamic gamma activity compared to the results reported by Gladden (1981) where three muscle spindles (only in two cats) out of 16 showed spontaneous activity. It seems that dynamic fusimotor neurones are more susceptible to anesthetics, as they come live just before animals need supplementary doses of anaesthetic. However, Gladden and McWilliam (1977a,b) and Gladden (1981) did not spend much time to observe the spontaneous intrafusal activity of muscle spindles under anaesthesia because they wanted to study the same objectives in decerebrated and spinal cats. Therefore, they carried out decerebration immediately after a short period of study under anaesthesia. This may explain the lesser incidence of spontaneous Db_1 activity in their experiments compared to ours.

The results generally agree with those of Gladden and McWilliam (1977a) where lightening of anaesthesia enabled recruitment of more types of intrafusal fibres. Moreover, these results helped to map the sensorimotor cortex topographically (previous section). Furthermore, exteriorised spindles helped to some degree to uncover intrafusal movements responsible for changes in afferent discharge due to cortical stimulation. Finally, the completely new finding was the assessment of independent control of two static gamma axons, one

which exclusively innervated chain fibres in the spindle (fig 61) was inhibited and the other, which innervated a chain fibre and a Sb_2 fibre was excited. Therefore, it is worth appreciating these experiments, because dorsal root recording with the present limited knowledge on their interpretation of sensory ending events could not have revealed the phenomenon of independent control of different static gamma axons.

On cortical stimulation, dynamic bag_1 fibres of 7 spindles (in five cats) were recruited. In all seven spindles, the static bag_2 fibres as well as nuclear chain fibres were recruited simultaneously, except in one case where only Sb_2 fibres were recruited with the Db_1 fibres. Again, this confirms the idea introduced by Gladden (1981) that a pure excitation of dynamic gamma motoneurone is difficult to obtain by cortical stimulation. At least two different possible mechanisms may be responsible for this phenomenon. One is derived from the fact that the Db_1 is more susceptible to anaesthesia, suggesting that once the dynamic gamma axons are spontaneously active, the static gamma axons are active too. Supposing a similar threshold level for the excitation of these different gamma axons at cortical level, at a time when they are all spontaneously active, might explain the recruitment of static intrafusal fibres joined with dynamic bag_1 fibre recruitment.

The other possible mechanism might be a divergence of descending pathways onto gamma motoneurones somewhere at the level of spinal cord, an idea which needs to be elaborated further. It is well known by now that gamma motoneurones in the spinal cord are at least of three types: one dynamic and two statics. There seems not to be a necessity to have three distinct descending descending pathways onto

gammas from the cortex to control the corresponding three types in the spinal cord. Having in mind the fact that the motor cortex is not a pioneer structure in initiation of voluntary movements (at least in primates and humans), one can imagine the presence of a single descending connections from a single type of neurone which under physiologic condition could control the activity of all different types of gamma motoneurones in the spinal cord providing a complex neuronal connection and various levels of excitability among different types of gamma motoneurones, the two facts that are known to exist in the central nervous system. One way of approaching a solution for this theory is by ablating techniques to see if abolishment of a structure or a pathway within the central nervous system dismisses the influence of the cortex on all types of gamma motoneurones. That, of course, does not contradict the fact that gamma motoneurones are under separate control. Information such as synaptic connections at different levels within the central nervous system, neurotransmitter and co-neurotransmitter release at the site of neurone to neurone junctions, variation in excitability within gamma motoneurone pool, and much more, is needed to prove the latter second possible mechanism stated above.

Gladden and McWilliam (1977 a,b) suggested firstly that their results were compatible with the conclusion that the central nervous system can control the dynamic bag_1 fibres of muscle spindles entirely separated from the static bag_2 fibres and nuclear chain fibres. The present results confirm their findings. The reason why these results support the view that dynamic bag_1 fibres are under separate control are as follows. Firstly, they were the last to become spontaneously active in light anaesthesia and the first to

stop during deepening anaesthesia. Secondly, contraction of dynamic bag_1 fibres often occurred sequentially with that of other intrafusal muscle fibres. Thirdly, additional evidence comes from findings of Gladden (1981) where intracellular recording of nuclear bag fibres showed no close correlation between junctional potentials of the two bags so that it could not be believed that the two bag fibres have possibly a common innervation.

