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SENSORY TRANSMISSION THROUGH THE LEMNISCAL PATHWAY DURING MOVEMENTS AND AROUSAL IN THE CAT

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SENSORY TRANSMISSION THROUGH THE LEMNISCAL PATHWAY

DURING MOVEMENTS AND AROUSAL IN THE CAT

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CHAPTER I

INTRODUCTION

A significant role in perceptual-motor coordination has been attributed to sensory changes produced in association with voluntary movement (36-39, 78, 81). Particularly, experiments in the visual modality, suggest that the central nervous system may be able to differentiate between neural input arising from purely exteroceptive origin and sensory input caused by self-produced actions of the organism. For example, there is the old question as to why the motion of the retinal image over the retina caused by the rapid voluntary movement of the eye from one fixation to another does not give rise to any sensation of movement. Obviously other displacements of the image relative to the retina do. One explanation of this phenomenon postulates a central mechanism, time locked with discrete voluntary movements and postural changes which would in some way modulate or prepare the sensory system for changes that occur as a result of intended movements (45, 46, 77). Thus the initiation of movements is assumed to be associated not only with an efferent discharge to the musculature, but also with a concurrent central discharge (corollary discharge [77]) into the

appropriate sensory system which serves to cancel out the self-produced sensations. Accordingly, afferency produced by changes in the environment is preceived directly whereas the afferent input caused by voluntary motor activity is not. Implicit in the model is the suggestion that the central processes involved with the initiation of voluntary motor activity are further accompanied by influences which modify the transmission of sensory information along ascending central nervous pathways.

The regulation of sensory input by higher nervous centers has also been implicated in the neural mechanisms underlying selective attention, orienting behavior and habituation to repetitive stimuli (see 41). Following the discovery (35) that electrical stimulation of various parts of the brain, through centrifugal pathways to sensory nuclei, could modify the transmission of sensory impulses at all levels of the specific afferent systems, it was suggested that such processes could serve to filter out or enhance certain types of information (40). For example, recordings from unanesthetized animals with implanted electrodes have shown that evoked potentials from the lowest sensory relays are reduced when the animal seems inattentive to a test stimulus. Thus, the tactile evoked potential recorded from the lateral column of the spinal cord diminishes when the animal is attentively sniffing a strong odor (43). Likewise, evoked potentials in afferent pathways are reduced with monotonous repetition of the same stimulus (40). It has been suggested that both types of sensory suppression are the result of active inhibitory influences arising from higher structures whose function is the filtering and selection of sensory input which may accompany such phenomena as the orienting response, habituation and attention (41, 42, 44).

The central modulation of afferent systems has been further implicated in the mechanisms underlying postural-motor coordination and the integration of sensory feedback generated in association with movements. Of particular interest are recent neurophysiological investigations of the sensory and motor events characterizing different stages of physiological sleep in the cat (See 69,70). Evidence has accumulated indicating that during the bursts of rapid eye movements (REM) of desynchronized electroencephalographic sleep there occurs a phasic inhibition of afferent transmission at the first relay stations of the ascending sensory pathways (see 70). At the same time, however, there is also a postsynaptic facilitation of the sensory volleys at the level of the specific thalamic relay nuclei (3, 18, 27). Furthermore, while the stage of desynchronized sleep is characterized by a tonic inhibition of the spinal motoneurons, there simultaneously occurs with the REM, a phasic enhancement of motor activity in both the pyramidal and extrapyramidal pathways which gives rise to brief muscular contractions and movements (25, 26, 61).

These observations have led to the hypothesis that the changes which occur in the sensory systems during the motor activities of REM sleep may also be manifested during voluntary movements in waking animals (27, 70). The central control of sensory input is assumed to be of importance for modulating the afferent feedback produced in conjunction with movements. Specifically, it is suggested that the inhibition of sensory impulses at the first synaptic relay which is subsequently followed by facilitation at the thalamic level results in a partial substitution of internally generated stimulation for the external sensory feedback arising from movements (27,70).

In summary, the active control of sensory processes is clearly implicated as an important factor in certain perceptual constancies, selective attention, and the integration of sensory feedback produced in association with voluntary movements. These considerations represent a divergence from the more traditional concept which assumes that impulses generated in receptors are simply relayed to higher centers, such as the cerebral cortex for their integration. At the heart of many of the newer formulations is the recognition that the relation of the central nervous system to the peripheral sensory and motor mechanisms is not that of a passive chain-reflex process. As Teuber (81) has pointed out, there may be little hope of understanding the central correlates of sensation and perception while conceiving the nervous system as a passive receiver of sensory input. Neither the view that sensations are converted to perception by past experience or memory, nor field theories which often ignore the orderliness of the underlying neural substrate are satisfactory in this respect. Both fail to appreciate that the senses may not merely convey stimulus energy, but that they are also systems for actively obtaining information about the environment and the relation of the organism to it. A further weakness of these older positions lies in their dependence upon the classical sensory pathways as the exclusive origin of perceptual behavior. As Gibson (29) recommends, the basic elements of perception arise from the classical sensory organs only when they are oriented to sources of stimulation by way of the body and when they are active; that is, when they adjust and explore so as to obtain information. Thus the nervous system operates upon its inputs, not only in selecting them, but by

providing an essential organization of these inputs relative to voluntary movement and motor function.

This newer approach may allow the function of the peripheral senses in relation to perceptual activity and motor coordination to be regarded from a new viewpoint. It can now be asked, for example, what effect is produced on the sensory pathways by the motor influences associated with the initiation of voluntary movements, and, furthermore, to what extent do the mechanisms responsible for the control and coordination of movements also participate in such processes as selective attention, orienting and habituation phenomena, and perceptual behavior in general.

The Dorsal Column-Medial Lemniscal Pathway as a Model System for the Study of Motor Influences on Sensory Process

The dorsal column-medial lemniscus system is a major afferent pathway for cutaneous tactile input. The dorsal columns occupy the extreme dorsal medial quadrant of the spinal cord and are composed mainly of first order sensory neurons. It is an uncrossed system throughout the length of the cord. The first order neurons synapse onto second order cells in the dorsal column nuclei in the medulla, and from here the second order neurons form the medial lemniscus which decussates at this level and continues upward to terminate in the posterolateral-ventral nucleus of the thalamus.

Sensory Functions of the Lemniscal Pathway

The sensory functions of the dorsal column-medial lemniscal system have been determined using a number of methods including the recording of single cell activity in response to natural stimulation in animals, the evaluation of sensory defects produced in neurological

patients by pathology of this system, and the analysis of the effects produced by lesions in experimental animals. A number of studies have shown that single units recorded in the dorsal column nuclei are responsive to hair movement and light touch or pressure applied to the skin, while other units are able to follow high frequency vibration (32, 53, 67). Still other cells respond to the position or movement of the limbs (51, 52, 88). These three classes of responses thus reflect the generally recognized sensory functions of the dorsal column system, namely the tactile, position and vibratory senses. Similar conclusions have been drawn from the impairment of sensory capacity following either experimental or pathological damage to this system. However, the degree of impairment resulting from such lesions is highly variable and may depend upon such factors as the type and extent of damage (see 66). It has recently been emphasized by Wall (87) that the dorsal columns may be of vital importance for processing the sensory information produced during exploratory movements.

Synaptic Mechanisms in Dorsal Column Nuclei

Since the dorsal column nuclei (nucleus gracilis and nucleus cuneatus) represent almost exclusively the single synaptic relay in the transmission pathway for the sensory information carried over the medial lemniscus to the thalamus, considerable interest has centered on their activity and function. The organization of these nuclei has turned out to be far more complex than was generally assumed only a few years ago when it was believed that they were simple relay nuclei. A wealth of studies have shown both excitatory and inhibitory influences to be imposed upon the second order cells of the dorsal column-medial lemniscal pathway

and indicate further that these effects may arise both from the periphery and from higher centers.

Afferent or "surround" inhibition is the most commonly noted effect and is found in units of the dorsal column nuclei when an area outside a cell's receptive field is stimulated (30, 32, 67). This depression is due to the mechanisms of both pre- and post-synaptic inhibition (5, 7). The presynaptic influence is suggested by the fact that afferent volleys are associated with depolarization of the terminals of primary afferents within the dorsal column nuclei (5, 7) and by the finding that there are interneurons with properties similar to those in the spinal cord that are considered to be interpolated as the presynaptic inhibitory pathway (6). The existence of a postsynaptic inhibitory mechanism has been suggested under similar conditions by the appearance of inhibitory postsynaptic potentials (IPSPs) recorded intracellularly from cuneothalamic (lemniscal) neurons and a decrease in the excitability of these cells to direct electrical stimulation (7). The significance of the afferent inhibition process is the creation of an excitatory receptive field with an inhibitory surround in a manner similar to the relations seen in the vertebrate eye. On this basis peripheral stimulation of afferent fibers which end in the dorsal column nuclei may inhibit the ongoing activity of certain units or when presented as a conditioning stimulus inhibit normal evoked activity in second order neurons. Such a mechanism along with the phenomenon of afferent facilitation (30, 32) has been considered an important process for the enhancement of spatial contrast in the incoming impulse pattern carried by the dorsal column-medial lemniscal pathway (65).

Central Influences on Synaptic Transmission Through the Dorsal Column Nuclei

In addition to perpheral influences, centrally induced modulation of activity in the dorsal column system has also been described. Both anatomical (16, 53, 54, 85) and physiological (5, 7, 19, 31, 33, 34, 55, 60, 82) evidence indicates that the sensorimotor cortex influences the transmission of impulses through the dorsal column via collaterals from the pyramidal tract which end mainly upon interneurons (6) within these nuclei and exert presynaptic and postsynaptic inhibition (5-7). Other investigations have also indicated that stimulation of the sensorimotor cortex may have excitatory effects which could be exerted via the pyramidal tract (31, 50, 60). However, there is no evidence to indicate that cuneothalamic neurons forming the medial lemniscus are actually activated by volleys descending from the cerebral cortex (7, 10). In this regard it would be expected that pyramidal tract influences arising from cortical stimulation would increase the firing rates of inhibitory interneurons located in the dorsal column nuclei (7, 10).

It has also been suggested that an alternative inhibitory pathway is by way of the reticular formation in the brainstem (14, 15, 34, 41, 43, 75).

In acute experiments, Hernandez-Peón and his colleagues found in the cat that brief electrical stimulation of the mesencephalic or pontine reticular formation inhibited the postsynaptic activity of the gracile nucleus evoked by single shocks applied directly to the dorsal columns of the spinal cord (43). Since, in chronic animals, electrical stimulation of the reticular formation as well as behavioral states

associated with reticular arousal can be shown to produce inhibition of sensory input over other ascending spinal pathways (see 41), it was suggested that inhibition in the dorsal column pathway is mediated under similar circumstances. However, these authors never validated this hypothesis by direct experimentation in freely moving, unanesthetized animals.

