ORGANIZATION OF DORSAL NECK AND EXTRAOCULAR MUSCLE AFFERENT INPUT IN THE CAT FRONTAL CORTEX

by

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ABSTRACT

Electrical nerve stimulation of dorsal neck muscles elicited excitatory and inhibitory responses in neurons of the cat frontal cortex. Regional variations in terms of the muscle origin of the afferent input, its group classification, and the latencies of the evoked unit responses, were noted in the dorsal and ventral banks of the cruciate sulcus, and in coronal and presylvian regions. Group 1 afferent projections depended on the integrity of the dorsal funiculus. Extraocular muscle afferents also projected to these regions, and showed excitatory and inhibitory converging effects with dorsal neck muscle afferents at the single-cell level at comparable latencies. The highest degree of convergence was observed between extraocular afferents and those neck afferents originating in muscles which cause large head deviations upon contraction. Vibratory stimuli to dorsal neck and extraocular muscles elicited EMG and tension increases in the muscle, and phasic and tonic unit responses in the frontal cortex. A sub-population of these cells increased their firing frequency with increases in the frequency of vibration at constant amplitude displacements as low as 20 um and 50 um. The results are interpreted as suggesting that regions of the cat frontal cortex are involved in neural mechanisms of eye-head coordination.

RESUME

La stimulation électrique des nerfs des muscles dorsaux du cou a évoqué des réponses excitatrices et inhibitrices au niveau des neurones du cortex frontal du chat. Des variations regionales furent observées en termes de l'origine musculaire des afférences, de leur classification par groupes et des latences des réponses évoquées unitaires dans les régions dorsales et ventrales du cruciatus sulcus et dans les régions coronale et présylvienne. Les projections afférentes du groupe 1 dépendaient de l'intégrité du funiculus dorsal. Des afférences des muscles extraoculaires envoyaient eux aussi des projections à ces régions et montraient des effets excitateurs et inhibiteurs convergeant avec des afférences des muscles dorsaux du cou, au niveau de la cellule isolée, avec des latences comparables. Le plus haut degré de convergence fut observé entre les afférences extraoculaires et les afférences du cou qui trouvent leur origine dans les muscles qui causent d'amples deviations de la tête en se contractant. Des stimuli vibratoires appliqués à ces muscles ont élicité une activité électromyographique, des augmentations de tension dans ces muscles, et des réponses évoquées unitaires toniques et phasiques au niveau du cortex frontal. Une sous-population de ces cellules augmentait sa fréquence de décharge avec des augmentations de fréquence de vibration pour des déplacements constants d'amplitude aussi bas que 20 µm et 50 µm. Les résultats sont interprétés comme suggérant que des régions du cortex frontal du chat sont impliquées dans les mécanismes neuronaux de la coordination des mouvements entre la tête et les yeux.

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INTRODUCTION

The work presented here deals with the organization of dorsal neck and extraocular muscle afferent input to regions of the cat frontal cortex in pericruciate, coronal and presylvian regions. Experimental and clinical evidence in various species during the past century has implicated frontal regions in eye and head movement, but their role in these activities is still obscure. Hitherto studies have investigated the motor consequences with cortical stimulation and ablation techniques, while the possibility of an afferent input from the muscles that move the eyes and the head to these regions remains largely unexplored. The purpose of this work was to investigate this latter question.

Chapter 1.1 presents a general introduction to the problem and a review of the background literature. In view of the lengthy extent of the literature accumulated over one hundred years, emphasis has been placed on those aspects most directly relevant to the presented experiments, and to the issues raised. Chapter 1.2 is a brief description of basic features of dorsal neck and extraocular muscles. Chapter 2.1 describes the input from the dorsal neck muscles to the frontal cortex, and the pathway involved for the electrophysiologically characterized group 1 afferents reaching these regions (2.2). Chapter 3 deals with the extraocular muscle projections, and their excitatory and inhibitory interactions with dorsal neck muscle afferents in the frontal cortex. The use of vibratory stimuli to dorsal neck and extraocular muscles in Chapter 4 enabled the characterization of the origin of the activated afferents and their specific effects on units in the frontal cortex, which could not be made with the use of electrical stimuli to the nerve.

Chapter 5 includes a general discussion and some conclusions reached as a result of the conducted studies.

Experimental methods are described in detail in Chapter 2, part 1, and procedures varying from, or in addition to these, are described in the individual studies. Some of the results of this investigation have been published (Barbas and Dubrovsky, 1977a and b; Barbas and Dubrovsky, 1978; Barbas et al, 1977; Dubrovsky and Barbas, 1977).

CHAPTER 1

1.1 INTRODUCTION

1.1.1 LOCALIZATION OF FRONTAL OCULOMOTOR AND/OR HEAD MOVEMENT ZONES

Regions within the frontal cortex of animals and man have been associated with eye and head movements for over a century now, but their role in these activities has not yet been clearly established. The characterization of an anterior region as the "frontal eye fields" (FEF) is historically based on cortical electrical stimulation experiments, which produced eye movements in man (Foerster, 1931: Penfield and Boldrey, 1937), in monkeys (Bender, 1955; Brucher, 1966; Chusid et al. 1948; Crosby et al. 1952; Ferrier, 1874; Grunbaum and Sherrington, 1901; Leyton and Sherrington, 1917; Marrocco, 1978; Risien Russell, 1894; Robinson and Fuchs, 1969; Sherrington, 1893; Wagman, 1964; Wagman, et al. 1961), and in dogs and/or cats (Berkowitz and Silverstone, 1956; Delgado and Livingston, 1955/56; Eliasson, 1966; Guitton and Mandl,1978a; Hassler, 1966; Livingston, 1950; Risien Russell 1895; Schlag and Schlag-Rey, 1970; Smith, 1940; Spiegel and Scala, 1936; Tsumoto and Suzuki, 1976) (see Holmes, 1938 for review of early work, and Robinson and Fuchs, 1969 for list of other review papers). The evoked eye movements depended on the region of stimulation (Guitton and Mandl,1978a; Leyton and Sherrington, 1917; Penfield and Boldrey, 1937; Risien-Russell, 1895; Spiegel and Scala, 1936), they were basically saccadic in nature, and included horizontal conjugate deviations toward the side contralateral to the stimulated side, and upward and downward deviations. Other eye movements included convergence and divergence of

the eyes but these were observed less frequently (Leyton and Sherrington, 1917; Spiegel and Scala, 1936) and were recently attributed to the use of anesthetics by Robinson and Fuchs (1969) who studied frontal oculomotor responses in the awake and anesthetized monkey.

The FEF of the monkey and man is situated in a frontal region rostral to the motor cortex, anterior the arcuate fissure.* The cytoarchitectonic area 8 in these species has generally been accepted as the frontal oculomotor region, although regions of area 6 (Mott and Schaffer, 1890) and 4 (Penfield and Boldrey, 1937) have at times been included as well. Stimulation of area 6, has more often been reported to result in eye and head movements (Foerster, 1931; Mott and Schaffer, 1890). These qualitative and quantitative discrepancies may be traced to technical variations, including the type of electrodes used, the level of anesthesia or lack of it, and the subjective measure of eye movements in some of the earlier experiments, all of which have been cited as crucial in evaluating evoked eye movements (Robinson and Fuchs, 1969).

In the cat, the experimental results are even less consistent, and neither the location of a region equivalent to area 8, nor the extent of a frontal oculomotor region are agreed upon. While the disagreement over the location of area 8 seems to rest largely on the criteria used to define it, the size seems to depend on the type of the experimental

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* Some investigators have suggested that there are really two frontal oculomotor regions in man, with one being a mirror image of the other in terms of the characteristics of the evoked movement upon stimulation. These are located in a long medio-lateral strip in the frontal cortex as described above (see Crosby et al, 1962).

preparation used. Both Hassler (1966) and Schlag and Schlag-Rey (1970), have suggested that area 8 might be in the presylvian sulcus because of its proximity with the face area, and the regional connections with the lateral part of the nucleus medialis dorsalis of the thalamus, while Nyberg-Hansen (1969) and Scollo-Lavizzari (1964) are in agreement with this view on the basis of the cytoarchitectonics of the region and its thalamic connections. On the other hand, Martínez-Moreno and Reinoso-Suárez (1977) using the thalamic connections criterion place area 8 on the proreal gyrus, somewhat more dorsal than the others. Akert (1964) has suggested that area 8 is below the ventral end of the coronal sulcus which forms the rostral pole of the compositus gyrus, on the basis of the cellular characteristics and layering of the region.

The size of a frontal oculomotor region in the cat is also ill-defined. Among the more recent studies Hassler's map (1966) is the largest and includes the ventral bank of the cruciate sulcus and both margins of the presylvian field. Two other recent studies report an excitable cortex largely situated in the presylvian and on a mesial region below the cruciate sulcus. (Guitton and Mandl, 1978a; Schlag and Schlag-Rey, 1970). Besides the methodological differences such as electrode tip size, currents and frequencies of stimulation used in these studies, perhaps the source of the discrepancies is the type of the experimental preparation used. Hassler's (1966) cats were freely moving, while in the other two studies (Guitton and Mandl, 1978a; Schlag and Schlag-Rey, 1970), the cats had their head fixed, and in the latter encéphale isolée preparations were used. Regions that might be involved in certain types of eye and head movement might have appeared unresponsive in preparations where the head

was fixed. In fact, both eye and head movements have been observed with stimulation of these regions by Hassler (1966) and a neck representation region overlapping with eye movement zones in the presylvian field has been described by Delgado (1952). That the differences may, in fact, have been largely due to this point and not to stimulation intensities, is suggested in Schlag and Schlag-Rey's (1970) report stating that increases in the strength of the current by fivefold did not result in eye movements in inexcitable regions.

The results of another recent study (Nieoullon and Rispal-Padel, 1976) with freely moving cats, cannot be directly compared with Hassler's map, as the stimulated frontal regions were restricted, for the most part, to superficial cortical regions. Whereas neck muscle activity was obtained with stimulation of regions within areas 4 and 6, no accompanying eye movements were obtained, a finding consistent with the location of excitable zones for eye movements in deeper regions (Guitton and Mandl, 1978a; Schlag and Schlag-Rey, 1970; Scollo-Lavizzari, 1964; Tsumoto and Suzuki, 1976).

COMMENTS ON LOCALIZATION

The site of a region in the cat brain homologous to the originally described area 8 of primates has been a controversial issue. The difficulties in the description of such a region may be due to attempts to make direct comparisons in the two species. However, according to Dobzhansky et al. (1977) "homology is correspondence of features in different organisms due to inheritance from a common ancestor" (see also Bock, 1969), and the carnivores are not ancestors of the primates

(Hodos, 1970). These two species have rather evolved in parallel (Dobzhansky et al, 1977). Hassler's data (1966) demonstrated that the evoked eye movements in the cat were closely associated with head and often whole body movements. This may be a crucial observation, as the anatomical position of the head with respect to the body is different in monkeys and cats, and neural mechanisms controlling eye and head movement may also differ in the two species.

The relative size of dorsal neck muscles varies considerably in different species (Napier, 1970), as animals hold their heads in different ways (De Beer, 1947); this imposes variable demands on the neck muscles in terms of the force they need to generate to hold and move the head. In man, the foramen magnum, through which the brain stem connects with the cerebral hemispheres, is situated in the middle of the base of the skull (Clark-Le Gros, 1965; Napier, 1970; Young, 1974). Movement of the atlantoccipital joint during the evolutionary process (Clark-Le Gros, 1965; Young, 1974) gave the dorsal neck muscles that insert in the lambdoidal ridge a long lever arm. This increased the turning effect of the force exerted by these muscles, so equilibrium of the head over the cervical spinal column could be maintained without great increase of the musculature size, a situation that would have hampered the necessary agility and mobility of the head (Thompson, 1917). On the other hand, in quadrupeds, like the cat, the foramen magnum is in the posterior part of the skull, the lever arm of the dorsal neck muscles is much shorter, and the head is carried "upon projecting arm or cantilever" (Thompson, 1917). In the cat, even small rotatory head movements produce shifts in the animal's center of gravity which elicit

reflex postural adjustments. The position of the head on the body, therefore, could have important consequences not only in the regional representation of movement, but also in those subserving vision and audition, whose sense organs are also on the head.

1.1.2 ABLATION OF FRONTAL CORTEX

FIXATION AND VISUAL RESPONSE DEFICITS

Phillips (1966) has stated that "the method of stimulation of the pia-covered cortical surface with currents adequate to provoke muscular contraction has already been pushed to the limits of its resolving power". Due to the limitations of this method, little information was provided concerning the functional significance of these frontal regions with respect to the eyes and the head. The interpretation of ablation studies has also been problematic, since the results are confounded with the effects of damage to adjacent structures. Very often results obtained with one experimental paradigm cannot be compared with those obtained with another. Nevertheless, several consistent findings across species have been described.

Unilateral lesions of the frontal cortex corresponding with the frontal eye fields result in visual neglect of all stimuli contralateral to the affected side in the monkey (Bianchi, 1895; Brucher, 1966; Clark and Lashley, 1947; Kennard, 1939; Latto and Cowey, 1972; Welch and Stuteville, 1958) and in humans (Silberpfenning, 1941-2). A transient persistence of gaze is observed in the monkey (Brucher, 1966; Latto and Cowey, 1972; Walker and Fulton, 1938) and the cat (Dreher and Zernicki, 1969; Jeannerod, Kiyono and Mouret, 1968), and deficits in

anticipatory visual attending and visual search in the cat (Schlag-Rey and Lindsley, 1970) and the monkey (Latto, 1978; Latto and Cowey, 1972; Latto and Iversen, 1972) have been reported. The search deficit is consistent with the searching responses in the cat elicited with electrical stimulation of regions within the anterior sigmoid gyrus; it is also consistent with the persistence of gaze phenomenon after frontal brain damage, since this would interfere with quick and effective scanning of the environment.

It has been proposed that the frontal cortex is not directly involved in the fixation reflex, but that it rather exerts an inhibitory influence on the occipital cortex which actually supports this function. Removal of this inhibition could, then, account for the enhanced fixation of gaze observed after the lesion (Dreher and Zernicki, 1969; Jeannerod et al, 1968). Henderson and Crosby (1952) present experimental evidence suggesting that the FEF exerts such inhibitory effects over the preoccipital cortex of both sides with respect to optokinetic responses, which are also supported in these posterior regions. However, Brucher (1966) reported a deficit in optokinetic responses in frontally lesioned monkeys, when the rapid phase was towards the side contralateral to the lesion, and suggested that the frontal cortex was involved in the production of this response. This finding is at variance with other reports which do not find optokinetic deficits, and could be accounted for by the sensitive quantitative measures used by Brucher (1966) to evaluate the response, as was suggested by Shanzer, who commented on Brucher's findings (1966). Experimental results in this and other studies, then, reflect the sensitivity and adequacy of the

experimental procedures in investigating the question under study, and seeming discrepancies may be traced to procedural differences.

POSTURAL AND PROPRIOCEPTIVE DEFICITS

In addition to the gaze and visual response deficits, several postural and equilibrium responses are disrupted after destruction of these frontal regions. Immediately following the lesion the head and eyes are turned towards the affected side (Kennard, 1939), and eye movements in response to passive head rotation are absent in cats (Jeannèrod et al, 1968). A disturbance of equilibrium is evident with continuous circling towards the lesioned side (Bianchi, 1895; Brucher, 1966; Kennard, 1939; Latto and Cowey, 1972). The limbs contralateral the damaged side are used less than the ipsilateral ones. These effects are transient and disappear in days, but the visual neglect outlasts these deficits, suggesting that it is not secondary to these other postural defects. Contact placing reactions in response to cutaneous stimuli are absent in cats with lesions of the gyrus proreus, the sigmoid gyri, and a small part of the coronal and longitudinal gyrus (Adkins, Cegnar and Rafuse, 1971; Bard, 1933; Chambers and Liu, 1957; Dubrovsky, Garcia-Rill and Surkes, 1974; Glassman, 1970). On the other hand, Forssberg, Grillner and Sjöström (1974) report the presence of placing reactions in chronic spinal kittens. Bridging the gap between these two extreme views is Massion's (1978) recent evidence that cats without motor cortex exhibit placing reactions, but the response, including its timing, is qualitatively different than that of intact cats.

Motor acts that are normally part of the animal's repertoire such as hopping and jumping are also disrupted after frontal cortical lesions (Adkins et al, 1970; Bard, 1933; Dreher and Zernicki, 1969; Dubrovsky et al, 1974). Glassman (1970) observed that cats with posterior sigmoid damage were able to direct the forelimb accurately to a target with vision but not while blindfolded, and suggested that a proprioceptive deficit might be present. In a subsequent experiment (Glassman, 1971), the author observed gross abnormal forelimb posture and deficits on a proprioceptive task involving the forelimb. A head turning response deficit was also observed in these cats, and neck rigidity has been reported with destruction of the gyrus proreus (McKibben and Wheelis, 1932). It may not be surprising then, that such complex behaviors as hopping and jumping which involve the coordinated use of the limbs, the head and the rest of the body are disrupted after these frontal lesions.

The frontal oculomotor regions have connections with the superior colliculus (Guitton and Mandl, 1974; Sprague, 1963) whose involvement in oculomotor responses is now well established, and with the internal medullary lamina of the thalamus (Auer, 1956; Orem and Schlag, 1971; Rinvik, 1968) which are also involved in visual and eye movement responses (Schlag and Schlag-Rey, 1977; Schlag-Rey and Schlag, 1974; 1977).

Taken together the available data suggest that the frontal cortex is involved in eye and head movement, but the nature of this involvement is still obscure. The transient and often subtle changes observed after ablation of these regions provide clues as to what this region does not, rather than as to what it does support. For example, these regions are

neither necessary nor sufficient for eye and head movement (Pasik and Pasik, 1964). The majority of the eye movement related neurons fire after eye movement, suggesting that they are not involved in the initiation of the response (Bizzi, 1967; 1968).

1.1.3 POLYMODAL INPUT

The question, therefore, still remains: What might be the role of these regions in eye and head movement? A look into the regional characteristics could perhaps provide clues to this general problem. A prominent feature of these regions which sets them apart from the classical primary somatosensory areas of the cerebral cortex, which are modality specific (Hubel and Wiesel, 1959; 1962; Mountcastle, 1957) is their polymodal nature. Studies in the monkey and in the cat have shown a visual (Buser and Bignall, 1967; Dubrovsky and Garcia-Rill, 1971; Garcia-Rill and Dubrovsky, 1973; Kitsikis et al, 1969; Mohler et al, 1973), auditory (Benevento et al, 1977; Buser and Imbert, 1961; Goldring et al, 1970; Teyler et al, 1971),vestibular (Boisacq-Schepens and Hanus, 1972; Boisacq-Schepens and Roucoux-Hanus, 1975; Odkvist et al, 1971) cutaneous somatosensory (Adrian, 1941; Amassian, 1953; Baker et al, 1971; Brooks et al, 1961a; 1961b; Clark et al, 1973; Goldring et al, 1970; Morse and Towe, 1964; Towe et al, 1964) and proprioceptive inputs (Albe-Fessard and Lieberskind, 1966; Amassian and Berlin, 1958; Clark et al, 1973; Grampp and Oscarsson, 1968; Landgren et al, 1967; Lucier et al, 1975; Oscarsson and Rosen, 1964; 1966; Oscarsson et al, 1966; Rosen and Anasuna, 1972; Silfvenius, 1968; Swett and Bourassa, 1967) to these cortical regions. These neurons at times receive afferent input from one sensory

modality only, and have receptive fields restricted to small peripheral regions, others receive input from more than one limb (Towe et al, 1964), while others receive afferent signals from two or more sensory modalities converging on one neuron (Buser and Imbert, 1961; Chu and Rutledge, 1971; Teyler et al, 1971).

Several lines of evidence indicate that the afferent input to these regions does not constitute a generalized excitation phenomenon, but is well organized to influence motor functions. The presence of peripheral inhibitory influences in addition to excitatory ones (Oscarsson et al, 1966), including surround inhibition through recurrent axon collaterals (Brooks, 1965) has been reported in regions of sensory convergence. The afferent input from the various sensory modalities is often unequal in the various polymodal regions, and there is often preferential input by one modality over the rest. The somatosensory projection is somatotopically organized (Sakata and Miyamoto, 1968), and the visual input shows a well organized topographical distribution, and is preferential to the proximal limb and body axis representation of the cortex (Garcia-Rill and Dubrovsky, 1973).

The polymodal characteristics of these regions suggest their involvement in sensory motor integration (Buser and Imbert, 1961). As early as 1895, Bianchi, who was the first to describe the visual and motor aspects of the disturbance following damage to the frontal cortex, stated: "...my hypothesis is that the frontal lobes are the seat of co-ordination and fusion of the incoming and outgoing products of the several sensory and motor areas of the cortex".

1.1.4 INPUT - OUTPUT RELATIONSHIPS

There is now ample evidence showing that peripheral sensory signals can influence motor activity (Murphy, Wong and Kwan, 1974; Sakata and Miyamoto, 1968; Woolsey, 1958). A combined cortical microstimulation and recording procedure using the same microelectrode, has revealed that cutaneous receptive fields of efferent neurons in the motorsensory cortex of the cat are located in a skin region above the muscles that are activated with stimulation of the cortical efferent zone (Asanuma et al, 1968). Similarly, cells receiving joint afferent input are involved in the contraction of the muscles that move that joint (Rosen and Asanuma, 1972).

The results of these studies suggest that peripheral afferent input can affect muscle contraction via long transcortical reflex loops (Phillips, 1969). That proprioceptive, cutaneous, joint, as well as afferent signals from other sensory modalities can influence motor behavior, is suggested by the activation of pyramidal tract neurons by these afferents (Buser and Ascher, 1960; Patton et al, 1962; Wall et al, 1953). Moreover, even though both pyramidal and extrapyramidal neurons receive converging afferent input, greater sensory convergence has been reported for the former (Brooks, 1965; Brooks et al, 1961; Chu and Rutledge, 1971). Most of the multimodal units are, in fact, located in cortical layers V and VI, which constitute the main source of corticofugal fibers (Chu and Rutledge, 1971). The sensory projection to the motor cortex is clearly related to movement. This characteristic of the motor cortex distinguishes it from the somatic sensory area, where, even

when movement is elicited upon stimulation, higher electrical currents are required for such movement to occur (Sakata and Miyamoto, 1968).

1.1.5 MOTOR BEHAVIOR: PERIPHERAL AND/OR CENTRAL INFLUENCES

In spite of the sensory-motor features of the regions, the sensory and motor deficits observed after their ablation, and the accumulating evidence that sensory input is important in fine motor control, it is surprising that an investigation of the afferent input to these frontal regions from the muscles that move the eyes and the head has not received much attention.

This could be partly due to the characterization of these regions as outflow centers with respect to the eyes and the head. The "efference copy" hypothesis proposed by Helmholtz (1867) and later propounded by Sperry (1950) supports a central initiation of movement expressed in two efferent command signals: One signal is sent to the effector muscle for contraction and movement, and another signal is simultaneously sent to sensory structures signalling the occurrence of movement. Thus if the eyes are to move, a signal is sent to the oculomotor neurons, and at the same time a signal, "corollary discharge", or "efference copy", is sent to some other sensory structure to cancel the disparity caused by the displacement of the image on the retina during the movement. The classical evidence invoked in support of this view is that upon voluntary movement of the eyes no movement of the environment is experienced, in spite the fact that the image on the retina is displaced; on the other hand, passive movement of the eye results in an illusory movement of the environment. In the latter case, since no

motor command moved the eye in the first place, no corollary discharge was sent to another brain region to cancel the movement illusion. Teuber (1960; 1966) adopted the hypothesis of a motor system acting on a sensory one, and implicated the frontal eye field region as one center where corollary discharges were sent (Teuber, 1964).

A role of extraocular proprioceptive sense in eye movement was originally denied (Brindley and Merton, 1960; Horridge, 1967; Irvine and Ludvigh, 1936), and Ludvigh later (1952) spoke only of a crude proprioceptive sense in the eye. The view that the muscle itself is insentient in general, with respect to position, and that the muscle receptors such as the spindles are merely the sensors in a feedback servo-loop subserving the spinal stretch reflex has been held by Merton (1964), who cited the experiments of Helmholtz in support of this view. However, careful studies in humans have shown that attempted movements of a totally paralyzed eye did not result in displacement of the visual field (Brindley et al, 1976), as Helmholtz would have predicted if position sense was indeed controlled by an outflow system alone and by the sense of effort (Merton, 1964). The earlier contrary evidence with the same procedure has been attributed to a partial, rather than total, paralysis (Brindley et al, 1976) in the original studies. Also, recent reports using both sensitive and non-traumatic psychophysical procedures in humans have shown that proprioceptive signals can be used to control eye position in the dark (Skavenski, 1972). Taken together these data suggest a functional proprioceptive role of the eye in controlling position.

This view is that classically held by another school of thought advanced by Sherrington, who proposed that peripheral signals were

important in motor control, and also suggested that these arise in muscle proprioceptors. Sherrington supported a functional extraocular proprioceptive sense subserving position sense (Sherrington, 1918; Tozer and Sherrington, 1910) on the basis of experimental evidence which showed that subjects were able to perform accurate eye movements in the dark while the conjuctiva, palpebral and ocular muscles were anesthetized with cocaine.

Both the centralists and the peripheralists, since the earlier days base their arguments on experimental evidence. Originally Mott and Sherrington (1895) observed that all movement in deafferented limbs was abolished, a finding which was later verified by Lassek (1953), Lassek and Moyer (1953), and Twitchell (1954). Supporting the Sherringtonian view are recent electromyographic studies in the monkey showing that after deafferentation the patterning of firing of agonistic and antagonistic muscles was altered during movement of the affected limb (Terzuolo et al, 1974). This result led the authors to conclude that the EMG pattern observed in the intact limb depended on sensory input, and to reject the notion that the motor output is determined by a central pre-programming. On the other hand, Lashley (1917) has long reported accurate movement of a deafferented limb joint in a human. Similarly Knapp, Taub and Berman (1963) Taub and Berman, (1968) Taub et al, (1975), and Bossom (1972; 1974) reported that monkeys with deafferented limbs were able to perform purposive movements and to learn a conditioned response using the affected limb which they could not view (Knapp et al, 1963).

Investigators from both schools agree that when one limb is deafferented, it is not used in locomotion, eating, grooming or other movement which normally involves the limb. However, when the intact limb is restrained, the animal is able to use the deafferented one in a purposive way (Bosson, 1974; Knapp et al, 1963). Another point of general agreement, is that even when motor acts are performed with the affected limb, the preoperative accuracy and fine motor control is never regained (Knapp et al, 1963; Bossom, 1974).

CONCLUSIONS

A choice between a central programming and a peripheral hypothesis is, though, not essential since the two hypotheses are not mutually exclusive (Evarts, 1971; Paillard and Brouchon, 1968). The extent of the motor deficits after deafferentation probably depends on the nature of the task, on the preoperative experience of the animal with the task, or a similar one, and on the cues that are available to the animal both pre- and post-operatively. Even though monkeys were able to perform several motor acts with deafferented limbs even in the absence of vision, when they were given a complex task which forced them to use proprioceptive cues for its accurate execution, they were unable to perform it (Eidelberg and Davis, 1976).

Behavioral compensation following removal of an input does not necessarily imply that the input is not involved in the task under normal circumstances. Such compensation has been observed in humans after an initial paralysis of a deafferented diaphragm (Nathan and Sears, 1960). A central programming hypothesis need not exclude or

undermine the importance of proprioceptive and other peripheral input, which Sperry (1950) regarded as essential in establishing a reference for all space perception.

1.1.6 PROPRIOCEPTIVE SIGNALS IN MOVEMENT

Given that proprioceptive signals play a role in motor control, the next question may be: Which are the relevant sensors, and what is their likely function in movement? One of the proposed functions, for which there is experimental evidence, is a role in position sense as already noted. This is an important function as it forms the basis of coordinated movement. But where do these afferent signals originate in the muscle if they are to signal position?

Muscles themselves contain several receptors including spindles, Golgi tendon organs, Pacinian corpuscles (Barker, 1959) and higher threshold receptors innervated by Group III afferent fibers, thought to function as muscle nociceptors at least in the limbs (Mense, 1977; Paintal, 1960). The Pacinian corpuscles respond to rapid tissue displacement and to high (150-300 Hz) vibration, but since they are activated only during transient mechanical changes and not during steady states, or during lower frequency displacements it is unlikely that they could effectively signal position. Nociceptors are activated during tissue pressure and have high thresholds. Since they rarely respond, and then only weakly, to muscle stretch (Paintal, 1960; 1961; Iggo, 1961) it is hard to see how they could be involved in position sense. Golgi tendon organs innervated by group Ib afferents are arranged in series with the extrafusal muscle fibers and detect changes

in tension in the muscle. Presumably these receptors should be active during both stretch and contraction of the muscle; however, experimental evidence indicates that their best stimulus for excitation is muscle contraction (Houk et al, 1971). In addition, the complex viscoelastic properties of muscles, and their exhibition of stretch relaxation showing a decrease in tension with time while the length of the muscle is constant (Abbott and Lowy, 1957; Little, 1969), make it unlikely that signals from tendon organs are used to signal position.

MUSCLE SPINDLES

Ever since the description of the spindles as muscle sense organs, the question whether these receptors are involved in position sense has been repeatedly raised ever since Sherrington suggested it (Sherrington, 1898). Muscle spindles are arranged in parallel with the extrafusal muscle fiber and respond to muscle stretch (Matthews, 1933). Two general types of endings have been identified, the primary, which are innervated by group la nerve afferents, and secondary endings of muscle spindles, innervated by group II afferent fibers; both are activated during muscle stretch. The rate of firing of the secondary ending increases with increases in fiber length, and attains the highest rate of discharge during the end of the displacement. The primary ending is also sensitive to the velocity of stretching, and fires at a higher rate during faster stretches with constant amplitude displacements.

These dynamic and static responses of the primary and the secondary endings, respectively, have been interpreted by models consistent with viscoelastic properties of the intrafusal muscle fiber. If the receptor

lies in series with a purely viscous region of the fiber, the force generated during stretch will be proportional to velocity. The displacement of the receptor will, therefore, be proportional to the velocity of stretch. If the receptor lies in series with an elastic region of the fiber, the displacement of the receptor will depend on the force generated during stretch and will be independent of velocity (Matthews, 1972). During release of the stretch, the secondary ending decreases its firing gradually, but the primary ending abruptly ceases firing. Muscle spindle afferents then convey signals concerning both changes in length and the rate of change in length. These signals may be used by the central nervous system to extrapolate and predict position (Matthews, 1977). Even though these receptors are unloaded and silenced during muscle contraction because of their in-parallel anatomical arrangement with the extrafusal muscle fibers, gamma efferent activity keeps the muscle spindles constantly in tune.

It is clearly possible that muscle spindles could subserve mechanisms underlying position sense and kinesthesis (Matthews, 1977), and experimental evidence suggests that they do. Vibration of muscles in humans causes illusory movement of the arm (Eklund, 1972; Goodwin et al, 1972), and subjects can follow with pursuit eye movements the illusory movement of their arms in a totally dark room (Lackner, 1975). Pulling on tendon digits gives an illusory movement of that digit (Matthews and Simmons, 1974). While these results suggest that muscle spindles can subserve kinesthetic mechamisms, it does not imply that they are the sole detectors of this complex function. A role of muscle spindles in position sense was, in fact, originally denied by reports

that signals arising from these receptors could not be used as conditioned stimuli in a discrimination task, whereas those of cutaneous nerves could (Swett and Bourassa, 1967). Also, stimulation of muscle afferent nerves at group 1 afferent excitation thresholds failed to elicit arousal responses in cats (Giaquinto, Pompeiano and Swett, 1963). Matthews has recently (1977) criticized the interpretation of these data, and suggested that the sensory signals could, rather, have been inappropriate in eliciting the response under consideration.

The signalling of position sense has been attributed to joint receptors (Mountcastle and Powell, 1959; Mountcastle et al, 1963) but their role in kinesthesis was recently refuted by the finding that most of these receptors in the cat knee joint respond during extreme angular movements while very few are active over the middle range (Burgess and Clark, 1969; Clark, 1975; Clark and Burgess, 1975; Grigg et al, 1973). It is conceivable that joint afferents could provide limb angular signals by some sort of neural integration as suggested by Boyd and Roberts (1953) and Mountcastle and Powell (1959). However, these receptors are at least not the sole detectors of angular movement, since patients without joints still have good kinesthetic sense (Grigg et al, 1973; Gross and McCloskey, 1973). It may be that joint and other receptors are all involved in signalling position under normal circumstances.

CONCLUSIONS

In view of the recent evidence, it is now reasonable to assume that afferent proprioceptive signals have a functional role, and could subserve a variety of motor control mechanisms at the suprasegmental level (see Bach-y-Rita, 1959; 1971; 1975; Matthews, 1977 for reviews).

This will be taken as the point of departure in the present investigation, which deals with the cortical afferent input of extraocular and dorsal neck muscles. Although the extraocular muscles of the cat do not possess the classically described muscle spindles (see Matthews, 1972), they have receptors which respond to stretch (Bach-y-Rita and Ito, 1966; Cooper and Fillenz, 1952; 1955). At least some of the extraocular receptors resemble simple spiral endings (Cooper et al, 1955). A series of experiments has been designed to activate dorsal neck and extraocular muscle receptors and afferents, and to investigate their input at the suprasegmental level and specifically in the frontal cortex of the cat.

CHAPTER 1, PART 2.

1.2 DORSAL NECK AND EXTRAOCULAR MUSCLE CHARACTERISTICS

1.2.1 DORSAL NECK MUSCLES

The dorsal neck muscles under study may be classified into two groups on the basis of their size and their relative depth on the dorsal neck region. One group includes the biventer cervicis and complexus, both of which are among the largest neck muscles (Fig. 1.2.1). These are situated at an intermediate depth on the neck, between the more superficially situated clavotrapezius, occipitoscapularis, and splenius, and the ventrally situated suboccipital muscles (Elliott, 1935). These latter are the deepest muscles of the dorsal neck and they are shorter and smaller in size than the biventer cervicis and complexus. They include the rectus capitis dorsalis major, medius, and minor, and the obliquus capitis caudalis and cranialis (Fig. 1.2.1). Hinoki and Terayama (1968) reported that injections of procaine into the sub-occipital muscles had marked effects on optokinetic responses in guinea pigs, while similar injections in the more superficially located larger neck muscles had no serious effects on these reflexes. Even though these results give physiological support to the classification of these muscles, the extent of spread of the drug to other muscles and structures was not established in those experiments.

1.2.2 ANATOMICAL AND INNERVATIONAL CHARACTERISTICS

Biventer cervicis and complexus

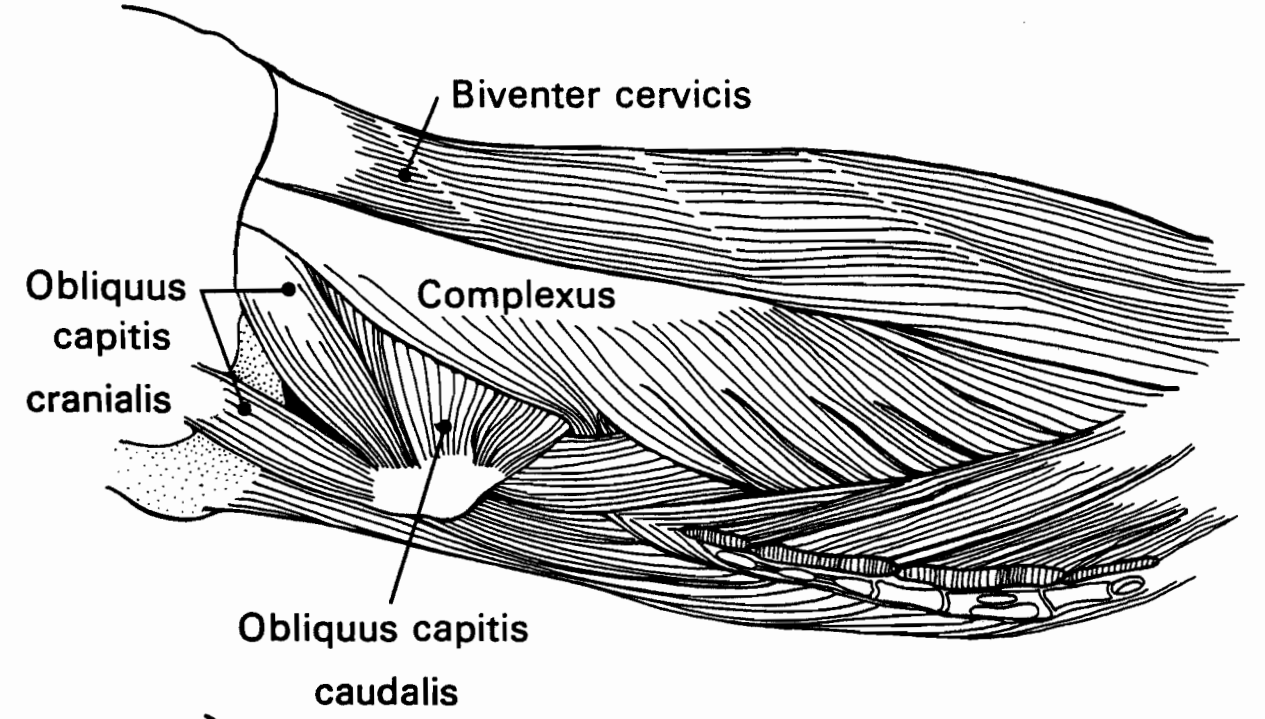
The biventer cervicis originates in the lower cervical and upper three thoracic vertebrae and inserts on the medial lambdoidal crest. It is innervated by nerves from the second, third and fourth cervical segments. Lateral to the biventer cervicis lies the complexus. Its origin is in the lower five or six cervical and 1-3 thoracic vertebrae, and it inserts on the lateral lambdoidal crest. It is innervated by branches from the first three cervical segments. The second and third cervical nerve branches from the biventer cervicis and complexus run close and parallel to each other (Fig. 1.2.2). These muscles have tendinous intersections across various levels (Elliott, 1935) (Fig. 1.2.1 and 1.2.2) which serve as insertion points for short fibers which do not reach the lambdoidal insertion (Richmond and Abrahams, 1975a).

Suboccipital muscles

The second group of muscles consists of the suboccipital group and includes the rectus capitis dorsalis major, medius, minor, and the obliquus capitis caudalis, and cranialis. These muscles are smaller and architecturally simpler than the biventer cervicis and complexus. They are innervated by branches from the suboccipital nerve at the first cervical (C_1) level. The rectus capitis dorsalis major lies ventral to the biventer cervicis (Fig. 1.2.1). It originates on the axis and inserts on the medial lambdoidal crest with its fibers running parallel from origin to insertion; it bears no tendinous intersections. Ventral to this muscle lies the rectus capitis dorsalis medius,

Fig. 1.2.1 Top: Diagram of lateral view of the cat dorsal neck; the skin and superficial neck muscles have been removed to show the biventer cervicis and complexus with tendinous intersections at various levels of the muscles.

Bottom: lateral view of the dorsal neck with the biventer cervicis and complexus removed to show four of the five suboccipital muscles. The rectus capitis dorsalis minor muscle lies beneath the medius and is not shown in diagram.