In addition, since Db_1 fibres could be exclusively recruited from a very confined area, the so-called "dynamic area", this increases the weight of evidence in favour of independent control of Db_1 fibres from static bag_2 fibres.

The present direct observation results neither support nor rule out the glycogen-depletion evidence where Barker et al. (1976b) and Laporte (1979) reported that gamma static axons innervated dynamic bag_1 fibres. Consistent recruitment of the Sb_2 fibre along with the Db_1 fibre in our experiments might apparently support the idea put forth by Barker et al. (1976b) and Laporte (1979). Intracellular recordings necessary to resolve the difficulty of the argument were done by Gladden (1981) which showed that the innervation of Db_1 and Sb_2 can not take place by means of a common static gamma axon. None of those intracellular technique were utilized in these experiments (for more details, refer to Gladden, 1981). However, in two out of four histologically sectioned spindles where there seem to be three thick intrafusal fibres, one was definitely a long nuclear chain having common innervation with Db_1 fibre (fig 45). The other spindle (also displayed in fig 44) has got a common innervation between the two thick intrafusal fibres, suspected to be a long chain again. However, it needs to be sectioned in the right pole in order to

confirm that it is a long chain, for they are usually thick in one pole and have an ordinary size of a nuclear chain fibre on the other pole.

One might argue that cortical stimulation may have actually excited dynamic or static gamma axons innervating Db_1 and Sb_2 fibres but these did not move during cortical stimulation, because the recruitment was so weak, with a rate less than 15 pulse per second. These results do not give a clue about that kind of recruitment. However in spite of that fact, all the points where a fusimotor response was not elicited, neither static nor dynamic, were stimulated with a stronger pulse up to a point where there was alpha motoneurone recruitment. Therefore, confining the analysis to only what could be observed on videotapes, is not a terribly bad limitation and observations can in fact reveal a great deal.

Because extrafusal contraction put the muscle spindle out of focus, concomitant intrafusal contraction was difficult to observe. However, it happened frequently that Sb_2 and Db_1 fibre contractions slightly preceded extrafusal contraction. That delay might be explained by the spatial summation phenomenon, where stimulation of some close-by points might bring a pyramidal tract neurone - PTN (and eventually alpha motoneurone in the spinal cord) into excitation. Phillips (1956) working on PTN's claimed that even below motor threshold, PTN's contained within a circle of radius 4 mm were firing a burst of impulses. With application of currents of stimulus strength just below alpha motoneurones' threshold, in order to recruit only gamma axons, it is not impossible at all to recruit alpha motoneurones if spatial summation happened.

On the other hand, beta axons are another possibility of being responsible for recruiting extrafusal fibres. According to Henneman's size principle (1965) beta dynamic motoneurones would be recruited before large alpha-motoneurones going exclusively to extrafusal muscle fibres. In fact McWilliam (1975) studied the β axons innervating spindles of tenuissimus muscle and reported a lower conduction velocity for the β_d axons than α axons although some overlap between α and β groups did occur. Therefore, β_d axons which are at the low end of the α range may have been recruited along with gamma axons during cortical stimulation.

Another important point to notice from exteriorised experiments is the information given in both tables 1 and 2 which show the spontaneous activity of intrafusal fibres preceding any cortical recruitment. As a rule, on cortical stimulation, the intrafusal fibres which were recruited were the same ones spontaneously active regardless of the type of intrafusal fibres, but there were a few exceptions (to see the exceptions, refer to table 1). That is an interesting point to pause on. It might imply that cortical stimulation under anaesthesia does not reveal the full version of cortical control of gamma motoneurones because the lighter the cat became, the better and more various results were obtained; and at the same time one can never carry out these experiments in conscious cats. Another implication may be the ability of the cortex to cause only a general facilitation over gamma populations in the spinal cord, since the incidence of inhibition was much less than the incidence of facilitation.