Following these early observations, the modulation of sensory transmission through the lemniscal pathway was investigated during different stages of sleep and arousal by Pompeiano and his colleagues. In a series of experiments it was shown that during the bursts of rapid eye movements (REM) of desynchronized sleep in the cat there was a reduction of the orthodromic lemniscal response to single shock stimulation of the superficial radial nerve (9). It was also found that at the same time there was a phasic enhancement of pyramidal tract activity which was associated with brief muscular jerks and movements that often accompany the bursts of REM (25, 61). Furthermore, the reduction of the lemniscal response and the increase in pyramidal tract activity were also observed during the "arousal reaction" produced by a brief acoustic stimulus (9). Subsequent investigations showed that the depression of the lemniscal response during bursts of REM could be attributed to the mechanisms of pre- and post-synaptic inhibition (10) and that lesions of the sensory motor cortex which prevented the appearance of the phasic increase in pyramidal tract activity also prevented the inhibition of the evoked lemniscal response at this time (11). In addition to lesions of the sensory motor cortex, it was shown that destruction of the medial and descending vestibular nuclei also prevented

the pyramidal discharges as well as the inhibition of the lemniscal response. However, this latter condition was associated with a complete absence of any of the phasic manifestations of desynchronized sleep including the bursts of REM (11, see 70). On the basis of these observations, it was concluded that the vestibular nuclei depress synaptic transmission through the dorsal column nuclei via the roundabout way of the sensory motor cortex and the pyramidal tract (11). Since it has also been shown that the vestibular nuclei are indirectly responsible for the blockade of afferent activity directed toward ventral motoneurons (64, 69, 72, 73) during the bursts of REM of desynchronized sleep in the cat, a further suggestion was made. When motoneurons are excited by supraspinal volleys originating from or triggered by the vestibular nuclei, it may be functionally important to uncouple both the motoneurons from their segmental reflex afferents as well as the supraspinal motor control centers from peripheral feedback (17, 70).

This last series of experiments remains virtually the only systematic study of the modulation of sensory input over the lemniscal pathway during different behavioral states in unrestrained, unanesthetized animals. Furthermore, it is the sole study demonstrating the origin of the central influences on sensory transmission at the synaptic level under such conditions. Although there has been one other report by Favale, Loeb, Manfredi and Sacco (23), that evoked potentials in the medial lemniscus show no change during different stages of sleep, these authors did not record eye movement activity during sleep. On the other hand, they did confirm the finding that during the "arousal reaction"

there may be a reduction in the lemniscal evoked responses which they suggested might be attributable to reticular formation influences. No further experiments were performed, however, to test this hypothesis.

A brief technical note on single unit activity in the dorsal column nuclei of the rat exhausts the small literature concerning changes in sensory transmission through the dorsal column-medial lemniscal pathway in unanesthetized animals during naturally occurring behavior. Ainsworth, Gaffen, O'Keefe and Sampson (2) reported that one unit responded to a threshold cutaneous stimulus with two spikes when the animal was sitting quietly, but with only one spike when it was engaged in some other activity such as walking about or grooming.

Sensorimotor Integration in the Lemniscal Pathway: Possible Relations to Mechanisms of Attention and Perception

Earlier it was mentioned that a significant role in perceptual-motor coordination has been attributed to sensory changes associated with voluntary movement (36-39, 78, 81). In this context a mechanism has been suggested which may account for how animals and man can distinguish the sensory consequences of their own movements apart from the results of stimulus events in the external environment (45, 46, 77). In the proposed model, the distinction between two types of afferent input is made by referring to sensory changes of exteroceptive origin as "ex-afference" and self-produced sensations resulting from movements as "re-afference" (45). According to this scheme ex-afference is perceived directly by the organism while re-afference is not because the organism when initiating any voluntary movement forms an "efference copy" which functions to cancel out the self-produced afferent input

(re-afference). In other words, the initiation of any voluntary movement is associated not only with a motor discharge to the appropriate effector organ, but also with a concurrent central discharge (corollary discharge [77]) back into the appropriate sensory system which normally matches or cancels out the sensations produced by the active movement. The concept of corollary discharge has proven useful in the analysis of the central control of eye movements and certain perceptual constancies in the visual system (see 81). It may also provide an interesting point of reference for analyzing the modulation of sensory input over the lemniscal pathway by activity originating in neural structures classically regarded as being solely involved in motor function.

In view of the anatomical and physiological relation of the pyramidal tract to the synaptic relays of the dorsal column-medial lemniscal system it would seem a likely possibility that downstream influences carried by the pyramidal tract in association with voluntary movement may simultaneously modulate sensory transmission over the lemniscal pathway. The results from numerous investigations of cortical influences on sensory transmission through the dorsal column nuclei performed in acute preparations could serve as a basis for directly testing whether or not voluntary movements in the unrestrained, unanesthetized animal are accompanied by a reduction of cutaneous sensory input over the dorsal column-medial lemniscal pathway. Confirmation of such a finding would be the first step in demonstrating the validity of the corollary discharge theory in reference to its actual operation at the neural level.

Other researches into the neural mechanisms of the orienting response, habituation and selective attention, provide a different approach for the interpretation of the central modulation of sensory input over the lemniscal pathway. Hernandez-Peón and others (see 48) have suggested that certain behavioral states associated with activation of the reticular formation may be accompanied by suppression or enhancement of sensory input at the lowest levels of the specific afferent pathways. During the orienting response to a novel stimulus it is thought that irrelevant sensory information is suppressed by the reticular system while the receptivity of the organism to a new stimulus may be enhanced (42). Such a conclusion may be supported by the findings of Carli, Diete-Spiff and Pompeiano (9) and Favale, et al (23) that in cats the evoked lemniscal response to brief cutaneous shocks is reduced during the arousal reaction produced by a novel auditory stimulus. On the other hand, neither of these studies investigated whether or not the reticular formation was directly participating in this phenomenon. Additionally, the possibility that the inhibition of the lemniscal response was attributable to a mechanism involving movement, similar to that just proposed cannot be ruled out. Finally, since the animals in both cases were free to move, the contribution of afferent inhibition (caused by movement stimulation of sensory receptors in the skin and muscles) to the reduction of the lemniscal response cannot be properly evaluated. Nevertheless, the hypothesis that activation of the reticular formation, which accompanies certain behavioral states, can directly modulate sensory input over the lemniscal pathway in the absence of movements remains to be investigated in unanesthesized, free-moving animals.

Still a third interpretation of the finding that sensory changes can be produced by supraspinal influences has been suggested by Pompeiano (17, 27, 70). Although bearing a similarity to the corollary discharge mechanism operating at the neural level which is proposed here, this approach has also emphasized the role of sensory modulation as important for coordinating the afferent feedback produced during phasic movements with the tonic mechanisms responsible for postural maintenance. Evidence that electrical stimulation of higher centers which evokes discharges in ventral motoneurons, also produces inhibition of sensory inputs in spinal reflex arcs (4, 12, 13, 63) has recommended the following hypothesis. It may be functionally important to reduce afferent input both at the segmental as well as more central levels at the time that spinal motoneurons are discharged by higher motor centers. Such a process would conceivably prevent instabilities in the motor system which would otherwise occur when the somatosensory volleys produced during movement were fed back along central nervous pathways to interact with the discharging motoneurons or the supraspinal motor control centers themselves (17, 70). Applying this interpretation to the modulation of sensory input through the lemniscal system it would be hypothesized that in association with voluntary movements in the unrestrained, unanesthetized animal there would be a simultaneous depression of synaptic transmission through the dorsal column nuclei. Furthermore, the depression of sensory input at lower levels may be accompanied by a facilitation at subsequent synaptic relays which would contribute also to the maintenance of "proper perception" during movements (27, 70). It should be added that this hypothesis predicts the

same phenomenon with respect to the transmission through the lemniscal pathway as does the adapted version of the corollary discharge mechanism proposed here. However, the latter theory originally postulated the cancellation of certain patterns of afferent input as being the essential mechanism for maintaining perceptual stability during voluntary movements.

Statement of the Problem

In the preceding section, recent physiological and anatomical evidence pertaining to the central modulation of sensory input over the dorsal column-lemniscal system has been reviewed. Also, several alternative interpretations concerning the role of inhibitory influences on afferent transmission along this pathway are discussed. However, in spite of the well documented existence of mechanisms for sensory control in the lemniscal system in acute surgical preparations, a systematic study of these processes during normal, waking behavior in intact subjects is yet to be reported. Therefore, the following section is devoted to the development of a research approach for investigating possible changes in sensory transmission through the lemniscal pathway in association with normally occurring behavior in freely moving, unanesthetized cats. More specifically, experiments will be performed with the aim of providing answers to the following questions.

1. Is the transmission of cutaneous sensory information through the lemniscal pathway modified during the arousal reaction or orienting response produced by the presentation of a novel stimulus in the unrestrained, unanesthetized cat?

2. Is the transmission of cutaneous sensory information through the lemniscal pathway modified during discrete voluntary movements?
3. To what influences, either central, peripheral, or both, can any modification of sensory transmission through the lemniscal pathway in the two preceding conditions be attributed?
4. To what extent can any modification of the sensory transmission through the lemniscal pathway by central and peripheral influences under the two conditions be interpreted by theories concerned with the active control of sensory processes in relation to perception, attention and motor coordination?

CHAPTER II

METHODS AND MATERIALS

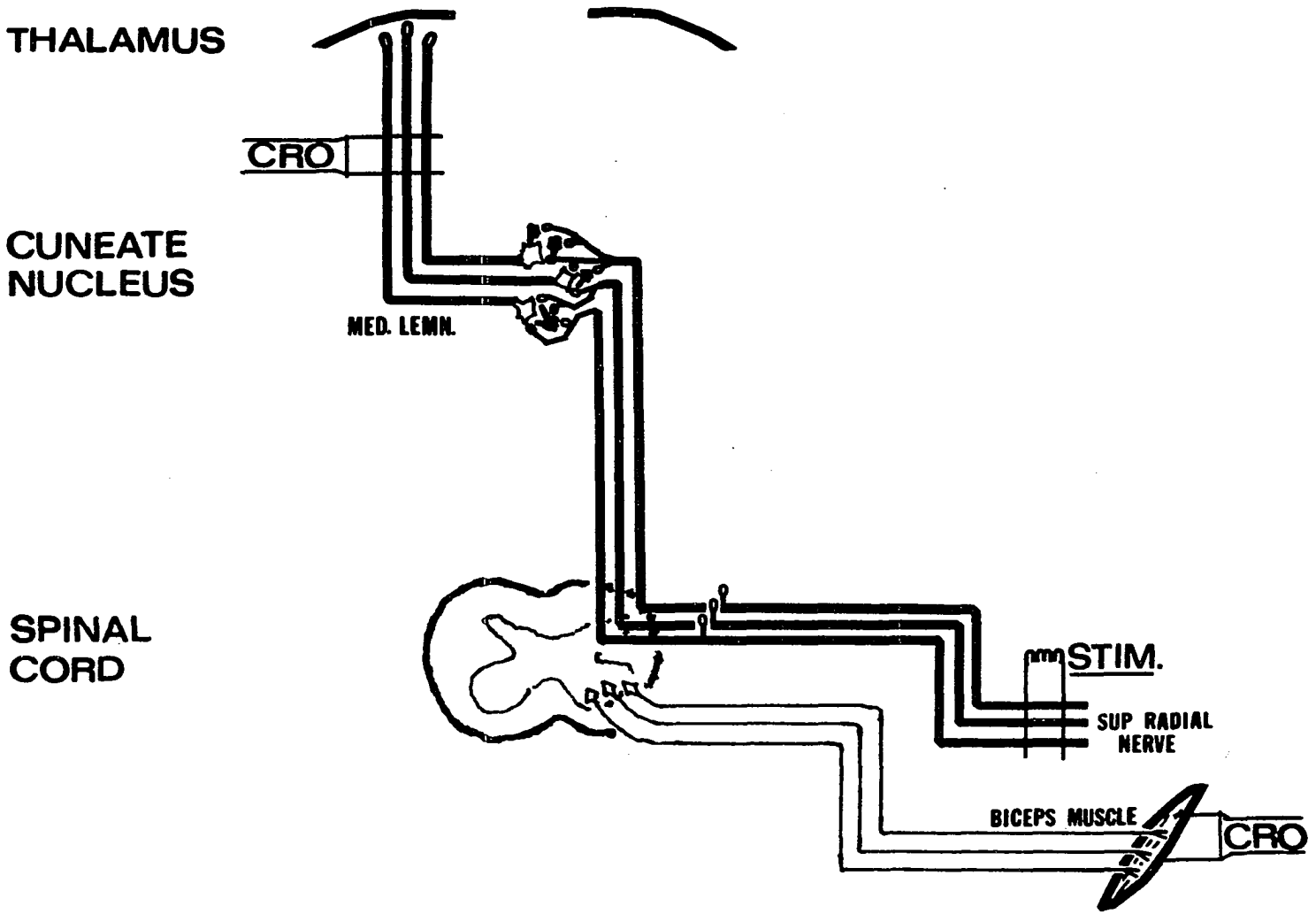
The experiments were performed on unanesthetized, freely moving cats bearing chronically implanted electrodes for stimulation and recording. Figure 1 shows the location of the electrodes for recording evoked responses in the left medial lemniscus to single shock stimulation of the right superficial radial nerve (a pure sensory cutaneous nerve) and for recording electromyographic activity (EMG) in the biceps muscle of the right forelimb.