Biventer cervicis
Obliquus capitis cranialis
Complexus
Obliquus capitis caudalis

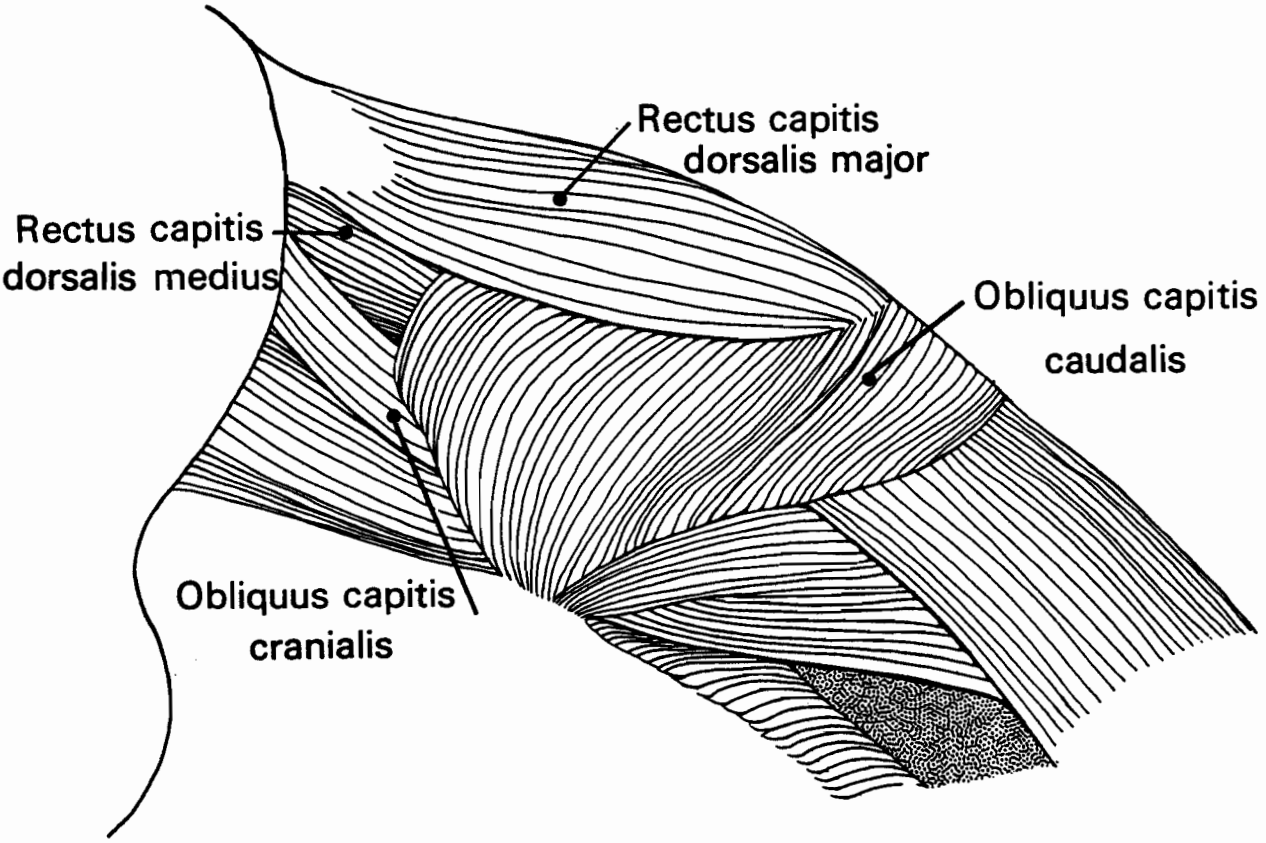
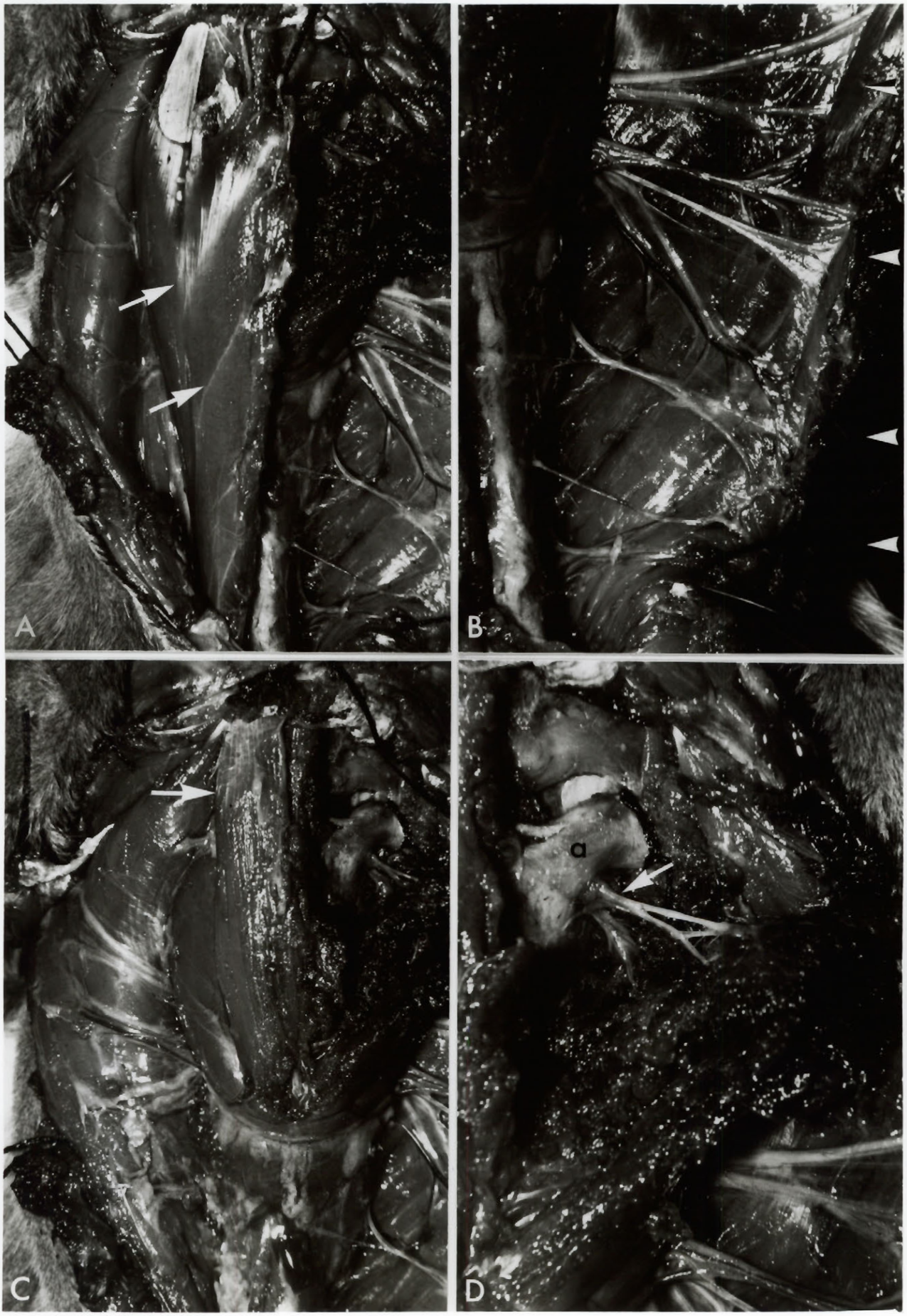

Rectus capitis dorsalis major
Rectus capitis dorsalis medius
Obliquus capitis caudalis
Obliquus capitis cranialis

Fig. 1.2.2 A- Photograph of the cat dorsal neck with the skin and superficial neck muscles retracted on the left side of the neck exposing the biventer cervicis medially, and the complexus laterally. Arrows point to two of several tendinous intersections on the biventer cervicis; these are also present on the complexus. B- The biventer cervicis and complexus muscles were detached from their insertion points on the right side of the neck and were retracted laterally to show the rich innervation of these muscles on the ventral side. The arrows on the right point to (from top to botton) nerve branches from the C_2 to C_5 levels. C- The biventer cervicis and complexus muscles on the left side of the neck were detached from their insertion points and retracted laterally to show the rectus capitis dorsalis major muscle (arrow) which is situated ventral to the former. Note parallel arrangement of fibers in this muscle, and absence of tendinous intersections. D- The suboccipital muscles on the right side of the neck were detached from their insertion points to show the ventrally emerging branches of the suboccipital nerve at the C_1 level, which innervate the five suboccipital muscles; a: atlas. All photographs show a dorsal view with the animal normally positioned in the stereotaxic apparatus.


A
B
C
D
a

which originates on the axis and inserts on the occipital bone below the lambdoidal crest. The smallest suboccipital muscle and the one with the shortest extent is the rectus capitis dorsalis minor; it originates on the atlas, which is the first cervical vertebra, and inserts on the occipital bone below the insertion of the rectus capitis dorsalis medius. The obliquus capitis caudalis muscle originates on the spine of the axis and runs obliquely with respect to the midline of the vertebral column to insert on the transverse process of the atlas. The obliquus capitis cranialis originates from the lateral edge of the atlas and inserts on the mastoid process of the temporal bone situated laterally with respect to the vertebral column.

1.2.3 HISTOCHEMICAL CHARACTERISTICS

The classification of muscle fibers into fast fatigue, fatigue resistant, and slow muscle fibers, was made on the basis of the extent of the ability of these fibers to maintain tension during repetitive stimulation. Muscles made up of fast fatigue fibers show a decrease in tension during repetitive stimulation, which is attributed to fatigue, since normal action potentials can still be generated. On the other extreme, muscles with slow fibers maintain tension well during repetitive stimulation. A number of cellular characteristics determine these properties, including myoglobin content, mitochondrial ATPase, number of mitochondria, and capillary supply per fiber, all of which are low in fast, and high in slow muscles. On the other hand, myofibrillar ATPase, glycogen content, and fiber area are high in fast, and low in slow muscles. These characteristics enable slow muscles dependent

on aerobic metabolism to maintain tension for long periods of time, and to participate in tonic postural mechanisms. Fast muscles depend on anaerobic glycolysis and are suited for fast phasic contractions (see Close, 1972 for review). The cellular variations in these fibers enable their description into these classes with the use of histochemical procedures.

On the basis of the relative proportions of these three fiber types classified by their histochemical characteristics, biventer cervicis has been described as a slow muscle, rectus capitis dorsalis major as a fast muscle, while complexus occupies an intermediate position in between these two (Richmond and Abrahams, 1975a).

1.2.4 ACTIONS

The main action of the biventer cervicis and complexus is to raise the head as is that of the rectus capitis dorsalis major with the assistance of the medius and minor. The obliquus capitis caudalis rotates the head, and the cranialis flexes it laterally (Elliott, 1935). Simultaneous contraction of combinations of these muscles results in a large variety of head movements. Due to the extensive connectivity and large cross-sectional area of the biventer cervicis and complexus, their contraction causes large head deviations with respect to the body axis. On the other hand, contraction of the suboccipital muscles results in small head movements, because of the relatively short extent of these muscles.

1.2.5 EXTRAOCULAR MUSCLES

Movement of the eyeball is achieved through the action of six muscles, which include the four recti and two obliques. They originate in the posterior part of the orbit and then diverge and attach to different parts of the globe. The muscles studied in the present investigation are the superior and lateral recti.

1.2.6 ANATOMICAL AND INNERVATIONAL CHARACTERISTICS

The superior rectus originates at the superior part of the apex of the orbit medial to the globe, and inserts somewhat obliquely on the globe forming an angle of approximately 23^{o} with the medial orbital wall (Fig. 1.2.3). It is innervated by the superior branch of the oculomotor nerve. The lateral rectus originates at the apex of the orbit and inserts on the temporal sclera approximately symmetrically above and below the horizontal plane of the eye. This muscle is innervated by the abducens nerve.

1.2.7 FIBER CHARACTERISTICS

The fibers of the extraocular muscles of the cat have been classified into two main categories, even though further subdivisions have been made morphologically (Alvarado and Van Horn, 1975; Peachey, 1971). The two main classes include large fibers which are singly-innervated and are located primarily in the muscle core, and small, multi-innervated slow fibers, located principally in an orbital layer (Bach-y-Rita and Ito, 1966b; Hess and Pilar, 1963). These two muscle fiber types show a

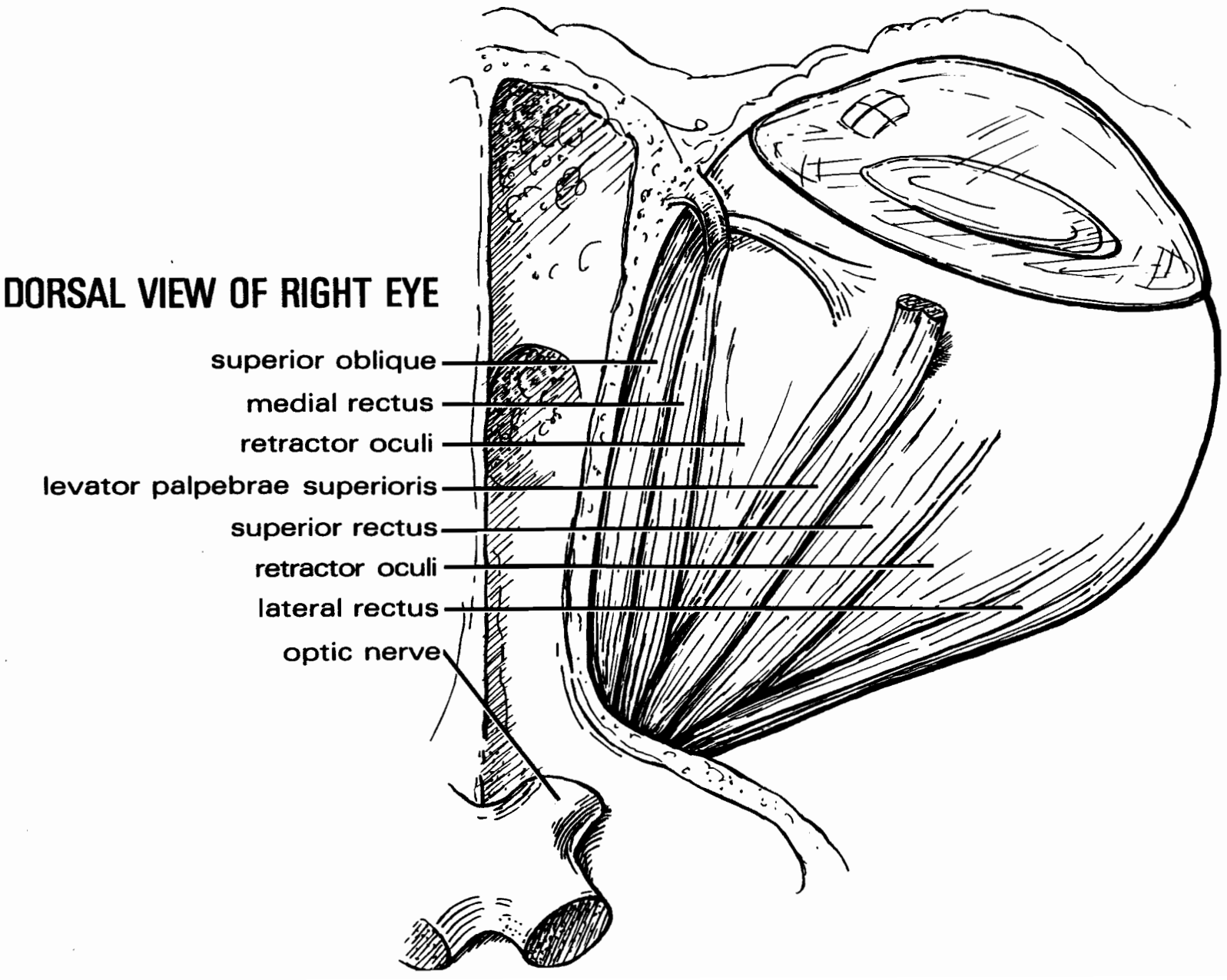
differential sensitivity to the depolarizing neuromuscular blocking agent succinylcholine, with the orbital multi-innervated fibers contracting, and the fast fibers showing blockade with administration of this agent (Bach-y-Rita and Ito, 1966b; Eakins and Katz, 1965; 1971). The slow fibers are active while the eyes are held at rest (Scott and Collins, 1973) paralleled by spontaneous activity in small nerve fibers (Yamanaka and Bach-y-Rita, 1968). These fibers are recruited early during eye movements, while the global ones become active later and during larger excursions of the eye (Scott and Collins, 1973).

1.2.8 ACTIONS

When the eye is in the straightforward position, the primary action of the superior rectus is in a vertical plane, acting to elevate the globe when it contracts. Because of its oblique insertion, (Fig. 1.2.3) this muscle exerts forces with medio-lateral and torsional components as well. The main secondary action of this muscle is in the horizontal plane, the direction depending on the position of the globe. When the globe is in the straightforward position, the superior rectus adducts the eye, and its action in this direction increases as the globe moves more nasally. This secondary action reduces to zero when the eye is abducted 23^{o}, and reverses to an abduction when the eye is abducted more than 23^{o}. During conjugate eye movements, such as nasal horizontal deviation, the medial rectus contracts, and the ipsilateral lateral rectus is stretched. The vertical recti and two obliques of the same eye actively maintain tone and tend to cancel the secondary actions of each other, ensuring that eye movements are effected smoothly without vertical

or torsional components. Contraction of the lateral rectus muscle produces pure horizontal movement.

Fig. 1.2.3 Diagram of dorsal view of right eye of the cat.


DORSAL VIEW OF RIGHT EYE
superior oblique
medial rectus
retractor oculi
levator palpebrae superioris
superior rectus
retractor oculi
lateral rectus
optic nerve

CHAPTER 2

2.1 FRONTAL PROJECTIONS OF DORSAL NECK MUSCLES

2.1.1 INTRODUCTION

Postural reflex responses of vestibular and neck origin have been clearly established (Roberts, 1967) and monosynaptic connections between neck motoneurons and the vestibular nuclei (Wilson and Yoshida, 1969), and between the otolith organs and neck motoneurons (Wilson et al, 1975) have been demonstrated. In addition to these reflex interactions at the spinal and brain stem level, telencephalic mechanisms controlling head position are also likely operative. In fact, because of the interactions of the head motor control system with the vestibular and oculomotor systems in coordinated eye and head movements, neck afferents originating in the numerous muscle spindles (Richmond and Abrahams, 1975a; Granit, 1970) may have a wider role at the suprasegmental than at the segmental level. The excitatory and inhibitory interactions of agonistic and antagonistic muscles observed in the limbs are not evident in neck muscles at the spinal cord level (Rapoport, 1977). Moreover, extracellular monosynaptic reflexes in neck motoneurons or in the muscle nerve are rare (Abrahams, Richmond and Rose, 1975), even though monosynaptic responses have been recorded intracellularly in neck motoneurons following stimulation of their nerve afferents (Anderson, 1977).

Experimental studies have disclosed that dorsal neck muscle afferents project to a number of suprasegmental regions known to be involved in equilibrium and head movement control, such as the cerebellum (Berthoz and

Llinas, 1974; Dubrovsky, 1974), the vestibulocerebellum (Schwartz and Milne, 1976; Wilson, Meada and Frank, 1975), the anterior suprasylvian cortex (Abrahams, 1970; Landgren and Silfvenius, 1968), the superior colliculus (Abrahams and Rose, 1975), the lateral reticular nucleus (Coulter, Mergner and Pompeiano, 1977), and the nucleus prepositus hypoglossi (Gresty and Baker, 1976). The possibility of afferent input from the dorsal neck to frontal regions which elicit head movements when stimulated (Hassler, 1966), has not received much attention yet. A group of units in cortical regions corresponding to the frontal eye fields fire before head movement in the monkey (Bizzi and Schiller, 1970; Robinson and Jarvis, 1974) and prior to initiation of activity in the biventer cervicis (Guitton and Mandl, 1978b), suggesting that these frontal regions may be involved in the initiation of head movement.

The first study investigated the projection of dorsal neck muscles to the cat frontal cortex, (Fig. 2.1.1) including regions within area 4 and 6 which are considered motor, and area 3a, which forms a transitional zone between the motor cortex rostrally and the somatic sensory cortex caudally (Hassler, 1966). Results showed that afferents from neck muscles project to these regions at latencies as short as 6 ms, and at least a sub-population of the units studied receive their afferent input from electrophysiologically characterized group 1 fibers.

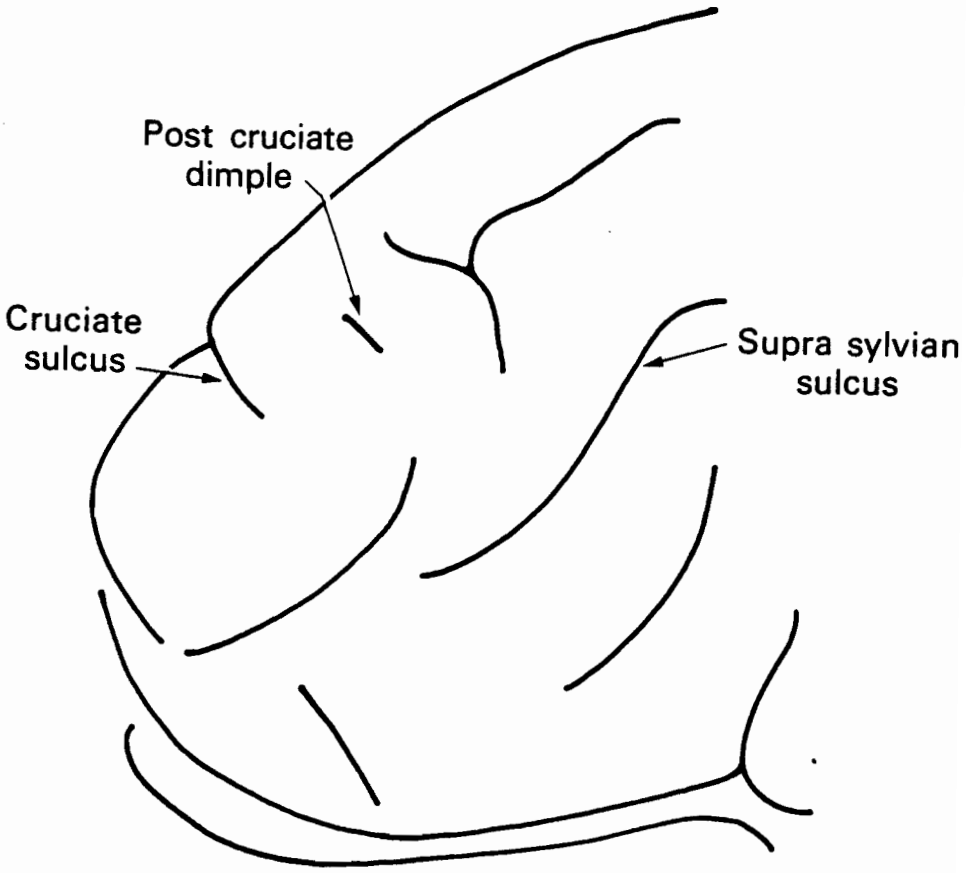
2.1.2 METHODS

SURGERY

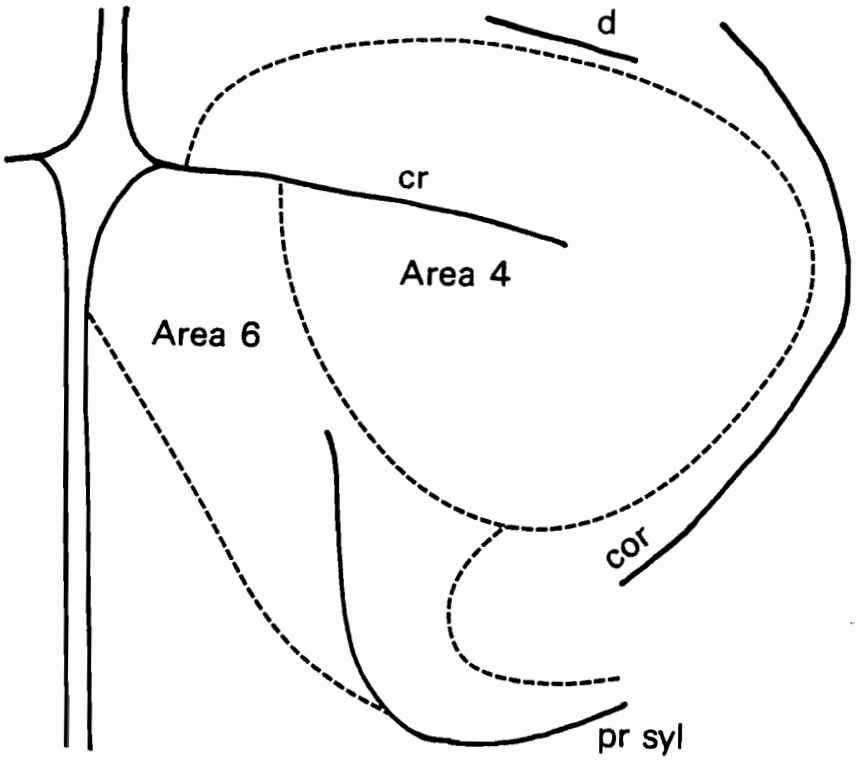
Experiments were performed on 26 cats anesthetized with alpha chloralose (60 mg/kg, intravenously, i.v.) dissolved in 25% urethane solution. The femoral artery and vein were cannulated. Blood pressure

Fig. 2.1.1 A- Diagram of dorsolateral view of the cat frontal cortex, and B- standard diagram of the cat frontal cortex showing the extent of the cytoarchitectonic areas 4 and 6 in relation to the frontal sulci. cr: cruciate sulcus, cor: coronal sulcus; pr syl: presylvian sulcus; d: postcruciate dimple.

A


Post cruciate
dimple
Cruciate
sulcus
Supra sylvian
sulcus

B


d
cr
Area 4
Area 6
cor
pr syl

was continuously monitored and kept above 100 mm Hg with intravenous infusions of physiological solutions (Ringer-Locke, see Lippold and Winton, 1968) when necessary. The trachea was intubated and the animal later paralyzed with gallamine triethiodide (Flaxedil, Poulenc, 8 mg/kg, i.v.) and artificially respired. Additional muscle relaxant was administered every hour (3 mg/kg). The temperature was kept at physiological range (37°-38°C), with a dc heating pad. Expired CO_2 level was periodically monitored with a capnograph (Godard-Statham B.E.) and kept at 3.8-4%. In order to prevent atelectasis (Collier and Mead, 1964) the lungs were occasionally filled to capacity and relieved for a few breaths.

A nerve branch from the second cervical level (C_2) innervating the biventer cervicis and complexus, and the branch of the suboccipital nerve to the rectus capitis dorsalis major and to the obliquus capitis caudalis muscles of the dorsal neck were prepared for stimulation bilaterally for the former, and unilaterally for the latter. In 16 experiments the suboccipital nerve was prepared for stimulation by positioning electrodes just before the nerve branches to supply the suboccipital muscles. In these cases, the muscle nerves stimulated included those of the rectus capitis dorsalis major, medius and minor, and the obliquus capitis caudalis and cranialis.

The left anterior brain area was exposed, the dura was retracted, and drying was prevented by a pool of warm mineral oil over the cortex. The dorsal funiculi were exposed by dissecting and retracting the muscles overlying the vertebral column, and by clipping the bone and retracting the dura until the rootlets of the C_1 and C_2 level were exposed for recording dorsal root potentials.

STIMULATION AND RECORDING

Nerve stimulation was bifocal through chlorided silver wires. The nerves and electrodes were covered with molten wax or a pool of warm mineral oil to insulate them from the surrounding tissues. Stimulation was delivered by a stimulator (Grass S8) through a stimulus isolation unit (Grass SIU5).

In order to monitor the group of fibers activated, afferent volleys were recorded from dorsal rootlets by means of cotton thread electrodes moistened with physiological saline and placed around individual rootlets at the C_1 and C_2 levels. The cotton threads were immersed in two small plastic containers filled with physiological saline with a coil of chlorided silver wire acting as the interface connection with the amplification system. Evoked potentials were amplified through a preamplifier (Tektronix 122) set at a time constant of 1 s (0.2 Hz frequency response for the low, and at 10 kHz for the high-frequency components of the response). This system enabled recording from a discrete population of the afferents with great stability and reliability. The stimulation required to elicit detectable activity in the rootlets was taken as the reference threshold value (T) required to activate group 1 fibers from the stimulated nerve. Strength of applied stimuli was expressed as a multiple of this reference value. Currents of 300 μA for 30 to 50 μs were usually sufficient to elicit detectable activity in the first and second rootlets. Occasionally train stimulation (three pulses of 0.25 ms, 1 ms total burst duration) was also used to activate nerve fibers.

Unit and evoked field recordings in the frontal cortex were made with platinum-iridium microelectrodes (Fredrick Haer and Co., Z = 10-14 MΩ

at 1000 Hz) connected through a cathode follower (Stoelting PAD 2A probe control) and amplified (Tektronix 2A61) for display on a cathode ray oscilloscope (Tektronix 565). The band width of recording was from 60 Hz to 6khz for single units and from 6 Hz to 6kHz for field activity. A storage oscilloscope (Tektronix 5103N) served as slave from which photographs were taken (Tektronix C5 camera). Frontal regions extending rostrocaudally 2 mm anterior,to 3.5 mm posterior the cruciate sulcus, 1 to 10 mm lateral from the midline, and up to 9 mm ventral from the surface of the cortex were explored in 52 penetrations. Microelectrodes were lowered with a microdrive that could be advanced in 1 μm steps, (Narishige). Electrolytic lesions produced by passing direct current (anode connected to the microelectrode) of 10 μA for 5 to 10 s were made at various recording levels for reconstruction of recording tracts and histological identification of responsive sites. A bigger lesion of 40 μA for 15-20 s was made at the most ventral point of the penetrations for easier identification of the tract. The depth of each unit from the surface of the cortex was recorded from the micromanipulator scale in μm.

HISTOLOGY

After each experiment the animals were perfused through the aorta with 10% formol saline. The brain and spinal cord were removed, fixed in formalin and embedded in paraffin. The explored frontal brain regions were cut in 10 μm sections and stained with cresyl violet for microscopic examination. Sites responsive to stimulation of dorsal neck muscle afferents were marked on diagrams of coronal sections of the cat frontal cortex.

2.1.3 RESULTS

FIELD AND SINGLE UNIT

Field and single cell activity was recorded in the postcruciate dimple in response to threshold electrical stimulation of the nerve of the biventer cervicis/complexus, as well as the suboccipital nerve to the five muscles or one of its branches to the rectus capitis dorsalis major and obliquus capitis caudalis muscles. These results are consistent with, and extend earlier findings of Landgren and Silfvenius (1968) who reported projections of group 1 afferents from the splenius, a dorsal neck muscle, to this region. The latency of evoked neural activity to this locus was 6 ± 2 ms.

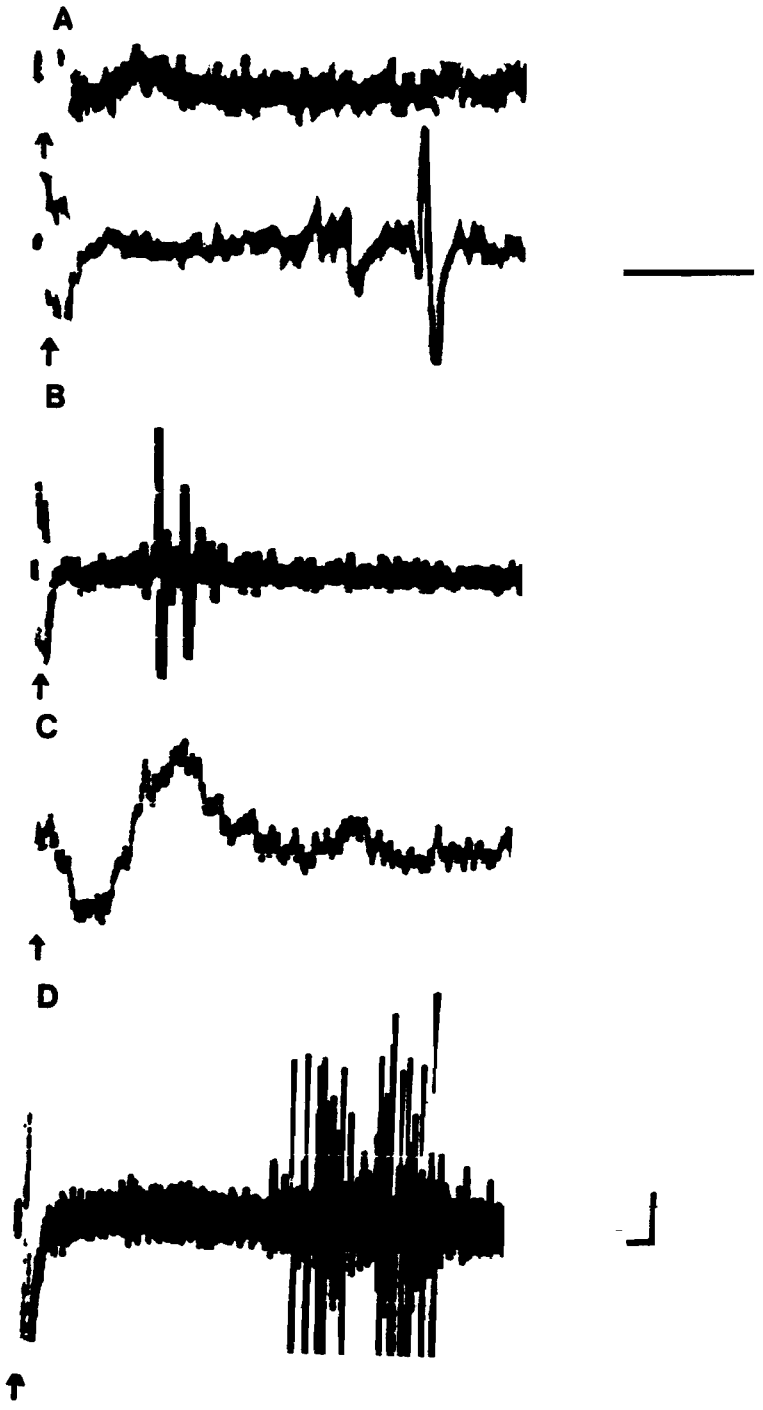
Rostral to the area of the postcruciate dimple, responses of 210 neurons to stimulation of dorsal neck muscle nerves were studied in 52 penetrations. Out of these units, 182 responded to stimulation of the nerve of the biventer cervicis/complexus contralateral, 58 units responded to the nerve of these muscles ipsilateral to the recording site, while 46 responded to the suboccipital nerve or its branches to the rectus capitis dorsalis major and obliquus capitis caudalis muscles. These figures represent an 84% response for the contralateral and a 59% for the ipsilateral biventer cervicis/complexus, and a 50% response for the suboccipital group of muscles. These results are summarized in Table 2.1.1. The neuronal response was a burst of 1-12 spikes per stimulus when the lowest intensity required to elicit an evoked response in the units was used. Twenty-seven per cent of these cells fired with 1-3 spikes, 56% with 4-6 spikes, 13% with 7-9 spikes, and 4% with 10-12 spikes. In 15% of all cases the evoked activity was in two bursts of spikes separated by 5-20 ms (Fig. 2.1.2D).

TABLE 2.1.1

Number of Responsive Units in Pericruciate and Presylvian Regions to Stimulation of Dorsal Neck Muscle Nerves

Muscle nerve stimulated	Number of units tested	Number of responsive units		Distribution of responsive units		
				Dorsal cruciate bank	Ventral cruciate bank	Presylvian cortex
Contralateral biventer cervicis/ complexus	216	182	(84%)	54	75	53
Ipsilateral biventer cervicis/ complexus	98	58	(59%)	20	25	13
Contralateral suboccipital or branches to rectus capitis dorsalis major and obliquus capitis caudalis	92	46	(50%)	7	9	30

Fig. 2.1.2 A- Top trace: afferent volley recorded with cotton thread electrode from dorsal rootlets of the first cervical segment to stimulation (1T) of the ipsilateral suboccipital nerve; lower trace: single cell activity recorded simultaneously with a microelectrode in the contralateral presylvian region in the frontal cortex. B- Single cell response in presylvian region to nerve stimulation (1.2T) of the contralateral biventer cervicis/ complexus muscles. C- Evoked field activity in presylvian region to electrical nerve stimulation (1.2T) of the contralateral biventer cervicis/complexus muscles. D- Unit response in the ventral bank of the cruciate to electrical stimulation (1.5T) of a nerve branch to the biventer cervicis/complexus. Note earlier evoked unit responses in presylvian regions (A, lower trace, and B), when compared with a response on the ventral cruciate (D). A-C show one sweep each, and D represents six superimposed sweeps showing that the evoked response in two bursts of spikes separated by 5 ms is consistent over repeated trials. Horizontal calibration 5 ms; vertical 80 μV.


A
B
C
D

Of 87 cells tested, 45 responded to stimulation of both the contralateral and ipsilateral nerve branch to the biventer cervicis/complexus, while convergence between the afferents from the biventer cervicis/complexus muscles with the suboccipital group was observed in 17 out of 82 cells (Table 2.1.2).

Field and single cell activity in response to contralateral stimulation of dorsal neck muscle afferents followed frequencies of up to 2/s. This finding is consistent with the frequency response of lateral eye movement stabilization by neck proprioceptors in man (Meiry, 1971). Responses to ipsilateral stimulation had longer latencies compared to contralateral ones (Fig. 2.1.3), and could follow consistently frequencies of only 0.5/s or less.

The latencies of response to contralateral nerve stimulation were 6-45 ms (Fig 2.1.3). The intensities necessary to evoke responses ranged from threshold to 3 T. Forty-four cells responded to threshold or 1.1-1.3 T intensities of stimulation of dorsal neck muscle nerves. However, for 80% of the 210 cells studied, intensities of 1.5 to 3 T were necessary to obtain responses.