Effects of Cortical Stimulation on Primary Afferents

According to the exteriorised muscle experiments, different patterns of influence on intrafusal fibres could be elicited on cortical stimulation: one nuclear chain fibre contraction, contraction of more than one nuclear chain fibre, static bag_2 fibre contraction, concomitant contraction of one or more nuclear chain fibre with Sb_2 fibre, dynamic bag_1 fibre contraction in combination with other static intrafusal fibres. Moreover, stimulation of the dynamic area might activate some chains (with or without Sb_2 fibre) while inhibiting others, each of which have different or even opposite effects on the afferent discharge. And probably there are many more possibilities for disparate effects brought about by order of recruitment of intrafusal fibres. Even with the limited number of possible recruitments mentioned above, the interpretation is very complicated. The degree of contraction of each intrafusal fibre in each case is another variable that makes interpretation even more difficult. Another variable is concomitant contraction of both poles of a spindle or contraction in one pole and inhibition of the other. However, to make discussion possible, it will be assumed that the possible recruitment of intrafusal fibres are those main types mentioned earlier and an attempt will be made to base intrafusal mechanisms underlying changes in primary afferents on those. I shall also try to match the findings not only to published findings of Boyd (1986) but also with those unpublished and other recent findings by his colleague, Dr. Gladden.

Generally our results confirm the existence of a functional relationship between the sensorimotor cortex on the one hand and fusimotor neurones on the other. The study of changes in static discharge and dynamic sensitivity of primaries and secondaries and their comparison with the effects obtained by Boyd and his colleagues (Boyd, 1986) on direct stimulation of fusimotor axons allowed us to define the action of the sensorimotor cortex on muscle proprioceptors and more particularly its role in modifying the activity of different types of gamma motoneurones, static and dynamic. Almost all the results obtained from the tenuissimus muscle were of an excitatory type, either static or dynamic, except one case each in different sets of experiments: in the afferent recording series reflected in fig 34 and in direct visualization series reflected in fig 61. Moreover, those results obtained from FDL were exclusively excitatory. These results are not inconsistent with results introduced by Vedel and Mouillac-Baudevin (1970). They were working on true physiological antagonists and reported different "facilitatory" and "depressor" effects on cortical stimulation depending on the level of anaesthesia. They claimed that under "light" anaesthesia (a persistently light level of EMG activity in the neck and shoulder muscles) stimulation of sensorimotor cortex (and pyramidal tract) strongly reduced static discharge and dynamic sensitivity of soleus primary sensory endings. However, in "deep" anaesthesia (having slight but permanent EMG activity in the neck and shoulder musculature), stimulation of sensorimotor cortex produced a reinforcement of both facilitatory effects: one with a dynamic character and the other one with a static character.

Different anaesthetic agents, barbiturates or chloralose in our case, and halothane in their experiments (Vedel and Mouillac-Baudevin, 1970), might account for the great variation of results. If one considers halothane to be one of those agents whose effects rapidly disappear, allowing the animal to become light quickly, then it may be rightly argued that in their "light" anaesthetic conditions, the cortex was actually not in a depressed condition, but rather in a excited one. Therefore, stimulation of the already excited cortex might be expected to have an opposite effect on volleys going corticofugally down to the gamma motoneurone population in spinal cord. It is worth pointing out that we never had our cats in a "light" anaesthesia as Vedel and Mouillac-Baudevin (1970) reported; and I think their "deep" anaesthesia was our light anaesthetic state. That might explain why they obtained a reproducible depressant effect on cortical stimulation. They discussed possible mechanisms responsible for the reduced fusimotor activity of the soleus muscle on cortical stimulation at two central and peripheral levels. At the central level one can argue that stimulating the pyramidal system blocks supraspinal input which entrains the activity of fusimotor neurones, thus ensuring a certain degree of sensitivity of the sensory terminals to stretching. At the peripheral level, although the respective roles of the two types of gamma motoneurones, under anaesthetic conditions, is difficult to define, however, assuming the presence of spontaneous activity in both types of gamma motoneurones, the depressant effect on primaries of the soleus muscle are evidence of a depression in static gamma activity. One possible mechanism at the central level might be due to activation of a cortical inhibitory mechanism, which itself is one of