Electrodes

Evoked potentials in the medial lemniscus were recorded via a pair of insulated 100 μ nichrome wires stuck together with electrode insulator varnish. These two wires were then inserted into a stainless steel capillary tube (length, 25 mm; diameter, 0.6 mm) and extended 10 to 12 mm from the end. The entire device was then insulated with varnish except at the very tip, where the inter-electrode distance was less than 0.4 mm. The other ends of the wires were soldered to small connector pins which mated with the lead wires to the amplifier.

Figure 1. Location of stimulating and recording electrodes in the lemniscal pathway.

The bipolar electrode (STIM.) implanted on the superficial radial nerve (SUP. RADIAL NERVE) of the right forelimb is used to evoke orthodromic responses in the contralateral medial lemniscus (MED. LEMN.) The lemniscal responses are recorded via a chronically implanted bipolar electrode and displayed on the cathode ray oscilloscope (CRO). An implanted EMG electrode in the biceps muscle of the right forelimb is used to record muscle activity during voluntary flexion movements of the limb. Also shown are both pre- and postsynaptic inhibitory paths in the cuneate nucleus (inhibitory interneurons in black).


THALAMUS
CRO
CUNEATE NUCLEUS
MED. LEMN.
SPINAL CORD
STIM.
SUP RADIAL NERVE
BICEPS MUSCLE
CRO

The EMG recording electrode consisted of a pair of 100 μ nichrome wires, 5 mm in length, and insulated, except at the tips, which were soldered to 36 gauge teflon insulated multistrand wire. The two nichrome wires were bent at a 90° angle and a small plastic piece was used between the wires to maintain an inter-electrode distance of approximately 5 mm. The entire device, consisting of the teflon lead wires and the plastic piece, was then threaded into a Silastic (Dow Corning) silicone elastomer tubing (outside diameter 1.9 mm) and sealed at the ends with Silastic medical adhesive silicone Type A. Small connector pins were soldered onto the lead wires to mate with the amplifier leads. A small hole through the plastic piece allowed the device to be sutured firmly to the muscle with the two electrode wires penetrating into the muscle to a depth of 2-4 mm. The length of the lead wires was sufficient (18 to 20 cm) to allow them to be carried under the skin up to a head connector.

The nerve stimulating electrode consisted of a pair of 38 gauge stainless steel suture wires (5 mm in length) which were soldered to 36 gauge teflon insulated multistrand wire and threaded into Silastic tubing, the ends being sealed with Silastic medical adhesive. Similarly, small pin connectors were soldered to the lead wires.

The teflon insulated lead wires used for the EMG and nerve stimulating electrodes were very resistant to mechanical damage but remained quite flexible and did not interfere in any observable way with the animal's mobility. The suitability of the stainless steel wires used for the various electrodes, as well as the Silastic material, for chronic implantation in tissues has been well documented (24, 79) and gross histological observations of the animals used here confirmed these findings.

Surgery and Electrode Implantation

Cats weighing between 2.0 and 3.5 kilograms were anesthetized with an intraperitoneal dose of sodium pentobarbital (Nembutal) 35-40 mg/kg with supplementary doses administered intravenously in order to maintain surgical anesthesia. Areas over the lateral aspect of the right forelimb and on the top of the head were shaved and washed with surgical soap. The animals were then fixed into the stereotaxic frame and draped.

The surgical procedure was aseptic in that all instruments, materials and drapes were sterilized by either autoclave or immersion in a solution of benzalkonium chloride (1:750).

Implantation of the nerve stimulating electrode generally followed the technique described by Pompeiano and Swett (71) and Straw and Mitchell (79). A 5 to 7 cm incision is made on the lateral aspect of the forelimb, just proximal to the elbow. Using care to preserve the blood supply to the tissues, approximately 12 mm of the superficial radial nerve is dissected free at the point where it passes between the lateral head of the triceps and the brachialis muscles. The bared stainless steel wires of the stimulating electrode are then carefully circled around the nerve, the interelectrode distance being about 4-6 mm. As recommended by Straw and Mitchell (79), Silastic RTV 382 diluted with 360 silicone medical fluid, approximately two parts RTV to one part fluid, is then catalyzed and immediately poured over the wires and the nerve. After the Silastic has solidified the edges of the mass are then fixed to the under side of the lateral head of the triceps muscle with dacron sutures (size 000) thus preventing any displacement of the electrode

during movements. The triceps muscle and the brachialis muscle are then sutured together over the electrode. Finally, the lead wires are passed under the skin of the foreleg, shoulder area and back to emerge through an incision on top of the animal's head. The lead wires were of sufficient length to allow a small amount of slack to be coiled subcutaneously to permit normal locomotion without pulling against the nerve in a damaging or painful way. This method proved extremely successful in that slipping of the nerve with reference to the stimulating electrode, changes in interelectrode distance or shorting of the electrodes into surrounding tissues was virtually impossible since the entire nerve and electrode assembly were completely encased in the soft silicone mass. As will be mentioned later, several physiological tests added further confirmation that the technique employed here meets all favorable criteria for the stimulation of peripheral nerves in the chronic, unanesthetized, free-moving animal.

Implanation of the EMG electrode was accomplished through the same incision used for implanting the nerve-stimulating leads. The two short nichrome wires which emerged perpendicular from the surface of the thin plastic piece were introduced deep into the biceps muscle until the plastic plate rested flush against the muscle surface. A small hole in the body of the plastic piece allowed the electrode to be firmly anchored in place with dacron sutures. The lead wires were then passed subcutaneously to emerge through the incision in the skin over the head. Routine surgical closure with a continuous suture (silk, size 000) was then made of the incision over the two implanted electrodes.

The electrode used for recording potentials in the medial lemniscus was introduced stereotaxically through a small opening in the parietal bone to reach the lemniscus at approximately a point just caudal to the red nucleus (Horsley-Clark coordinates A:2.5, L:4.5, H:-4.0). During introduction of the electrode evoked potentials were elicited by single shocks delivered via the implanted electrode on the superficial radial nerve in order to have an accurate test for the localization of the recording electrode in the medial lemniscus. When suitable recordings were obtained the electrode was anchored in place with dental acrylic. A small screw electrode located over the frontal sinus served as electrical ground. Figure 2 illustrates the location of the recording electrodes in the left medial lemniscus for the 8 animals used in the experiments.

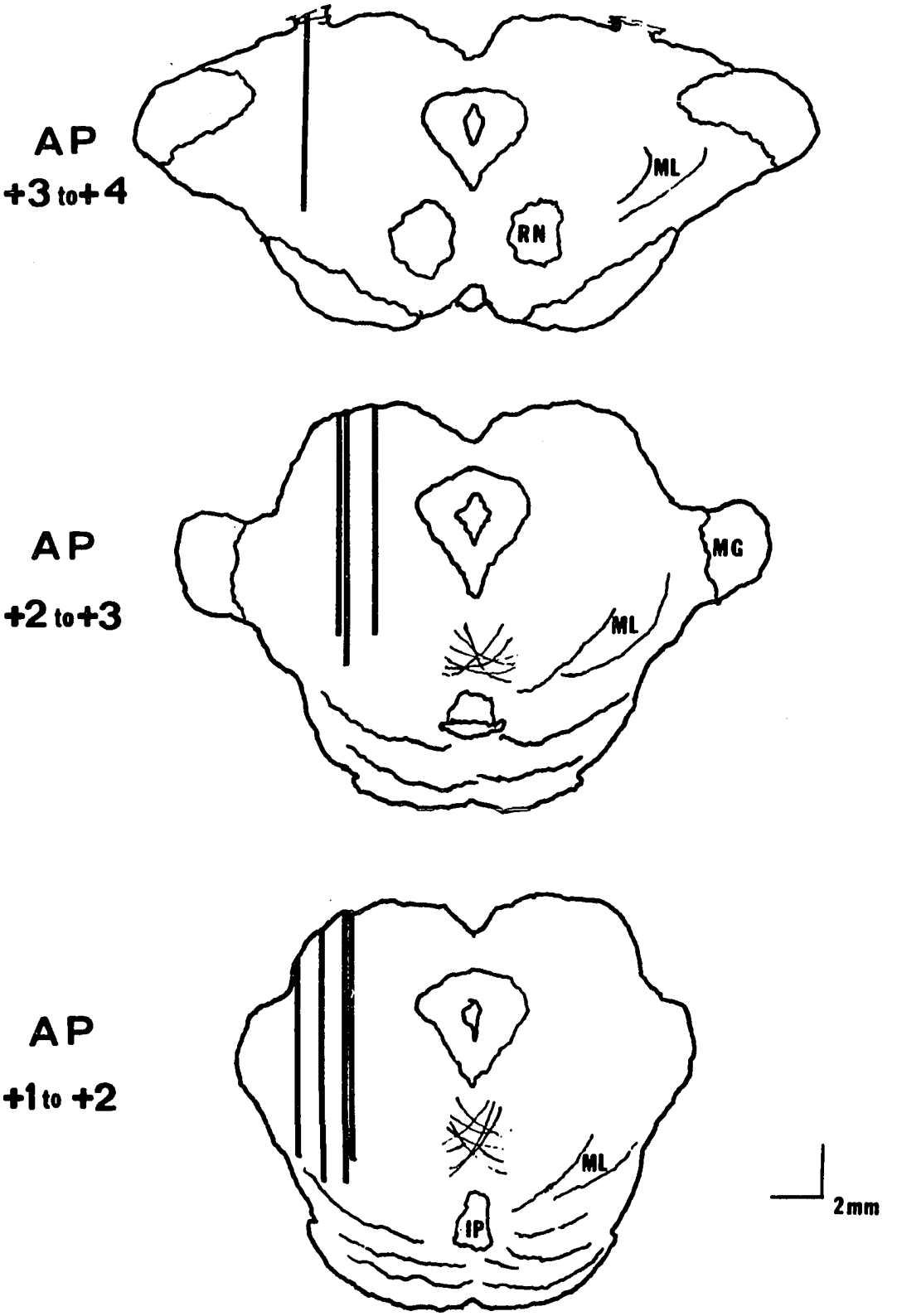
All of the electrode leads were inserted into a light weight plastic connector plug (Amphenol; diameter, 1.6 cm; length, 2.0 cm) which was secured to the head with dental acrylic and finally the surgical incision was closed with tightly spaced interrupted sutures. The animals routinely received 300,000 units of penicillin for several days following the operation to prevent infection.