HISTOLOGICAL RESULTS

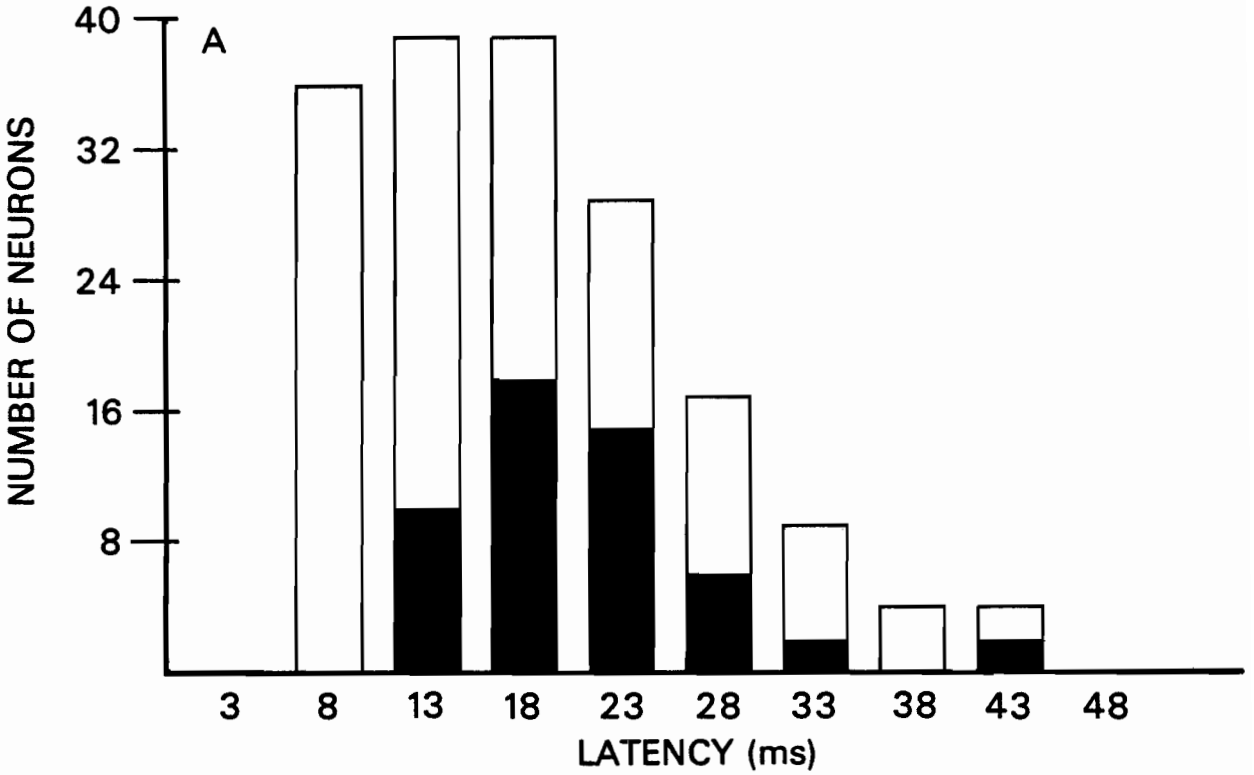
Examination of recording sites responsive to stimulation of dorsal neck muscle nerves showed a double distribution. One of these included the dorsal and ventral banks of the cruciate sulcus. The other site encompassed regions of both margins of the presylvian sulcus. Figure 2.1.4 is a series of composite maps reconstructed from histological examination of coronal sections of the frontal pole of the brain, showing the

TABLE 2.1.2

Convergence of Dorsal Neck Muscle Afferents in Pericruciate and Presylvian Regions

Muscle nerves stimulated	Number of units tested	Number of units showing convergence	
Contralateral biventer cervicis/complexus and ipsilateral biventer cervicis/complexus	87	45	(52%)
Contralateral biventer cervicis/complexus and contralateral suboccipital or branches to rectus capitis dorsalis major and obliquus capitis caudalis	82	17	(21%)

Fig. 2.1.3 A- Interval histogram illustrating the distribution of the response latencies of neurons in pericruciate and presylvian regions following electrical nerve stimulation of the biventer cervicis/complexus muscles contralateral (hollow bars) and ipsilateral (black bars) to the recording site. B- latency responses to stimulation of the suboccipital nerve, or its branches to the rectus capitis dorsalis major and obliquus capitis caudalis muscles contralateral to the recording site. The numbers along the abscissae indicate the midpoint of each latency interval.


A
40
32
24
16
8
NUMBER OF NEURONS
3
8
13
18
23
28
33
38
43
48
LATENCY (ms)

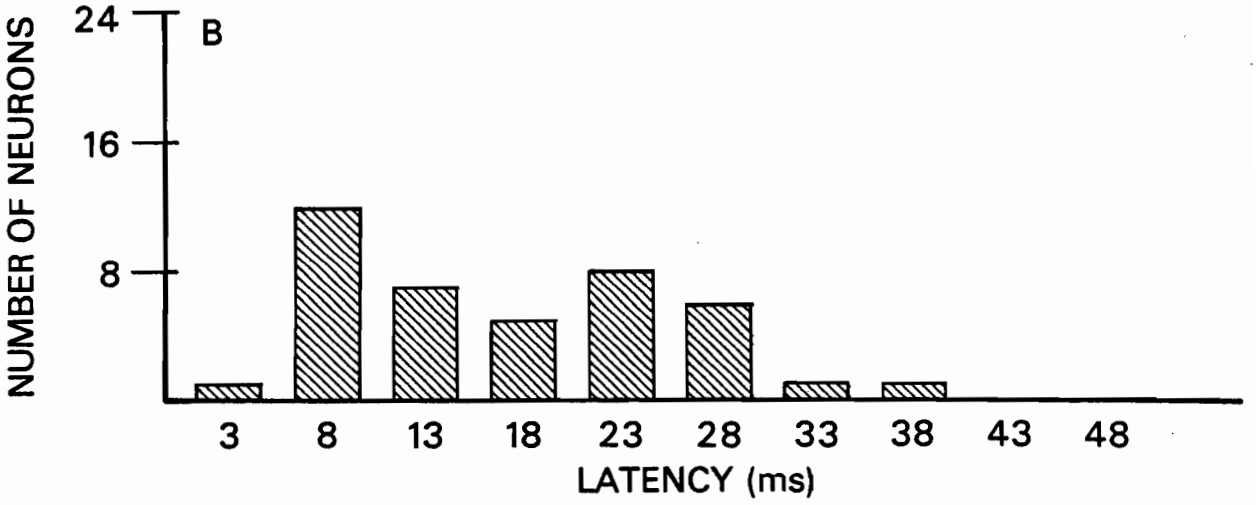
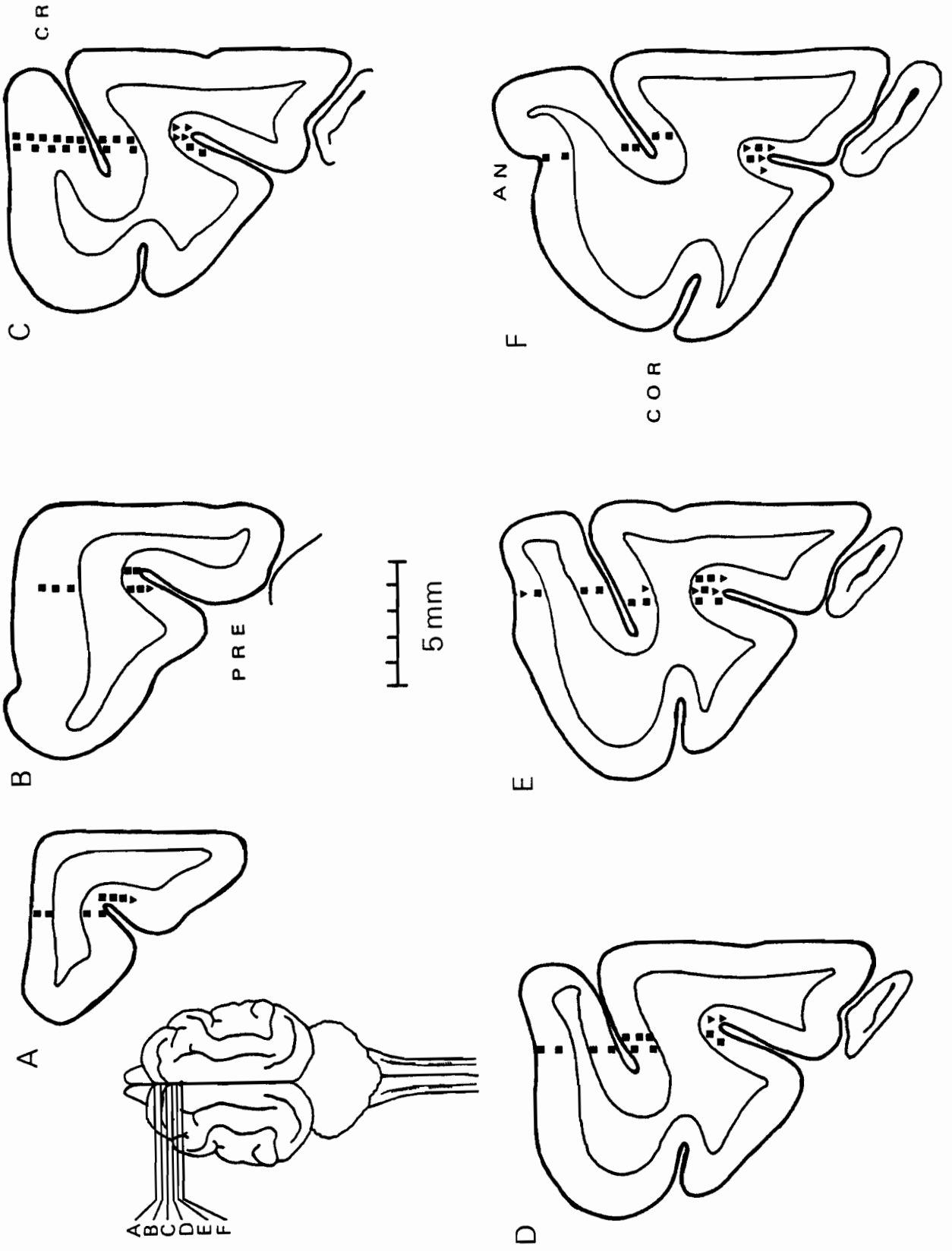

B
24
16
8
NUMBER OF NEURONS
3
8
13
18
23
28
33
38
43
48
LATENCY (ms)

Fig. 2.1.4 Coronal diagrams of the cat frontal cortex (left) showing responsive sites to electrical stimulation of afferents from dorsal neck muscles. Squares show responses to the biventer cervicis/complexus nerve, triangles to the suboccipital nerve. Nerve stimulation was contralateral to the recording site (A-F). CR: cruciate sulcus; COR: coronal sulcus; AN: ansate sulcus; Pre: presylvian sulcus.


A
B
C
D
E
F
A B C D E F
PRE
CR
AN
COR
5 mm

responsive sites. Figure 2.1.5 shows a photograph of a brain section through the anterior sigmoid gyrus with a lesion at a responsive site on the medial bank of the presylvian sulcus.

The dorsal neck muscle afferent input was not uniform to the two loci, and several other differences were also noted between the two regions. The suboccipital nerve projected mainly to presylvian regions, whereas afferents from the biventer cervicis/complexus projected to both loci. The relative number of units activated by low threshold afferent input was different in the two regions, with a predominance of these in presylvian regions. Of 44 such cells 30 were situated in presylvian and 14 in pericruciate regions. The latencies of responses within the presylvian regions were characteristically short (6-15 ms Fig. 2.1.2A). The longest latencies (30-45 ms) were observed on the dorsal bank of the cruciate sulcus, with the latencies being shorter as the microelectrode advanced deeper (Fig. 2.1.6).

The presylvian was a region of low convergence of dorsal neck muscle afferent input when compared with pericruciate regions. Of 45 units responding to contralateral and ipsilateral nerve stimulation of the biventer cervicis/complexus, 41 were in pericruciate and only four were in presylvian regions. Also, of 17 units responding to both the contralateral biventer cervicis/complexus, as well as to the suboccipital nerve, 14 were in pericruciate, and three in presylvian regions.

2.1.4 DISCUSSION

The results of the present study showed that electrical stimulation of dorsal neck muscle afferents evoked field and single cell activity in

Fig. 2.1.5 Coronal section through the left anterior sigmoid gyrus rostral to the cruciate sulcus showing electrolytic lesion on the most ventral point of one penetration marking a responsive site to dorsal neck muscle afferent stimulation. The lesion is on the gyrus proreus, on the medial bank of the presylvian sulcus. Cresyl violet; magnification, 21X.

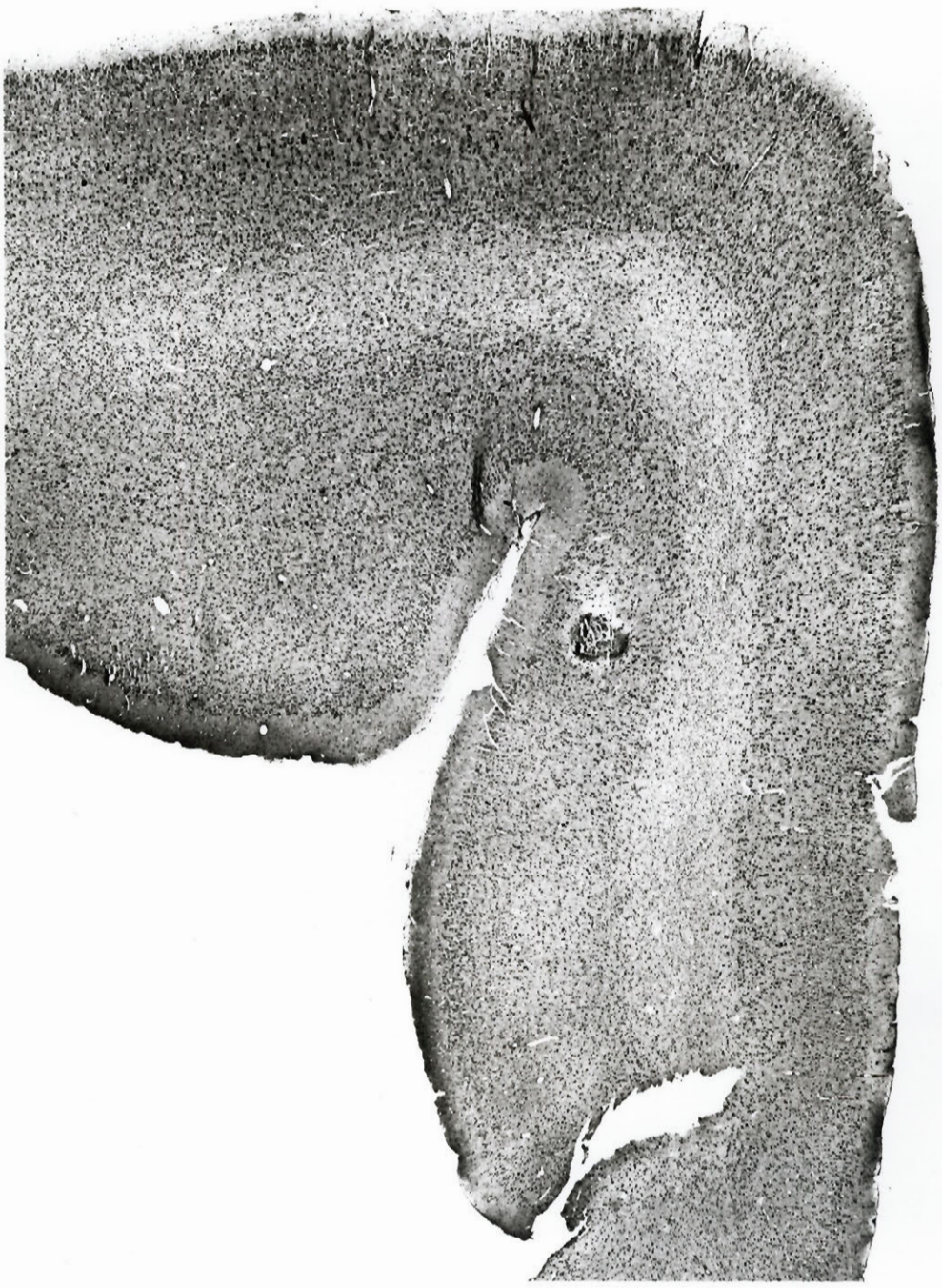
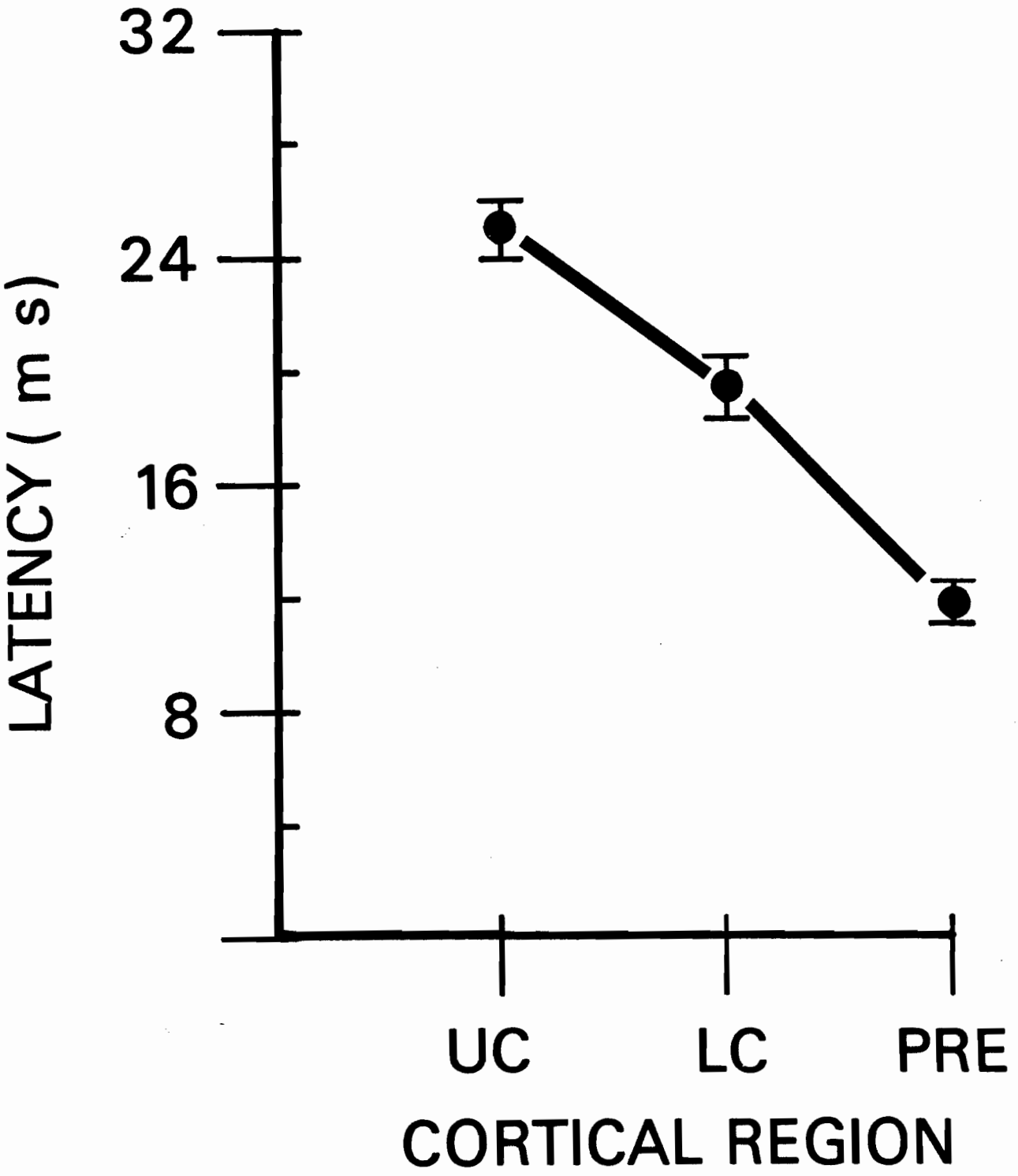


Fig. 2.1.6 Mean unit response latencies to stimulation of contralateral dorsal neck muscle afferents in the various frontal regions. Responses to the biventer cervicis/complexus and suboccipital nerve are pooled. Note descending latency trend as the microelectrode traverses the dorsal bank of the cruciate (UC), to the ventral bank of the cruciate (LC) and to the margins of the presylvian sulcus (PRE). Vertical bar at each point indicates ± standard error.


32
24
16
8
LATENCY (m s)
UC
LC
PRE
CORTICAL REGION

frontal regions of the cat brain. Regions which overlap with the ones investigated in the present study have been implicated in head movement as a result of stimulation (Hassler, 1966) and ablation studies (McKibben and Wheelis, 1932), and on the basis of single unit responses prior to head movement (Bizzi and Schiller, 1970; Robinson and Jarvis, 1974) or neck muscle activity (Guitton and Mandl, 1978b). The present findings of low threshold afferent input from muscles that hold and move the head to regions of the frontal lobe at short latencies is consistent with the idea that these regions are involved in neural mechanisms of head movement control. Since the head has considerable inertia, and during coordinated eye and head movement, in response to an unexpected appearance of a stimulus to the side, it lags the eyes by 10-25 ms (Morasso, Bizzi and Dichgans, 1973), it is conceivable that the short latency input from neck proprioceptors could serve to signal the state of the muscle prior to, as well as during ongoing head movement.

The present investigation also showed that dorsal neck muscle afferents project to two different loci. One involved regions of the pericruciate, and the other the presylvian cortex. The dorsal and ventral banks of the cruciate sulcus received afferents mainly from dorsal neck muscles which extend across the cervical spine from origin to insertion. In the cat, the contraction of these muscles produces movements which deviate the cantilevered head from both the body axis and the gravitational axis; these two axes coincide in man but not in quadrupeds.

While signals concerning head position in space are conveyed to the central nervous system by the vestibular system, neck afferents are the

primary source of information of the angle formed by the head and the body (Cohen, 1961). These afferents may, then, be a relatively important control factor in situations where the head deviates simultaneously from both the gravitational and the body axes (Dubrovsky and Garcia-Rill, 1973; Mittelstaedt, 1964). This task requires information from both the vestibular and dorsal neck systems. It has already been shown that vestibular (Boisacq-Schepens and Roucoux-Hanus, 1975) as well as visual (Garcia-Rill and Dubrovsky, 1973) afferents project to frontal regions corresponding to the body axis and overlap with those receiving dorsal neck muscle afferents in the pericruciate cortex as shown in this study.

The two margins of the presylvian sulcus received projections from both the more superficially and longitudinally extended, and the sub-occipital group of dorsal neck muscles. Contraction of the suboccipital group results in small head movements, and Granit (1970) has suggested that these muscles may play an important role in head stabilization, a necessary condition for appropriate function of the distance receptors (Sherrington, 1906). Those results, and the short latencies of unit evoked responses in presylvian zones, suggest that these regions may be involved, although not exclusively with fine control of head position.

CONCLUSION

The results presented showed that dorsal neck muscle afferents project to pericruciate and presylvian regions at latencies of 6-45 ms. It is suggested that some of these signals may be used in mechanisms underlying head movement control. In addition, the shorter latency responses in presylvian regions, the bias of low threshold afferent input

there, and the preferential input by the suboccipital group when compared with pericruciate regions, suggest that the processing of these signals may be different in the two regions.

2.2 CHARACTERISTICS OF DORSAL NECK MUSCLE AFFERENT INPUT TO THE FRONTAL CORTEX BEFORE AND AFTER DORSAL FUNICULUS SECTION

2.2.1 INTRODUCTION

The previous study showed that dorsal neck muscle afferents project to the cat frontal cortex within pericruciate and presylvian regions. A sub-population of the units recorded in the frontal cortex responded within 6-10 ms to stimulation of dorsal neck afferents which were electrophysiologically characterized as belonging to group 1. These afferents originate in the primary endings of muscle spindles and in tendon organs.

The next study had two general objectives, these included: A. To determine the exact regions of influence of group 1 neck muscle afferents, and to investigate their course to the frontal cortex. The aim of this objective was to further examine the regional distribution and characteristics of dorsal neck muscle afferents in the frontal cortex. The role of the dorsal funiculus in the group 1 frontal projections was examined as this pathway contains afferent fibers of muscle nerves (see McIntyre, 1974), is the exclusive pathway for group 1 muscle afferents from the forelimb (Landgren et al, 1967; Oscarsson and Rosen, 1963; 1965), and also carries dorsal neck muscle afferents to the cat flocculus (Wilson et al, 1975). Also, an anatomical pathway from the ventrobasal thalamus to the neck muscle afferent receiving presylvian regions exists (Hand and Morrison, 1972; Ruderman et al, 1972), and this could convey signals from the dorsal neck to the frontal cortex. B. The second objective of this study was to investigate whether the dorsal neck muscle afferents

have inhibitory as well as excitatory influences on units in the frontal cortex.

Results showed that electrophysiologically characterized group 1 muscle afferents from the dorsal neck reach discrete regions of the cat frontal cortex via the dorsal funiculus, and have both excitatory and inhibitory effects on frontal cortical units. However, dorsal neck muscle afferent fibers with an excitatory or inhibitory input to at least 80% of the responsive units, and which required intensities of stimulation higher than 1.5T to elicit evoked activity in the frontal cortex reach these regions through other conductive path(s).

2.2.2 METHODS

Experiments were performed on 26 cats anesthetized with alpha chloralose (60 mg/kg, i.v.). Animal preparation, surgery, stimulating and recording procedures have been described in detail in Experiment 1, Chapter 2. In this experiment field activity was also summated (64 sweeps, 125 ms total sweep time) with a digital memory oscilloscope (Enhancetron 1024, Nuclear Data, Inc.).

Transection of the dorsal funiculus was made with dissecting forceps just above the C_1 level (Fig. 2.2.5 G), where ascending fibers are principally interrupted (Bromberg and Towe, 1977). Care was taken to avoid damage of the vascular bed and thus avoid ischemic lesions in adjacent tracts.

In order to test for inhibitory effects elicited by dorsal neck muscle afferents, double-barrelled glass pipettes were used in 10 experiments. The recording barrel was filled with 1 M NaCl; the other

barrel was filled with 1 M sodium glutamate and was linked to an iontophoretic unit. Iontophoretic release of glutamate by passing cathodal currents of 4-15 nA, monitored with a galvanometer (Guildline SR 21), provided a background of neuronal excitation against which inhibitory effects with stimulation of dorsal neck muscle afferents could be evaluated. The impedance of the pipette electrodes measured at 200 Hz was 6 to 10 MΩ. A small steady braking current was used to prevent spontaneous leakage of glutamate between testings.

HISTOLOGY

Histological procedures for the brain and spinal cord were as described in Experiment 1.

In cases where glass pipettes were used, the electrode was left in the brain and subsequently in formalin for one week so that a trace of the electrode remained in the brain when it was removed. The results reported are all from histologically identified sites.

The dorsal funiculus lesions were reconstructed by microscopic examination of serial sections through the lesion. The extent of sparing was evaluated by projecting and magnifying histological slides (20X), and measuring the intact and partially damaged tissue area by planimetry. Separate measurements were made for the fasciculus gracilis, and the medial and lateral fasciculus cuneatus, and each of these regions was expressed as a percentage of the homologous contralateral control region. The center-most dorsal extent of the dorsal horn was used as the line of demarcation dividing the medial from the lateral fasciculus cuneatus. The justification for the division is based on the assumption

that dorsal neck muscle afferents lie in the lateral part of the fasciculus cuneatus. Studies have reported a medial arrangement within the dorsal funiculus of fibers originating in the caudal periphery, with a progression laterally for more rostrally originating peripheral fibers (Chang and Ruch, 1947; Ferraro and Barrera, 1935; Walker and Weaver, 1942). Even though some overlap has been reported (Shriver, Stein and Carpenter, 1968; Walker and Weaver, 1942), fibers from the upper cervical levels such as those of neck origin course generally laterally, in the fasciculus cuneatus.

2.2.3 RESULTS

Before dorsal funiculus section

Field and single cell activity was recorded in 40 penetrations in pericruciate, presylvian, and coronal gyrus regions in response to threshold or 1.1-3T stimulation of a nerve branch to the biventer cervicis/complexus, and of the suboccipital nerve to the rectus capitis dorsalis major and obliquus capitis caudalis muscles. Responses of 222 cells were recorded to peripheral electrical nerve stimulation, of which 136 responded to the contralateral and 58 to the ipsilateral biventer cervicis/complexus, while 43 responded to the contralateral rectus capitis dorsalis major/obliquus capitis caudalis muscles. (Table 2.2.1). Convergence between two or more nerve afferents was tested in 100 cells, of which 53 responded to more than one afferent input. Afferents from the contralateral and ipsilateral biventer cervicis converged onto 40 out of 70 cells tested, while of 67 cells, 17 responded to stimulation of both the contralateral biventer cervicis/

TABLE 2.2.1

Number and Distribution of Responsive Units in Pericruciate, Coronal and Presylvian Regions to Stimulation of Dorsal Neck Muscle Nerves.

Muscle nerve stimulated	Before dorsal funiculus section						After dorsal funiculus section					
	Number of units tested*	Number of responsive units	Distribution of responsive units				Number of units tested*	Number of responsive units	Distribution of responsive units			
			UC	LC	COR	PRE			UC	LC	COR	PRE
Contralateral biventer cervicis and complexus	203	136 (67%)	47	46	24	19	64	32 (50%)	9	9	10	4
Ipsilateral biventer cervicis and complexus	123	58 (47%)	23	24	5	6	40	19 (48%)	4	6	3	6
Contralateral suboccipital to rectus capitis dorsalis major and obliquus capitis caudalis	110	43 (39%)	5	7	15	16	47	9 (19%)	1	2	3	3

UC: Dorsal bank of cruciate sulcus; LC: Ventral bank of cruciate sulcus; COR: Dorsal and Ventral banks of coronal sulcus; PRE: Medial and Lateral banks of presylvian sulcus.

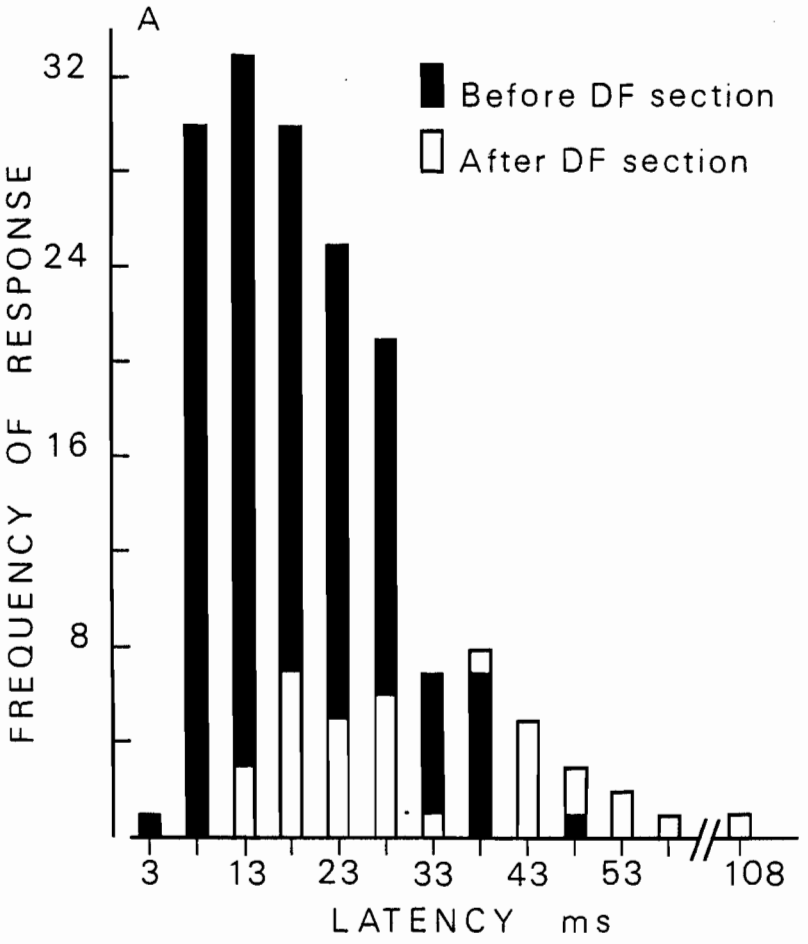
*The number of units tested in each sub-region was uniform.

complexus and to the contralateral rectus capitis dorsalis major/obliquus capitis caudalis muscle nerves.

The latencies of response to stimulation of dorsal neck muscle nerves were 5-46 ms (Fig. 2.2.1). The longest latencies were recorded for units in the dorsal bank of the cruciate sulcus. Units with progressively shorter latencies were encountered as the microelectrode advanced deeper, with the shortest latencies observed in the presylvian field (Fig. 2.2.2). A one-way analysis of variance showed significant differences in neuronal latency responses to contralateral nerve stimulation in the four cortical regions explored, which included the dorsal and ventral bank of the cruciate, coronal, and presylvian regions ($p<0.01$). Unit following frequencies were 0.1-2.0/s. Responses to threshold or 1.1-1.3T intensities of stimulation were observed in 40 out of 200 units tested (20%). These units had the highest (0.5-2/s) following frequencies, and the shortest latencies (5-10 ms). However, for 25% of these units the latencies were longer (12-30 ms); these latter units were all in peri-cruciate regions. For the majority (80%) of all responsive units, intensities of 1.5-3T were necessary to obtain responses, the latencies were longer (12-46 ms), and unit following frequencies were 0.1-0.5/s.

Inhibition was also observed in the frontal cortex with stimulation of dorsal neck muscle nerves against a background of glutamate induced neuronal activity. Inhibitory effects were noted in 12 out of 40 cells tested (30%), and were characterized by a general reduction in the background activity, observed in six cases (three for each contralateral nerve), or a decrease in spike activity within 10-20 ms (Fig. 2.2.3 B) or 50-90 ms following nerve stimulation. These effects could be overcome

Fig. 2.2.1 Interval histogram illustrating the distribution of the response latencies of neurons in pericruciate, coronal, and presylvian regions following electrical stimulation of afferents from a nerve branch to the biventer cervicis/complexus, and to the rectus capitis dorsalis major/obliquus capitis caudalis muscles of the dorsal neck contralateral to the recording site, A. The unit latencies of response to stimulation of these two contralateral nerves to the four neck muscles are pooled in A, and in Fig. 2.2.2. Response latencies to ipsilateral nerve stimulation of the biventer cervicis/complexus are shown in B. The numbers along the abscissae indicate the midpoint of each latency interval; DF: dorsal funiculus.


A
32
24
16
8
FREQUENCY OF RESPONSE
Before DF section
After DF section
3
13
23
33
43
53
108
LATENCY ms

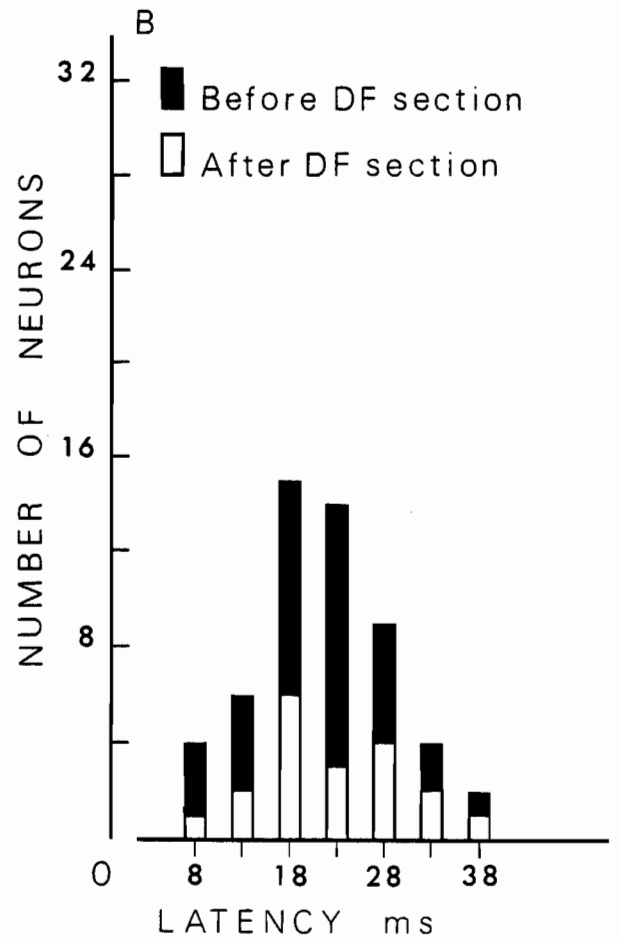

B
32
24
16
8
0
NUMBER OF NEURONS
Before DF section
After DF section
8
18
28
38
LATENCY ms

Fig. 2.2.2 Mean unit response latencies to stimulation of contralateral dorsal neck muscle afferents in frontal cortical regions before, and after dorsal funiculus section. Note mean latency increase in the dorsal bank of the cruciate sulcus (UC), coronal (COR), and presylvian (PRE) regions, but not in the ventral bank of the cruciate (LC), after dorsal funiculus section. Vertical bar at each point indicates ± standard error.

Before DF section N= 52 (UC); 53 (LC); 39 (COR); 35 (PRE).

After DF section N= 10(UC); 11(LC); 13 (COR) and 7 (PRE).