the components of the cortex. If one assumes that an excitatory cortical condition might be achieved in very light halothane anaesthesia (stage I of Guedel), all components, both excitatory and inhibitory, might either increase their activity or at least be brought to a subthreshold level. In that condition, the cortical inhibitory mechanisms are no exceptions. Unfortunately, this theory can not be proven by our results and remains to be tested. It is worth noting that the evidence which illustrates that it does not take much time for the cat under halothane anaesthetic to lose the desired and necessary surgical anaesthetic state (stage III of Guedel) is given by Winters et al., 1972. Halothane, according to them, is believed to be one of those anaesthetic agents that induces stage III of anaesthesia directly from stage I (Excitation) without going to stage II (Delirium). The stages of anaesthesia were first introduced by Guedel (1937).

FDL in our case, being functionally closer to a physiologic extensor as the soleus is, did not show any very obvious inhibitory effects. However, in the case of fig 35,B something definitely was inhibited (probably a nuclear chain), as the scattery rebound activity is obvious immediately at the "off" of the stimulus. This response, of course, is not comparable to those reported by Vedel and Mouillac-Baudevin (1970) where the static firing and the maximum response (to the ramp) diminishes. On stimulation of the dynamic area in the present study both static and dynamic excitatory fusimotor effects were obtained. However, when the animals became lighter, the chances were greater of producing a response with a dynamic character.

In the case of figures 34 and 61 where some intrafusal fibres were inhibited, the dynamic area was the target of stimulation. However, that does not mean the cats were too light at the time. In fact, in both cases, cats were not light enough to expect Db_1 fibre recruitment! On the other hand, by referring to the criteria given, it seems more likely that Vedel and Mouillac-Baudevin's deep anaesthesia were comparable to our light anaesthesia and therefore there is a strong possibility that we did not achieve their condition of "light anaesthesia" ever. Hence, that might explain why a clear-cut inhibitory response which was repetitively obtained in their experiments was absent in the present study. At the end what is important to note is the ability of sensorimotor cortex to inhibit as easily as to excite providing that the cortex is in the proper state of excitation; this concept is confirmed both by theirs and our results, as well as others (Vedel and Mouillac-Baudevin, 1970; Gladden and McWilliam, 1977a,b; Gladden, 1981).

Rather than generalize, considering that there are only two inhibitory examples, one can assume that the "dynamic area" is not exclusively an excitatory area, and in more physiologic conditions, it might be able to excite one set of static gamma axons and inhibit others.

Looking at fig 1 of Vedel and Mouillac-Baudevin (1970), the point where they elicited a depressor effect of a soleus primary afferent corresponds to our point 7, and does not fall into the "dynamic area". Our inhibitory results were obtained frequently from stimulation within "dynamic area". Therefore, this may be further evidence that the state of anaesthesia accounts for the big variation in the results. Paying attention to the intrafusal movements in the

case of fig 61 where the two chains were inhibited, and at the same time the rebound activity in the primary afferents after stoppage of stimulus in many figures such as 30 and 35 one can attribute the two together without much dispute. In fact, what I am suggesting, is that if the corresponding changes in the primary afferent of the spindle shown in fig 61 had been recorded, the results might have been very similar to that shown in fig 30,B and C. For the case of fig 34 where the dynamic gamma axon was apparently inhibited (with or without chain fibres), there was no analog in the direct visualizing experiments.