Instrumentation and Recording Procedures

Following recovery from the effects of the anesthesia (36-48 hours) the animal was placed in a sound attenuated electrically shielded recording chamber (length, 1.2 m; height, 1.0 m; depth, 1.0 m) and connected to the recording apparatus via a double shielded cable. The chamber as well as the cable did not restrict movement of the animal to

Figure 2. Location of the bipolar recording electrode in the left medial lemniscus.

The placement of the bipolar recording electrode in the left medial lemniscus was confirmed on frozen serial sections (sectioned at 50 μ) for each of the 8 animals used in this study. The diagrams indicate the anterior-posterior (AP) interval, in millimeters, according to the Horsley-Clark stereotaxic coordinates, in which the electrode tips were found to be located. For 1 animal, the electrode was located between 3 and 4 millimeters anterior (AP +3 to +4) to stereotaxic zero; for 3 animals, between AP +2 and +3; and for the remaining 4 animals between AP +1 and +2. IP: interpeduncular nucleus; MG: medial geniculate; ML: medial lemniscus; RN: red nucleus.


AP
+3 to +4
ML
RN
AP
+2 to +3
MG
ML
AP
+1 to +2
ML
IP
2mm

any appreciable extent, while a one-way glass allowed the experimenter to observe the animal's behavior.

The potentials evoked in the left medial lemniscus to single shock stimulation of the right superficial radial nerve were led to a Grass Model P15 A.C. preamplifier having half-amplitude band pass settings of 3 Hz and 300 Hz. The output of the preamplifier was then displayed on a Tektronix Model RM 565 dual beam, dual time base oscilloscope and photographed with a Lehigh Valley Electronics Model PC-2A 35 mm Continuous Recording Oscilloscope Camera.

EMG activity in the right forelimb biceps muscle was amplified with a similar Grass AC preamplifier with a half-amplitude band pass setting of 10 Hz and 1 K Hz, displayed on the oscilloscope and photographed. Additionally, the output of the AC preamplifier was rectified and fed to a passive resistor-capacitor integrator network with a discharge time constant of 0.10 sec. This type of integrator provides a unidirectional voltage deflection proportional to the average level of the incoming signal but does not represent true integration in the mathematical sense. It is often referred to as a "lag circuit" but has the advantage over other types of integrators in that the output is a continuous analog function (see 76). Despite the inherent inaccuracy of the device for determining exactly the amount of EMG activity at any given time it did prove extremely useful for detecting even very slight fluctuations in frequency and/or amplitude of the EMG signal. The output of the integrator was also displayed on the oscilloscope and photographed.

Stimulation of the right superficial radial nerve via the implanted electrode was accomplished by a Devices Mark IV isolated stimulator. The nerve was stimulated with single rectangular pulses of 0.05 msec duration, anode distal, at a rate of once per 2 seconds. The timing of the stimulation pulses, as well as the triggering of the oscilloscope, the camera shutter and other associated equipment was controlled by a Devices Digitimer Mark II using a 10 K Hz quartz crystal oscillator as a reference source. All timing operations were accurate to within less than 0.05 percent.

Experimental Procedure

In general, data were obtained for each animal on three different recording sessions on three separate days. Typically a single recording session lasted from one and a half to two hours, and followed a routine pattern. First of all, the animal was connected to the recording apparatus and stimulation of the right superficial radial nerve was begun while recordings from the medial lemniscus and the right biceps muscle were monitored on the oscilloscope. When the stimulus strength was just sufficient to evoke a small potential in the medial lemniscus a series of photographs of the recorded traces was begun as the stimulus strength was gradually increased. The stimulus strength just sufficient to evoke the lemniscal potential was noted and referred to as one times threshold (1 x T) for the response. Ten to 15 evoked responses were then photographed for each intensity level beginning at 1 x threshold and at each 1 + 0.25-times-threshold interval up to a maximum of 4 times the threshold (4 x T) strength for the response. All of these recordings were made while the animal rested quietly.

It should be noted at this point that although the animal often moved about for a few minutes upon first being placed into the recording chamber, the repetitive stimulation of cutaneous nerves has been shown to be associated with relaxation and maybe even sleep (71). Although not measured in these experiments, this effect undoubtedly contributed to the settling of the animal into a resting posture and the absence of gross movements during much of the recording session. In fact, the most often observed activity, when any was present, consisted of licking the fur and other such grooming behavior. However, recording of data during such occasions, as well as during the rare instances of obvious exploratory behavior, was strictly avoided by instantly stopping the camera when the behavior was first observed. In the few cases where a short segment of recording was made during these undesired behaviors, a mark on the film identified these segments and the data was not included in any of the analysis.

After obtaining the stimulus intensity data, the next experiment involved the presentation of a series of auditory stimuli (tones). During this time the lemniscal response was being evoked once per 2 seconds to a constant nerve stimulus corresponding to between 1.9 and 2.5 times threshold for the lemniscal response for different animals. At the same time the EMG activity from the biceps muscle, a time scale marker, and auditory stimulus marker were monitored continuously and photographed along with the evoked lemniscal responses.

The tones, presented over a loud speaker mounted in the ceiling of the recording chamber, were generated by a Hewlett Packard Model 200 AB Audio Oscillator, while the duration of the tones, 500 msec, was

controlled by the Digitimer. The intensity of all the tones was 15 db above a background noise of 72 db as measured by a General Radio, model 1551-C sound level meter inside the recording chamber. Three different tones, at 800 Hz, 1150 Hz and 1400 Hz frequencies, were presented on the first, second and third recording sessions respectively. The interval between successive tones was random within the following limits: tones were presented no closer than 8 seconds, nor longer than 40 seconds apart. Between 20 and 30 tones were presented per session.

Before beginning the presentation of the tones, behavioral observation always indicated that the animals were awake. Furthermore, during the sequence of the tones the animal was carefully observed to insure that no tones were presented during movements or during any other signs of behavioral arousal. The EMG recording from the biceps muscle also served to insure that none of the tones were presented during movements of the right forelimb.

In the third section of the recording session evoked lemniscal responses along with continuous recordings of EMG activity in the right forelimb biceps muscle were obtained during discrete voluntary movements of the animal. Since the animals were generally immobile for the greatest portion of the time, movements were obtained by gently lifting the animal to its feet. The door to the recording chamber was then closed and an interval of about 5 seconds was allowed before the camera was turned on to begin the recording. The stimulus to the nerve was of constant intensity, once per two seconds, as in the previous experiments, and remained on during the whole of these experiments. Upon being placed on its feet, the cat often stood still for a few seconds before

taking several steps and resuming the original resting posture. This type of behavior was often very consistent so that the majority of movements recorded were obtained as the animal lay down and made small adjustments of the limbs in conjunction with assumption of a resting, relaxed posture. As mentioned before, no recordings were made when the animal was involved in grooming behavior or where there were any overt signs of arousal and exploratory behavior. As will be described later, several additional criteria were employed to insure that the analysis included only data recorded during spontaneous, discrete voluntary movements.

At the end of the last recording session each animal was anesthetized with 35 mg/kg Nembutal, intraperitoneally, in order to study the effects of passive forelimb movements on evoked lemniscal responses. Thirty minutes after the time of the injection, the animal was placed on its side in the recording chamber and reconnected to the recording apparatus. A special device consisting of a potentiometer with a small armature connected to the wiper was then attached by means of a thread to the animal's forepaw. In this way, passive movements of the paw caused the armature to move while the resultant voltage change through the potentiometer was fed to the oscilloscope to indicate both the speed and direction of the passive movement. A small, low tension spring returned the armature to a stop position with full limb extension. A complete cycle from extension to flexion and back to extension, and covering an arc of about 40° to 60° was completed within less than 2 seconds and in all experiments was varied between this value and a value of less than one second. By this means, the effect of either

passive flexion, extension, or no movement while holding the limb in a variety of positions could be studied. Actual passive movement was accomplished by the experimenter's gently grasping the forelimb just behind the paw and, with as steady a pressure as possible, moving the limb. The movements occurred with respect to both the elbow and shoulder joints.

Scoring and Analysis of Data

At the end of each experimental session, the film on which all the data were recorded was developed by standard photographic procedures. Since the oscilloscope light beam was photographed against the darkened screen face, the developed film yielded a negative with black traces upon a light background. The film was then projected by a Dietzgen 35 mm film reader upon an eight by ten inch sheet of graph paper. Using calibration marks and scales photographed at the beginning of each film record, a grid which corresponded to lines on the graph paper was constructed. This grid then allowed for alignment of the recorded traces along the horizontal axis and was marked off in milliseconds, while the vertical scale was calibrated in microvolts. In measuring the amplitude of the evoked lemniscal response the stimulus artifact as well as the corresponding time marker indicating the triggering of the nerve stimulus were used as a reference. Since the latency of onset of the initial deflection of the lemniscal potential varied between 3.0 and 3.6 milliseconds, the lowest point at which the trace fell within this interval was used as the "zero" point. The amplitude in microvolts from the zero point to the top of the initial deflection of the potential wave, as indicated by reversal of wave,

was then used as the approximate measure of the total amount of evoked neural activity recorded in the massed potential discharge. Since the potentials themselves were generally monophasic in form the amplitude of the potential represents a relatively accurate measurement of the amount of evoked activity carried through the dorsal column-medial lemniscal pathway (9, 56).

For the EMG data, the output of the integrator was used as a rough measure of the amount of muscle activity occurring at any given time. Since the integrator circuit was sensitive to both amplitude and frequency changes it was not calibrated in microvolts but in arbitrary units. The analog EMG signal, which was simultaneously recorded, was used to verify that changes in the integrator output reflected real changes in EMG activity especially with regard to the exact time of onset of bursts of muscle activity.