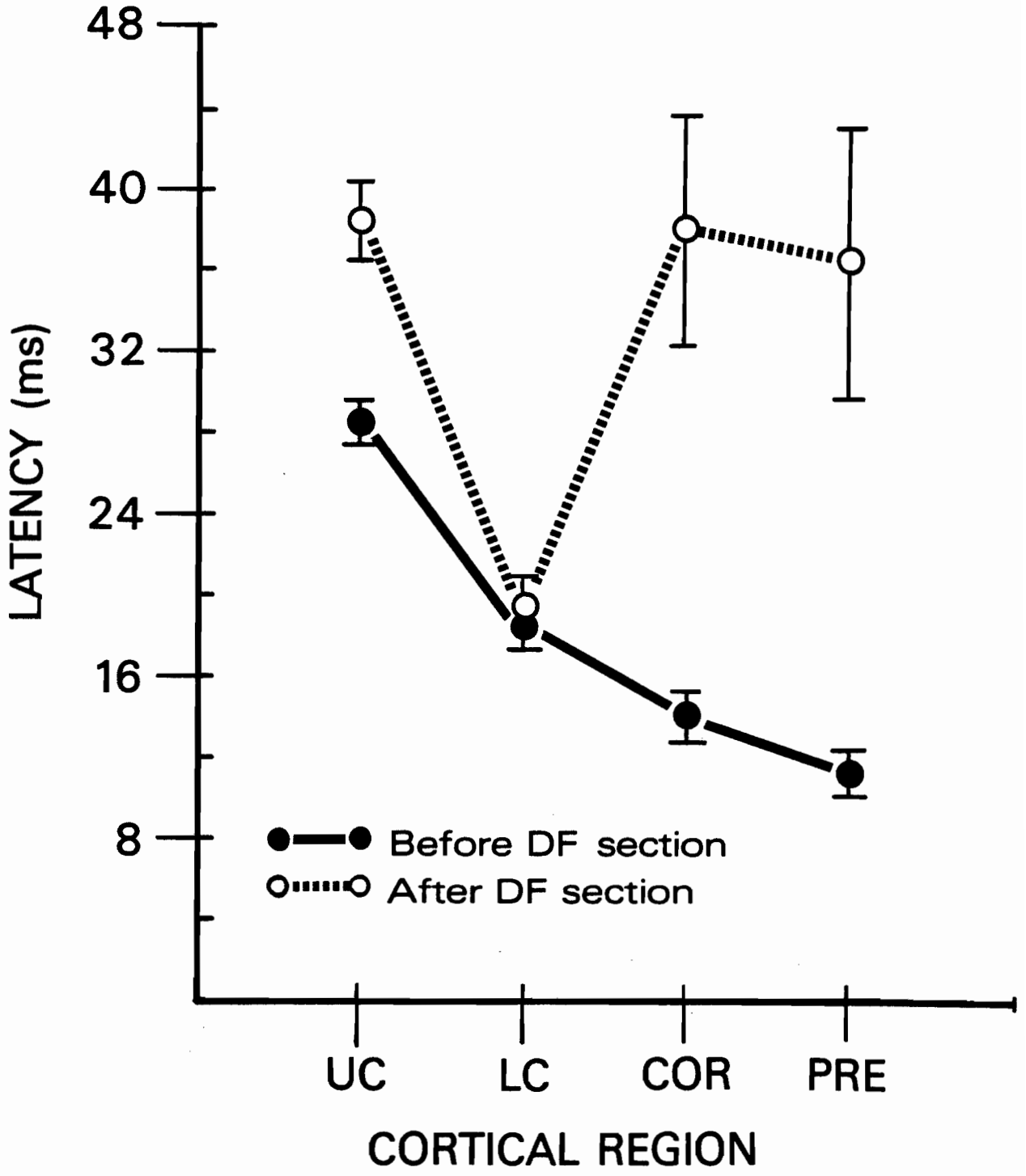
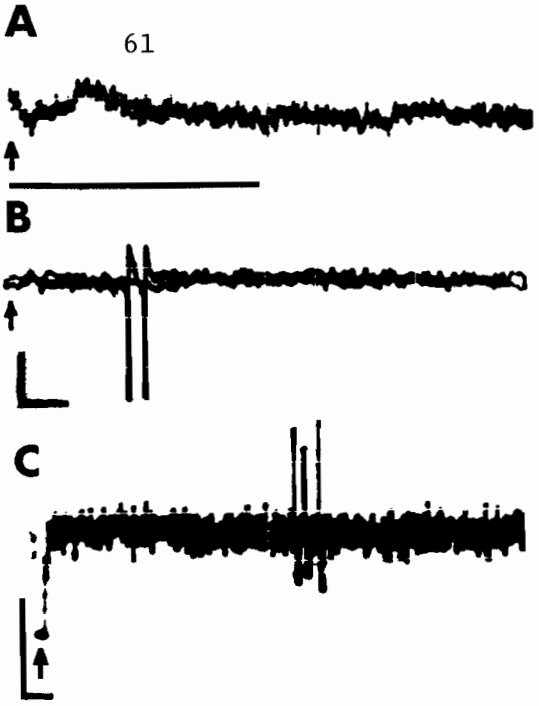
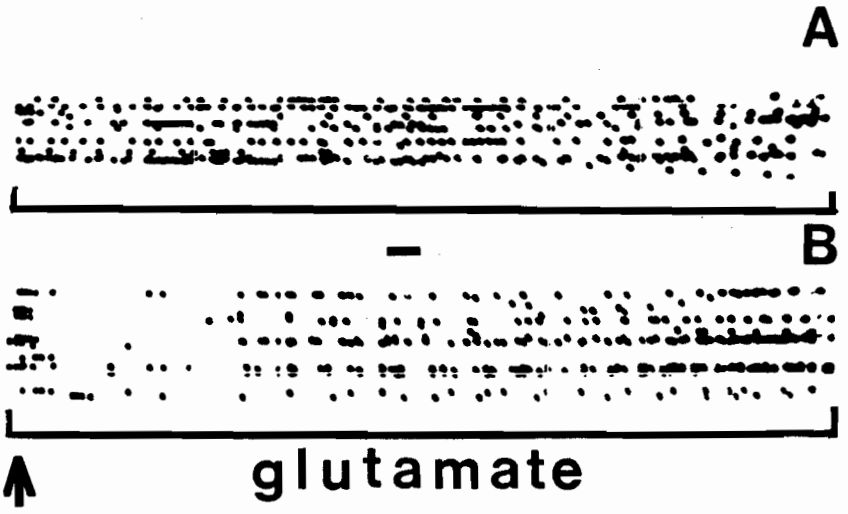

48
40
32
24
16
8
LATENCY (ms)
Before DF section
After DF section
UC
LC
COR
PRE
CORTICAL REGION

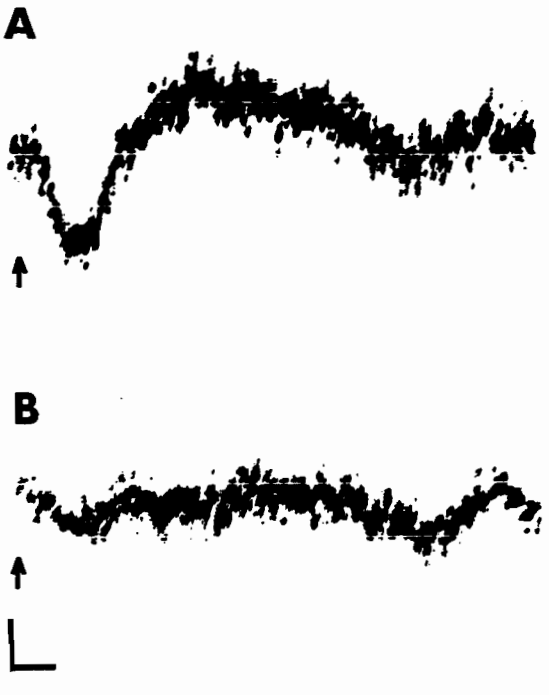
Fig. 2.2.3 Composite figure showing: first three traces, A- afferent volley recorded from dorsal rootlets of the first cervical segment to stimulation (1.1T) of the ipsilateral suboccipital nerve to the rectus capitis dorsalis major and obliquus capitis caudalis muscles of the dorsal neck; B- short latency unit response evoked in contralateral presylvian region to stimulation (1.1 T) of the suboccipital nerve, as above, before dorsal funiculus section; C- late response of another cell in presylvian region to stimulation of the suboccipital nerve (2.0 T), after the lesion.

Middle traces: A- Raster display of glutamate-induced activity of unit in presylvian region; B- the glutamate induced activity is decreased with 1.2T intensity of stimulation of the contralateral suboccipital nerve.

Lower two traces: A- averaged evoked field activity (64 sweeps, 125 ms sweep time) in the ventral bank of the cruciate sulcus to threshold electrical nerve stimulation of the contralateral biventer cervicis/complexus muscles before dorsal funiculus section; B- recording location, intensity, and nerve stimulated, as above, after dorsal funiculus section. Vertical calibration: 80 μV; horizontal calibration, 5 ms; stimulation at arrows.


A
B
C


A
B
glutamate


A
B

with increased release of glutamate, indicating that a true inhibitory process was involved (Krnjevic, Randic and Stranghan, 1966). Stimulation of the contralateral biventer cervicis/complexus nerve elicited inhibitory effects in five units, while that of the suboccipital nerve decreased the firing frequency of six units. Converging inhibitory effects with stimulation of each of these nerves were observed in one unit. Thresholds for inhibition varied between 1-2.5T, with three of the units inhibited with stimulus intensities at, or near (1.1-1.3T) threshold.

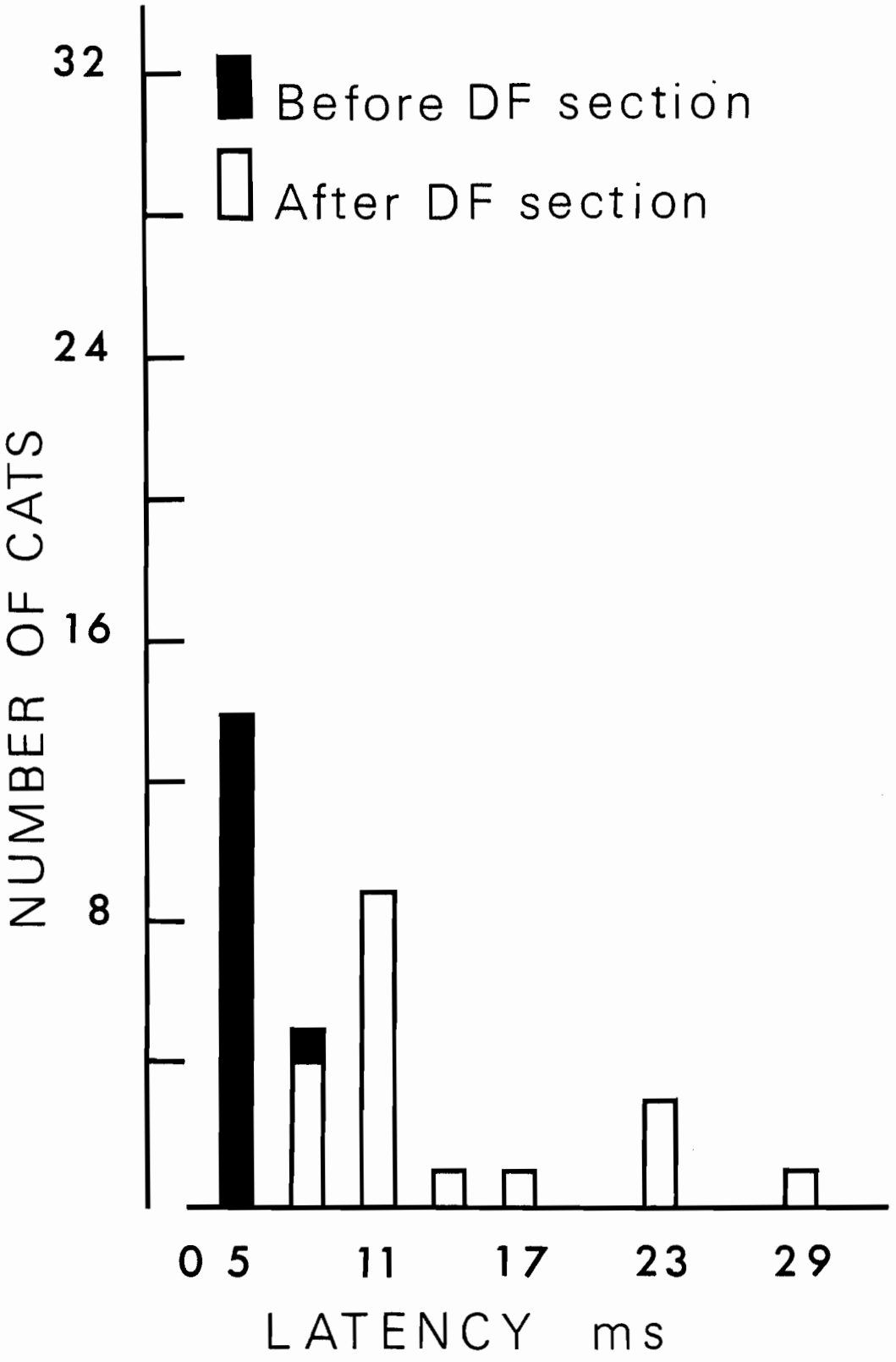
After dorsal funiculus section

Following recording from a sample of units which included neurons responding with stimulus intensities at, or near, threshold, the dorsal funiculus was sectioned unilaterally contralateral to the recording site above the C_1 level (Fig. 2.2.5G). Unit recording was continued with the same penetration as preoperatively, or in a penetration adjacent to the previous one.

After dorsal funiculus section, field and unit activity to threshold stimulation of dorsal neck muscle nerves was abolished (Fig. 2.2.3). With increased intensities of stimulation (1.5-3T), field activity with significantly longer latencies (7-29 ms compared with 4-9 ms pre-operatively), could still be recorded ($p<.01$ by t-test for dependent samples, see also Fig. 2.2.4). The interval of onset to peak amplitude of evoked field activity was also significantly increased after the lesion ($p<.01$).

Seventy-two cells were recorded after dorsal funiculus section. Five units which responded with threshold intensity of contralateral

Fig. 2.2.4 Onset of averaged field activity (64 sweeps) at various sites in the frontal cortex following threshold stimulation of dorsal neck muscle nerves in 19 cats before dorsal funiculus (DF) section, and evoked activity at longer latencies with 1.8-3T nerve stimulation after dorsal funiculus section. Stimulation was contralateral to the recording site.


32
24
16
8
NUMBER OF CATS
Before DF section
After DF section
0 5
11
17
23
29
LATENCY ms

dorsal neck muscle nerve stimulation before the section were not responsive postoperatively, even though their background activity could still be recorded in the frontal cortex indicating that the cells were not lost. It was not possible to test more units in this manner, since units were usually lost during the microdissection. Stimulation of the contralateral biventer cervicis/complexus nerve resulted in evoked responses in 32 out of 64 cells tested (50%), while responses to the contralateral suboccipital nerve to the rectus capitis dorsalis major/ obliquus capitis caudalis muscles resulted in 9 out of 47 cells tested (19%). These values show 17% and 20% decreases to stimulation of the two muscle nerves, respectively, when compared with pre-operative values (Table 2.2.1). In contrast, the number of units responsive to stimulation of the biventer cervicis/complexus ipsilateral to the recording site was 19 out of 39 cells tested (48%), a value which is comparable to the preoperative figure of 47% responsive units (Table 2.2.1). This indicates that the decrease in responsive units with contralateral nerve stimulation on the side of the lesion was not a result of general unresponsiveness of the brain due to the lesion, but rather due to interruption of a pathway involved in the transmission of these peripheral signals to the frontal cortex. Further, the absence of response to threshold stimulation after the lesion was not due to an increase in the postoperative threshold itself, since dorsal root potentials were recorded at the previous threshold levels after the lesion, whereas single cell and field activity in the frontal cortex were not. The percentage of cells which were unresponsive to stimulation of dorsal neck muscle nerves was 36% after the lesion compared with 14% preoperatively.

There was also a reduction in the proportion of units showing inhibitory effects to stimulation of dorsal neck muscle nerves. Five out of 24 units tested (21%) showed inhibitory effects with postoperative stimulation of dorsal neck muscle nerves compared with 30% of the units inhibited preoperatively. Three of these units were inhibited with stimulation of the contralateral biventer cervicis/complexus, and two with stimulation of the suboccipital nerve. These results, and the fact that inhibition of neuronal responses was observed with threshold intensities of stimulation of dorsal neck muscle nerves before but not after dorsal funiculus section, suggest that this pathway is at least partly involved in the transmission of inhibitory signals to these frontal brain regions as well.

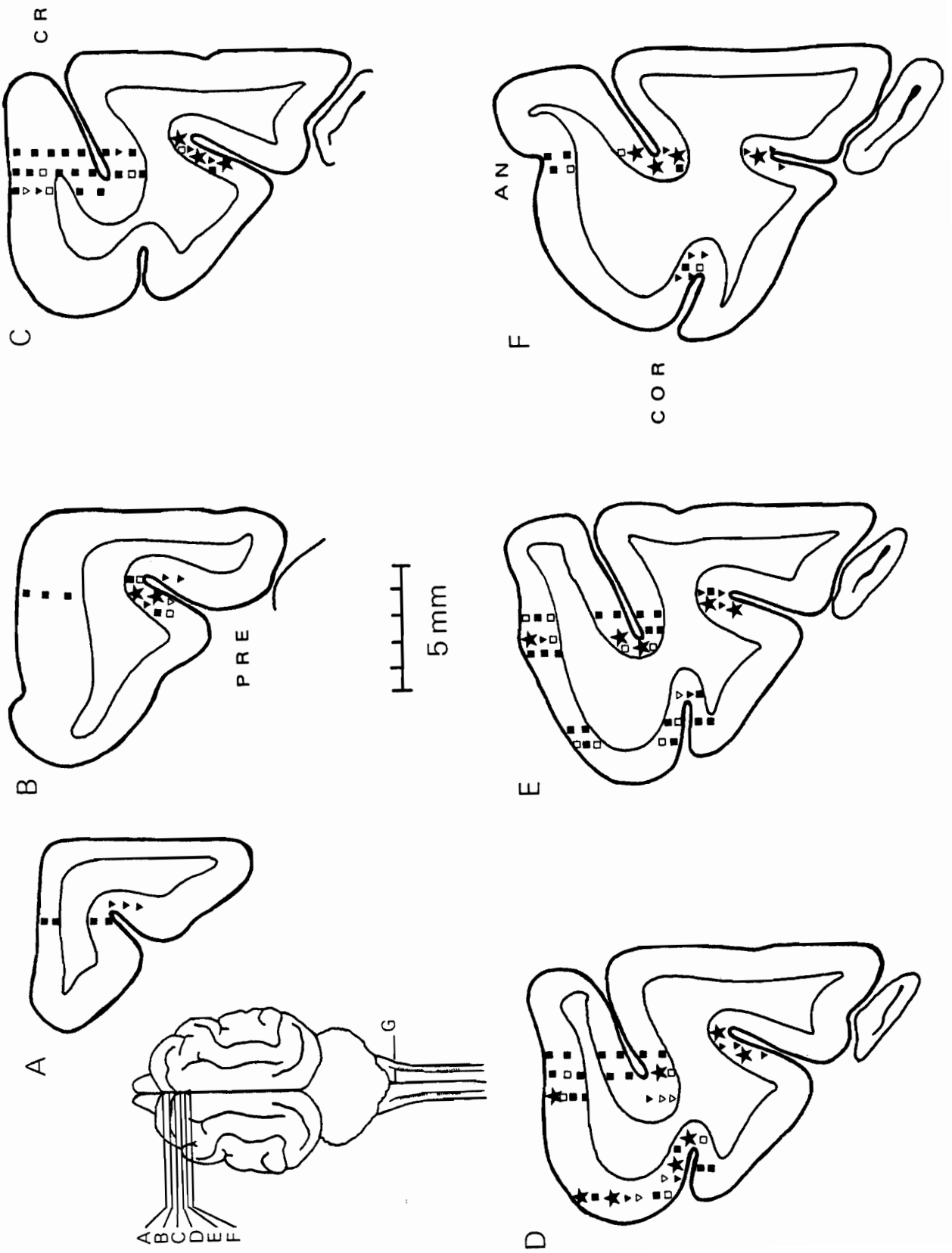
Unit following frequencies were 0.1-0.3/s, and the latencies of response to contralateral nerve stimulation were 12-110 ms (Fig. 2.2.1). A one-way analysis of variance showed overall significant differences between pre- and postoperative neuronal latency responses to stimulation of contralateral neck muscle nerves ($p<0.01$). No significant differences were observed with ipsilateral nerve stimulation ($p>0.05$). The relationship between postoperative mean latency response and cortical region was different than the preoperative trend (Fig. 2.2.2). Units with early (5-10 ms) latencies were never recorded postoperatively. Moreover, units with latencies of 56-110 ms were recorded after but not before the lesion (Fig.2.2.1), suggesting that other organizational changes also took place, as has been noted in other systems after dorsal funiculi lesions, or deafferentation (Bowsher, 1971; Dostrovsky and Millar, 1977; Dostrovsky, Millar and Wall, 1976; Dreyer et al, 1974; Fadiga and

Manzoni, 1969; Millar, Basbaum and Wall, 1976). These relatively long latency units were recorded in coronal and presylvian regions and account for the variability at these levels seen in Fig. 2.2.2. With the exception of these very long latencies, the four sub-regions were more homogeneous with respect to latency responses to contralateral nerve stimulation after the lesion. A one-way analysis of variance of latencies in the dorsal cruciate, ventral cruciate, coronal, and presylvian cortex showed no statistically significant differences among these four cortical regions, $p>.05$. The mean latency response was significantly increased after the lesion in the dorsal bank of the cruciate sulcus, and in coronal and presylvian regions ($p<.01$), but was not significantly affected in the lower bank of the cruciate sulcus, ($p>.05$ by t-test comparisons).

HISTOLOGICAL RESULTS

Responsive sites before and after dorsal funiculus section were determined through microscopic examination of histological slides with the explored regions using the electrolytic lesions and the micro-manipulator scale readings recorded during the experiment, to calculate the depth of the units. The identified responsive sites were marked on diagrams of coronal sections of the frontal cortex of the cat (Fig. 2.2.5). In agreement with earlier findings, (Experiment 1, Chapter 2, and Dubrovsky and Barbas, 1977), responsive units to dorsal neck muscle afferents were located in pericruciate and presylvian regions. In addition, a projection to the lateral sigmoid gyrus, and on the dorsal and ventral banks of the coronal sulcus was also identified (Fig. 2.2.5). The distribution of responsive units in the various regions is shown in Table 2.2.1.

Fig. 2.2.5 Coronal diagrams of the cat frontal cortex (left) showing responsive sites to electrical stimulation of afferents from dorsal neck muscles. Squares show responses to the biventer cervicis/complexus nerve; triangles, to the suboccipital nerve; stars show responses with threshold electrical nerve stimulation of both contralateral dorsal neck muscle nerves tested; black symbols before, and hollow symbols after dorsal funiculus section. G on the dorsal view of the cat brain (left), shows the level of transection of the dorsal funiculus above the C_1 level contralateral to the recording site (A-F). CR: cruciate sulcus; COR: coronal sulcus; AN: ansate sulcus; Pre: presylvian sulcus. All above represent responsive sites to contralateral nerve stimulation.


A
B
C
D
E
F
G
PRE
CR
AN
COR
5mm
A B C D E F

The electrophysiologically characterized group 1 muscle afferents projected in small cortical bands within regions corresponding with the cytoarchitectonic areas 3, 4, and 6 (Hassler, 1966; Hassler and Muhs-Clement, 1964), posterior the cruciate sulcus, and in presylvian regions. Some of the more dorsally situated projection sites overlap with the ones which receive group 1 muscle afferents from the forelimb of the cat in area 3a, which reach these regions via the dorsal funiculus also (Landgren et al, 1967; Oscarsson and Rosen, 1964; 1966; Silfvenius, 1968). Out of 40 units responding to threshold stimulation of contralateral muscle nerves, 10 were in pericruciate, 12 in coronal, and 18 in presylvian regions.

Units showing inhibitory effects to dorsal neck muscle nerve stimulation preoperatively were distributed in pericruciate (7 units) and presylvian (5 units) regions; none were recorded in the lateral sigmoid and coronal gyrus regions. After the lesion, one unit inhibited with contralateral nerve stimulation was recorded in a pericruciate region, two in presylvian, and two in coronal gyrus regions.

The summary of the histological results of the dorsal funiculus lesions is shown in Table 2.2.2 and representative photographs of complete and partially sectioned dorsal funiculi are shown in Fig. 2.2.6. The extent of sparing in Table 2.2.2 is expressed as a percentage of the area of the contralateral control homologous region for each brain. Edematous tissue is indicated with an asterisk; the percentage figures in these cases are likely exaggerated since this tissue was expanded. In 14 animals the lesions were complete, and except in two, were restricted to the dorsal funiculus. In these cases there was 25% and 15% damage to

TABLE 2.2.2

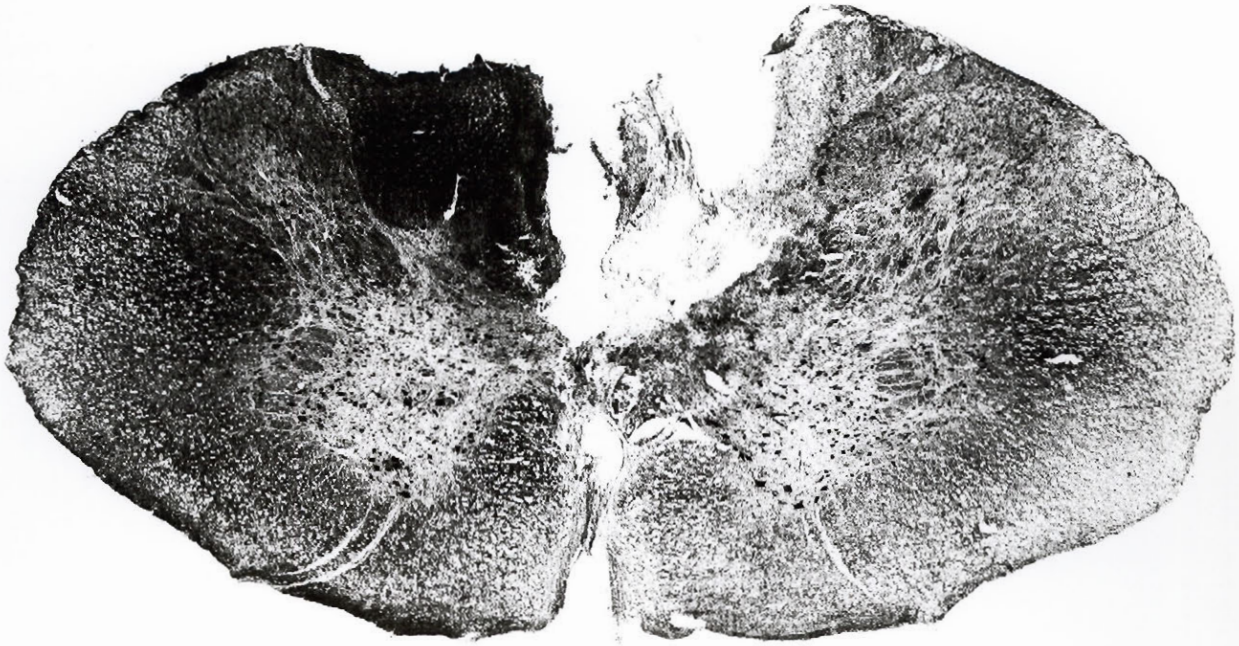
Percent Sparing of Dorsal Funiculus Regions Compared with the Area of the Contralateral Control Side.

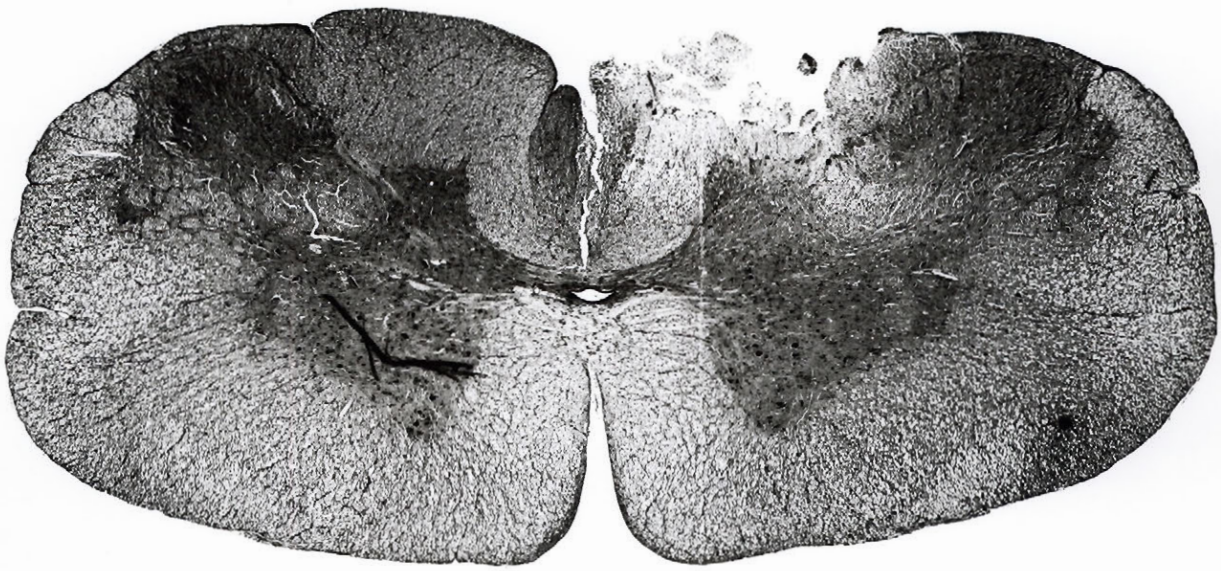
Cat. No.	Gracilis	Medial Cuneate	Lateral Cuneate
18	0%	14% 35%*	0%
21	90%	50%	0%
33	90%	40%	0%
36	63%*	0%	10%*
37	63%	34%	11%
38	25%, 30%*	14%, 50%*	10%*
39	20%, 70%*	20%, 50%*	0%
42	65%	23%, 42%*	35%*
44	50%*	49%*	49%*
45	70%	30%	0%
46	30%, 50%*	80%	48%*

In 14 cases (not shown in Table 2.2.2) the dorsal funiculus was complete and except in two was restricted to the dorsal funiculus. In these two, there was a 25% and 15% damage to the dorsal horn, respectively.

*edematous tissue.

Fig. 2.2.6 Photograph of coronal sections of the spinal cord in two cats showing complete destruction of the dorsal funiculus (top), and partial damage (bottom). Note complete destruction of the lateral fasciculus cuneatus on the bottom section and edematous tissue in the medial fasciculus cuneatus and gracilis; also note apparent sparing ventromedially within the medial fasciculus cuneatus. Cresyl violet; magnification, 19.5X.





the dorsal horn. The rest of the brains showed various degrees of sparing mostly restricted to the medial fasciculus cuneatus and fasciculus gracilis. The lateral fasciculus cuneatus, which is expected to carry the neck afferents, was completely lesioned in all but five cases, where edematous tissue of 10-49% was noted, and in one case in which there was 11% sparing ventromedially. Since there were no differences in the results in cases with extensive edematous tissue in the lateral part of the cuneate, such as number 44 compared with others with complete lesions, it is likely that edematous tissue is non-functional.

2.2.4 DISCUSSION

The results presented indicate that the units recorded in frontal brain regions in response to stimulation of contralateral dorsal neck muscle afferents come from two populations. One of these consists of those cells which could be activated with threshold or 1.1-1.3 T intensities of peripheral nerve stimulation, had generally short (5-12 ms) latencies, and could follow stimulus frequencies of 0.5-2.0/s. The second group consists of those cells which were activated with higher electrical stimuli (1.8-3T), had latencies of activation of 12-46 ms, and could only follow consistently stimuli 0.1-0.4/s. Transmission of dorsal neck muscle afferent signals to the first group of cells, which comprised approximately 20% of the sample studied, is via the dorsal funiculus, since no cells with these characteristics were recorded after transection of this pathway ipsilateral to the stimulated side. The afferents influencing these cells were electrophysiologically characterized

as belonging to group 1. The second group of cells received their afferent input via pathways other than the dorsal funiculi, since a sample of units with characteristics similar to those in the second group responded to neck muscle afferent stimulation after the lesion.

Dorsal funiculus section, therefore, resulted in a decrease in the relative number of responsive units to contralateral dorsal neck muscle afferent stimulation (Table 2.2.1), and to an increase in their mean latency (Fig. 2.2.2). These results parallel those of Dobry and Casey (1972) where a decrease in the number of units with short latency responses to somatic stimuli was observed in the coronal somatosensory cortex in cats with chronic dorsal funiculi lesions. Their results in cats with acute lesions were more variable, which might be due to the smaller lesions in these animals. However, when latencies of evoked responses were recorded both before and after dorsal funiculi section in the same unit, the latencies to somatic stimuli were increased postoperatively for at least some of these units.

The ventral zone of the cuneate nucleus, which receives group 1 muscle afferents from the forelimb (Rosen, 1969; Rosen and Sjölund, 1973) and includes a representation of the neck region (Millar and Basbaum, 1975), projects to the nucleus ventralis posterolateralis (VPL) of the thalamus (Hand and Van Winkle 1977), which in turn projects to the coronal somatosensory cortex (Hand and Morrison, 1972). In addition, the cuneate nucleus sends some afferents to the nucleus ventralis posteromedialis (VPM) of the thalamus, which has an input to the presylvian cortex. The group 1 afferents from the dorsal neck may course through the dorsal funiculus via these known anatomical routes to the coronal and presylvian cortex.

Regions within the cytoarchitectonic areas 4 and 6, (Hassler and Muhs-Clement, 1964) however, do not receive direct projections from the VPL and the VPM which together comprise the ventrobasal complex of the thalamus, (Hand and Morrison, 1972); these cortical regions receive an input from the nucleus ventralis lateralis (VL) (Asanuma and Fernandez, 1974a; 1974b; Hand and Morrison, 1972; Rispal-Padel, Massion and Grangetto, 1973; Strick, 1970). However, ventral zones of the cuneate which receive afferents from deep structures, also project to a number of brainstem and other thalamic nuclei (Hand and Van Winkle, 1977) and group 1 afferents to pericruciate regions may course through these other routes. An additional possibility is that pericruciate units receive this group 1 afferent input via the sensory cortex, a hypothesis which is supported by both physiological (Thompson, Stoney and Asanuma, 1970; Zarzecki, Shinoda and Asanuma, 1976), and anatomical (Grant, Landgren and Silfvenius, 1975; Jones and Powell, 1968) data. A group 1 projection from the forelimb muscles to area 3a in cats (Oscarsson and Rosen, 1963) and monkeys (Lucier et al, 1975; Phillips, Powell and Wiesendanger, 1971) has been demonstrated, and projections from neck muscles (Dubrovsky and Barbas, 1977; Landgren and Silfvenius, 1968) reach the postcruciate dimple in area 3a, which forms a transitional region between the sensory and motor cortices (Hassler, 1966). The latencies of response of all cells, including those receiving group 1 afferents, were longer in pericruciate than in coronal and presylvian regions in the present study. This finding is consistent with both a subcortical indirect route of these afferents, and with a cortico-cortical input from sensory to pericruciate motor regions. If evoked neuronal responses in pericruciate regions depended on an initial activation of a

sensory area, then similar changes might be expected to occur in neuronal responses in both regions after interference with the primary response. This was indeed the case for neurons recorded on the dorsal bank of the cruciate sulcus after dorsal funiculus section, but not for neurons on the ventral bank of this sulcus (Fig. 2.2.2), even though both regions had an approximately equal number of units influenced by group 1 afferents preoperatively and even though this input was removed in both regions after the lesion. Whereas there was a predominance of unit evoked responses at latencies in the range of 40-49 ms on the dorsal bank of the cruciate sulcus with an increase in the mean post-operative latency, neither the mean, nor the range of latencies were affected for units on the ventral bank of this sulcus postoperatively. A mean latency increase was also observed for units in the coronal and presylvian cortex, and further, latencies of 50-110 ms were recorded after but not before the lesion in these regions. The parallel increases in the unit postoperative mean latency in coronal, presylvian, as well as those on the dorsal bank of the cruciate, coupled with the fact that the former two regions receive direct thalamic input from the ventrobasal complex but the latter does not, suggest that a group 1 input from neck muscles to units of the dorsal bank of the cruciate may depend on a cortico-cortical projection from area 3a or from coronal and presylvian regions. The ventral bank of the cruciate may receive group 1 afferent input via other subcortical routes. That the organization of the dorsal and ventral banks of the cruciate may be different, is also suggested by the fact that these regions receive afferent input from two different regions of the VL (Strick, Hand and Morrison, 1972).

As was reported in the last experiment, the dorsal and ventral banks of the cruciate sulcus received afferents mainly from the biventer cervicis and complexus muscles, and presylvian regions received input from these muscles and also from the suboccipital. The present results confirm those findings and extend the regions of influence of neck muscle afferents to the dorsal and ventral banks of the coronal sulcus which have characteristics similar to those of presylvian regions with respect to the dorsal neck muscle afferent input.

The present results showed that it is the dorsal funiculus which is largely involved in these low threshold projections which evoke short latency responses in the frontal cortex. Even though the actual reduction in responsive units after dorsal funiculus section was only 20%, the significant increases in the mean latency response in three of the four cortical regions studied could have important consequences on fine motor control. Lesions of the posterior sigmoid gyrus in the cat, which include the pericruciate regions reported here, have been shown to result in a deficit on a proprioceptive-dependent task involving the forelimb, and a head turning response deficit (Glassman, 1971).

The evolution of the dorsal funiculus is associated in phylogeny with the differentiation of the limbs, and is more developed in animals with high limb agility (see Norton, 1973 for review). Consequent to these developments, the coordinated use of the limbs and the head, which carries the distance receptors of vision and audition, made exploration of the environment possible. The fact that signals from the neck and the forelimb (Landgren et al, 1967; Oscarsson

and Rosen, 1963; 1966) project via the dorsal funiculus and partly overlap in the frontal cortex is not surprising. These brain regions may be involved in the control of coordinated movement. Even though head and limb movement can proceed in the absence of proprioceptive afferents (Bizzi, Polit and Morasso, 1976; Bossom, 1972; 1974; Knapp, Taub and Berman, 1963; Taub and Berman, 1968; Taub, Goldberg and Taub, 1975), the preoperative quality of movement and fine motor control is affected (Dubrovsky and Garcia-Rill, 1973). Proprioceptive signals from the neck and the limbs via the dorsal funiculus to the frontal cortex may be involved in this latter aspect of movement.

CHAPTER 3

3.1 FRONTAL PROJECTIONS OF EXTRAOCULAR MUSCLES

3.1.1 INTRODUCTION

The previous two studies demonstrated that dorsal neck muscle afferents project to regions of the cat frontal cortex at latencies of 5-46 ms. These results, and previous findings of single unit discharge activity preceding head movement in monkeys (Bizzi and Schiller, 1970; Robinson and Jarvis, 1974), or dorsal neck muscle activity in cats (Guitton and Mandl, 1978b), suggest that these regions may be involved in the neural control of head movement. However, since head movement elicits eye movements in a direction opposite to that of the head, a reflex which is necessary for distinct vision, head and eye movements must be coordinated. In fact, electrical stimulation of regions within the ventral bank of the cruciate sulcus and in the presylvian field results in coordinated eye-head movement in the cat (Hassler, 1966). Since dorsal neck muscle afferents reach frontal regions which overlap with those eliciting eye and head movement upon stimulation, the experimental question I posed was whether extraocular muscle afferent signals also reach these regions.

The results showed that extraocular muscle afferents reach and have both excitatory and inhibitory effects in frontal cortical regions, where they converge with dorsal neck muscle afferents at the single cell level.

3.1.2 METHODS

Experiments were performed on 34 cats anesthetized with alpha chloralose (60 mg/kg, i.v.) dissolved in 25% urethane solution.

Exposure of the globe and the superior and lateral rectus muscles was achieved after removal of the frontal sinus, the overlying soft tissues, and the levator palpebrae superioris muscle. The branch of the third nerve to the superior rectus, and the sixth nerve to the lateral rectus were exposed and prepared for stimulation contralateral to the recording site after the superior and lateral walls of the orbit were removed, and the globe was collapsed by removal of the aqueous and vitreous humor and the crystalline lens. In 12 experiments the superior rectus nerve was prepared for stimulation bilaterally. Nerve stimulation consisted of single pulses of 3-9 V for 50-90 μs, or train stimuli (see Experiment 1 Chapter 2).

The frontal cortex was exposed unilaterally as previously described. Stimulation and recording procedures were also already described.

3.1.3 RESULTS

FIELD AND SINGLE CELL

Field and single cell activity was recorded in pericruciate, lateral sigmoid, presylvian, and on the dorsal and ventral banks of the coronal sulcus, in response to electrical nerve stimulation of the superior rectus and the lateral rectus muscles of the eye. Responses of 318 units were recorded, of which 54 responded to the ipsilateral and 126 to the contralateral superior rectus muscle nerve, while 75 responded to the contralateral lateral rectus muscle nerve (Table 3.1.1).

TABLE 3.1.1

Number of Responsive Units to Stimulation of Extraocular Muscle Nerves in the Cat Frontal Cortex.

Muscle nerve stimulated	Number of units tested	Number of responsive units		Distribution of responsive units			
				UC	LC	COR	PRE
Contralateral superior rectus	313	126	(40%)	46	50	10	20
Ipsilateral superior rectus	163	54	(33%)	20	15	14	5
Contralateral lateral rectus	161	75	(47%)	33	13	20	9

Abbreviations:

UC: dorsal bank of cruciate sulcus; LC: ventral bank of cruciate sulcus; COR: dorsal and ventral banks of coronal sulcus; PRE: presylvian field.