This, itself is stronger evidence for independent control of static gamma motoneurones compared with that given by Gladden and McWilliam (1977a,b), where Sb_2 fibre could be recruited without nuclear chain fibres. Recently Wand and Schwarz (1985) worked on the influence of the reticular part of substantia nigra on the primary and secondary afferent discharges of the soleus in barbiturate-anaesthetized cats by injection of picrotoxin (a GABA antagonist). They claimed that static fusimotor input to flexor muscle spindle primary and secondary endings is not necessarily activated in parallel by the central nervous system. The underlying mechanism is believed to be that functional activation, by blocking the τ-aminobutyric acid (GABA)-mediated inhibition, of output neurones of the reticular part of the cat substantia nigra, can gate static fusimotor action on flexor muscle spindle primary and secondary endings. Their conclusion is consistent with the idea that the central nervous system can control the activity of static gamma motoneurones innervating Sb_2 fibres (whose contraction excites primary endings, with little or no effect on secondary endings)

independently of those innervating nuclear chain fibres (whose contraction excites both primary and secondary endings). Although these findings add new weight to the likely hypothesis of the existence of two types of static fusimotor neurones (Boyd, Gladden and Ward, 1983) there is a need for further investigation, probably using a different approach, to confirm the existence of independent control of different static gamma population.

Linked to the consideration of inhibitory responses, the phenomenon of rebound activity should be discussed. This phenomenon is evident in some of the figures occurring on the "off" of the stimulus (e.g. figures 30; 23,B and 35,B). It certainly signifies inhibition of some intrafusal fibres within the corresponding muscle spindle; however, this inhibition is either not strong enough to reduce the afferent discharge drastically during the cortical stimulation, or is masked by powerful recruitment of other intrafusal fibres (e.g. Sb_2 fibre). It could even be caused by cortical inhibition of an active gamma axon innervating one pole of the spindle in which another gamma axon(s) innervating the opposite pole has been excited. Unfortunately, by referring to results from uncovered spindles, where there was only one example of inhibition, neither of the above possibilities could be favoured. However, it is thought that slight inhibition of a static gamma axon supplying nuclear chain fibres may account for this type of change because the rebound activity results in a very erratic discharge such as one might expect if chain fibres were contracting.

Could primary afferent recordings reveal recruitment of the Db_1 fibre alone, without recruitment of static intrafusal fibres? The evidence shows no positive answer to the question. Although some of

the afferents did not fire during the ramp release during the course course of stimulation (e.g. figures 16, 17, 18, 21), it does not mean necessarily that static intrafusal fibres were not recruited. Emonet-Dénand et al. (1977) working on peroneus brevis muscle afferents demonstrated that on combined stimulation of dynamic and static gamma axons, the primary discharge goes silent on ramp release. Even on stimulation of a static gamma axon the primary can fall silent during the release (Emonet-Dénand et al. 1977). Therefore referring to those results obtained from direct observation of intrafusal fibres where the Db_1 was never individually recruited on cortical stimulation, one can conclude almost with certainty that if the anaesthetic condition of the cat is light enough for dynamic gamma motoneurones to be recruited, then the excitability of the cortex is definitely good enough for static gamma axons (of any type) to be jointly recruited as well.

Static Intrafusal Fibre Recruitment

Figures 26, 27, 29 and 30 demonstrate changes of afferent responses that are most probably a consequence of at least one type of static intrafusal fibre, either static bag_2 or nuclear chain fibres. According to Boyd (1986) if the afferent firing goes very irregular, as in fig 27, nuclear chains must be mainly responsible with or without concomitant contraction of Sb_2 fibre. In most cases recruitment was not very strong and it was mostly nuclear chain and weak static bag_2 fibre contraction. As a result of the irregularity of the afferent firing due to static intrafusal fibre contraction, the ramp response is abolished too!