Statistical Analysis

The results obtained in the following experiments were submitted, for the most part, to the most standard parametric statistical tests, the details of their application being presented along with the analyzed data in the text. However, there are several general features which all of the analyses shared in common. For all of the experiments, each animal served as its own control. Thus, for a given experiment on a particular recording session, a difference score, or more often a set of difference scores, were obtained by subtracting the value of a certain variable measured under a specific condition from the value of that variable obtained during some specified control period. These

difference scores were then statistically evaluated using tests which take into account the existence of a correlation between the means of two sets of scores on given variable obtained from the same individual subject (t test for correlated means). Furthermore, these difference scores, generally expressed as percent change scores, allowed comparisons between subjects as well as comparisons of the same subject on different occasions to be carried out without the necessity of controlling for differences in the absolute value of a particular variable. Since, for most of the experiments, an average percent change score could be computed for each individual subject, overall tests against hypotheses, using the zero mu t test (t_{ou}, two-tailed test), as well as the combining of the individual subject's scores into an average representative of the entire group were easily performed.

CHAPTER III

EVOKED LEMNISCAL RESPONSES IN ACUTE AND CHRONIC CATS

Evoked Lemniscal Responses in Acutely Anesthetized Cats

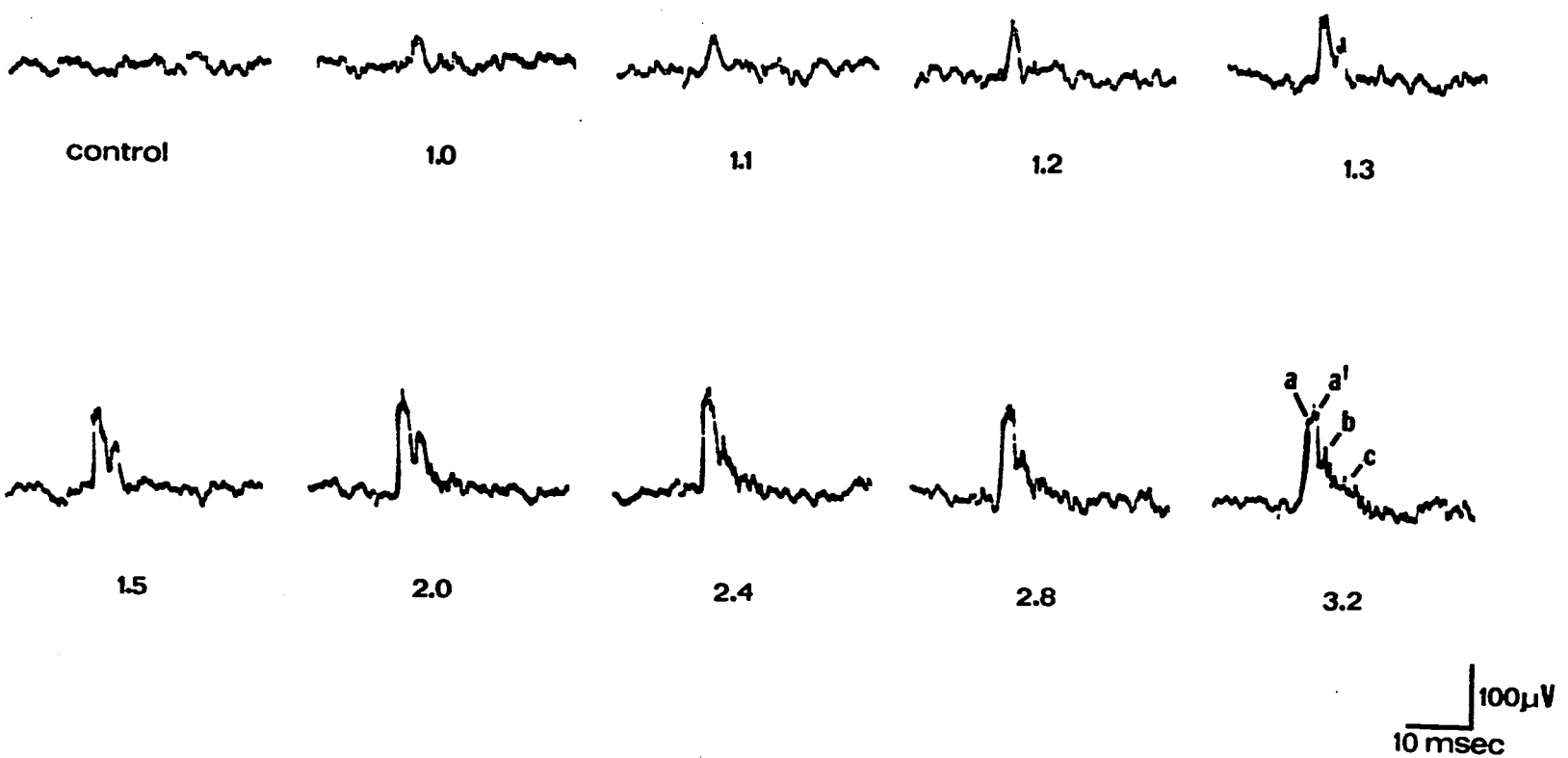
Single shock stimulation of the superficial radial nerve elicits a large evoked potential in the contralateral medial lemniscus of the acutely anesthetized cat. The latency of the response remains fairly constant at 3.3 msec (range 3.0-3.6 msec) while the amplitude of the response increases with increasing stimulus strengths up to a maximum corresponding to 2.0 to 2.5 times the intensity just sufficient to evoke the response (Figure 3).

The latency of the response is entirely consistent with the single synaptic relay interposed in the dorsal column-medial lemniscal pathway. Other studies have indicated that the afferent fibers contributing to the lemniscal system have conduction velocities in the order of 35 to 80 m/sec (8, 10, 68, 83), while the synaptic delay reportedly ranges from 0.7 to 0.8 msec (5, 10). In this study, while the evoked response started at a latency of about 3.3 msec, the duration of the initial component of the response lasted as long as 1.7 msec. The distance from the stimulating to the recording electrodes was approximately 180 mm. Assuming a synaptic delay of 0.75 msec yields a nerve conduction time of between 2.55 and 4.25 msec and hence a figure for conduction velocity of between 42 and 71 m/sec. Since there is a 30-50% decrement in conduction velocity when the afferent fibers enter the cord (8, 68, 83),

Figure 3. Development of the evoked lemniscal response with increasing stimulus strengths.

Acute, anesthetized cat. The lemniscal responses, recorded via a bipolar electrode in the left medial lemniscus, were evoked once per 2 seconds by stimulation of the right superficial radial nerve with 0.05 msec duration rectangular pulses. Stimulus intensities are expressed in times threshold (T) for the lemniscal response. In this experiment the threshold (1 x T) for the evoked response was 0.20 volts as read from the stimulator dial. The stimulus to the nerve was delivered 10 msec following the onset of the oscilloscope trace.

The lemniscal response amplitude shows a progressive increase with higher stimulus intensities up to a maximum corresponding to stimulus strengths between 2.0 and 2.4 x T. The early component of the evoked response is made up of two small peaks labeled a and a'. At a stimulus intensity of 1.3 x T there is a second later component (b) and at higher stimulus strengths (2.0 x T) an even later peak appears labeled c.


control
1.0
1.1
1.2
1.3
1.5
2.0
2.4
2.8
3.2
a
a'
b
c
100μV
10 msec

a figure between 47 and 85 m/sec gives a closer approximation of the conduction velocities in the peripheral afferent fibers activated by the nerve stimulation. This range corresponds very well with previously reported measurements of the conduction velocities of group II cutaneous afferents which ascend in the dorsal columns and make synaptic contacts in the cuneate nucleus with neurons forming the medial lemniscus (8, 10, 68, 83).

In Figure 3 it will be noticed that in addition to the largest early component, there are a number of small wavelets which make up the later portion of the evoked potential and generally appear with stimulus strengths above 1.2 to 1.3 times threshold. The small wave labeled a', which is seen even at threshold intensity, may represent activity evoked in fibers having just slightly slower conduction velocities than those contributing to the primary response (a). The peaks of the succeeding smaller waves labeled b and c are separated by a fairly constant interval, i.e., about 4 msec, and may be attributable to repetitive firing of cuneo-thalamic neurons, a phenomenon which is known to occur in response to single shock stimulation of peripheral nerves (6, 30). In other experiments, however, the evoked potential had a simpler configuration with only a single large late component occurring at a latency of 7 to 8 msec with a duration of about 4 msec. Thus the possibility that these late components are attributable to repetitive firing of cuneothalamic neurons may be only one of several alternatives. The existence of synaptically driven units in the deep fascicles of the dorsal columns has been recently demonstrated (84) and presumably these fibers could contribute to evoked responses in the

medial lemniscus. Also, a further anatomical factor should not be neglected, namely, that the lateral cervical nucleus, the second relay in Morin's tract (62) contributes, together with the dorsal column nuclei, to the medial lemniscus (9).

Despite the consistent and distinct appearance of the late components of the lemniscal responses evoked in the anesthetized cat, these small potential waves were often barely visible in the recordings obtained from the same animals after recovery from the effects of the anesthesia. In several instances, however, small inflections on the later part of the evoked potential wave remained and undoubtedly contributed to the widening of the response. Also, the appearance of the later components was facilitated when the chronic animals were anesthetized at the end of the experiments (4-5 days after implantation of electrodes).

The growth in amplitude of the evoked potential with increasing stimulus strengths corresponds closely with the results obtained by others (9) and undoubtedly reflects the recruitment of activity in increasingly larger numbers of first order sensory fibers. That the size of the evoked potential does not increase with stimulus intensities above 2.0-2.5 times threshold agrees with the finding that group II cutaneous afferents in the dorsal columns and peripheral nerves all show thresholds to electrical stimulation at or below 2.2 x T (83). Thus, with stimulus strengths above this value, the evoked lemniscal potential presumably represents activity generated in the near maximum number of afferent fibers in the superficial radial nerve which ascend via the dorsal column-medial lemniscal pathway.

The considerable amount of investigation on the receptor characteristics of the cutaneous afferents which contribute to the lemniscal

pathway is also relevant to the recording of evoked potentials in this system. Based upon responses to natural skin stimulation, there is generally good agreement that the roughly 3 to 1 ratio of fast adapting to slowly adapting fibers observed in peripheral nerves (48, 49), is maintained through the dorsal columns to the cuneate and gracile nuclei (8, 32, 52, 67, 68). For the most part fast adapting fibers are represented by "hair" units (see 48) which show a short burst of activity with bending of hairs but show no activity when the hair remains in a fixed position. Furthermore, they show maximal discharge as a function of the rate of movement (67), and otherwise have little or no spontaneous activity. Of all cutaneous afferents they have the smallest receptive fields, the lowest thresholds to electrical stimulation, and are among the largest and most rapidly conducting fibers innervating the skin (see 83). Thus, by virtue of number, as well as by low threshold to electrical stimulation and fast conduction velocity, evoked activity in these afferents would likely be heavily represented in the primary component of the lemniscal response.

In summary, single shock stimulation of the superficial radial nerve in anesthetized cats produces an evoked potential which can be recorded in the contralateral medial lemniscus of the brain stem. The latency of the primary wave of the potential is consistent with the transmission of impulses over fast conducting cutaneous afferents and through the single synaptic relay interposed in the dorsal column-medial lemniscal pathway. The maximum amplitude of the response appears to correspond with stimulus intensities just above threshold for activation of cutaneous afferents which ascend in the dorsal columns. An analysis

of the distribution of receptor types and functional characteristics of the sensory fibers which contribute to this system from cutaneous sources suggests that the lemniscal response may represent mainly activity evoked in fibers which show rapid adaptation to naturally occurring stimuli applied to the skin.