Several units responded to stimulation of more than one muscle nerve. Converging excitatory effects of afferents from the superior rectus of both eyes were observed in 46% of the cells tested. Afferents from the contralateral lateral rectus converged with those from the ipsilateral and the contralateral superior rectus in 51% and 42% of the units tested, respectively, while 28% of the units responded to all these nerves stimulated (Table 3.1.2).

The response latencies to stimulation of extraocular muscle nerves contralateral to the recording site, varied between 7 and 50 ms, while ipsilateral responses occurred at 11-50 ms (Fig. 3.1.1). The shortest response latencies were recorded for units 5-7 mm ventral to the surface of the cortex, and were in regions within the presylvian field or the coronal cortex, depending on the medio-lateral site of the microelectrode penetration (see coronal diagrams in Fig. 3.1.6). The longest responses were dorsal to the cruciate sulcus near the cortical surface. For responses to contralateral nerve stimulation, the curves relating latency and depth show a similar trend, (Fig. 3.1.2) suggesting that these afferents reach the frontal cortex via parallel pathways. Ipsilateral responses were generally longer, even though considerable overlap occurred at various cortical depths. Unit following frequencies with contralateral nerve stimulation were 0.5-1.5/s.

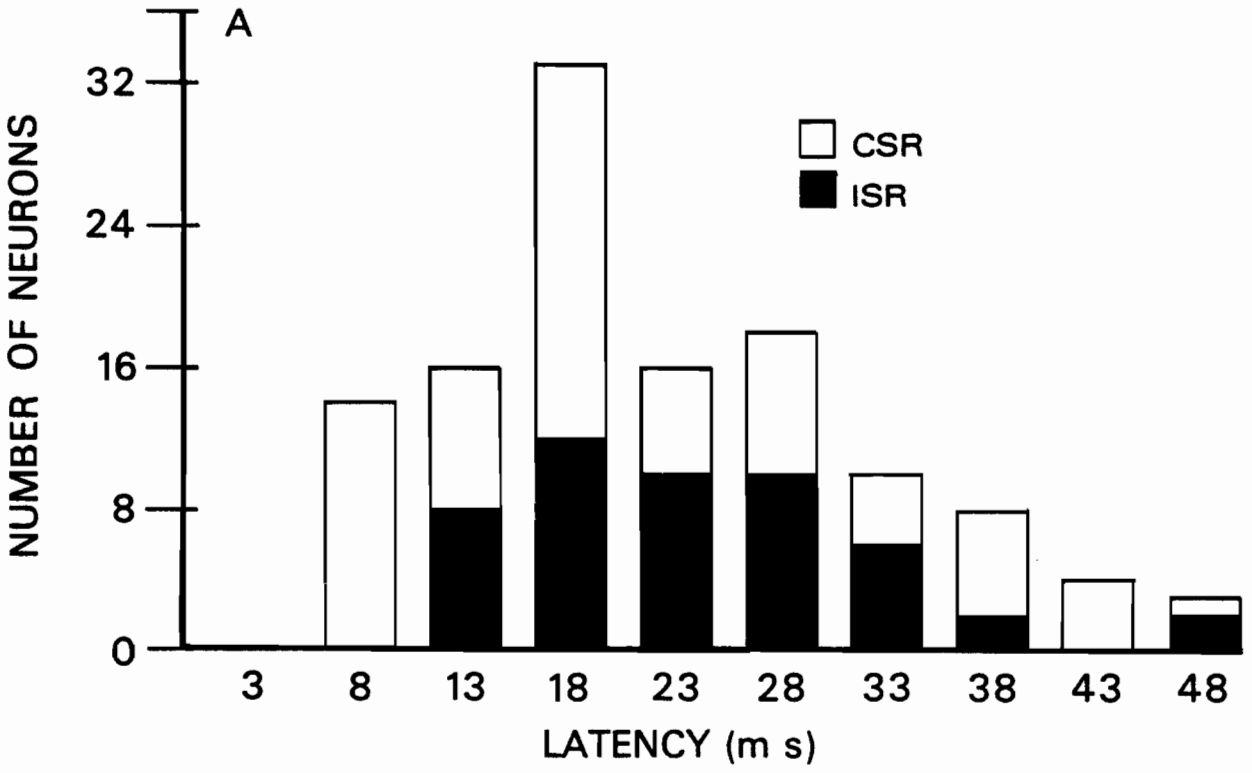
Inhibitory effects were also observed with stimulation of extraocular muscle nerves, as evaluated extracellularly against a background of glutamate-induced excitation (see Experiment 1, Chapter 2). These effects were either in the form of a general reduction of the background activity (observed in 7 units), or complete cessation of neuronal activity during a fixed time interval (observed in 13 units).

TABLE 3.1.2

Convergence of Extraocular Afferents in the Frontal Cortex

Muscle nerves stimulated	Number of units tested	Number of units showing convergence
Contralateral superior rectus and ipsilateral superior rectus	72	33 (46%)
Contralateral superior rectus and contralateral lateral rectus	78	33 (42%)
Ipsilateral superior rectus and contralateral lateral rectus	73	37 (51%)
Contralateral superior rectus and ipsilateral superior rectus and contralateral lateral rectus	67	19 (28%)

Fig. 3.1.1 Interval histogram illustrating the distribution of the response latencies of neurons in pericruciate, presylvian and coronal gyrus regions following electrical nerve slimulation of the contralateral (CSR) and ipsilateral (ISR) superior rectus muscle, A, and the contralateral lateral rectus muscle (CLR) of the eye, B. The numbers along the abscissae indicate the midpoint of each latency interval.


A
NUMBER OF NEURONS
32
24
16
8
0
CSR
ISR
3
8
13
18
23
28
33
38
43
48
LATENCY (m s)

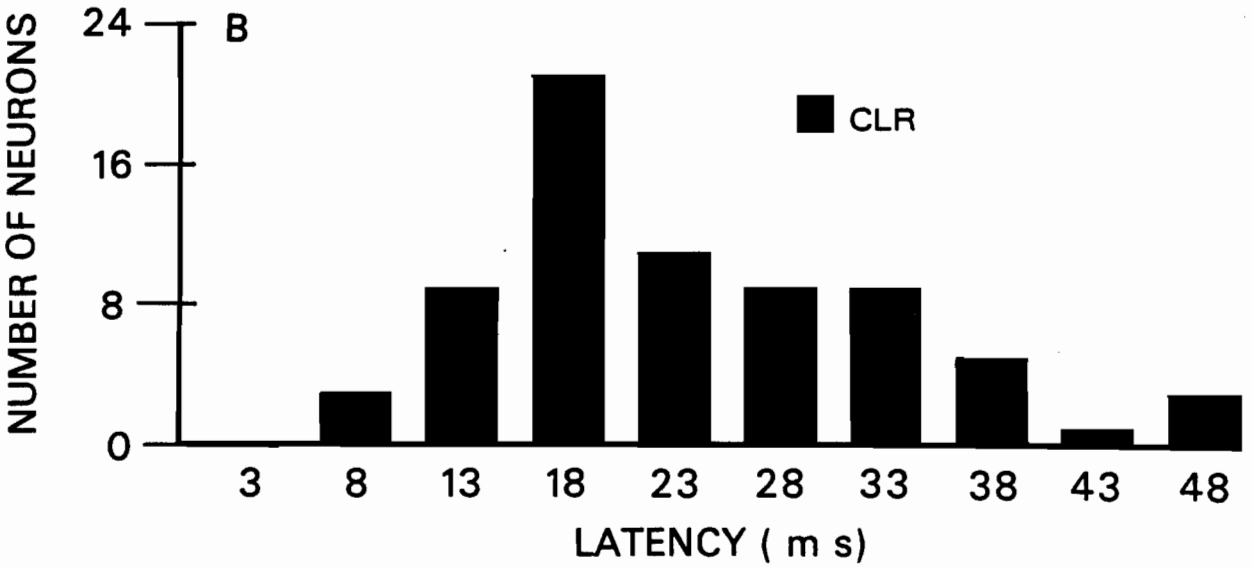
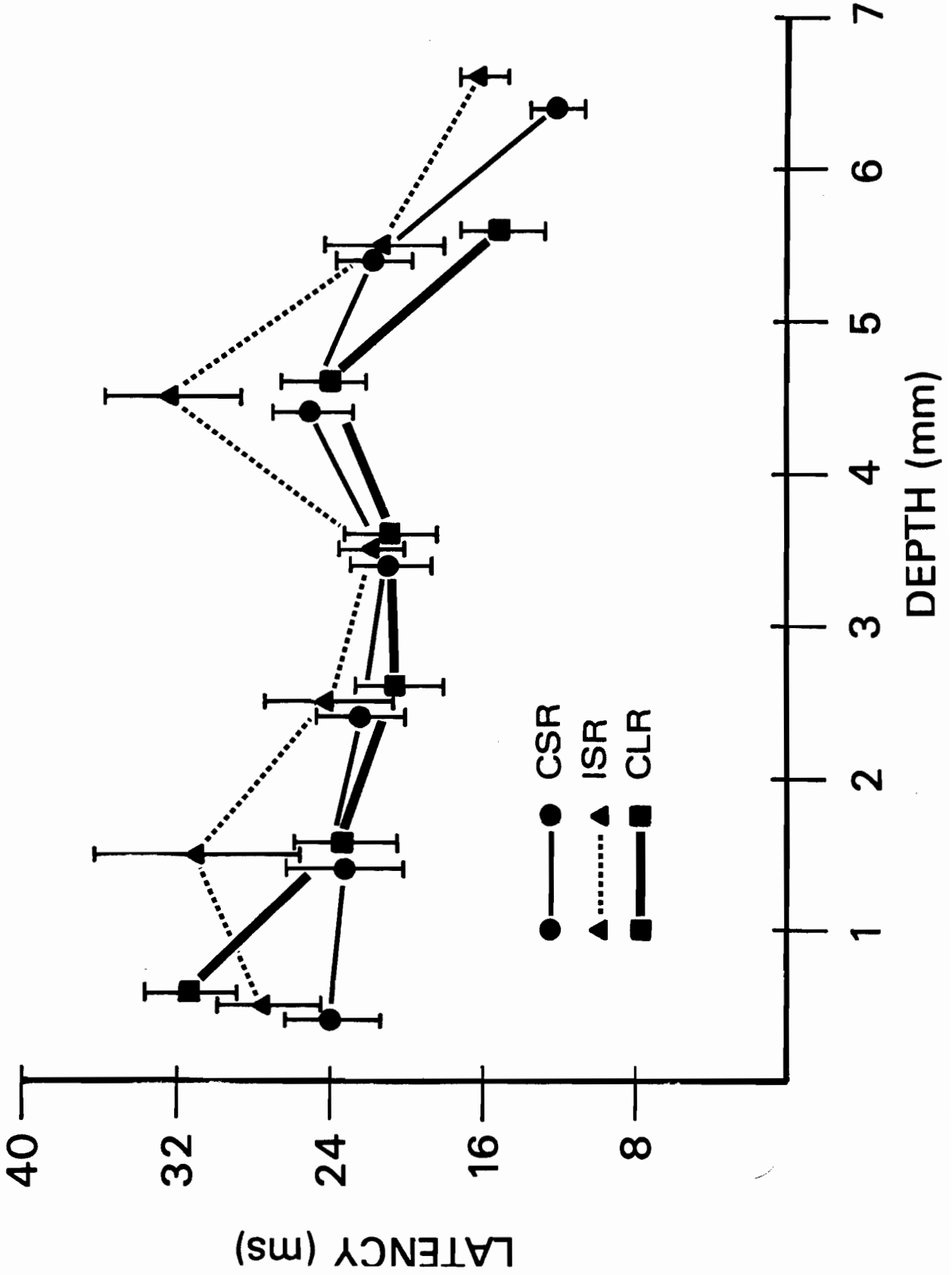

B
NUMBER OF NEURONS
24
16
8
0
CLR
3
8
13
18
23
28
33
38
43
48
LATENCY (m s)

Fig. 3.1.2 Mean unit response latencies to stimulation of extraocular muscle nerves as a function of the depth of the recording site in relation to the surface of the cortex above the cruciate sulcus. Each point represents the mean of latencies recorded within one mm steps. Vertical bar at each point indicates ± standard error. CSR: contralateral superior rectus; ISR: ipsilateral superior rectus; CLR: contralateral lateral rectus.


LATENCY (ms)
40
32
24
16
8
1
2
3
4
5
6
7
DEPTH (mm)
CSR
ISR
CLR

Out of 93 cells tested in 11 experiments, 20 were inhibited with stimulation of one extraocular nerve. In 19 cases it was impossible to achieve a sustained response with glutamate release to test for inhibitory effects, as these cells responded for an initial 3 to 4 s and subsequently ceased firing.

Eleven of 63 cells tested showed inhibitory effects with stimulation of one extraocular muscle nerve and were otherwise unresponsive to the other nerves tested. One of these showed a generalized decrease of its firing frequency with stimulation of the contralateral superior rectus. Stimulation of the ipsilateral superior rectus decreased the firing frequency of two units at latencies greater than 50 ms, and throughout a 200 ms interval in two others. A decrease in unit activity between 10-20 ms, 40-80 ms, and 45-75 ms (Fig. 3.1.3D), time intervals was observed in three units following stimulation of the contralateral lateral rectus, while three others showed a generalized decrease of their firing activity over an interval of 200 or 400 ms.

The rest of the units inhibited were also activated by at least one other extraocular muscle nerve stimulation. Excitatory and inhibitory responses assumed a well defined pattern for the superior rectus whose nerves were prepared for stimulation in both eyes in 10 experiments. Thus, whereas units were excited with stimulation of the superior rectus muscle nerve of one eye, they were inhibited with stimulation of the homologous muscle nerve of the contralateral eye. This pattern was observed in 9 of 30 cells tested. Two of these units were also responsive to stimulation of the lateral rectus muscle nerve. The latency of excitation by one input and that of inhibition by the other overlapped in 6 cases,

Fig. 3.1.3 Composite figure showing:

A - Unit response in ventral bank of the cruciate sulcus to electrical nerve stimulation of the ipsilateral superior rectus muscle; B- Glutamate-induced excitation of the cell is decreased with stimulation of the nerve of the superior rectus muscle of the contralateral eye. Note that the interval of excitation in A, and that of inhibition in B overlap.

C- Raster display showing glutamate-induced excitation of unit on the dorsal bank of the coronal sulcus; D- the glutamate-induced excitation of the unit is decreased starting at 50 ms after electrical nerve stimulation of the contralateral lateral rectus muscle nerve.

E- Glutamate-induced excitation of unit on the dorsal bank of the cruciate sulcus; the induced excitation is decreased with electrical nerve stimulation of the contralateral lateral rectus muscle of the eye, F, and with the biventer cervicis/complexus nerve of the dorsal neck, G. E-G represent eight superimposed sweeps. Nerve stimulation only at arrows.

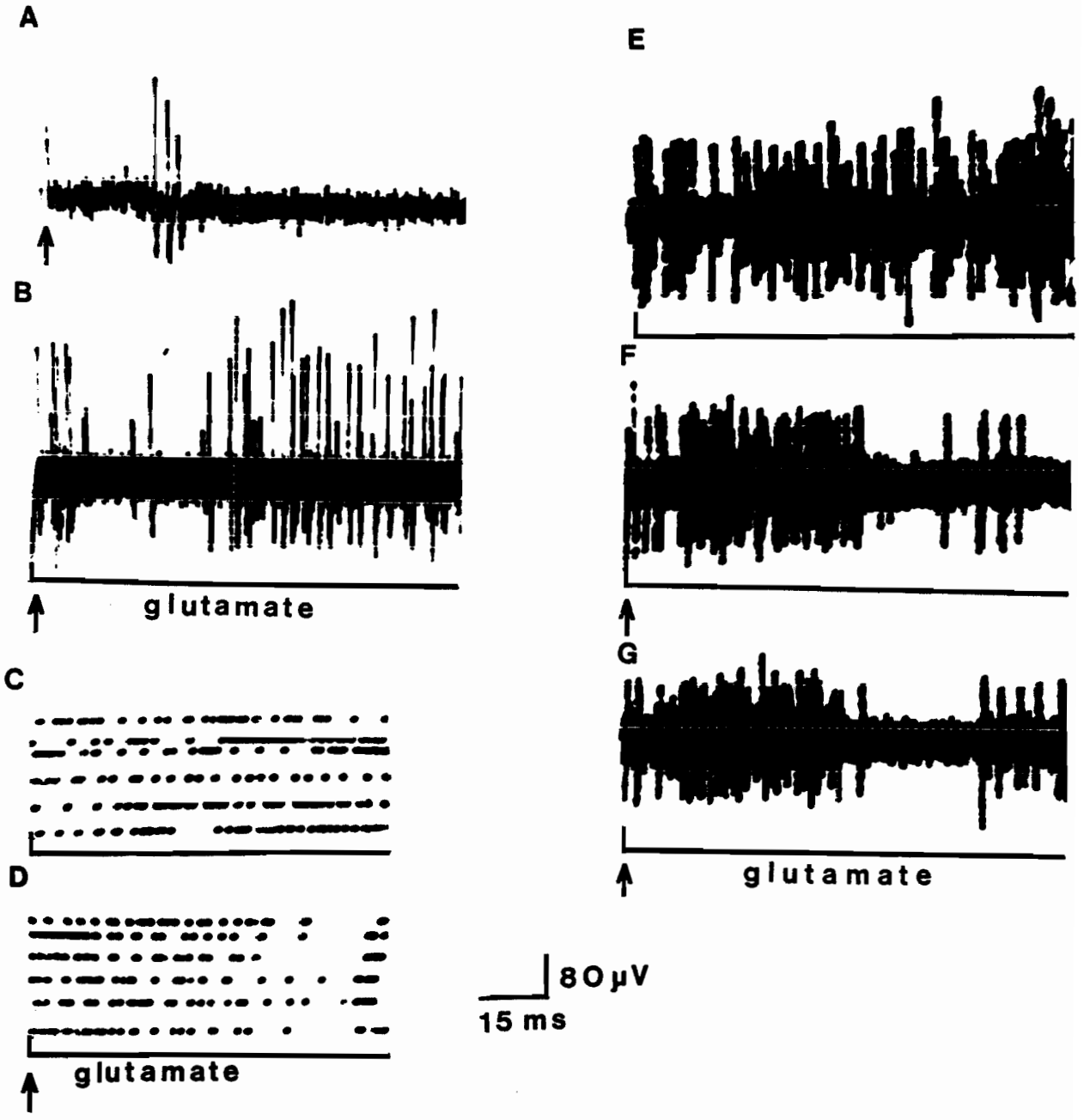

A
B
glutamate
C
D
glutamate
E
F
G
glutamate
80 µV
15 ms

Fig. 3.1.4 Cell response with two spikes in the dorsal bank of the cruciate sulcus following electrical nerve stimulation of the biventer cervicis/complexus, A, the rectus capitis dorsalis major/ obliquus capitis caudalis of the dorsal neck, B, and the superior rectus muscle of the eye, C, contralateral to the recording site.

Neuronal response in lower bank of the cruciate sulcus following electrical nerve stimulation of the contralateral biventer cervicis/complexus of the dorsal neck, D, the ipsilateral superior rectus, E, and the contralateral superior rectus of the eye, F, Note response with two spikes in D and E and two bursts of three spikes in F. Stimulation at arrows.

(Fig. 3.1.3 A and B), whereas in two others unit activity decrease was observed later. The last of these units showed a generalized reduction of the frequency of its background firing activity. Decrease of neuronal activity with stimulation of more than one of the nerves tested was never observed.

The initial experiments in this study showed that the extraocular muscle projection sites were in regions which overlapped with those receiving projections from the dorsal neck muscles. In order to determine whether afferents from the extraocular and dorsal neck muscles have an input onto the same frontal units, nerves from both extraocular and neck muscles were prepared for stimulation in 30 experiments.

3.2 CONVERGENCE OF EXTRAOCULAR AND DORSAL NECK MUSCLE AFFERENTS ON FRONTAL CORTICAL UNITS.

EXCITATORY CONVERGENCE

Convergence between one extraocular and one neck muscle nerve was observed in 136 of 213 cells tested (64%), and included both contralateral and ipsilateral nerves from both dorsal neck and extraocular muscles. This degree of convergence was higher than that observed between pairs of extraocular muscle nerves (Table 3.1.2), or between pairs of dorsal neck muscle nerves (Table 2.1.2). Extraocular muscle afferents showed the highest degree of convergence with afferents from the longitudinally extended dorsal neck muscles which included the biventer cervicis and complexus. These converged with afferents from the contralateral superior rectus in 85 of 137 units tested (62%), and with afferents from the contralateral lateral rectus in 37 out of 70 cells tested (53%).

On the other hand, afferents from the smaller suboccipital neck muscles, rectus capitis dorsalis major and obliquus capitis caudalis converged to a lesser extent with extraocular muscle afferents. Responses to suboccipital muscle nerve afferents and to the contralateral superior rectus occurred in 24 out of 91 cells tested (26%), and in 14 out of 47 cells (30%) they converged with afferents from the lateral rectus muscle of the eye (Table 3.2.1).

Stimulation of extraocular and dorsal neck muscle afferents with the lowest intensities required to elicit neuronal activity resulted in approximately the same number of spikes in 60% of the units, which received converging input (Fig. 3.1.4) while in 40% of the units stimulation of one nerve elicited more spikes than stimulation of one other, or others (Fig. 3.1.5).

Although not systematically studied, it was observed that simultaneous stimulation of one dorsal neck and one extraocular muscle nerve resulted in a greater number of spikes than stimulation of each nerve separately, indicating that spatial and/or temporal summation occurred. Additional evidence of this phenomenon was revealed with apparent increases in the number of spikes as single pulse stimuli to the nerve were changed to trains. It was also noted that simultaneous stimulation of two muscle nerves resulted in unit evoked responses, while no response was elicited when each of the nerves was stimulated separately. This was more commonly observed with pairs of extraocular muscle nerves, than with dorsal neck/extraocular, or two dorsal neck muscle nerves.

TABLE 3.2.1

Convergence of Extraocular and Dorsal Neck Muscle Afferents in the Frontal Cortex

Muscle nerves stimulated	Number of units tested	Number of units showing convergence
Contralateral biventer cervicis/ complexus, and contralateral superior rectus	137	85 (62%)
Contralateral biventer cervicis/ complexus, and contralateral lateral rectus	70	37 (53%)
Contralateral superior rectus and contralateral rectus capitis dorsalis major/obliquus capitis caudalis	91	24 (26%)
Contralateral lateral rectus and contralateral suboccipital	47	14 (30%)

Fig. 3.1.4 Cell response with two spikes in the dorsal bank of the cruciate sulcus following electrical nerve stimulation of the biventer cervicis/complexus, A, the rectus capitis dorsalis major/ obliquus capitis caudalis of the dorsal neck, B, and the superior rectus muscle of the eye, C, contralateral to the recording site.

Neuronal response in lower bank of the cruciate sulcus following electrical nerve stimulation of the contralateral biventer cervicis/complexus of the dorsal neck, D, the ipsilateral superior rectus, E, and the contralateral superior rectus of the eye, F, Note response with two spikes in D and E and two bursts of three spikes in F. Stimulation at arrows.

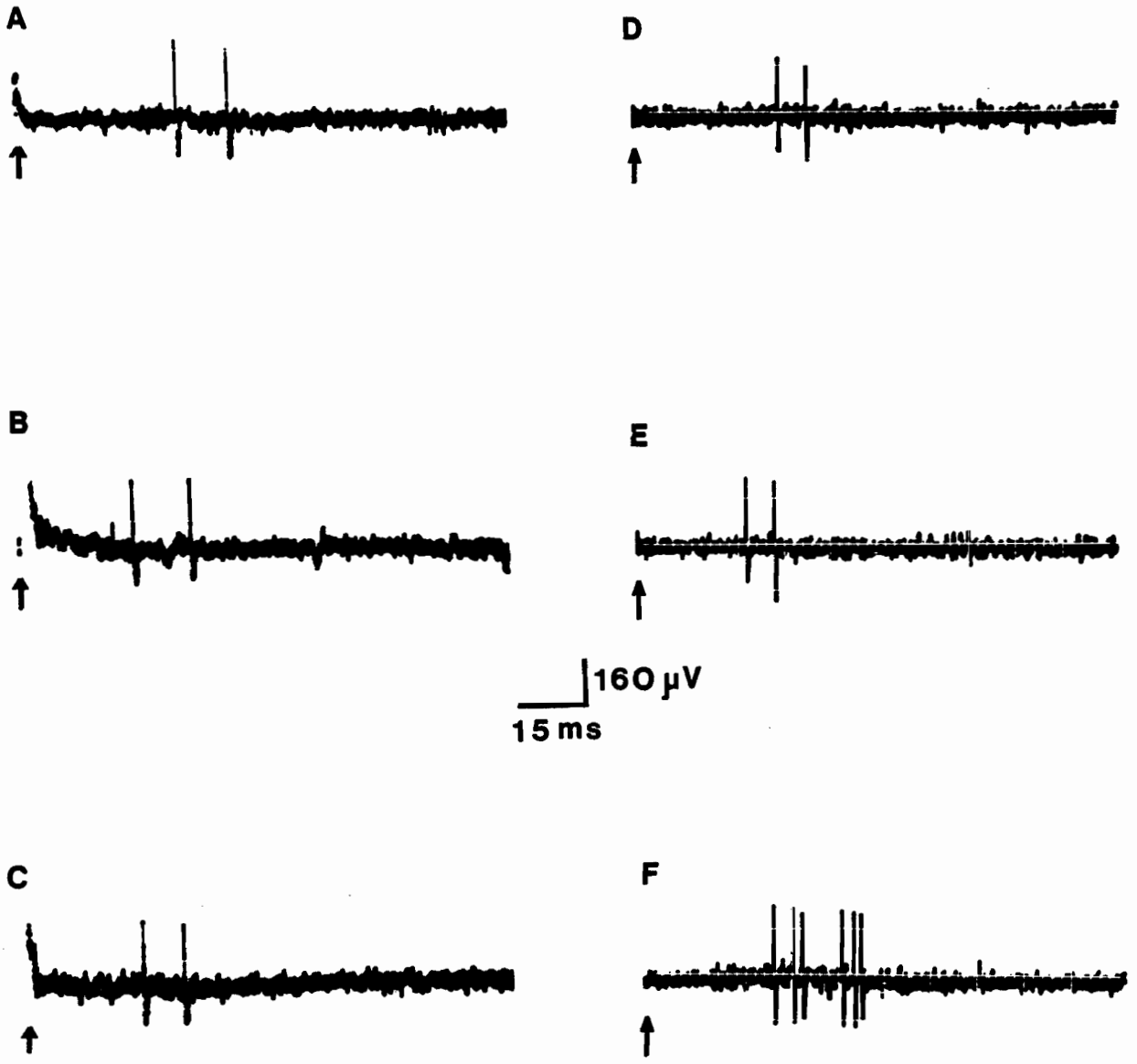
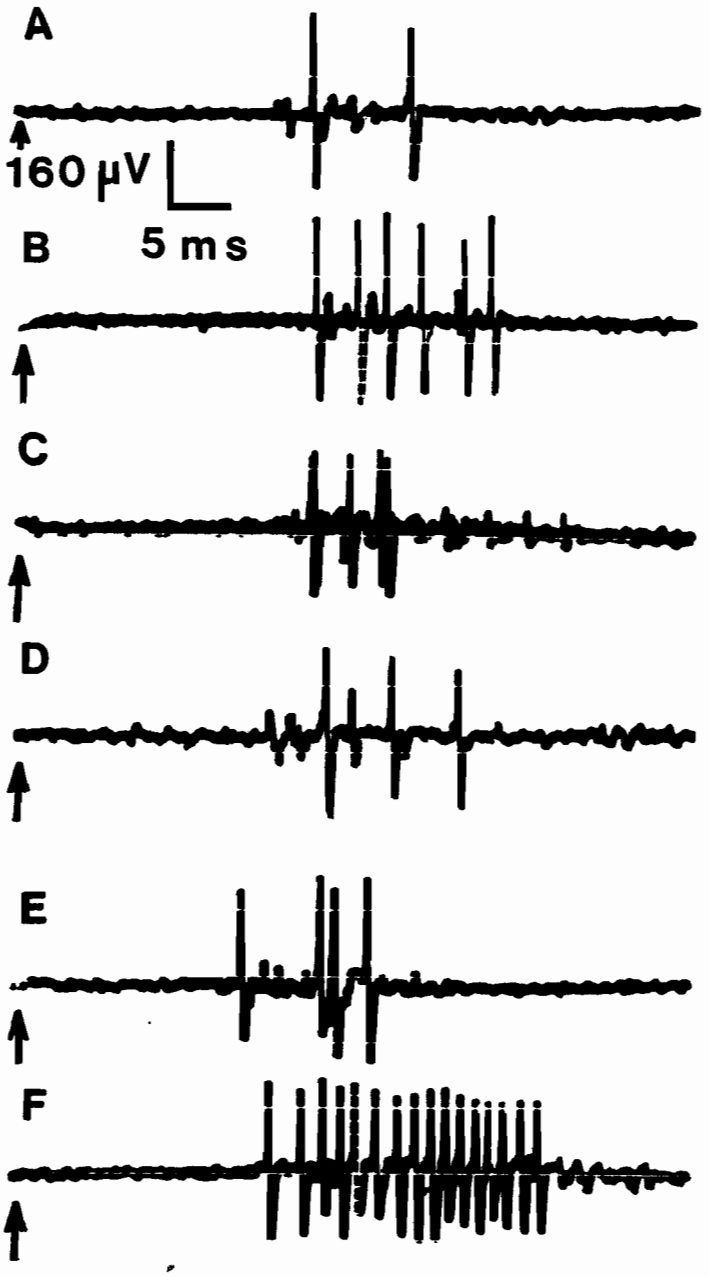

A
D
B
E
160 µV
15 ms
C
F

Fig. 3.1.5 Converging effects of dorsal neck (A-C) and extra-ocular (D-F) muscle afferents on neuron in the ventral bank of the cruciate sulcus. Stimulating the ipsilateral, A, and contra-lateral biventer cervicis/complexus, B; the contralateral rectus capitis dorsalis major/obliquus capitis caudalis, C; the contra-lateral lateral rectus, D; and the contralateral, E, and ipsi-lateral superior rectus, F. Note that the number of spikes differs with stimulation of the various nerves. Nerve stimulation at arrows.


A
160 µV
5 ms
B
C
D
E
F

INHIBITORY CONVERGENCE

Extraocular and dorsal neck muscle afferents also showed converging inhibitory effects on four frontal cortical units. All these cells were inhibited with stimulation of the biventer cervicis and complexus nerve; in addition, three were inhibited with stimulation of the contralateral lateral rectus and one with stimulation of the contralateral superior rectus. The interval of inhibition by the pair of extraocular and dorsal neck muscle afferents overlapped in three cases, and was 10-20 ms, 40-80 ms, and 45-75 ms, respectively (Fig. 3.1.3 right). In one case both the neck and extraocular muscle nerve stimulation resulted in a generalized decrease in the glutamate induced excitation of the unit. None of these inhibited units showed other excitatory or inhibitory effects with stimulation of the other extraocular or dorsal neck muscle nerves tested.

LATENCIES

Extraocular muscle afferents converged with afferents from dorsal neck muscles that were activated with threshold intensities of electrical nerve stimulation in 24 out of 35 cases tested, and with dorsal neck muscle afferents that required 1.5-2T intensities for activation in the rest of the cases. The latencies of the units receiving both extraocular and dorsal neck muscle afferent input were 7 ms to 45 ms, depending on the site of recording. Seventy-one percent of the units receiving converging afferents showed an evoked response at the same latency or varied by 1 to 3 ms with stimulation of one dorsal neck and one extraocular muscle nerve, both contralateral to the recording site. In 24% of the units there

was a difference of 5-10 ms with stimulation of each of these afferents, with the shortest latency evoked with dorsal neck afferent stimulation in 80% of these. For the rest of the units (5%) there was a difference of 11-25 ms, with contralateral dorsal neck muscle afferents always evoking the shorter latencies of response.

HISTOLOGICAL RESULTS

The responsive sites to extraocular muscle nerve stimulation were in narrow bands within 1 mm anterior, to 2 mm posterior the cruciate sulcus rostro-caudally,2.5 to 10.5 mm from the midline, and 0.5-8 mm dorso-ventrally (Fig. 3.1.6). The distribution of responsive units in the various regions is shown in Table 3.1.1).

Sixty-four per cent of the units receiving both extraocular and dorsal neck muscle afferent input were on the anterior, posterior and lateral sigmoid gyrus, in pericruciate regions, (A-D on the dorsal view of the cat brain in Fig. 3.1.6). The rest of the units were approximately equally distributed in the dorsal and ventral banks of the coronal sulcus, and in the presylvian field. Photographs of samples of the four main cortical regions explored are shown in Fig. 3.1.7.

3.2.1 DISCUSSION

The present findings showed that stimulation of extraocular muscle nerves elicited single unit activity in the cat frontal cortex at latencies of 7 to 50 ms. The wide distribution of response latencies of frontal units may be a reflection of the varied conduction velocities of afferent fibers observed in these nerves (Bach-y-Rita and Ito, 1966a).

Fig. 3.1.6 Coronal diagrams of the cat frontal cortex (left) showing responsive sites to electrical nerve stimulation of extraocular muscles. CSR: contralateral superior rectus; CLR: contralateral lateral rectus; INH: sites of neurons showing inhibitory effects with extraocular muscle nerve stimulation.

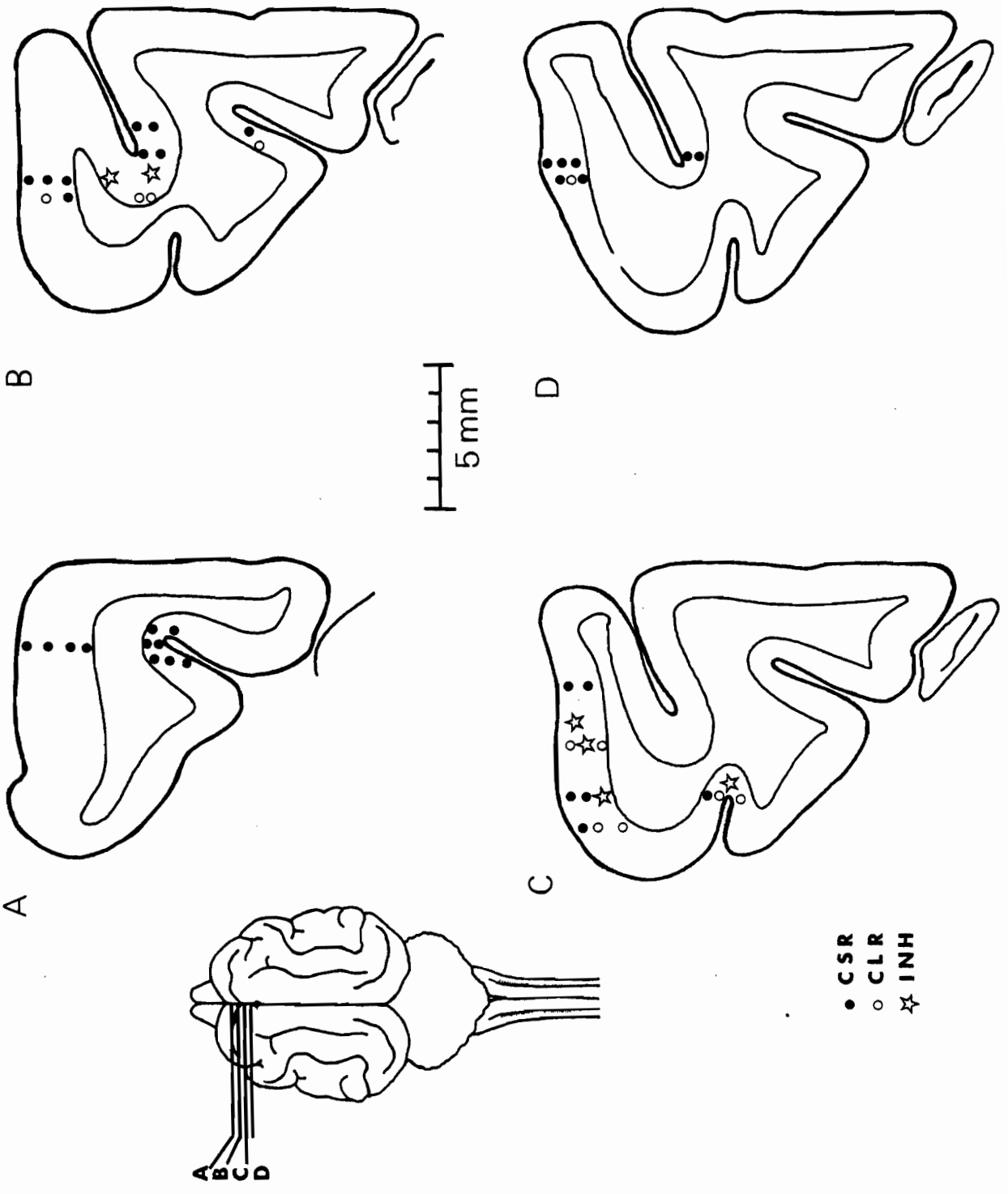
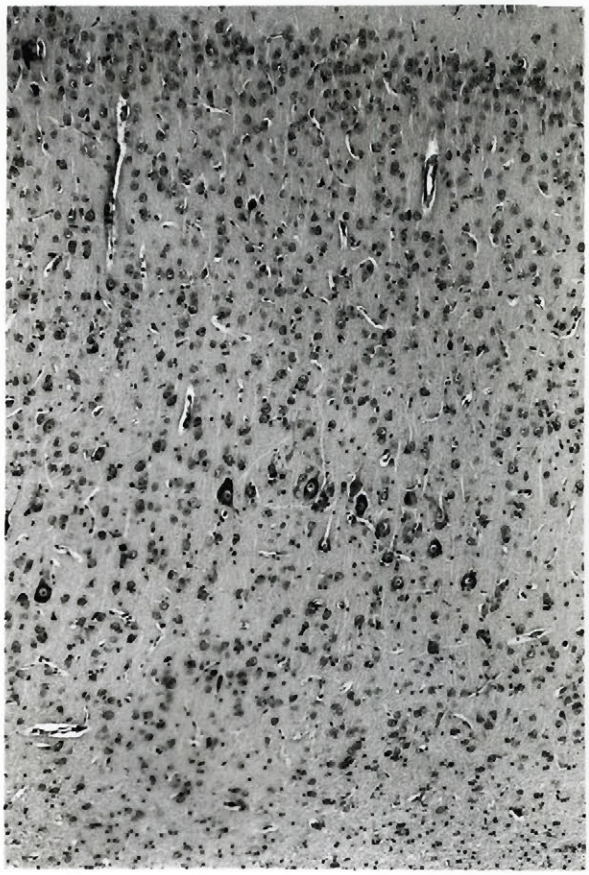
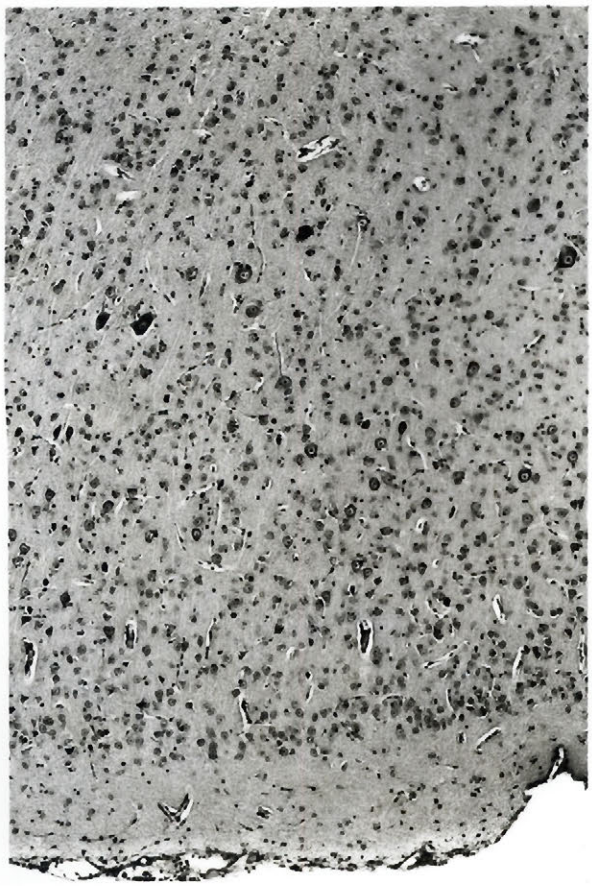
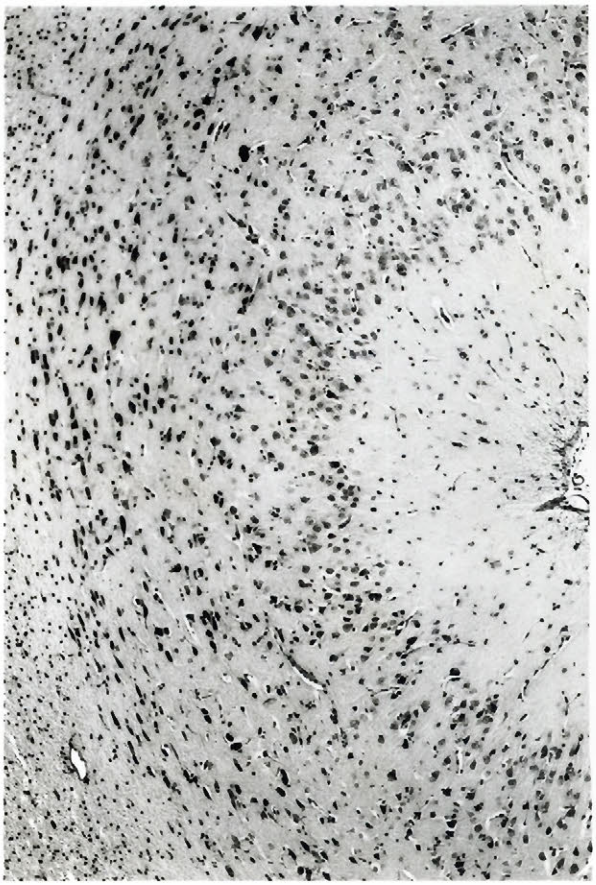

A
B
C
D
5 mm
• CSR
○ CLR
☆ INH
A
B
C
D

Fig. 3.1.7 Photomicrograph showing samples of the frontal regions traversed in the microelectrode penetrations where responsive units to electrical nerve stimulation of extraocular and dorsal neck muscles were located. The samples were taken from, top (left): dorso-lateral bank of the cruciate sulcus; top (right): ventro-lateral bank of the cruciate sulcus; bottom (left): dorsal back of the coronal sulcus; bottom (right): cortical region above the presylvian sulcus (partly shown on the right). All four samples were photographed from a single coronal section 1 mm posterior the cruciate sulcus. Cresyl violet; magnification, 63X.