Sometimes when the intrafusal fibres were observed directly, Db_1 contraction was seen accompanying that of Sb_2 and nuclear chain fibres, and one might expect to see both an increase in the dynamic response and scattery static firing on ramp hold (as in figure 20). But because, except in one case, nuclear bag fibres were not contracting on their own in the direct observation experiments, it seems reasonable not to restrict the interpretation of these afferent responses to Sb_2 and Db_1 fibres and leave it to be more open. It is interesting to know that 10% of dynamic gamma axons also co-innervate a single chain fibre. Therefore, if a dynamic gamma axon innervating both Db_1 and a single nuclear chain fibre is recruited along with a static gamma axon on cortical stimulation, then one might have expected to see a similar pattern of response.

It is also believed that cortical stimulation imposes some changes on the sarcomere length of intrafusal fibres during the course of stimulation which is sustained even after the stimulus is off (Emonet-Dénand, Hunt and Laporte, 1985; Proske and Morgan, 1985). In interpreting the results one should be aware that the after-effect phenomenon exists. It certainly is something that happens during movement in conscious man and is not an artifact that is being produced during laboratory experiments (Gregory, Morgan and Proske, 1987). Gregory, Morgan and Proske recently in a comparative study attributed the changes in the size of the stretch reflex in a conditioned muscle of the cat and man to the formation of stable cross-bridges between actin and myosin filaments when the muscle was shortened several seconds after a contraction at a long length (1987). Figures 30,A; 29,B and 35,A show examples of after-effects during our experiments. It seems that once the intrafusal fibre(s) is contracted and shortens during the course of cortical stimulation, the myosin heads have a chance to form cross bridges and the fibre remains shortened after the stimulation ceases. The cross bridges would not break right away and as a result of their stiffness the primary afferent may have a higher static firing than previously recorded. On the next ramp stretch where the cross bridges are broken apart, they will be formed again at the release of the stretch but only at the usual length. As long as those changes usually disappear at the subsequent ramp stretch, it does not imply on sustained alterations of gamma axon discharge continuing after the cessation of cortical stimulation (figures 30,A, 29,B and 35,A). Such a sustained gamma motoneurone excitation must have followed cortical stimulation in fig 36 because the raised discharge at initial length persisted

through many stretches, and the response to all the subsequent stretches were also altered; the initial bursts are noticeably changed.

Alpha-Motoneurone Recruitment on Cortical Stimulation

If the stimulus strength is high enough (depending of course on the anaesthetic level of the cat) to recruit slow and/or fast alpha motoneurones, then it is almost definitely strong enough to recruit almost all gamma axons supplying different intrafusal fibres in a spindle (exceptions are those gamma motoneurones which we could not recruit on cortical stimulation). In figures 31, 32 and 33 where EMG activity signaled extrafusal contractions as well as intrafusal ones, then the afferent firing is increased dramatically to a level where it could be claimed that both static gamma axons innervating nuclear chain and static bag_2 fibre were recruited. Dynamic gamma motoneurones could have been recruited as well, since they were frequently excited when alpha motoneurones became active (in lightening the anaesthesia). The high frequency, between 150-200 Hz, signifies such strong engagement of Sb_2 and nuclear chain (and possibly Db_1) fibres that it can even mask the unloading of the muscle spindle due to concomitant extrafusal muscle fibre contraction. In the direct observation experiments, it happened many times that extrafusal fibres were recruited on cortical stimulation after the intrafusal fibres, but only with a short delay. Therefore, if intrafusal fibres' contraction precedes that of extrafusal's, one may not see any drop in afferent firing when the muscle spindle gets unloaded (if the intrafusal contraction is such that length dependence is suppressed). Those figures also disclose another

possibility and that is saturation of the activity of the fusimotor system. As soon as the afferent firing reached a high level of frequency, it dropped down toward a basal level regardless of the existence of the stimulus. That "habituation" might happen at all levels, cortical neurones, spinal gamma motoneurones, intrafusal fibres or even at the level of the sensory ending. It might have happened at more than one level too. There is no evidence in our results to specify the exact location of that habituation.