Evoked Lemniscal Responses in Unanesthetized, Unrestrained Cats

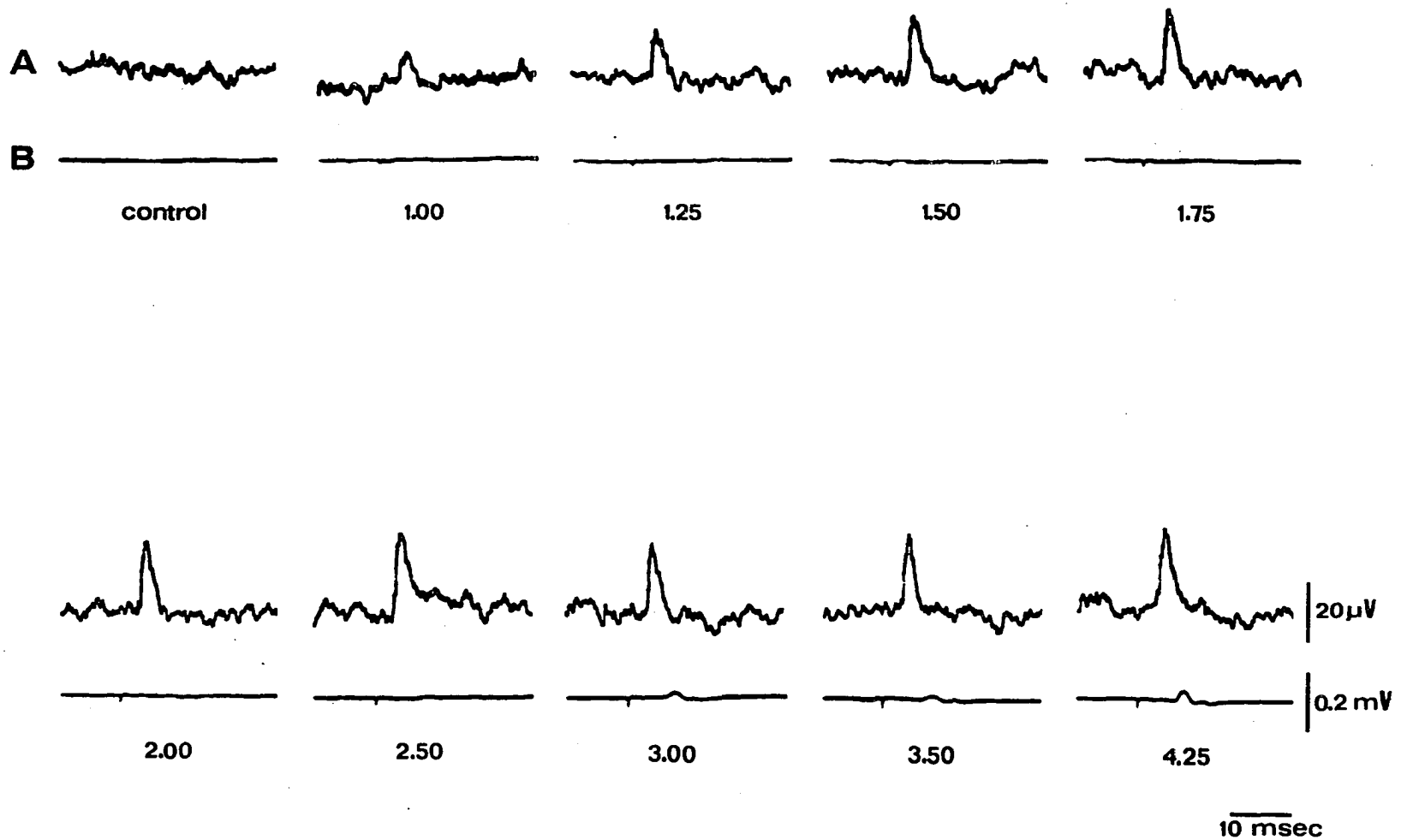
Figure 4 shows recordings from the left medial lemniscus of the responses evoked by single shocks applied to the contralateral superficial radial nerve at increasing stimulus intensities in the unrestrained, unanesthetized cat. Below these traces appear the bipolar EMG recordings obtained at the same time from the right forelimb biceps muscle. Similar to the responses observed in anesthetized animals, the latency of the lemniscal response remains fairly constant, while the amplitude of the potential increases to a maximum value corresponding to stimulus intensities above 2.0 to 2.5 times threshold for the response.

As mentioned before, the later components of the evoked potential are absent or greatly attenuated. Also, the response as a whole is lower in amplitude than that obtained during the surgical implantation of the electrodes, and, in fact, in several animals lemniscal response amplitudes showed a slow but progressive decline over the course of several days. These phenomena were presumably the result of trauma coincidental with the positioning of the recording electrode in the medial lemniscus and with the implantation of the peripheral nerve stimulating electrode. Both increased excitability of the afferent pathway attributable to surgical irritation and conceivably

Figure 4. Development of the evoked lemniscal response and ipsilateral biceps EMG responses with increasing stimulus strengths.

Unrestrained, unanesthetized cat, 3 days after chronic implantation of the electrodes. The lemniscal responses (A), along with the EMG responses (B) recorded via a bipolar electrode in the right forelimb biceps muscle, were evoked once per 2 seconds by stimulation of the right superficial radial nerve with 0.05 msec rectangular pulses. Stimulus intensities are expressed in times threshold (T) for the lemniscal response. The stimulus to the nerve was delivered 10 msec following the onset of the oscilloscope trace.

The lemniscal response amplitude shows a progressive increase with higher stimulus intensities up to a maximum corresponding to stimulus strengths between 2.0 and 2.5 x T. At a stimulus strength of 2.5 x T there appears a very small response in the biceps EMG recording which increases slightly in amplitude with higher stimulus intensities. This early response is followed by a later and smaller EMG response at stimulus intensities above 3.5 x T.


A
B
control
1.00
1.25
1.50
1.75
2.00
2.50
3.00
3.50
4.25
20 µV
0.2 mV
10 msec

leading to large evoked response, as well as depression of the response due to the ultimate manifestation of tissue damage several days later, could have produced those differences. However, for 6 animals tested across three recording sessions, the voltage just sufficient to evoke responses in the medial lemniscus (1 x T) varied no more than plus or minus 20% of the value obtained on the first recording session. Since this amount of variability is slight (compare to +100% = 2 x threshold), changes in the stimulating conditions did not appear to be responsible for changes in lemniscal response amplitudes.

Returning to Figure 4, the EMG recordings from the right forelimb biceps muscle indicate the occurrence of a small reflex response lasting about 3 to 4 msec at stimulus intensities above 2.0 x T for the lemniscal response. At even higher stimulus strength, i.e., above 3.0 x T, a second response is observable which is partially superimposed on the earlier wave. At stimulus intensities sufficient to evoke both these responses, their frequency of occurrence as well as amplitudes were quite variable. With regard to latency, the first response regularly occurred at about 6.0 to 7.0 msec after the stimulus. Allowing between 3.1 and 4.0 msec for synaptic delay plus transmission from the cord through the efferent fibers to the muscle, the conduction velocity over the afferent limb of the reflex pathway would be between 32 and 59 m/sec. The minimum latency of the second wave appeared to be about 11 to 13 msec and yields a corresponding figure of 12 to 30 m/sec. Based upon conduction velocity as well as differences in threshold to electrical stimulation, the first and second reflex responses may be attributable to activity evoked in the slower conducting group II and group III cutaneous afferents respectively. On the other hand, it must be emphasized

that the second inflection seen in the EMG recordings may not represent a second independent response. Rather, it may be part of a single muscular response which, because of the recording conditions in a volumn conductor, is manifested as a polyphasic evoked potential. Nevertheless, the two waves have been treated separately in these experiments.

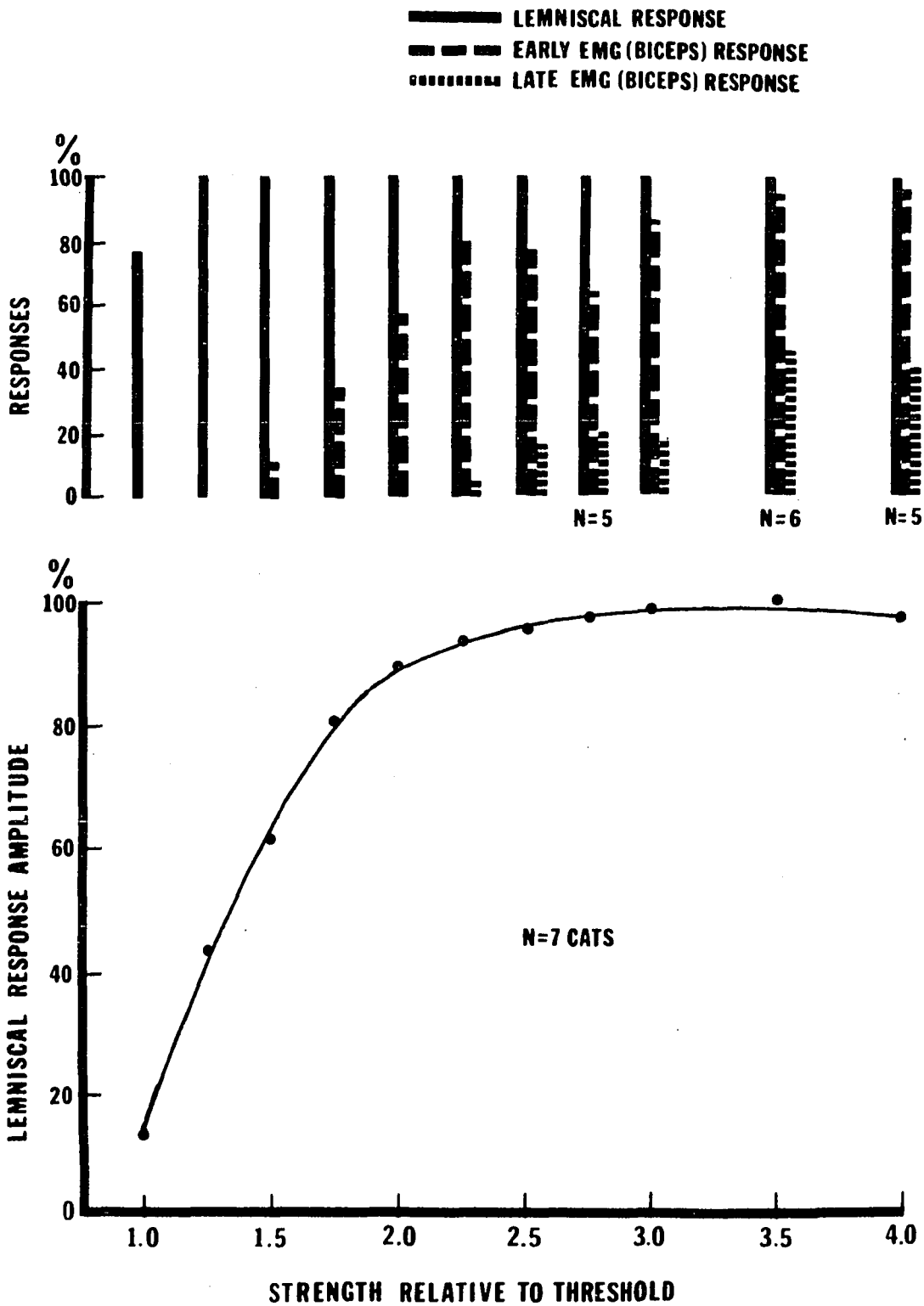
While the functional significance of ipsilateral flexion reflexes evoked by stimulation of group II afferents remains unclear (see 47), it is worth noting that the appearance of this early muscle response occurred at stimulus strength above threshold but below maximum stimulus intensities for group II afferent volleys which ascend through the lemniscal pathway. Low rate repetitive nerve stimulation at intensities which evoked this early response but were below three times threshold (3.00 x T) for the lemniscal response consistently failed to elicit behavioral changes in the resting animal as indicated by gross visual observation. In contrast, however, was the frequently observed arousal and movement of the animal when stimulation was carried out at higher strengths, which corresponded to the occurrence of the later muscle response. Taken together, the occurrence of the late reflex response in association with overt behavioral arousal is consistent with the finding that threshold stimulation of group III cutaneous afferents, which may contribute to reflex responses to nociceptive stimuli, occurs at stimulus strengths above 3.5 to 4.0 times threshold for the lemniscal response (9).