In addition, differences of synapses along the way may have also contributed to these varied latency responses. The course of the pathway(s) of afferent fibers from the extraocular muscles of the cat to the central nervous system has been a matter of considerable debate. Extraocular afferents run peripherally along the motor nerves and then separate and join the ophthalmic branch of the trigeminal nerve (Batini and Buisseret, 1974; Batini et al, 1975). However, at least some of the afferents of the abducens nerve to the lateral rectus remain in the motor nerve (Bach-y-Rita and Murata, 1964; Batini and Buisseret, 1974). The location of the cell bodies of the primary afferents has also not been clearly established (Corbin and Harrison 1942; Fillenz, 1955). However, recent experimental evidence indicates that some of the cell bodies of the lateral rectus afferents are in the trigeminal mesencephalic nucleus (Alvarado-Mallart et al, 1975). The course of the extraocular muscle afferents to the frontal cortex is not known beyond the presumed brain stem level, and it is not known if it is the same for all the extraocular muscle nerves studied. The functions relating latency of response and depth of the units below the surface of the cortex for the three nerves tested (Fig. 3.1.2) indicate that the latency of response is largely dependent on the site of the units; this suggests that for a given site the superior and lateral rectus muscle afferents follow parallel pathways to these frontal cortical regions.

Stimulation of extraocular muscle nerves also had inhibitory effects on units in the frontal cortex. The excitatory and inhibitory effects observed were quite complex. For example, it is not immediately apparent why stimulation of the superior rectus nerve of one eye activated, while

that of the contralateral eye inhibited the same unit, while on other occasions afferents from the superior rectus of both eyes showed converging excitatory effects on frontal units (Table 3.1.2). On the efferent side, as a consequence of the anatomical arrangement of the extraocular muscles on the globe, complex mechanical changes occur in these muscles during the various types of eye movements (Davson, 1972). The afferent signals conveyed to a particular unit in the frontal cortex may depend on the state of the muscle. In the case of the superior rectus, this is different during upward vertical deviation of the eye, when this muscle contracts, than during horizontal eye movement, when this muscle actively maintains tension (Davson, 1972). It has been argued that the constraints implicit in the kinematic laws of eye movement are imposed by neural mechanisms (Nakayama, 1975), and that the neurally determined agonistic-antagonistic interactions in extraocular muscle pairs depend on the state of the organism, such as wakefulness and sleep (Nakayama, 1975). It may be that these relationships are also different in the awake and anesthetized preparation.

Complex patterns of excitation and inhibition with natural stimulation of wrist muscles (which also exert forces in various directions upon contraction) were also observed in the external cuneate nucleus, including excitation with natural stimulation of one muscle, and inhibition with stimulation of one of its synergists (Rosen and Sjölund, 1973). It is clear that the agonistic-antagonistic interactions observed at the segmental level do not necessarily hold at the suprasegmental level (Eyzaquirre and Fidone, 1975). The complex excitatory-inhibitory interactions observed in the present study may reflect a different level of analysis of these peripheral signals in the frontal cortex.

Extraocular muscle afferents project to a number of brain regions, including the brainstem (Fillenz, 1955), the superior colliculus (Abrahams and Rose, 1975), the cerebellum (Baker et al, 1972; Batini et al, 1974; Fuchs and Kornhuber, 1969; Schwartz and Tomlinson, 1977), and the cerebral cortex (Buisseret and Maffei, 1977; Dubrovsky and Barbas, 1977; Landgren and Silfvenius, 1968). The function of extraocular proprioceptors is a much-debated subject, and several hypotheses have been proposed, including their participation in mechanisms underlying saccadic correction in the cerebellum (Fuchs and Kornhuber, 1969), position sense (for review see Bach-y-Rita, 1971, 1975) and in binocular interactions in the cat visual cortex (Buisseret and Maffei, 1977). The wide projections of extraocular muscle afferents suggest multiple roles of these proprioceptors, and the significance of a given projection should, perhaps, be evaluated on the basis of the known types of processing occurring in each cortical region.

As it pertains to the frontal cortex, the present study demonstrated a 60% convergence between extraocular and dorsal neck muscle afferents at the single cell level. Regions of the frontal cortex have been implicated in eye and head movement as a result of stimulation (Hassler, 1966), lesion (Latto and Cowey, 1972), and single unit responses (Bizzi and Schiller, 1970; Guitton and Mandl, 1978b). The interaction of afferent eye and neck muscle signals at comparable latencies in the frontal cortex may be a step in the sensory-motor integration necessary for eye-head coordination. Coordinated eye-head movement must operate in a system that takes into account the position of the head in relation to the body, and the position of the eyes in their orbits (Bizzi, 1975; Ludvigh, 1952). The angle

formed by the head and the body is signalled by neck proprioceptors (Cohen, 1961), while the position of the eye in the orbit may be signalled by extraocular proprioceptors (Brindley et al, 1976; Skavenski, 1972). In this context it is of interest to note that the highest degree of convergence was found between the large and longitudinally extended dorsal neck muscles and extraocular muscles (Table 3.2.1), since it is contraction of the former which causes large head deviations which elicit eye saccades opposite the head movement.

The significance of this observation should, however, be evaluated on the basis of the relative involvement of neck afferents in coordinated eye-head movement, in general. Head position in space, for example, is signalled to the central nervous system by the vestibular system. The relative contribution of the vestibular and dorsal neck muscle systems in feedback mechanisms during coordinated eye-head movement was recently investigated in nonanesthetized monkeys (Bizzi, 1975; Bizzi et al, 1972; Morasso et al, 1973). Those results indicated that behavioral coordination of head and eye movements depended on a central program accompanied by peripheral feedback. The experimental paradigm employed in those studies involved head rotation to the side, with the vestibular system being the main source of peripheral feedback signals for the eye movements accompanying the head rotation. However, when saccadic eye movements were initiated while the head was in motion, signals from the neck region became a relevant control factor of the eye movements (Morasso et al, 1973).

The relative involvement of the neck afferents in coordinated eye-head movement, and coordinated head, limb and body movement, in general, is likely to differ not only as a result of postural deviations during

movement, but their role may also vary across species. The angle formed by the head and the body is different in cats and monkeys. In the cat, the head is carried on a projecting arm, with the result that even small head deviations shift the animal's center of gravity and elicit reflex postural adjustments. Not only does the dorsal neck play a role in these mechanisms during movement (Roberts, 1967), but the demands placed on these muscles in terms of the force required to hold the head stationary are also different when compared with man and monkey.

CONCLUSION

The evidence presented showed that proprioceptive signals from extraocular and dorsal neck muscles project and exhibit converging excitatory and inhibitory effects on frontal cortical units of the cat brain. The highest degree of convergence was observed between extraocular and the large neck muscles which result in big head deviations upon contraction. The converging signals from these muscles may have a role in coordinated eye-head movement.

CHAPTER 4

RESPONSES OF FRONTAL CORTICAL UNITS TO DORSAL NECK AND EXTRAOCULAR MUSCLE VIBRATION

4.1 INTRODUCTION

The previous studies demonstrated that afferents from dorsal neck and extraocular muscles project to the cat frontal cortex. A group of those afferents from the dorsal neck were electrophysiologically characterized as belonging to group 1. These afferents consist of group 1a and 1b, which originate in the primary endings of muscle spindles, and in tendon organs, respectively. Group 1b afferents from Golgi tendon organs have only slightly higher electrical thresholds than group 1a. Due to overlaps in electrical threshold for group 1a and 1b (Jack and MacLennan, 1971), and between 1b and group II (Eccles and Lundberg, 1959), no specific statement can be made on the type of receptors from where the activated fibers originated. On the other hand, sinusoidal vibration of the muscle can be used to activate selectively the primary endings of muscle spindles, since these follow higher frequencies of vibration and are activated with lower amplitudes (less than 50 μm, Matthews, 1972) of displacement of the muscle, than the secondary endings. The latter are innervated by afferent fibers in the group II range. Tendon organs are arranged in series with respect to the extrafusal muscle fibers and can be activated by both muscle stretch and contraction. However, experimental evidence indicates that their best stimulus for activation is muscle contraction (Houk et al, 1971).

In Experiments 1 and 2 of Chapter 2, afferent nerve fibers from dorsal neck muscles were electrophysiologically characterized as group 1 if the intensity required to activate them was 1.3T or less. In view of these stringent criteria, at least some of the group 1 fibers described must have originated in the primary endings of muscle spindles. These receptors are arranged in parallel with the extrafusal muscle fiber, and are activated during muscle stretch. They provide signals proportional to muscle length, and the rate of change in length at the segmental level (Matthews, 1972). It is not known if any of these specific signals from the neck reach the frontal cortex, since electrical nerve stimulation does not render such an analysis possible.

Even less is known about the nature of signals conveyed by the extraocular muscle projections to the frontal cortex. Since afferent thresholds for activation could not be easily monitored in the case of the extraocular muscles as it was done for neck muscles, the afferent nature of the activated fibers might even be disputed. This is based on the possibility that efferent axons may branch and then project to the frontal cortex, even though this branching has not been demonstrated. With the use of vibratory stimuli, which activate selectively muscle receptors, this possibility is eliminated.

Unlike human extraocular muscles and those of the higher apes and ungulates which possess muscle spindles (Buzzard, 1908; Cooper et al, 1955; Daniel, 1946; Manni et al, 1970) the extraocular muscles of lower monkeys, cats and dogs have no muscle spindles (Cooper and Daniel, 1949). However, the presence of a variety of receptors has been demonstrated physiologically and anatomically in these species (Bach-y-Rita and Ito,

1966a; Baker et al, 1972; Cooper and Fillenz, 1952; 1955; Fillenz, 1955; Fuchs and Kornhuber, 1969; Manni et al, 1970; Schwartz and Tomlinson, 1977), and these respond to stretch.

The purpose of the next study was to investigate the responses of frontal cortical neurons to dorsal neck and extraocular muscle vibration. An attempt was made to give a qualitative description of the nature of the afferents involved in these frontal projections and to show their effects on frontal neurons with changes in the amplitude and frequency of muscle vibration.

4.2 METHODS

Experiments were performed on 19 adult cats weighing 2.3-3.2 kg. Only one muscle was vibrated in each experiment, except in two cases in which one neck muscle was vibrated and the superior rectus muscle of the eye was manually stretched. The vibrated muscles included the biventer cervicis of the neck (6 cats), the rectus capitis dorsalis major of the neck (6 cats), and the superior rectus muscle of the eye (9 cats).

SURGERY

Induction of anesthesia and animal preparation were as described in Experiment 1, Chapter 2, except that the animals were not initially paralyzed, so that electromyographic activity (EMG) could be recorded. The vibrated muscles were kept moist with warm mineral oil.

The neck muscles were isolated from the neighboring muscles and insulated copper sutures were placed on their tendons which were then

carefully detached from their insertion point. The muscles were rigidly attached to the vibrator. A strain gauge (Grass FT 03) connected to the bridge mode of the dc preamplifier (Grass 7P1A) was also attached in series with the tendon of the rectus capitis dorsalis major of the neck, and the superior rectus muscle of the eye. The biventer cervicis and rectus capitis dorsalis major were prestretched, by 5 and 6 mm respectively, from a length they held with the head of the cat normally positioned in the stereotaxic apparatus (Fig. 1.2.2), in order to enhance the sensitivity of the muscle spindles to the vibratory stimuli and muscle stretch (Lucier et al, 1975). Vibration of the muscle from this prestretching proved effective in eliciting evoked responses in frontal cortical units during the initial stages of the experiment. The corresponding initial tension of the rectus capitis dorsalis major at this length was 26-28 g in the six animals used. The muscles adjoining the one vibrated were denervated.

For vibrating the superior rectus, this muscle was isolated and insulated copper sutures were placed on its tendon and part of the underlying sclera. The sutured sclera with the intact attached tendon was subsequently cut from the globe, which was collapsed in five experiments and left intact in four others. The muscle was then rigidly attached to the vibrator and to the strain gauge in series with the muscle tendon. The superior rectus was stretched and lifted from the globe to prevent pressure against the ventrally situated retractor bulbus muscle which contracts and draws the globe in the orbit (Bach-y-Rita, 1973). The muscle was prestretched from its primary position by 4 mm to an initial tension of 2.5 g. This value coincides with that reported as optimal

for producing the vestibulo-ocular reflex in the rabbit (Barmack, 1978), and has been reported to be close to movement threshold in primary position in the cat (Tomlinson and Schwartz, 1977). Vibration of the superior rectus from this initial position proved effective in activating units in the frontal cortex during preliminary stages of the experiment.

The muscles adjacent the superior rectus, including facial muscles innervated by trigeminal afferents in the orbital region, were denervated. In cases where the globe was left intact, it was not possible to denervate the ventrally situated extraocular muscles. Controls used to ensure that activation of frontal cortical units was not due to transmission of vibrations to these adjoining muscles are described in the Results.

The anterior brain region was exposed contralateral to the stimulated side as described in Experiment 1, Chapter 2. EMG activity was recorded with a pair of needle tungsten electrodes insulated except for 1 mm at the tips which were separated by 5 mm. The activity was amplified through an ac amplifier (Grass 7P5A, 0.15 Hz frequency response for the low, and at 75 Hz for the high-frequency components of the response) and written on the polygraph (Grass 7P). EMG activity was at times amplified (Tektronix 122) and displayed on a storage oscilloscope (Tektronix 5103N). Tension changes over the preset baseline were recorded on another channel of the polygraph. The higher cutoff frequency was 15 Hz to filter out interference from the vibratory stimuli. Single unit EMG and neuronal action potentials were occasionally passed through a window discriminator consisting of a voltage-gating circuit which converted the action potentials to pulses of constant

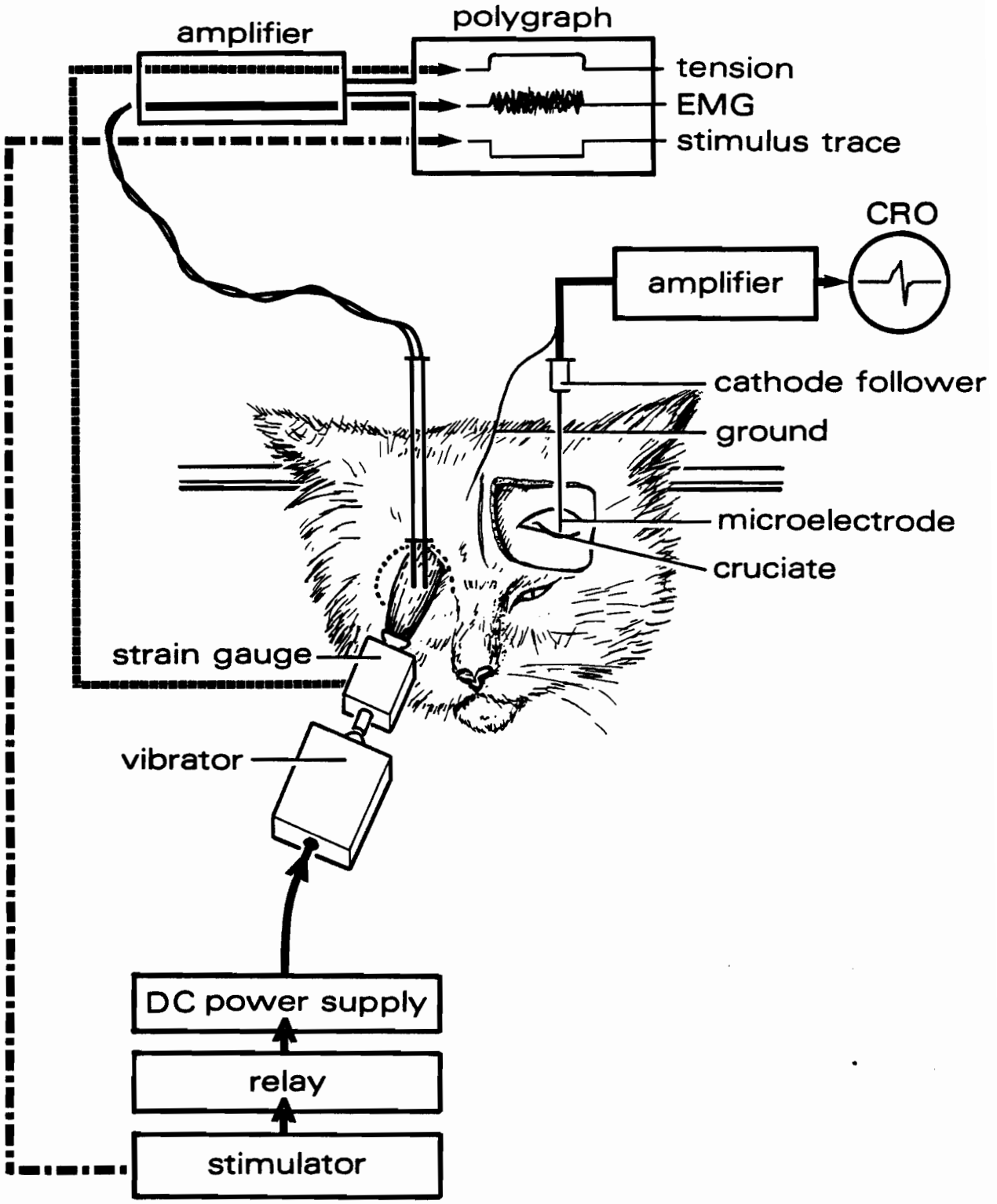
voltage. These were integrated over 1 s intervals (for EMG) and over 2 s (for frontal cortical cell activity) by a linear rate meter, and were written on another channel of the polygraph.

Electrical nerve stimulation and single unit recording were as described in Experiment 1, Chapter 2. During initial experiments, electrical thresholds of dorsal neck muscle afferents were determined by recording dorsal root potentials (see Experiment 1, Chapter 2).

A diagram of the experimental setup for muscle vibration, tension, EMG and single unit recording is shown in Fig. 4.1.

MUSCLE VIBRATION

Mechanical stimulation of the muscle was effected by means of a vibrator of variable frequency and amplitude. The vibration frequency was in the range of 20 to 350 Hz and the amplitude 20 to 200 μm. The constructed vibrator consisted of a lever (50 mm long) pivoted at a short distance from one end, and cam operated at the other. The pivot acted as the fulcrum of the lever system, and the cam, which was fitted in an elongated slot along the lever could be alligned at different distances from the fulcrum. Hence a variable amplitude vibrating system was achieved, in which the "short arm" was the working or stimulating end. A loop was attached to this end, and the muscle was later fastened to this. The specified range of vibration frequency was achieved by varying the voltage supplied to an electric dc motor of the series type (the current was 700 mA at 28 V and 10,000 RPM; dimensions: diameter 5 cm, and length 7 cm). The cam was fixed on the shaft of the dc motor. A variable speed rotational movement was, thus, transformed to variable


amplifier
polygraph
tension
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stimulus trace
CRO
amplifier
cathode follower
ground
microelectrode
cruciate
strain gauge
vibrator
DC power supply
relay
stimulator

frequency translational or vibrating system by means of a cam and a lever.

The amplitude of displacement was measured with a displacement indicator (Mahr) statically, and also with the use of stroboscopic light (General Radio Co. type 1531-AB) dynamically. The frequency of vibration at different voltage levels was measured with a tachometer (Smith Industries Ltd., ATH 6), and also with the use of stroboscopic light with and without a muscle load. No differences were observed in the two situations even during tensions often exceeding 100 g in the rectus capitis dorsalis major muscle of the dorsal neck produced by tetanizing electrical stimuli to a branch of the suboccipital nerve. This was due to the use of a relatively strong motor, so that the muscle load contributed a negligible amount to the damping of the system and to its total mass. When loaded such a system behaved, in effect, as in the free-run situation, and its output remained constant as predetermined.

The duration of stimulation was determined by interrupting the dc current to the motor and turning it on for the desired interval by means of a relay controlled by a pulse stimulator (Grass S8). Hence a repetitive fixed duration stimulation could be obtained.

A dc motor of this type is inherently noisy and interferes with electrophysiological recording. Also, interruption of dc current through the motor windings develops back Electro Motive Force (EMF). Filtering in the latter case is usually accomplished by connecting a diode across the motor input. A Zener diode and a 0.01 μF capacitor parallel with it connected in such a polarity as to eliminate the developed back EMF as well as to clamp any voltage above the maximum

operating voltage provided all the necessary filtering.

In order to eliminate transmission of the vibration through routes other than the muscle stimulated, the vibrator was placed on a holder whose base rested on a table which was physically separated from the one with the preparation. In addition, the muscles adjacent to the vibrated one were routinely denervated.

EXPERIMENTAL DESIGN

The experimental protocol used included vibratory stimuli of 25, 50, 100, 200, and 300 Hz frequencies at 20 and 50 μm displacements of the muscle for low threshold units, and 70, 100 and 140 μm for higher threshold units. Electrical stimulation of the nerves of the vibrated neck muscles was also used.

The neck muscle vibrated in initial experiments was the biventer cervicis, since the probability of response in the frontal cortex when the nerve to this muscle was stimulated electrically was higher than any other neck muscle (Table 2.1.1). In addition, this muscle projects widely within all the regions studied in the previous experiments (Fig. 2.1.4 and 2.2.5). Once the vibratory stimuli to the biventer cervicis proved effective in eliciting frontal cortical unit responses, a more detailed investigation was conducted with the rectus capitis dorsalis major in which tension and EMG changes during vibration were also recorded. This muscle was selected for study among those of the dorsal neck because it is architecturally simple compared with the biventer cervicis and complexus, is easily accessible, and its afferent

innervation is through the first cervical segment only. Tension and EMG changes were recorded at 20 and 70 μm amplitudes of displacement and 50, 100, 200 and 300 Hz frequencies. A minimum of six trials were recorded for each amplitude and frequency level in each cat.

The superior rectus muscle of the eye was selected for vibration because its projections to the frontal cortex were already investigated in Chapter 3. Also, its dorsal anatomical location and easy accessibility make this muscle ideal for the study.

4.3 RESULTS

Microelectrode penetrations in the frontal cortex were made on the basis of the maps constructed in the previous experiments. These included regions between the postcruciate dimple and 1 mm anterior the cruciate sulcus, where most of the units receiving electrophysiologically characterized group 1 afferents from the dorsal neck were located (Chapter 2), and which also included the extraocular muscle projection sites (Chapter 3). A total of 79 units were recorded in these regions in 19 cats. Of these 68 responded to vibration of the biventer cervicis or the rectus capitis dorsalis major of the neck, or to vibration and/or stretch of the superior rectus muscle of the eye. Eleven units were unresponsive to these afferent stimuli.

General Observations

The evoked unit response latencies of 18-90 ms were generally longer than those previously observed with electrical nerve stimulation.

Comparisons of latencies of evoked responses in the same units confirmed this general observation (Fig. 4.2 D-E) and showed the difference in evoked latencies to the two stimuli to be 10-30 ms. This finding is consistent with the time required to activate muscle receptors and their receiving afferents (Whitteridge, 1959). Increasing the frequency of vibration from 100 Hz to 300 Hz often shortened the latency of evoked activity, a finding consistent with the faster and more efficient activation of muscle receptors at these frequencies.

Two general types of evoked responses to muscle vibration were noted in the frontal cortex. One type was characterized by a phasic burst of evoked unit activity 18-90 ms after the onset of stimulation and showed no further evoked responses during the rest of the stimulation period which lasted for 2-10 s. The other general type of response had tonic characteristics such that the evoked activity generally initiated 18-90 ms after the onset of stimulation continued while the stimulus was on. These two types of responses were observed with vibration of both dorsal neck muscles, and the superior rectus muscle of the eye, but the relative proportion of these differed in the three muscles studied, and will be described for each muscle below. Units could further be classified into those that showed frequency-dependent evoked responses and those that did not. Each of these groups included both phasic and tonic types of units. A composite figure (4.2) illustrates some of these observed responses.

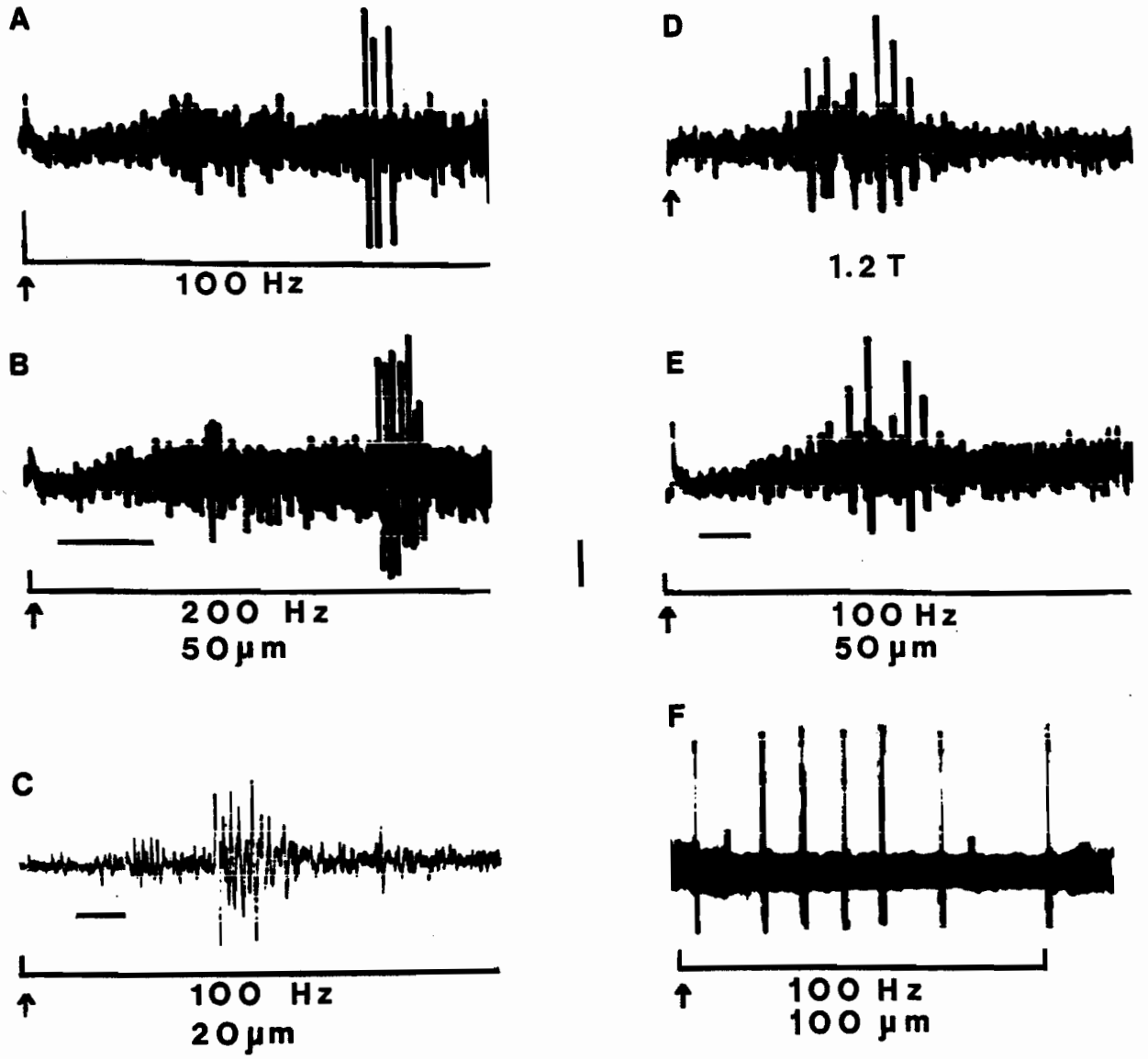
Fig. 4.2 Composite figure showing: A-B Cell in the dorsal bank of the cruciate sulcus showing phasic evoked activity with vibration of the rectus capitis dorsalis major of the dorsal neck at 100 Hz, 50 μm (A) and 200 Hz, 50 μm (B).

C- Cell in presylvian region showing phasic response to vibration of the rectus capitis dorsalis major muscle of the dorsal neck (100 Hz, 20 μm).

D- Cell response in the ventral bank of the cruciate following electrical nerve stimulation (1.2T) of the rectus capitis dorsalis major, and E- after vibration of the same muscle; note later response of the neuron in the latter.

F- Neuronal response in the dorsal bank of the cruciate sulcus showing tonic response over a 4 s vibration interval (100 Hz, 100 μm) of the biventer cervicis muscle of the dorsal neck.

Stimulation onset at arrows, and throughout horizontal line trace below brain activity traces. Vertical calibration: 80 μV; horizontal: A - E, 10 ms and F-, 4 s interval.

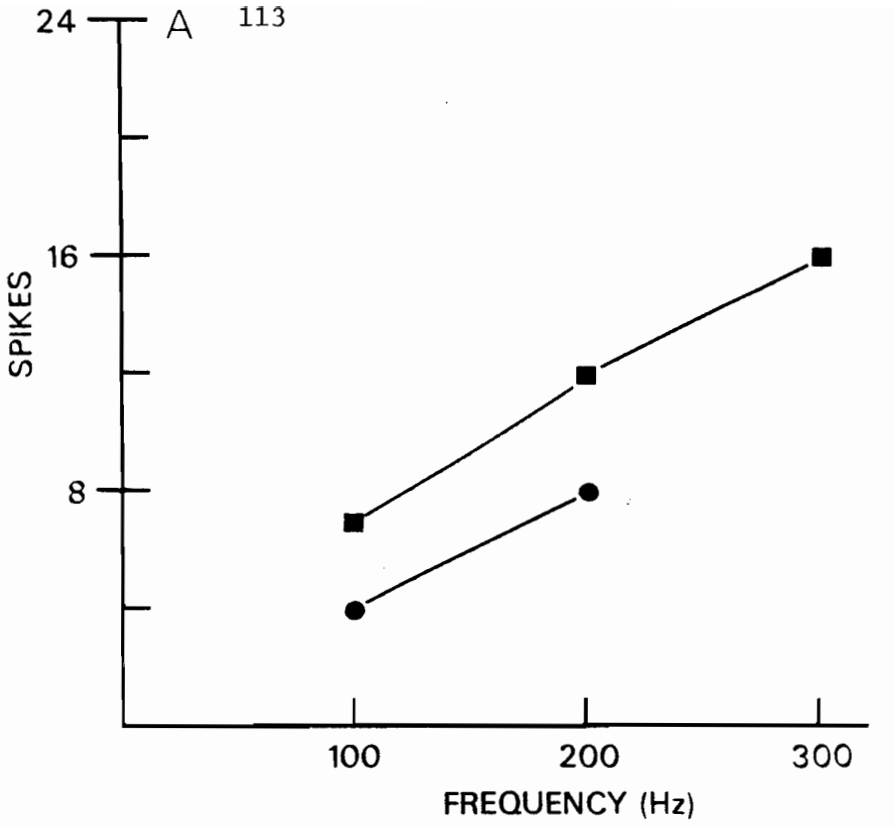

A
100 Hz
B
200 Hz
50µm
C
100 Hz
20µm
D
1.2 T
E
100 Hz
50µm
F
100 Hz
100 µm

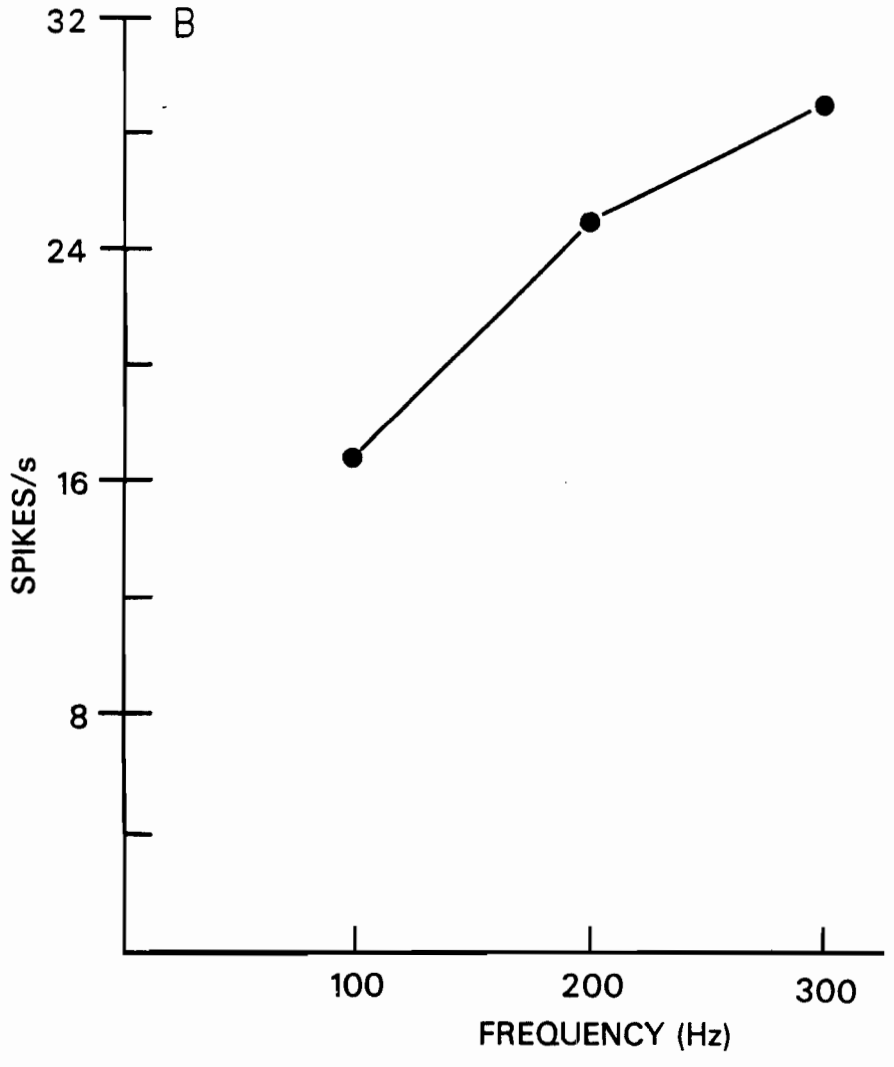
Responses to the biventer cervicis

In six cats, 15 units in the frontal cortex showed consistent evoked responses to vibration of this muscle at 70-120 μm amplitudes of displacement and 25-300 Hz frequencies. Of these, one group (n = 9) showed no consistent increases in firing activity as the frequency of vibration was increased from 100-300 Hz at 100 μm and 140 μm displacements of the muscle. The majority of these units (n = 8) showed a phasic type of response which was a burst of 2-20 spikes 20-80 ms after the onset of stimulation. One unit showed a tonic type of increase in firing activity over its background firing rate which spread throughout the period of stimulation (Fig. 4.2 F). The electrical threshold was determined in three of these units and was 1.9-2.2 T, suggesting that the evoked responses were due to activation of afferents belonging to group II or III.

In order to test whether afferents electrophysiologically characterized as belonging to group 1 cause frequency-dependent increases in unit firing activity when activated with vibratory stimuli, three units responding to threshold electrical stimuli were selected for study. All three showed an increase in firing activity as the vibration frequencies were increased from 100 to 200 Hz, or from 100 to 300 Hz (Fig. 4.3). Two of these showed a phasic type of increase in firing activity at 20-40 ms after the onset of vibration (Fig. 4.3 A), while one unit showed a tonic type of increase which lasted throughout the three second vibration period (Fig. 4.3 B). In addition, three units that showed inhibitory effects with threshold electrical nerve

Fig. 4.3 A- Graph representing number of evoked neuronal responses of two units which showed phasic (A) and of one unit which showed a tonic response (B) following vibration of the contralateral biventer cervicis muscle of the dorsal neck. The magnitude of the evoked response depended on the frequency of vibration. The neurons in A were recorded in the ventral bank of the cruciate sulcus, and in B in the dorsal bank of this sulcus. The lowest amplitudes of displacement at which all these responses were still obtained was 70 μm.