Effect of Cortical Stimulation on Tenuissimus Secondary Afferent Discharge

In contrast to primary afferents, secondary afferent recordings did not disclose much information about intrafusal contractions. Having said that, one should appreciate the fact that they of course can only be influenced by static gamma and beta axons. Their number was also considerably less in our experiments compared to those of primaries (almost a 1 to 5 ratio).

The biassing effect of the stretch on secondary discharge tended to be short-lived as indicated by fig 38 and 39. Since Sb_2 fibre contraction has little or no effect on the secondary firing frequency, the short-lived biassing effect can be interpreted in two ways: either the frequency of recruited descending neurones were decreasing, habituation, or the contraction of the chain fibres was failing due to fatigue, thus reducing the extension the sensory endings. Fig 42 indicates that some sort of "habituation" might have happened somewhere along the fusimotor path, for the secondary ending only responded to the first second or so of stimulation and no more. That brief response seems to be of a type involving both Sb_2 fibres

and nuclear chain fibres (Boyd, 1986). A similar situation, where Sb_2 and nuclear chain fibres contracted briefly and then failed to respond during the rest of the stimulation, was seen frequently during direct visual observation.

In figures 38,B and 39,B the length sensitivity of the secondary afferent to ramp stretch is increased during cortical stimulation. Contraction of chain fibres seem to be the cause for the increase in the length sensitivity of the secondary afferent, however, one should remember that not all chain fibre contraction increases length sensitivity of the secondary ending (Jami and Petit, 1978). In fact, Jami and Petit reported that of the three to six gamma axons acting on a secondary ending only one or two elicited a significant increase in discharge frequency produced by 1 mm lengthening of the peroneus tertius muscle of the cat.

Chain fibre contraction can either abolish or decrease the length sensitivity of the secondary to stretching, as in fig 40. Even in the absence of the cortical stimulation on the fourth ramp stretch in fig 40,B, the response is not as it was prior to cortical stimulation. Excitation of chain fibres on cortical stimulation can outlast the stimulation and therefore can decrease the length sensitivity of the secondary afferent to stretching.

Important points to notice in figures 38-41 (concerning secondary afferents) are the absence of a decrease in the secondary static discharge or unloading of nuclear chain fibres by bag contraction on cortical stimulation. Although the latter event does take place in spindles, however, not only it was absent in those secondary records, it was not observed in direct visualizing experiments either.

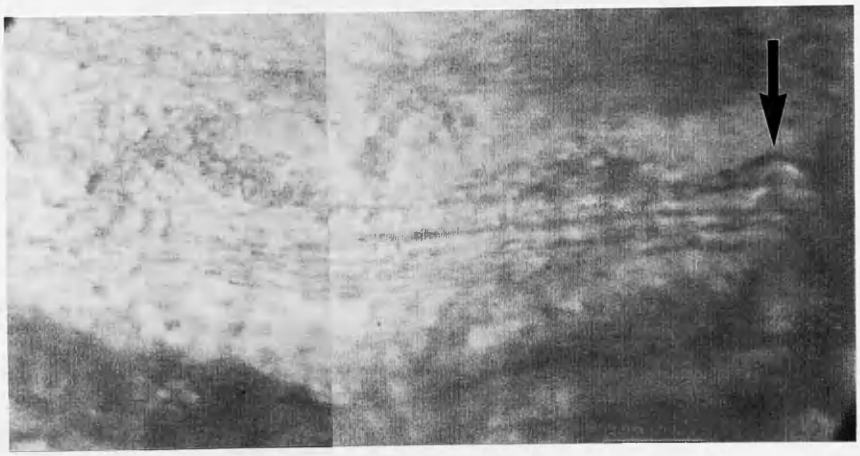
* * *

APPENDIX

A

Arrow indicating the area where the unusual bursting spontaneous activity was seen (see text page 87).

B



Arrow indicating a kinked nuclear bag fibre (see text page 91).

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