The lower part of Figure 5 graphically shows the amplitude of the lemniscal response as a function of increasing stimulus strengths

Figure 5. Graph of development of the evoked lemniscal response and biceps EMG responses with increasing stimulus intensities.

The lower figure shows the lemniscal potential amplitude plotted for stimulus strengths applied to the right superficial radial nerve. The mean of 10 responses per animal, averaged over 7 animals, are shown for each stimulus value. Lemniscal response amplitude is expressed as percent of maximum amplitude. At stimulus strengths corresponding to 2.0 x T, the lemniscal response achieves 90 percent of maximum amplitude and increases only slightly with intensities as high as 4.0 x T.

In the upper portion of the figure, lemniscal responses, along with the EMG responses, are plotted in terms of their probability of occurrence at each of the stimulus strengths. The ordinate gives percent number of stimuli, out of 10, on which a response could be observed, averaged across 7 animals. The abcissa corresponds to stimulus strengths as shown in the lower part of the figure. The short latency (early) EMG responses are first detectable at 1.5 x T, occur an average of 55 percent of the time at 2.0 x T and finally appear at the 95 percent level at strengths above 3.5 x T for the lemniscal response. Later muscle responses do not occur until 2.25 x T is reached and appear less than 50 percent of the time even at stimulus strengths as high as 4.0 x T for lemniscal potential. For two animals, no stimuli were presented at 2.75 and 4.0 x T levels while one animal was not tested at 3.5 x T stimulus level.


LEMNISCAL RESPONSE
EARLY EMG (BICEPS) RESPONSE
LATE EMG (BICEPS) RESPONSE
%
100
80
60
40
20
0
RESPONSES
N=5
N=6
N=5
%
100
80
60
40
20
0
LEMNISCAL RESPONSE AMPLITUDE
N=7 CATS
1.0
1.5
2.0
2.5
3.0
3.5
4.0
STRENGTH RELATIVE TO THRESHOLD

for all animals tested. Similar to the responses illustrated previously for single animals, the amplitude of the lemniscal response increases markedly up to about 2.0 times threshold strength, then increases by only about 10% more with stimulus strengths as high as 4 times threshold intensity. Since each point represents the average of 10 responses from each animal, it is possible to calculate an average standard deviation of the lemniscal responses for a given amplitude. At a stimulus strength of 2.5 x T, the standard deviation across animals ranged from plus or minus 20 percent to as low as 6 percent of the mean amplitude and yielded an average value of plus or minus 12 percent. Similar values were obtained in other experiments and thus serve to illustrate the stability of evoked lemniscal responses recorded in unrestrained, unanesthetized cats.

The upper part of Figure 5 shows the lemniscal responses for the same animals, along with the two muscle responses plotted as an average probability of their occurrence for ten stimuli at each of the indicated stimulus strengths. At what has been arbitrarily defined as threshold (1 x T) the lemniscal response occurred on the average about 75% of the time (range 50% to just at 100%). At higher stimulus strengths the lemniscal responses occurred 100% of the time in all animals.

One animal showed the presence of the earliest muscle response at a stimulus intensity as low as 1.50 x T, but this response was not present in all animals until the stimulus strength was raised to 2.25 x T. Similarly, the later muscle response occurred in the most responsive animal at 2.25 x T, while it was present in 4 out of 6 animals at a strength of 3.5 times threshold and 3 out of 5 animals at a strength of

4.0 x T for the lemniscal response. In summary, for a given animal, the early muscle response generally occurred at a stimulus intensity which produced a lemniscal response of about 80-90% of maximum amplitude. It then required a 50% to 100% increase in this stimulus strength to produce the late reflex response by which time the lemniscal response had always attained its maximum amplitude. Thus, the threshold for the early reflex muscle response occurred below stimulus strengths which produce maximal amplitude lemniscal responses. This finding lends further support to the conclusion that the early response is mediated by cutaneous afferents having the same general characteristics as those which ascend in the dorsal column-medial lemniscal system. On the other hand, stimuli of sufficient intensity to evoke the late muscle response do not produce a further increase in the amplitude of the lemniscal response. Thus, the later muscle response may be related to stimulation of cutaneous afferents which mediate painful sensations and ascend in such pathways as the spinothalamic and spinoreticular systems. This conclusion is supported by the observation of behavioral arousal induced by high intensity electrical stimulation of the superficial radial nerve.

On the basis of the experimental results just described, the stimulus intensities to be used for the rest of the experiments were determined. For ethical reasons, as well as because of the nature of the studies to be conducted, stimuli which produced arousal and activation of the animal were strictly avoided. On the other hand, it was desired that the nerve stimulation be of sufficient intensity to activate the greatest possible number of peripheral afferent fibers which contributed to the evoked responses in the medial lemniscus. Otherwise, changes

in sensory transmission through the lemniscal pathway might occur in reference to afferents with higher thresholds to electrical stimulation but such changes would not be reflected in the amplitude of the evoked lemniscal response if these same fibers did not contribute to the evoked response itself. Therefore, the initial procedure for each animal on every recording session was to set the stimulus intensity for evoking the lemniscal response at a value which appeared to produce the largest amplitude response but was below the strength sufficient to produce the late reflex muscle response. The occurrence of the first muscle response generally served as a reference with stimulus strength being set at a value which yielded this response less than 50% of the time. Across animals, this strength varied from between 1.9 to 2.5 times threshold intensity for the lemniscal response, but for a given animal remained very constant between separate recording sessions.

In summary, similar to the results obtained in the anesthetized cat, single shock stimulation of the superficial radial nerve produces an evoked response in the contralateral medial lemniscus which attains its maximum amplitude at stimulus strengths between 1.9 and 2.5 times threshold for the response. At this stimulus intensity, a small, short latency reflex response can be recorded in the ipsilateral forelimb biceps muscle while at higher stimulus strengths a later reflex muscle response may occur. An analysis of the calculated conduction velocities and thresholds for electrical stimulation evoking these two responses suggested they may be produced by activity in group II and group III cutaneous afferents, respectively. Since stimuli which evoked the late reflex response were associated with behavioral arousal, this

finding, in conjunction with the stimulus intensity function for lemniscal response amplitudes, was used as a basis for determining the stimulus strengths used to evoke the lemniscal responses in future experiments.

CHAPTER IV

EVOKED LEMNISCAL RESPONSES DURING INDUCED AROUSAL

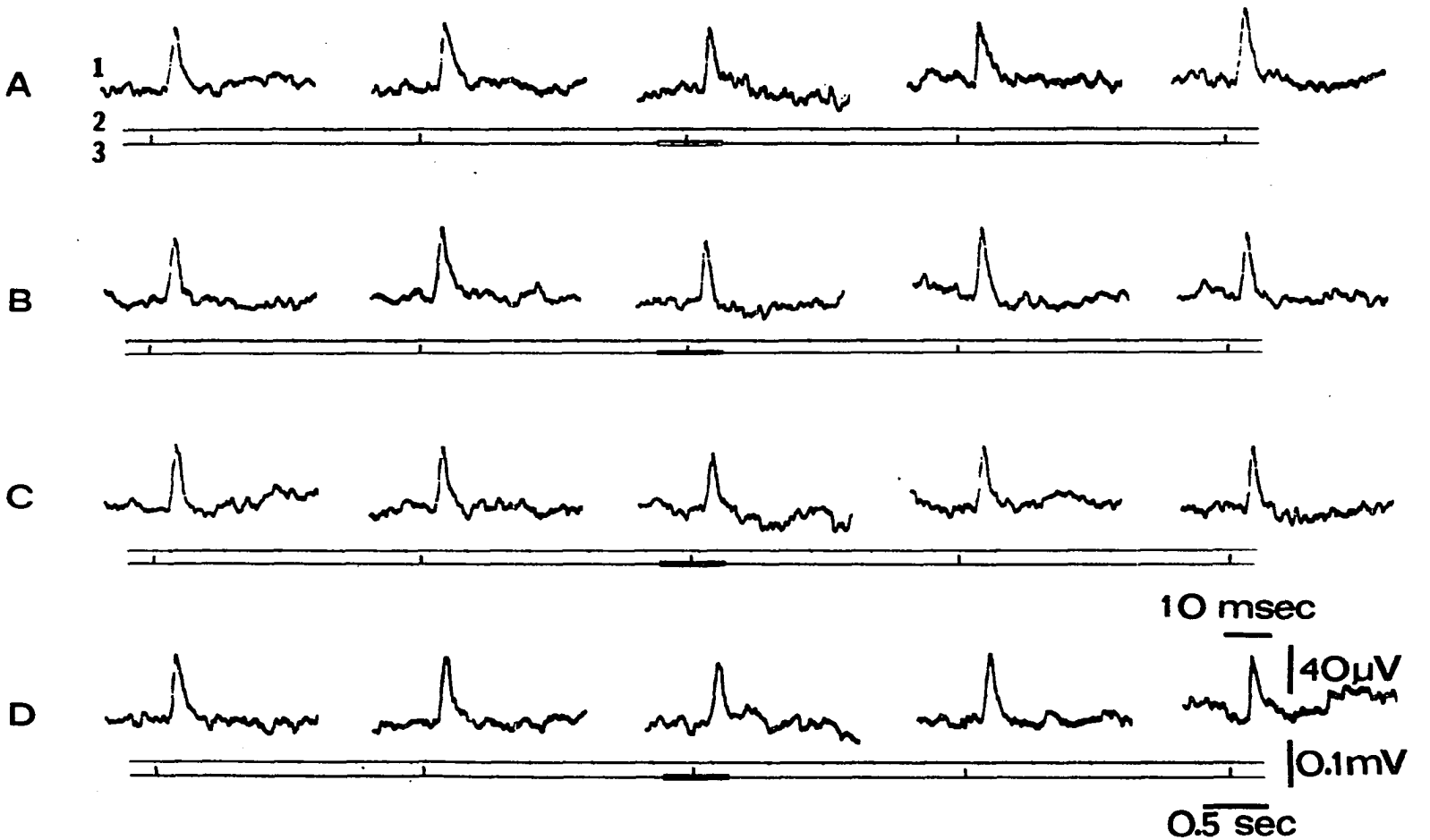
In seven animals bearing chronically implanted electrodes, the effect of presenting a brief auditory stimulus on the amplitude of the evoked lemniscal response was studied. As described previously, the lemniscal response was evoked repetitively at a constant rate of once per 2 seconds and at a constant stimulus intensity corresponding to a value determined for each animal by the methods outlined in the preceding section. During presentation of the tones the animals were closely observed to insure that none of the tones were presented during movement, while continuous recording of the EMG activity from the forelimb biceps muscle was used to further confirm these observations. The animals were always awake at the beginning of the experiment and, as noted previously, there were rarely any movements over the entire course of the tone series. No tone trials from any sessions for any animal were excluded from the analyses.