24
A
16
8
SPIKES
100
200
300
FREQUENCY (Hz)


32
B
24
16
8
SPIKES/s
100
200
300
FREQUENCY (Hz)

stimulation showed similar effects with 70 μm amplitude and 50-200 Hz frequencies of vibration of the muscle. One of these units was inhibited within an interval of 100-180 ms after the onset of stimulation, and the other two showed a general decrease of their glutamate-induced background activity. The lowest amplitude at which these responses were still obtainable was 70 μm, a figure which although lower than the 100-140 μm range observed in all the cells in the first group, is still higher than those required to activate group 1 afferents in the limbs (Lucier et al, 1975; Matthews, 1972). This finding is not likely to reflect a disadvantageous initial position of the biventer cervicis, since changes in its length did not lower the amplitude requirements. This result could rather reflect general differences between neck muscles and limb muscles and in addition, could be due to the complex architectural structure of this muscle. Since fibers of this muscle insert at various levels of the muscle on tendinous intersections (Richmond and Abrahams, 1975a), fibers distal to this insertion may not be effectively vibrated when the stimuli are applied longitudinally to the insertion tendon.

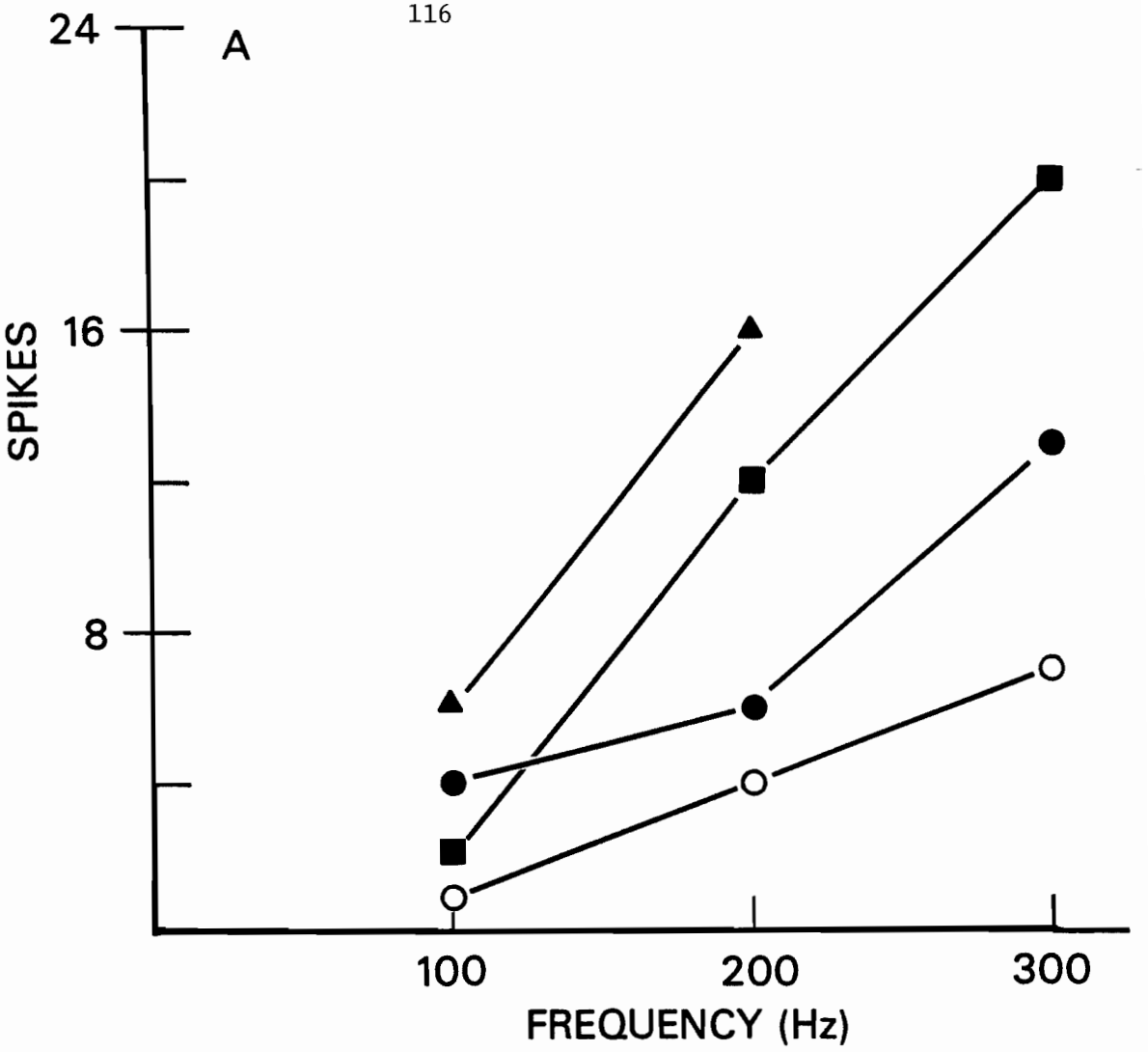
In order to determine whether this higher amplitude requirement was a general characteristic of neck muscles, or was particular to the biventer cervicis, the rectus capitis dorsalis major was prepared for vibration in six experiments. This muscle bears no tendinous intersections, and is architecturally simpler than the biventer cervicis (Fig. 1.2.1 and 1.2.2).

Responses to the rectus capitis dorsalis major

In six cats, 22 units showed consistent responses to vibration of the contralateral rectus capitis dorsalis major muscle of the neck at 20, 50, 70 and 100 μm amplitudes of displacement, and 25 to 300 Hz frequencies. The amplitudes of muscle displacement required to elicit unit evoked responses were, thus, lower than those required for the biventer cervicis, which is consistent with the previous contention that vibratory stimuli may be more effective in activating receptors in an architecturally simple muscle. The evoked unit activity was either a phasic burst of 2-20 spikes 18-80 ms after the onset of stimulation, or tonic activity spread throughout the period of stimulation. Several units also showed frequency-dependent activity; these will be discussed first.

Phasically responding units (n = 4) showed consistent increases in the number of spikes fired as the stimulation frequency increased from 100-200 Hz or 100-300 Hz (Fig. 4.4). Figure 4.4 B shows that while the responses with a given frequency varied somewhat over repeated trials, the trend remained unchanged. This was observed in all four units. Frequency-dependent increases in tonic type of firing activity were also observed (n = 2) (Fig. 4.5). The displacement amplitudes required to activate all of the frequency dependent units was 20 μm. Unit responses were also obtained with 25-50 Hz frequencies when the amplitude of displacement was raised from 20 μm to 50 μm. Two of these units were stimulated electrically and required intensities of stimulation at or near threshold for activation.

Fig. 4.4 A- Graph showing the number of evoked responses of four units in pericruciate, presylvian and coronal cortical regions, which showed a phasic response to vibration of the contralateral rectus capitis dorsalis major (20 μm - 50 μm). The magnitude of the evoked response depended on the frequency of vibration. B- Number of spikes of one of above units (black circles in A) over repeated trials. Note consistent increasing trend in the number of responses from 100 Hz to 300 Hz, even though inter-trial variation in spikes at each frequency is evident.


24
A
16
8
SPIKES
100
200
300
FREQUENCY (Hz)

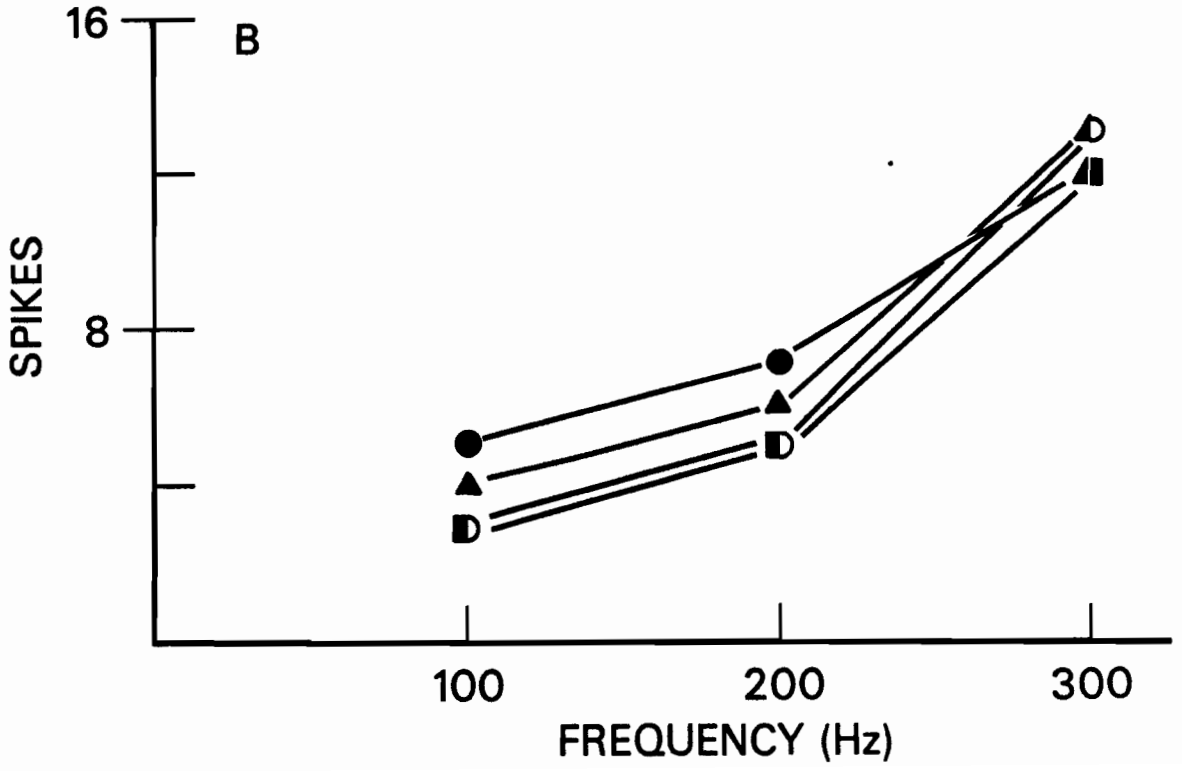
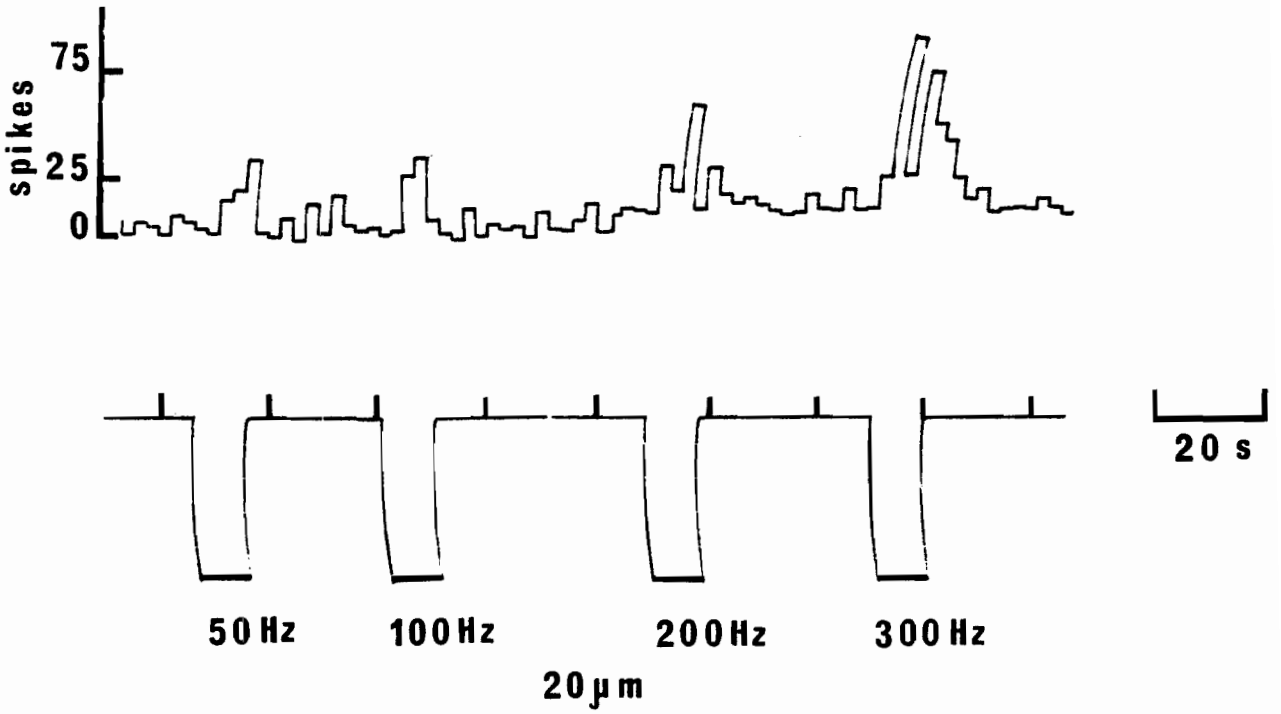
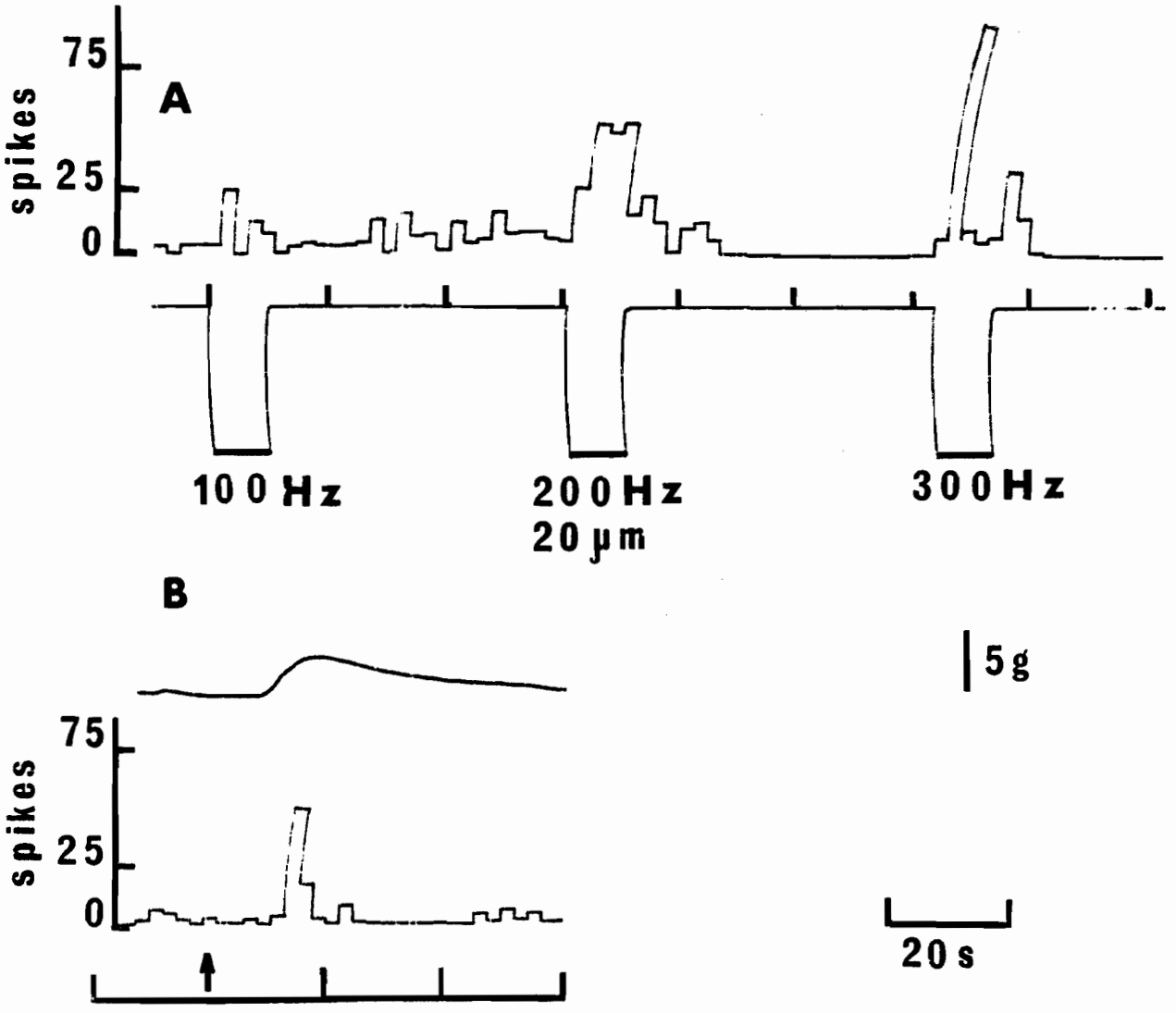

16
B
8
SPIKES
100
200
300
FREQUENCY (Hz)

Fig. 4.5 Top trace: Integrated (2 s intervals, see METHODS) spike activity of neuron on coronal cortex which showed tonic responses to vibration of the rectus capitis dorsalis major muscle of the dorsal neck. The magnitude of the evoked firing activity depended on the frequency of vibration. The lower trace shows the duration of vibration; the vertical lines on this trace show 20 s time intervals. Note earlier onset of activity at 200 Hz and 300 Hz compared with 50 Hz and 100 Hz. The amplitude of displacement was 20 μm in all cases.


spikes
75
25
0
20 s
50 Hz
100 Hz
200 Hz
300 Hz
20 µm

The frequency-dependent characteristics of these units, the decrease in the amplitude of muscle displacement required to activate them as the frequency of vibration was increased, and their activation by low electrical threshold afferents, are consistent with the view that they receive afferent input which originates in the primary endings of muscle spindles. The responses of three of these units were, in addition, tested with 30-40 µg/kg intravenous injections of succinylcholine, a depolarizing neuromuscular blocking agent known to activate preferentially the primary endings of muscle spindles, and to a much lesser extent secondaries (Fehr, 1965). The firing frequency of all three cells increased with administration of this drug (Fig. 4.6). Coinciding with the neuronal responses was an increase in the muscle tension (Fig. 4.6 B), indicating that the spindles of this muscle were activated, and resulted in an increase in the muscle tension probably due to activation of segmental and/or suprasegmental circuits. Moreover, the frontal cortical unit responses correlated with the administration of succinylcholine showed the tonic (Fig. 4.6) or phasic characteristic responses also observed with vibration of the neck muscle. Although the succinylcholine-induced responses add confidence to the idea that afferent signals originating in the primary endings of muscle spindles from the cat neck reach the frontal cortex, this evidence is indirect, for the intravenous administration of this drug results in a general activation of these receptors in other muscles as well, and the latter could also have an input to these frontal cells. One unit with a frequency-dependent increase in firing activity between 160 Hz and 300 Hz at 50 µm amplitudes of displacement differed from the rest as it did not respond

Fig. 4.6 A- Top trace: Integrated (2 s intervals, see METHODS) spike activity of neuron in lateral sigmoid gyrus at the level of the cruciate sulcus, which showed tonic responses to vibration of the rectus capitis dorsalis major muscle of the dorsal neck. The magnitude of the response depended on the frequency of vibration. The lower trace shows the duration of vibration; vertical lines on this trace show 20 s time intervals. B- Injection of succinylcholine (30 µg/kg, at arrow) resulted in an increase in the background activity of this neuron (middle trace) with a concomitant increase in the tension of the muscle (top trace). Lower trace shows 20 s time intervals.


75
spikes
25
0
A
100 Hz
200 Hz
20 µm
300 Hz
B
5g
75
spikes
25
0
20 s

with frequencies below 160 Hz even with increased amplitudes of displacement of the muscle up to 140 μm. These characteristics suggest that the activated afferents in this case might not have originated in the primary endings of muscle spindles, and could be due to activation of other receptors, including Pacinian corpuscles.

The rest of the units which responded to vibration of the rectus capitis dorsalis major (n = 15) showed no consistent increases in firing activity with increases in stimulation frequency from 100 Hz to 300 Hz at amplitudes of 20 μm to 100 μm. The majority of these units (n = 14) showed phasic bursts of 2-20 spikes with vibration of 50 Hz to 200 Hz or 25 Hz to 300 Hz, and were unresponsive for the rest of the trial which extended 2-6 seconds. The rest of the units showed tonic type of activity with muscle vibration. These results, combined with those described above, show that afferents of this muscle evoked phasic types of responses in 18 out of 22 cells (82%). It may be noted here that this muscle has the histochemical profile of a fast muscle (Richmond and Abrahams, 1975a) suggesting that it is involved in phasic movement.

TENSION AND EMG

The tension developed during 3-10 s vibration of the muscle at displacements of 20 and 70 μm and frequencies of 50, 100, 200 and 300 Hz was recorded. An example of the mean increase in tension at these amplitudes is shown in Table 4.1 for one cat. Variations in the tension developed with a given displacement amplitude and frequency occurred,

TABLE 4.1

Mean Tension (mg) Developed in the Rectus Capitis Dorsalis Major of the Neck and the Superior Rectus Muscle of the Eye during Vibration

Muscle vibrated	Amplitude	Frequency			
		50 Hz	100 Hz	200 Hz	300 Hz
Rectus capitis dorsalis major	70 μm	261 ±5%	547 ±8%	1190 ±10%	1548 ±10%
	20 μm	148 ±12%	214 ±13%	464 ±5%	859 ±8%
Superior rectus	70 μm	190 ±13%	457 ±7%	897 ±8%	1172 ±8%
	20 μm	37 ±40%	86 ±30%	318 ±10%	412 ±7%

Since the cats were of different weights, an average tension of all animals was not computed for each frequency; instead, the standard error was computed for each animal at each amplitude and frequency over repeated trials , and this was expressed as a percentage of the mean developed tension. The average of these normalized values in the six cats used is shown for each level below the tension values.

Fig. 4.7 Tension (top traces) and integrated (1 s intervals, see METHODS) single unit EMG (second traces) of rectus capitis dorsalis major muscle of the dorsal neck following vibration of this muscle (bottom traces) at 20 μm amplitude displacements and 200 Hz (A), and 300 Hz (B) frequencies. Note example where tension was not well maintained during the vibration interval (A, top trace), and note that the EMG activity of this unit corresponded well with tension variations (A, second trace). Vertical bars below integrated EMG traces show 10 s intervals.

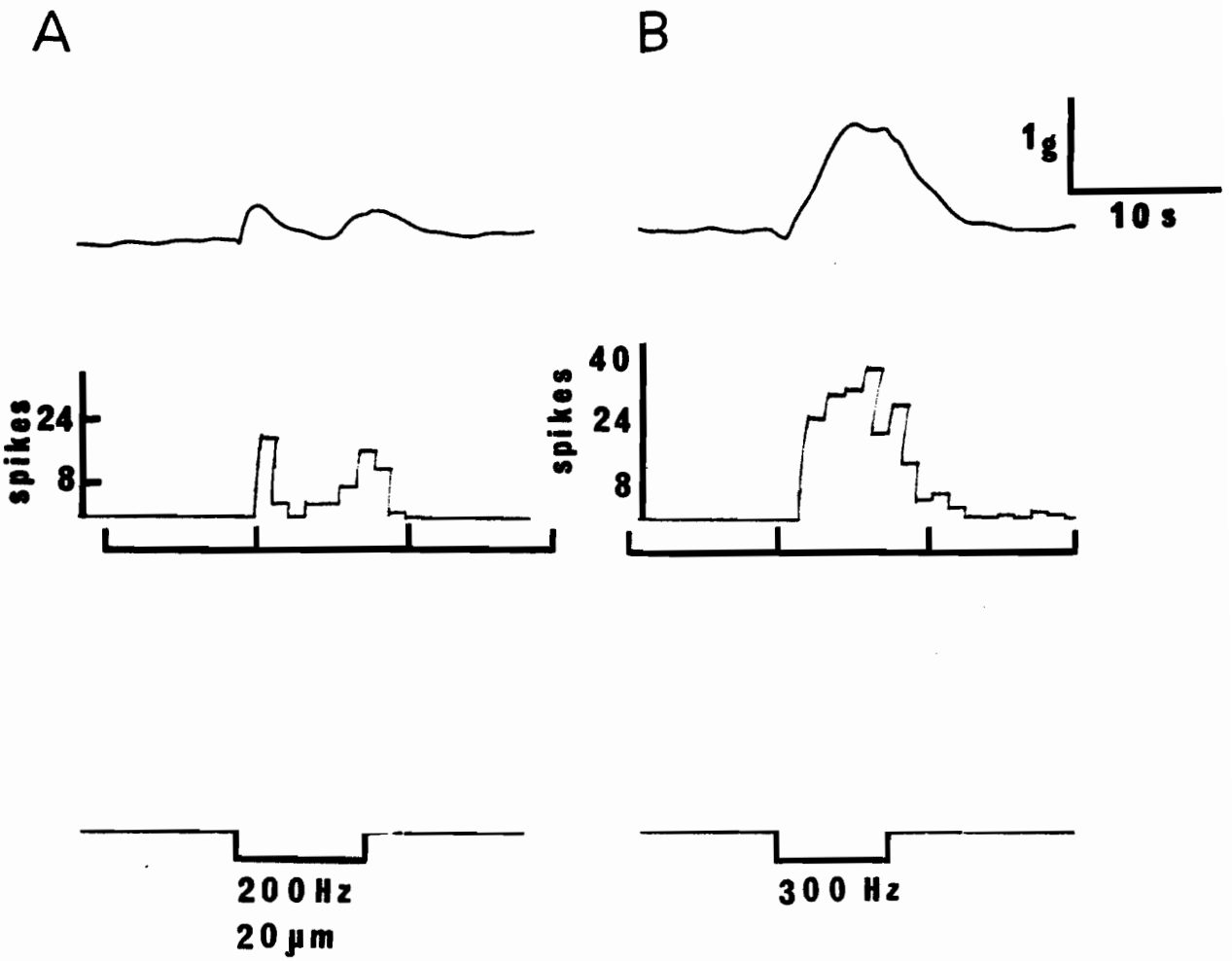

A
B
1g
10 s
spikes
24
8
spikes
40
24
8
200 Hz
20 µm
300 Hz

Fig. 4.8 Single unit EMG (integrated in 1 s intervals) recorded from the rectus capitis dorsalis major muscle of the dorsal neck in response to vibration of this muscle at: A- 300 Hz; B- 200 Hz; C- 100 Hz; D- 50 Hz; the amplitude of displacement of the muscle was 70 μm peak to peak in all cases.

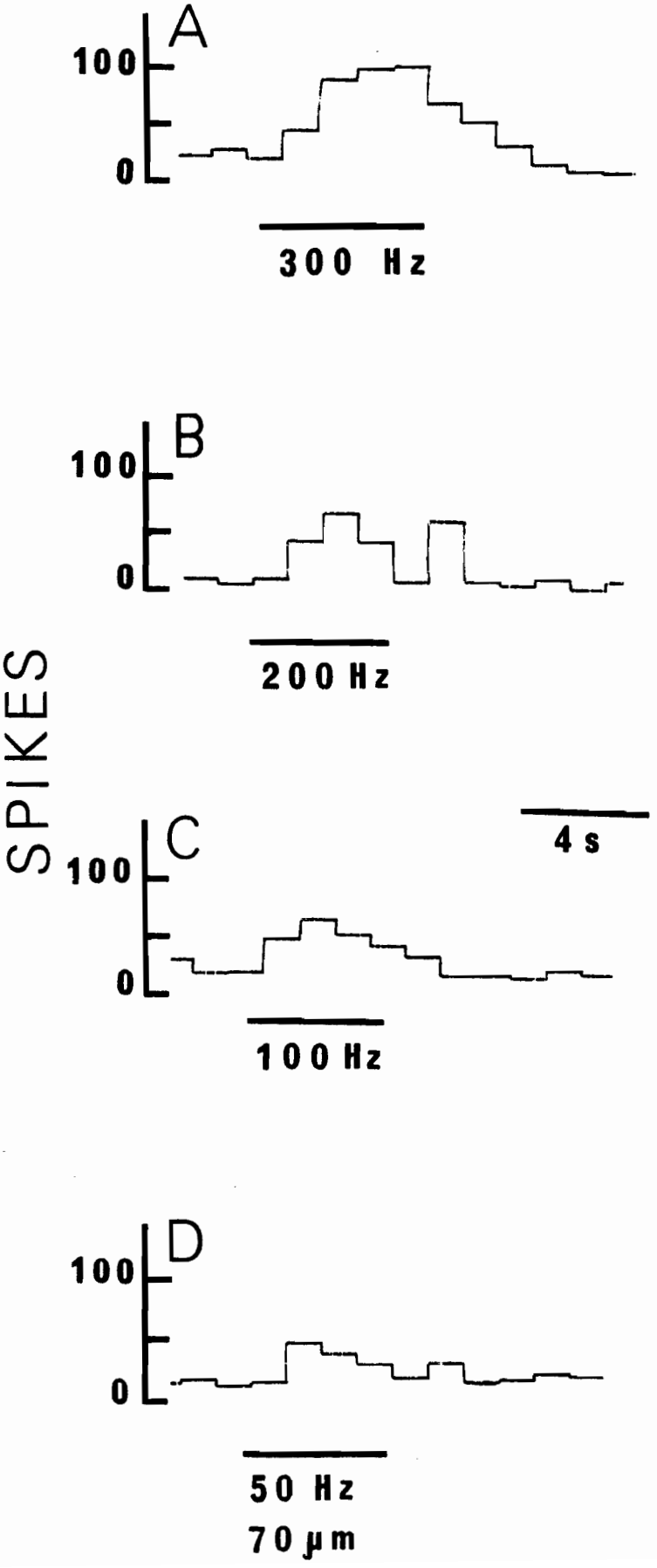
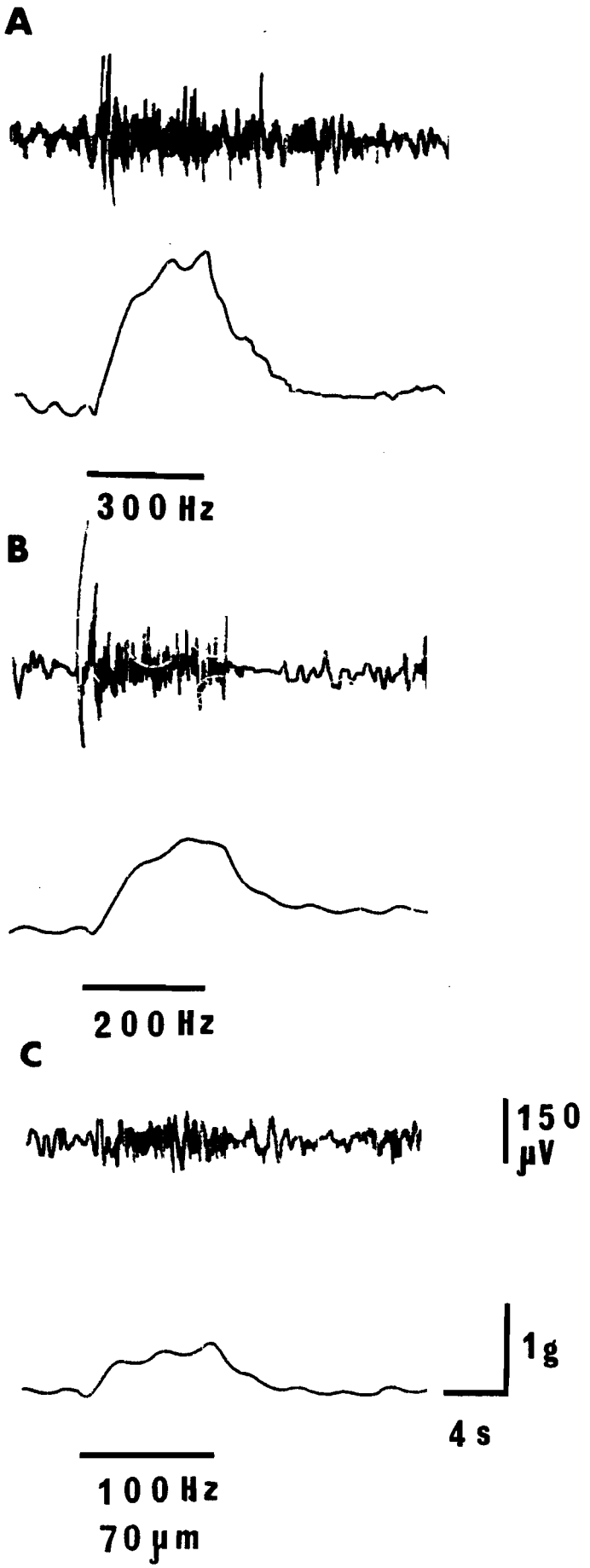

A
100
0
300 Hz
B
100
0
200 Hz
SPIKES
C
4 s
100
0
100 Hz
D
100
0
50 Hz
70 µm

Fig. 4.9 EMG activity (top traces in A, B and C), and concomitant tension increases (below each EMG trace) recorded from the rectus capitis dorsalis major muscle of the dorsal neck following vibration of this muscle at; A- 300 Hz, B- 200 Hz, and C- 100 Hz at 70 μm displacements peak to peak.


A
300 Hz
B
200 Hz
C
150 µV
1g
4 s
100 Hz
70 µm

but these were small (Table 4.1 see s.e.). At 20 μm displacements of the muscle and 50 and 100 Hz frequencies no measurable tensions were recorded in 60% and 50% of the trials, respectively, and when present they were no larger than 250 mg (Table 4.1). In approximately 5% of all trials at 200 and 300 Hz and 20 μm displacements, there was no tension developed, and in another 5% of the trials at these frequencies, the developed tension was not well maintained throughout the duration of vibration (Fig. 4.7). These variations are likely to reflect moment to moment changes in the state of the muscle. Unit responses were, however, observed at times when little or before measurable tensions developed, suggesting that frontal cortical units respond with small displacements of the muscle. This is also suggested by the evoked phasic responses at latencies of 20-30 ms. The developed tension was accompanied by an increase in single unit (Fig. 4.8) or gross EMG (Fig. 4.9) which could be recorded along the entire extent of the muscle.

Responses to the superior rectus

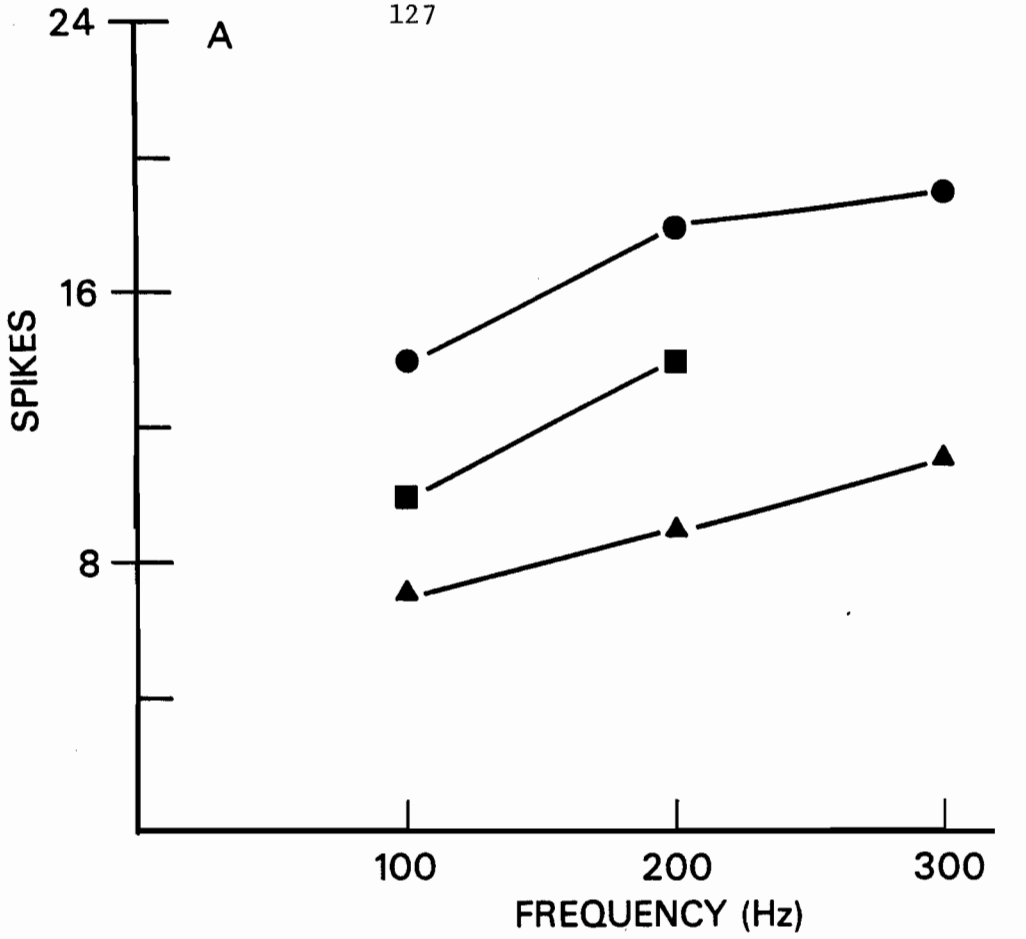
Neuronal responses in the frontal cortex to vibration of the superior rectus muscle of the eye were recorded in nine animals. Thirty-nine units showed consistent responses to vibration of this muscle at 50-140 μm amplitudes and 25-300 Hz frequencies or 0.5-1.5 mm single stretches of the muscle. Consistent increases in firing activity with increases in vibration frequencies from 100 Hz to 200 Hz, or from 100 Hz to 300 Hz were observed in five units, including three that displayed

phasic type of evoked activity (Fig. 4.10 A), and two which showed tonic type of activity (Fig. 4.10 B) which lasted throughout the stimulation period of 3-6 s after the onset of the response. One of these units (Fig. 4.10 B, circles), showed a mixed response: at 50 Hz it fired phasically with a burst of two spikes, but at 200 Hz and 300 Hz it fired tonically. The higher frequencies of vibration may have resulted in a more efficient and faster activation of the muscle receptors, and therefore afferents, as is suggested by the earlier activation of units showing tonic responses with higher stimulus frequencies (Fig. 4.11 E-G).

A second group of responsive units (n = 20) with the above stimulus parameters did not show consistent increases in firing frequencies with increased stimulus frequencies. The background firing activity of most of these units (n = 18) was 1-2 bursts of 2-3 spikes every 2-3 seconds. The spontaneous activity of two units was high, and showed a tonic type of increase during muscle vibration at 50 Hz to 300 Hz (Fig. 4.11 A-D).

A last group of neurons (n = 14) responded to single stretches of 0.5-1.5 mm applied manually to the muscle. Three of the units in this group were previously shown to respond to vibration of this muscle also; the rest were not tested with vibratory stimuli. Faster pulls were more effective in eliciting evoked responses in two of these units. All units responded phasically or with a prolonged tonic type of response during stretch, and none did so on release. This result suggests that activation of the cells was due to stretch of this muscle and not due to mechanical disturbances of other proximal muscles, since

Fig. 4.10 Graph showing number of evoked responses of units in pericruciate, presylvian and coronal cortical regions which showed a phasic (A) and tonic (B) response to vibration of the contralateral superior rectus muscle of the eye. The magnitude of the evoked response depended on the frequency of vibration. The phasic response in A was in the form of one burst irrespective of the duration of vibration, while in B the evoked activity lasted throughout the 3 to 6 s vibration interval.


24
A
16
8
SPIKES
100
200
300
FREQUENCY (Hz)

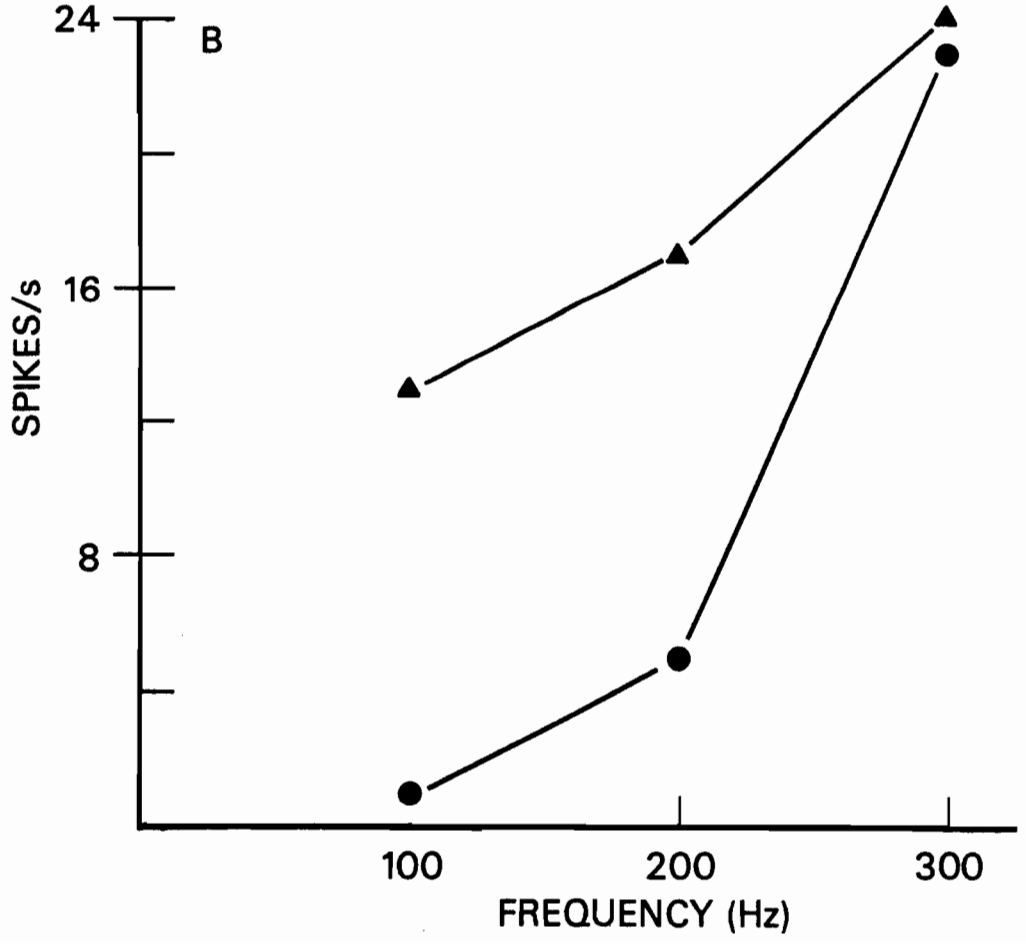
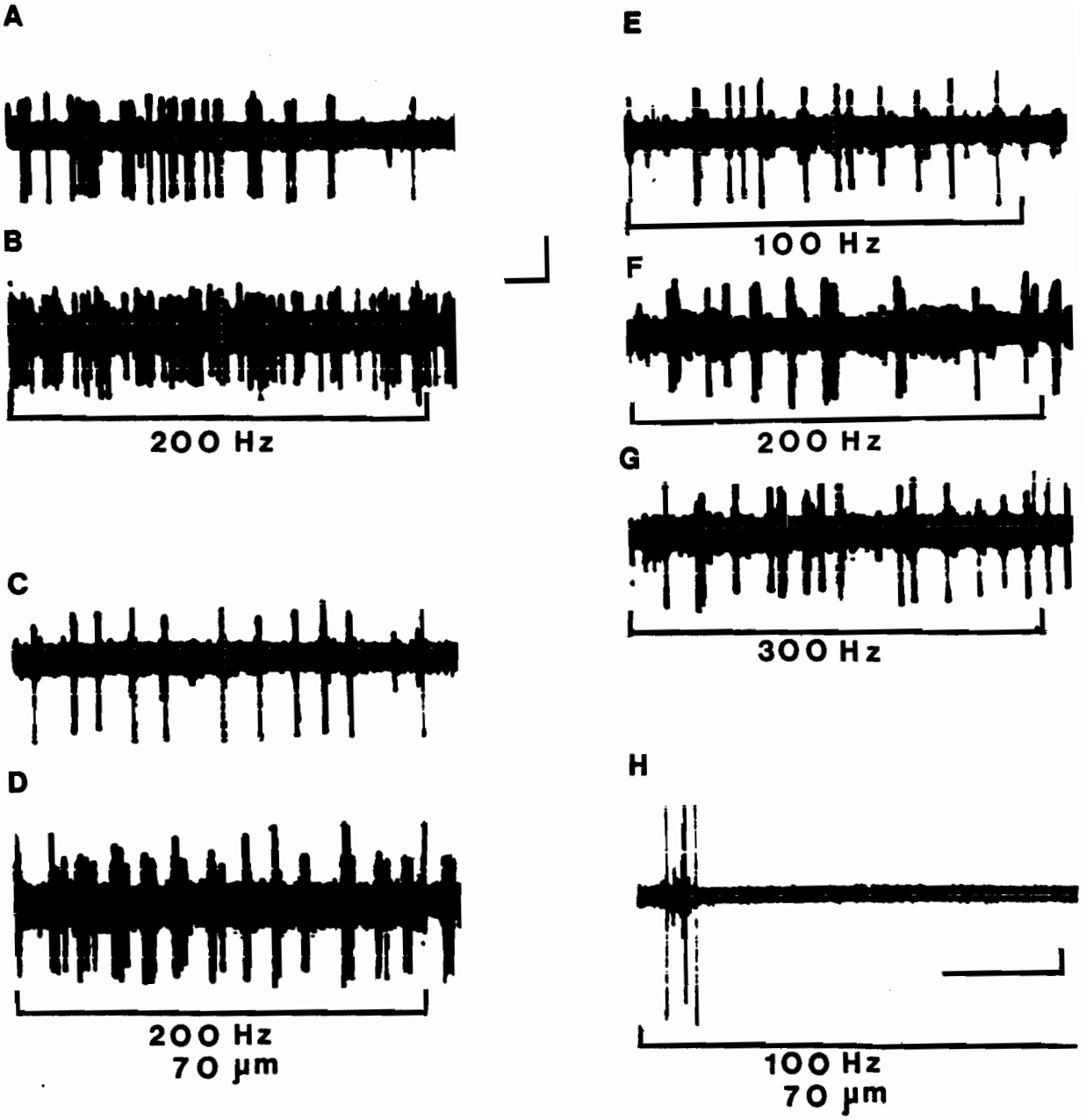

24
B
16
8
SPIKES/s
100
200
300
FREQUENCY (Hz)

Fig. 4.11 Composite figure illustrating: A- and C- the background activity of each of two neurons in the lower bank of the cruciate sulcus and an increase in their firing frequency B- and D-, induced with vibration (200 Hz, 70 μm) of the superior rectus muscle of the eye.

E-G Cell response in coronal cortical region with vibration of the superior rectus (100 Hz, 200 Hz, and 300 Hz, 70 μm). Note earlier onset of unit activity at 200 Hz and 300 Hz compared with 100 Hz frequencies.

H- Phasically responding cell in the dorsal bank of the cruciate sulcus to vibration (100 Hz, 70 μm for 3 s) of the superior rectus muscle. Vertical calibration ; 160 μV; horizontal: 200 ms.


A
B
200 Hz
C
D
200 Hz
70 µm
E
100 Hz
F
200 Hz
G
300 Hz
H
100 Hz
70 µm

these frictional disturbances are the same during stretch and during release.

Among the units responsive to extraocular muscle vibration or stretch those which showed tonic responses predominated, with 27 (69%) of these belonging to this group (see examples in Fig. 4.11 B and D and E-G). The rest of the units showed phasic responses 20-90 ms after the onset of stimulation (Fig. 4.11 H) much like those described for dorsal neck muscles above.

Eight of the responsive units exhibited an upper frequency limit within the 300 Hz range employed, above which they abruptly ceased firing. A shift to a lower frequency promptly resulted in a resumption of the firing activity. This behavior suggested a contraction of the muscle fibers containing the activated receptors, a condition which would then unload the receptors and stop the afferent firing. Tension developments in the muscle at the frequencies where unit activity ceased in the present study were 0.4-1.2 g, which correspond to muscle twitch tensions observed during nerve stimulation.

In two experiments, the biventer cervicis of the neck was vibrated, and the superior rectus muscle of the eye was stretched, in order to test whether afferent convergence similar to that noted in Experiment 3 could also be observed with these stimuli. Eight out of twelve cells tested this way responded to vibration of the biventer cervicis and to stretch of the superior rectus, thus confirming and extending the results of the previous experiment.

TENSION AND EMG

The mean tension developed in the superior rectus over the baseline level with 70 μm and 20 μm amplitudes of displacement of the muscle at 50, 100, 200 and 300 Hz frequencies is shown in Table 4.1 for one cat. When the amplitude of displacement was 20 μm, no measurable tension was observed in 85% of the trials at 50 Hz and in 20% of the cases at this amplitude and 100 Hz frequencies in all cats. Occasionally, the developed tension recorded with 20 μm amplitudes and 200 and 300 Hz frequencies was not well maintained throughout the vibration interval. Accompanying the tension changes were EMG activity increases over the baseline level, at latencies compatible with polysynaptic activation (Fig. 4.12 and 4.13). No single unit EMG was ever recorded in this muscle as reported for the neck. This might be due to the small and tightly packed fiber arrangement of the extraocular muscles. In approximately 15% of all trials, in which tension increases up to 407 mg were observed with vibratory stimuli, there were no apparent EMG responses. EMG was best recorded from the outer, orbital muscle layer, and recording was less effective when the electrode penetrated the muscle core. These results suggest that with the stimuli employed in the present study, the slow orbital fibers are important contributors to the EMG activity observed. Paralytic doses of gallamine triethiodide diminished the EMG activity with muscle vibration of both extraocular and dorsal neck muscles.

In order to test whether transmission of vibration to the frontal cortex occurred through the afferents of the vibrated muscles, and not

Fig. 4.12 EMG activity (left traces) recorded from the superior rectus following vibration of this muscle: A- 300 Hz; B- 200 Hz; C- 100 Hz (70 μm displacements peak to peak in all cases); tension increases in the muscle are shown on the right. Note long latency onset of EMG compared with that of the rectus capitis dorsalis major (Fig. 4.9). Vibration throughout horizontal bar below each trace.

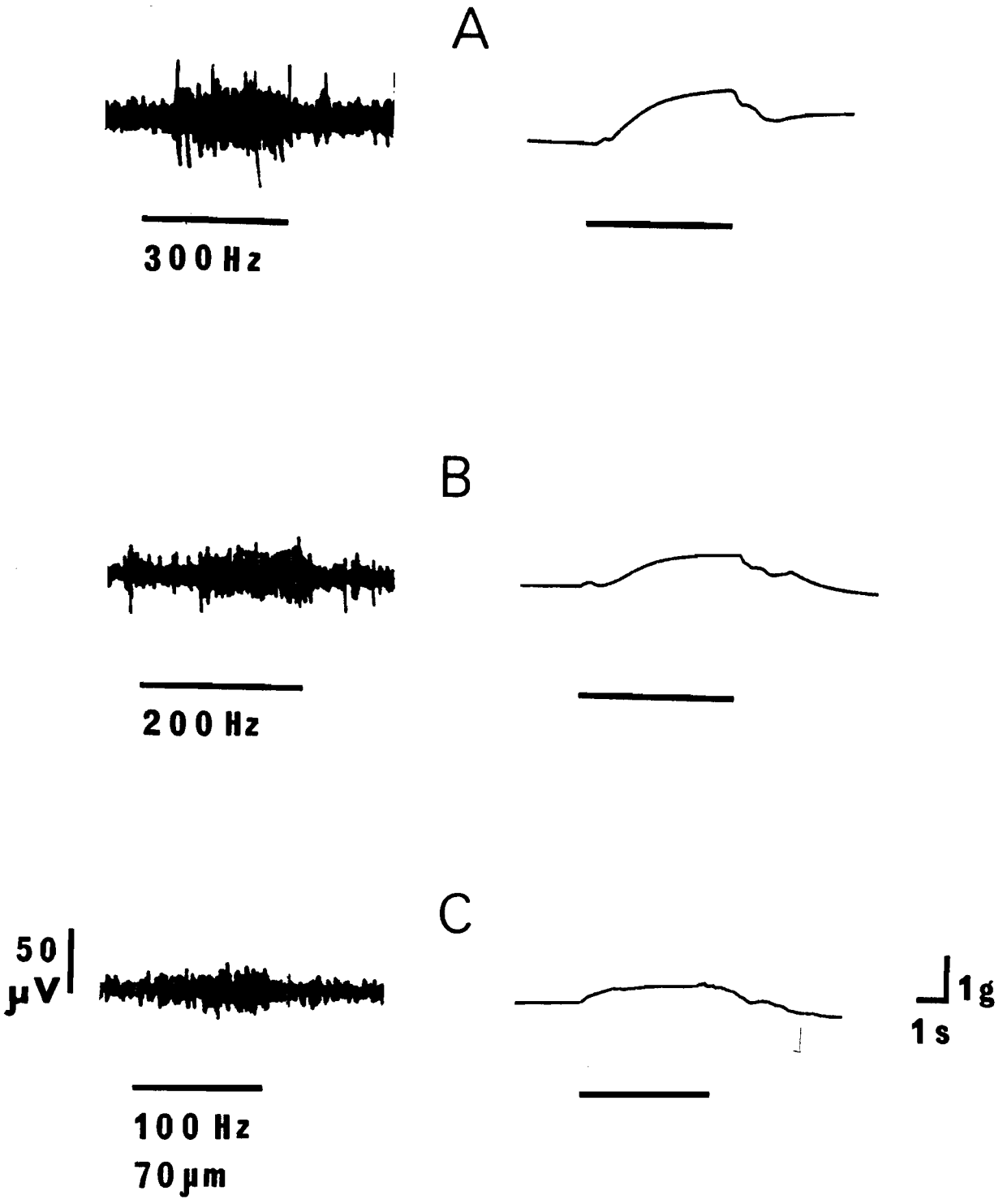
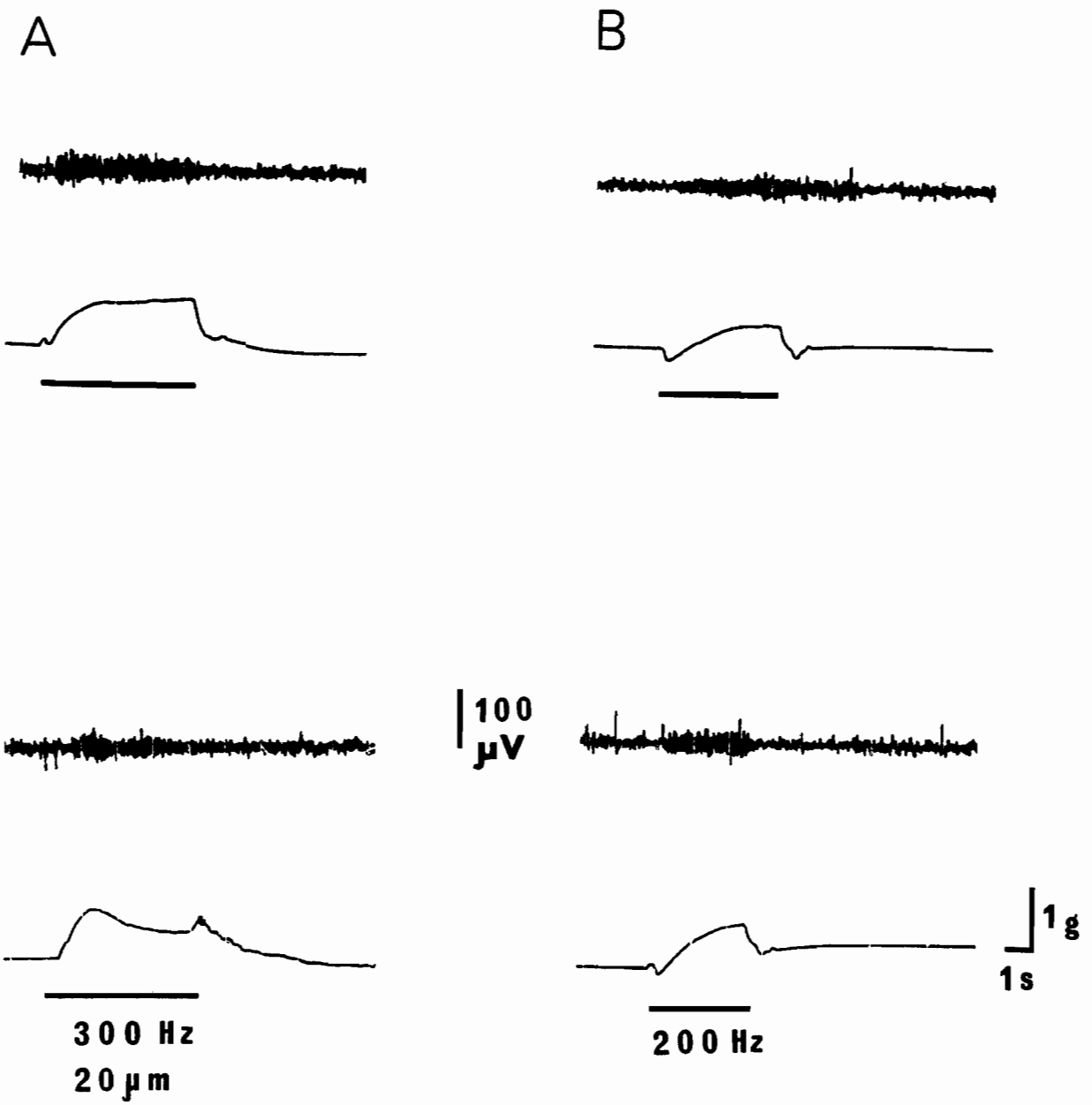

A
300 Hz
B
200 Hz
C
50
µV
1g
1s
100 Hz
70µm

Fig. 4.13 A- and B- show two examples each of EMG (top traces) and tension (shown below EMG traces) recorded from the superior rectus muscle of the eye following vibration of this muscle at: A- 300 Hz, 20 μm, and B- 200 Hz, 20 μm. Note variability in tension traces with identical vibratory stimuli in A which was observed occasionally at this amplitude of displacement (see RESULTS for details).


A
B
100
μV
1g
1s
300 Hz
20 μm
200 Hz

through adjoining structures through volume conduction, the nerve of the vibrated muscle was cut after examination of the last responsive unit in each experiment. This test is especially crucial for the superior rectus muscle of the eye, where frictional disturbances of other extra-ocular muscles converging posteriorly in the orbit are likely to occur. After transection of the nerves, vibration of dorsal neck muscles, or the superior rectus muscle of the eye did not elicit responses in frontal projection regions either immediately after or two hours following nerve transection.

4.4 DISCUSSION

In the first two experiments a sub-population of dorsal neck muscle afferents projecting to the cat frontal cortex were electrophysiologically characterized as belonging to group 1. This category, however, consists of group 1a and 1b afferents which originate in the primary endings of muscle spindles and in tendon organs, respectively. Those studies did not, therefore, identify the receptor origin of the low threshold afferents eliciting the evoked neuronal responses. The present study demonstrated that group 1 afferents originating in the primary endings of muscle spindles project to at least a sub-population of neurons in the cat frontal cortex. Several characteristics of the evoked responses are compatible with activation of group 1a afferents. These include: 1) The increase in unit firing activity with increases in vibration frequencies from 100 Hz to 300 Hz at constant amplitude displacements as low as 20 μm. These stimuli activate powerfully the primary endings of muscle spindles, but hardly any secondaries (Matthews, 1972).

2) The decrease in amplitude displacements required to elicit unit evoked responses as the frequency of vibration was increased. 3) Frequency-dependent activity of units also activated with threshold intensities of electrical nerve stimulation, and their response with intravenous injection of succinylcholine, reported to activate the primary endings of muscle spindles (Smith, 1966; Fehr, 1965). This latter point, though suggestive, is indirect. It indicates that the recorded units received input from afferents originating in the primary endings of muscle spindles, but does not necessarily imply that this was due to activation of the spindles of the muscle in question only, since the receptors of other muscles with a possible projection to these frontal regions were also activated. However, taken with the rest of the evidence, this additional observation increases the confidence of the idea that afferents originating in the primary endings of muscle spindles of the cat dorsal neck project to the frontal cortex in regions corresponding with the cytoarchitectonic areas 4 and 6 (Hassler and Muhs-Clement, 1964). Dorsal neck muscles have already been noted as having one of the richest supplies of muscle spindles in the body (Granit, 1970; Richmond and Abrahams, 1975b).

Golgi tendon organs are low threshold receptors also, and since they are arranged in series with the extrafusal muscle fibers, they can be activated during muscle stretch and contraction. Experimental evidence, however, indicates that the latter is their best stimulus for activation (Houk et al, 1971). The tensions developed with the vibratory stimuli employed were less than 2.0 g, and even though tendon organs must have been activated as was indicated with the increase in the EMG activity,

several units in the frontal cortex responded to the vibratory stimuli before appreciable tensions and EMG responses developed in the muscle. Tendon organs, could not, therefore have appreciably contributed to those evoked responses. It should be noted in this context, that extracellular monosynaptic responses in neck motoneurons with activation of their nerve afferents are rare in the cat neck (Abrahams et al, 1975), pointing to an involvement of neck afferents in suprasegmental activities (Rapoport, 1977). The activation of units in the cat frontal cortex prior to overt influences on the stimulated muscle, suggests that regions of the frontal cortex may have a role in neural mechanisms of head movement control.

The possibility that the evoked unit responses might have been due to activation of Pacinian corpuscles should also be considered. These receptors respond well to frequencies of 100-300 Hz at displacements as low as 1 μm, and have been considered as vibration receptors (see Burgess and Perl, 1973 for review). However, these are not easily activated with frequencies below 50 Hz even with large amplitude displacements. In this experiment, with the exception of one unit, the rest responded to both low (25 Hz), and high frequencies (300 Hz) at displacement amplitudes of 20 and 50 μm.

Muscular nociceptors with afferent fiber diameter in the group III range have also been described (Mense, 1977; Paintal, 1960; 1961). Activation of these afferents by the present stimuli can be excluded on several grounds. Very few of the nociceptors respond to muscle stretch (Paintal, 1960; 1961; Iggo, 1961), whereas all the responses in this study were evoked by these stimuli. Moreover, the vibration displacement

amplitudes were kept at low levels and within physiological range, making it unlikely that these receptors, known to respond to tissue pressure and damage, were activated.

At least some of the evoked responses to vibration of the rectus capitis dorsalis major occurred during very low or before measurable tensions developed in the muscle. This finding suggests that even small displacements of the muscle, thought to play a role in head stability (Granit, 1970), activate these frontal cortical units. This observation is consistent with the idea that regions within the presylvian cortex, which receive input primarily from the suboccipital muscles, may be involved in mechanisms subserving fine head movement control, as was suggested in Chapter 2. An interesting observation emerging from this study is the apparent higher amplitude requirement for activation of biventer cervicis afferents electrophysiologically characterized as group 1. These afferents are activated with lower amplitudes of displacement in limb muscles (see Matthews, 1972), and even in another dorsal neck muscle as shown here. This might be a particular characteristic of the biventer cervicis, and its complex architecture was cited earlier as a possible cause of a relatively inefficient transmission of the vibration to the fibers of the muscle. However, muscle properties, including architectural characteristics reflect function. The tendinous intersections at various levels of the muscle enable the insertion of an increased number of muscle fibers, thus increasing the total cross sectional area of the muscle, and the maximum force that it can develop. Contraction of this muscle in the cat causes large head deviations, and its properties are well suited

for this action. The input from these two neck muscles to the frontal cortex may be related with their peripheral actions.

As has already been noted, large head deviations result in eye movements opposite the head movement, and it is afferents from the long and large muscles like the biventer cervicis and complexus that show the highest degree of convergence with extraocular muscle afferents (Chapter 3). The present study confirmed those results with the demonstration that vibratory stimuli to the biventer cervicis and single stretches of the superior rectus muscle activated the same frontal units in 67% of the cells thus tested. These results further establish that the fibers from both muscles involved in this projection system originate in muscle receptors.

The presented data also demonstrated that vibration and/or stretch of the extraocular superior rectus muscle also elicited single cell responses in the frontal cortex. The majority of evoked neuronal responses were tonic in nature, and these might be due to activation of slowly adapting stretch receptors which are present in cat extraocular muscles (Bach-y-Rita and Ito, 1966a). These receptors respond linearly to changes in muscle load rather than to changes in muscle length (Bach-y-Rita and Ito, 1966a), a situation mimicked by increases in vibration frequencies at constant length displacements in the present study (Table 4.1). The increased unit responses in the frontal cortex with increased frequencies of vibration observed in a sub-population of the units studied, is consistent with the activation of these receptors. Phasic unit activity in the frontal cortex may have been due to activation of afferents originating in fast adapting receptors, also described in cat extraocular muscles (Bach-y-Rita and Ito, 1966a).

The predominance of tonic cell responses in the frontal cortex with stretch of extraocular muscles, could have various implications concerning the processing of extraocular afferent projections to these regions. Cat extraocular muscles include both fast and slow muscle fibers. Although the site of the activated receptors in the present study is not known, the nature of the neuronal evoked responses suggests a predominant activation of receptors associated with slow muscle fibers. If this is indeed the case, a tonic input from extraocular muscles to the frontal cortex may be signalling the state of the muscle while the eyes are at rest, and also during a variety of eye movements, since these muscle fibers are active during most eye movements, including times when the eyes are in the primary position (Scott and Collins, 1973).

An interesting additional finding in the present study is the increased tension and EMG activity with muscle vibration, since this suggests a feedback control system in this extraocular muscle. Even though it was not the aim of the present experiment to investigate in depth this point, the observation merits discussion in view of the controversy over the significance, and at times even the existence of extraocular reflexes. Reports on the absence of extraocular reflexes have been largely based on experiments where passive pull of eye muscles failed to elicit the myotatic reflex response (McCouch and Adler, 1932; Irvine and Ludvigh, 1936; Whitteridge, 1960), known to occur in limb muscles. Keller and Robinson (1971) base their claim of the absence of such reflexes in the monkey, on the failure to detect changes in the firing rate of units in the abducens nucleus during normal

conjugate eye movements in the alert monkey when the eye muscles were stretched or shortened. On the other hand, evidence of reflexive control in extraocular muscles has been observed with the use of EMG techniques in the cat (Marek and Markel, 1971), and in humans (Maruo, 1964). Moreover, Sears et al. (1959) observed a decrease in muscle discharge during contraction, if that muscle itself, its antagonist, or yoke was stretched during the contraction phase. Inhibitory effects on extraocular nerve fiber activity were also unraveled in cat extraocular muscles during active contraction, while passive stretch did not produce such effects (Bach-y-Rita, 1972).

Indirect support on the presence of proprioceptive feedback in extraocular muscles has been provided by Collins (1971) with the demonstration of a series of parallel tension-extension curves in human extraocular muscles "at whatever angle of gaze stretching is begun" (Granit, 1971). Commenting on those data, Granit stated that this was an indication of the existence of feedback control in extraocular muscles, since experimental evidence has demonstrated that "in pure alpha activity stretch should produce a set of curves of different slopes depending on the number and firing rate of the alpha fibres" (Granit, 1971).

Reports of negative results in the literature with respect to the existence of extraocular feedback mechanisms, seem to be based on limited experimental conditions using passive stretch, while Keller and Robinson's (1971) method does not exclude the possibility that small motoneurons which are not easily sampled with extracellular microelectrode techniques might, in fact, be involved in extraocular stretch reflexes.

While all of the authors reporting negative results seem to have been in search of a phasic myotatic reflex, the possibility of a role of the tonic component of the stretch reflex (Matthews, 1970), although alluded to (Keller and Robinson, 1971), seems to have been generally neglected by these authors. A critical appraisal of these studies in the light of available information on the central connections of extraocular muscle afferents reveals some of the limitations of the procedures employed. The phasic component of the stretch reflex constitutes,by definition,the monosynaptic activation of motoneurons consequent to Ia afferent activation originating in the primary endings of muscle spindles of the homonymous muscle. The cell bodies of at least some extraocular afferents are in the trigeminal nucleus in the cat (Alvarado-Mallart et al, 1975), and in the Gasserian ganglion in goats and pigs (Manni, Bortolami and Desole, 1966). Neurophysiological reports indicate long latency responses in oculomotor nuclei to extraocular muscle stretch (Cooper Daniel and Whitteridge, 1951; Tomlinson and Schwartz, 1977) suggesting second order or later responses. If the primary afferents are in nuclei other than those containing the motoneurons of the extraocular muscles, as existing data suggest, an eye reflex loop is at least disynaptic, and probably polysynaptic. A monosynaptic stretch reflex is, by necessity, excluded in these cases. An additional point may further indicate why phasic reflexes may be the exception rather than the rule in extraocular muscles. These muscles are generally stretched during contraction of their antagonist, and fixation of gaze requires prolonged stretch of antagonistic muscles during contraction of the agonist. If a phasic stretch reflex was

readily elicited during muscle stretch, fixation would be impossible. This is not to deny that phasic reflexes may be operative in special circumstances, such as during optokinetic and vestibular nystagmus. On the other hand, the tonic component of the stretch reflex could have a role during eye movement. Commenting on this component, Matthews (1970) stated: "The essential thing to be kept in mind in thinking about the tonic component of the stretch reflex, is that it is a steady motor output to a steady barrage of afferent input, and that this allows for integrative neural mechanisms of a far higher order of complexity than one can hope to find displayed in the tendon jerk resulting from a single synchronous input". In fact, Baichenko (1967) has described a tonic polysynaptic reflex in the extraocular muscles of rabbits. The present data are in agreement with Baichenko's results as the presently observed EMG responses were also consistent with polysynaptic activation of reflex extraocular loops (see Fig. 4.12 and 4.13).

The EMG activity recorded in the orbital layer of the superior rectus muscle was presumably due to activation of multi-innervated slow tonic fibers which are capable of propagated action potentials (Bach-y-Rita and Ito, 1966b; Bach-y-Rita, 1967). These fibers would cause an increase in muscle tension upon contraction, but slow fibers with non-propagated impulse activity (Hess and Pilar, 1963) must have also contributed to the developed tension, as was indicated by an increase in muscle tension with no apparent EMG changes at times.

CONCLUSION

The results presented demonstrated that vibratory stimuli to dorsal neck muscles elicited single cell responses in the cat frontal cortex. A sub-population of the activated neurons exhibited responses compatible with the activation of the primary endings of muscle spindles. Vibration and/or stretch of extraocular muscles also evoked responses in frontal neurons, and included a sub-population which were also activated with vibration of the biventer cervicis muscle of the dorsal neck. The effects of the afferent signals originating in the activated receptors from both dorsal neck and extraocular muscles were varied in nature. These included both phasic and tonic evoked neuronal responses, which showed frequency-dependent characteristics in some neurons and in others did not. These multiple responses of frontal cortical units to dorsal neck and extraocular muscle vibration, suggest that afferents from these muscles reaching the frontal cortex may have a variety of roles in mechanisms underlying eye, head, and eye-head movement.

CHAPTER 5

DISCUSSION AND CONCLUSIONS

Although the exact mechanisms of the neural control of locomotion have not yet been elucidated, information on distinct brain regions involved in these processes, and the input-output relations between sensory afferents and motor output is now available. However, a similar picture concerning brain regions controlling extraocular movement, and eye-head movement has yet to be described. In recent years a great deal of work has been done on the brain stem organization of these movements. However, a system of eye and head movement which by nature involves the visual, auditory and olfactory senses in exploration of the environment, must involve telencephalic brain regions.

Early experimenters described that eye and head movements were elicited in primates with electrical stimulation of frontal brain regions, and thus implicated the so-called frontal eye fields in these activities. However, later workers demonstrated that these regions were neither necessary nor sufficient for eye and head movement, and their role in these actions remained unclear.

Recent experimental work on eye movement has been largely modelled after Helmholtz's (1867) outflow theory, which stated that the retinal image displacement signals caused during eye movement are cancelled by centrally originating signals commanding the eyes to move. Sherrington's inflow theory, on the other hand, stated that these displacement signals are cancelled by signals from the eye muscles to the brain.

The relative contribution of inflow and outflow systems in movement, should, perhaps, be evaluated on the basis of the behavioral situation under study. With regard to a frontal oculomotor region, reports on the absence of effects in eye movements following destruction of frontal cortical regions may have been the result of the restricted questions asked in the past. These regions receive converging signals from afferents originating in various sensory modalities, a prerequisite for central integration of mechanisms underlying the behavioral coordination of complex movement. These characteristics of the frontal cortex point to the need for an investigation of hypotheses other than those concerned with an involvement of these regions in eye movement under static conditions. Yet previous discussions have largely centered on the role of the frontal cortex in eye movement, per se.

The present study posed a different question: Is there, and how is a peripheral afferent input from the muscles that move the eyes and the head organized in the frontal cortex? As such, the present data provide strong support for the concept of centripetal input affecting neural events involved in mechanisms of eye and head movement. The description of an afferent input from the dorsal neck originating in muscle spindles, and the short latencies of neuronal responses evoked by these afferents in the frontal cortex are in keeping with current ideas of a role of these receptors in kinesthesia (for review see Matthews, 1977). Although the current work does not provide direct behavioral evidence for this, it is clear that an afferent input is prerequisite in suprasegmental events concerned with these functions.

The present experimental results defined the organization of dorsal neck and extraocular muscle afferents to the frontal cortex in terms of their regional distribution, thresholds for activation, the latencies of the evoked neural responses and following frequencies, the pathway(s) involved, the phasic and tonic nature of the evoked responses, and the excitatory and inhibitory interactions of afferents from dorsal neck and extraocular muscles. Included in the latter was the observation that the highest degree of convergence was between extraocular and dorsal neck muscle afferents originating in muscles that cause large head deviations upon contraction and result in eye movements in the opposite direction than the head rotation. The interaction of these signals in the frontal cortex may be a step in the sensory motor integration necessary for eye-head coordination.

The results presented also provided evidence that activation of muscle receptors of both dorsal neck and extraocular muscles activated circuits that elicited responses in the extrafusal muscle fibers of these same muscles. It is not known whether the cells receiving these afferents project back to the homonymous muscles, a question open for future study. However, given the high probability of response of the cells with stimulation of these afferents, and the fact that the majority were located in regions which constitute major corticofugal fiber systems, it would be surprising if they were not thus involved.

Having defined some physiological properties of the neural connections between extraocular and dorsal neck muscles with the frontal cortex, investigations in non-anesthetized animals are now needed to explore

specifically the types of movement in which these afferents may be involved. The response characteristics of these units may, for example, vary during altered head and body positions of the animal. The use of alert animals may help specify the functional significance of the complex excitatory-inhibitory interactions between afferents from the various muscles observed in the present studies.

At the anatomical level, experiments may be designed to test directly the cortico-cortical connections hypothesis (see Chapter 2, Experiment 2) in the various sub-regions which receive dorsal neck and extraocular muscle afferents. These experiments will speak further on the regional characteristics and variations of the afferent input. The course of the extraocular afferents to the frontal cortex may also be investigated anatomically, and recent advances in the study of afferent polysynaptic pathways with the use of metabolic labelling techniques of active neurons may also be applied here.

Ablation studies may further increase the understanding of the role of the frontal cortex in eye-head movements, if tasks are specifically designed to ensure a dependence of the animal on proprioceptive signals originating in these peripheral muscles. Alternative cues, which are likely to obscure deficits which might otherwise be evident, should be carefully eliminated. Studies which have reported concrete impairments in various species with frontal cortex damage in the past, showed a definite pattern: deficits were always present in complex movements which often required the use of coordinated eye-head and often limb and whole body movements. Even though with the use of complex tasks more deficits

will be evident in any ablation study, those results pointed to the significance of the frontal cortex in another aspect of movement, and specifically that which is likely to affect fine motor control. Asanuma's work (Asanuma et al, 1968) on input-output relationships emphasized the close coupling of afferent-efferent relationships at the electrophysiological level. Other investigators pointed to the importance of peripheral signals for fine motor control, which become increasingly crucial as the movement grows more complex and additional demands are imposed on the animal (see Introduction). In view of the present demonstration of an afferent interaction of extraocular and dorsal neck muscles, and on previous accounts on the importance of proprioceptive signals in complex motor tasks requiring fine motor control, perhaps it is experiments emphasizing this latter aspect of movement that will further elucidate the role of the frontal cortex in eye and head movement.

SUMMARY

Electrical nerve stimulation of dorsal neck muscles elicited single cell activity in the frontal cortex of chloralose anesthetized cats at latencies of 6-45 ms. Biventer cervicis and complexus afferents projected within pericruciate, presylvian, and coronal cortical regions, whereas the suboccipital muscles projected mainly to presylvian and coronal regions. The highest mean latencies of neuronal evoked responses were recorded in pericruciate regions, and the latencies were progressively shorter in coronal and presylvian regions. Approximately 20% of the responsive neurons were activated by afferents that were electrophysiologically characterized as

as belonging to group 1. These afferent projections depended on the integrity of the dorsal funiculus. Electrical nerve stimulation of dorsal neck muscles also elicited inhibitory effects in 30% of the cells tested. The presence of inhibition was evaluated against a background of neuronal excitation induced through the iontrophoretic release of glutamate.

Extraocular muscle afferents also projected to frontal brain regions at latencies of 7 - 50 ms, and showed excitatory and inhibitory converging effects with dorsal neck muscle afferents at the single cell level. There was a higher degree of convergence between the large neck muscles, biventer cervicis/complexus and extraocular muscles (53-62%), than between the smaller suboccipital muscles and extraocular muscles (26-30%). Vibratory stimuli to dorsal neck and extraocular muscles elicited phasic and tonic neuronal responses in the frontal cortex, and EMG and tension increases in the muscles. A sub-population of these cells increased their firing activity as the frequency of vibration was increased from 100 to 300 Hz at constant amplitude displacements as low as 20μ and 50μm. These data demonstrate that cells in the frontal cortex are influenced by afferents originating in low threshold receptors in these muscles. The excitatory and inhibitory interactions of dorsal neck and extraoccular muscle afferents in the cat frontal cortex suggest that these cortical regions are involved in coordinated eye-head movement.*

*The results summarized above, and described in detail in Chapters 2, 3, and 4 are original.

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