Figure 6 shows evoked lemniscal responses along with EMG activity in the right forelimb biceps muscle, recorded from an unrestrained, unanesthetized cat during presentation of a 500-msec duration tone at 1150 Hz, with intensity 15 db above background noise. While the lemniscal response remains otherwise very stable, those responses evoked immediately following the onset of the tone are consistently reduced in size.

Figure 6. Reduction of the evoked lemniscal response amplitude during presentation of a novel auditory stimulus.

Unrestrained, unanesthetized cat, 2 days after chronic implantation of electrodes. 1: lemniscal responses recorded in the left medial lemniscus to single shock stimulation of the right superficial radial nerve; 2: continuously recorded EMG activity from the right forelimb biceps muscle; 3: signal marker of the shocks to the superficial radial nerve once per 2 seconds, 0.05 msec duration pulse, 2.0 x T stimulus intensity. The lemniscal responses are aligned with respect to the occurrence of the shocks delivered to the superficial radial nerve, i.e., the nerve stimulus occurs 10 msec following the onset of the lemniscal response trace, this point being synchronized with the stimulus marker.

A, B, C and D show 4 different sequences of 5 evoked responses each, recorded for 4 presentations of a 500 msec duration tone, 1150 Hz, with intensity 15 db above background noise (channel 3 shows the occurrence and duration of the tone stimulus). In each set of traces the lemniscal response evoked during the tone is reduced in amplitude, compared to the lemniscal responses evoked before the tone stimulus. Although the effect is very slight the reduction of the lemniscal response during the tones was not accompanied by movements, as indicated by the EMG recording.


A
1
2
3
B
C
10 msec
D
40μV
0.1mV
0.5 sec

Furthermore, there is a slight tendency for the lemniscal response evoked 2 seconds later to also be decreased. Direct visual observation as well as the EMG recording indicated that these effects were not associated with movements of the animal nor in particular movements of the right forelimb.

Table 1 summarizes the results of the statistical analysis for the first 11 tone trials (out of 21) on the first recording session for each of the 7 animals. The analyses compare the average amplitude of the two lemniscal responses occurring just before each tone with the average amplitude of the two evoked responses just following the tone. Mean amplitudes (in microvolts) of the evoked responses both before and after the tones are in the first column while the second column shows the average percent difference (average amplitude reduction) computed from the percent change scores on each tone trial. The number of tones, out of 11, which were associated with a decrease in the evoked response appear in column 3 expressed as a percent.

These data indicate that in every animal the tone stimulus produced a reduction of the evoked lemniscal response amplitude, although this effect was very modest in most cases. The amount of reduction ranged from less than one percent to as high as 6.7 percent. Out of the first 11 tones presented, between 55 and 82 percent were associated with a decrease in the evoked response amplitude.

In the lower part of Table 1 appear the overall averages and statistical tests (zero mu $\underline{t}$ tests, $\underline{t}_{ou}$) showing that the evoked response amplitude was reduced on the average by 3.5 percent ($p<.05$). Similarly, the average number of tones accompanied by a depression of the

Table 1

EFFECT OF NOVEL AUDITORY STIMULUS ON EVOKED LEMNISCAL RESPONSE AMPLITUDE

Cat		Before Tone (μV)	After Tone (μV)	Amplitude Reduction (%)	t test value[1]	Number of Lemniscal Responses Reduced (%)
4852	$\bar{x}$	22.6	21.6	4.4	-0.73 (NS)[2]	55.0
	S	2.8	2.5			
4702	$\bar{x}$	67.7	67.2	0.7	-0.24 (NS)	73.0
	S	3.9	4.2			
5034	$\bar{x}$	21.1	20.9	1.0	-1.07 (NS)	64.0
	S	2.4	2.9			
5044	$\bar{x}$	26.8	25.0	6.7	-3.50 ($p<.01$)	82.0
	S	1.7	1.8			
4849	$\bar{x}$	24.8	23.3	6.1	-1.58 (NS)	73.0
	S	2.8	2.9			
3772	$\bar{x}$	29.8	28.2	5.4	-1.29 (NS)	64.0
	S	1.9	3.7			
4853	$\bar{x}$	52.6	52.3	0.6	-0.04 (NS)	64.0
	S	3.8	6.2			
Trials 1-11 (Above)				$\bar{x}$ 3.56		67.9
				t_{ou} 3.48 ($p<.05$)		$t_{u=50\%}$ 5.38 ($p<.01$)
Trials 12-21				$\bar{x}$ 0.52		50.9
				t_{ou} 0.57 (NS)		$t_{u=50\%}$ 0.94 (NS)

[1] t-test for correlated means computed from percent difference scores for each tone stimulus.

[2] Not significant (NS).

lemniscal response amplitude amounted to almost 68 percent ($p<.01$). On the other hand, a similar analysis of the remaining 10 trials (tones 12 through 21), which appears at the bottom of the table, indicates no systematic effect of the tones, suggesting that the novel stimulus became rapidly ineffective with repeated presentations.

Effect of Repeated Presentations of the Novel Stimulus on the Evoked Lemniscal Response

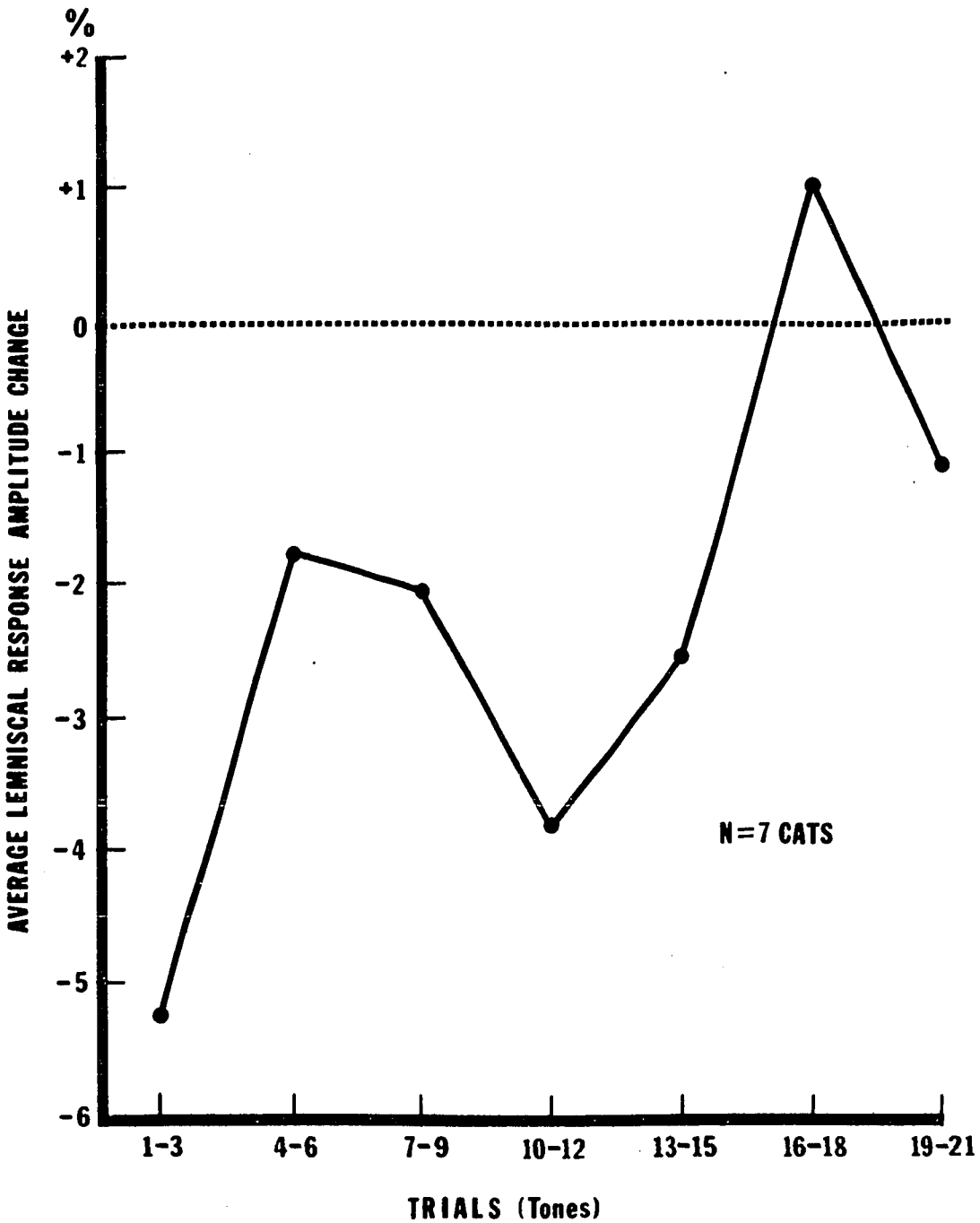
Figure 7 illustrates the combined data from the 7 animals on the reduction of the evoked lemniscal response amplitude as a function of repeated presentations of the novel stimulus. The average percent decrease in lemniscal response amplitude is plotted, in blocks of three trials, across the entire session of 21 trials, the basis for the figure being the same data as that shown in Table 1. The first three presentations of the tone were associated with an average reduction in the evoked lemniscal response amplitude of slightly over five percent ($p<.05$, t_{ou}), while the average decrease with tones 19 through 21 amounts to only about one percent (not significant, t_{ou}). This result would indicate that the first few presentations of the tone produce the greatest reduction of the evoked response but that after 15 to 20 tones the effects becomes largely unobservable.

In order to study in more detail the effects of repeated presentations of the novel auditory stimulus, six of the seven animals were run on the same experiment for two additional sessions, on separate days and using a different tone on each of the sessions. The data were analyzed in the same way as the previous experiments with the percent difference scores, as well as the percent number of tones associated

Figure 7. Effect of repeated presentations of a novel auditory stimulus on the evoked lemniscal response amplitude.

The average value of the evoked lemniscal response amplitude across the 7 animals is calculated as a percentage of the pre-tone control value and plotted in blocks of 3 trials (tones) for 21 trials. The figure is based upon the same data as shown in Table 1.

The initial presentations of the tone are associated with the greatest decrease of the evoked lemniscal response amplitude. Later presentations of the tone produce little if any change in the evoked response amplitude.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-6
AVERAGE LEMNISCAL RESPONSE AMPLITUDE CHANGE
N=7 CATS
1-3
4-6
7-9
10-12
13-15
16-18
19-21
TRIALS (Tones)

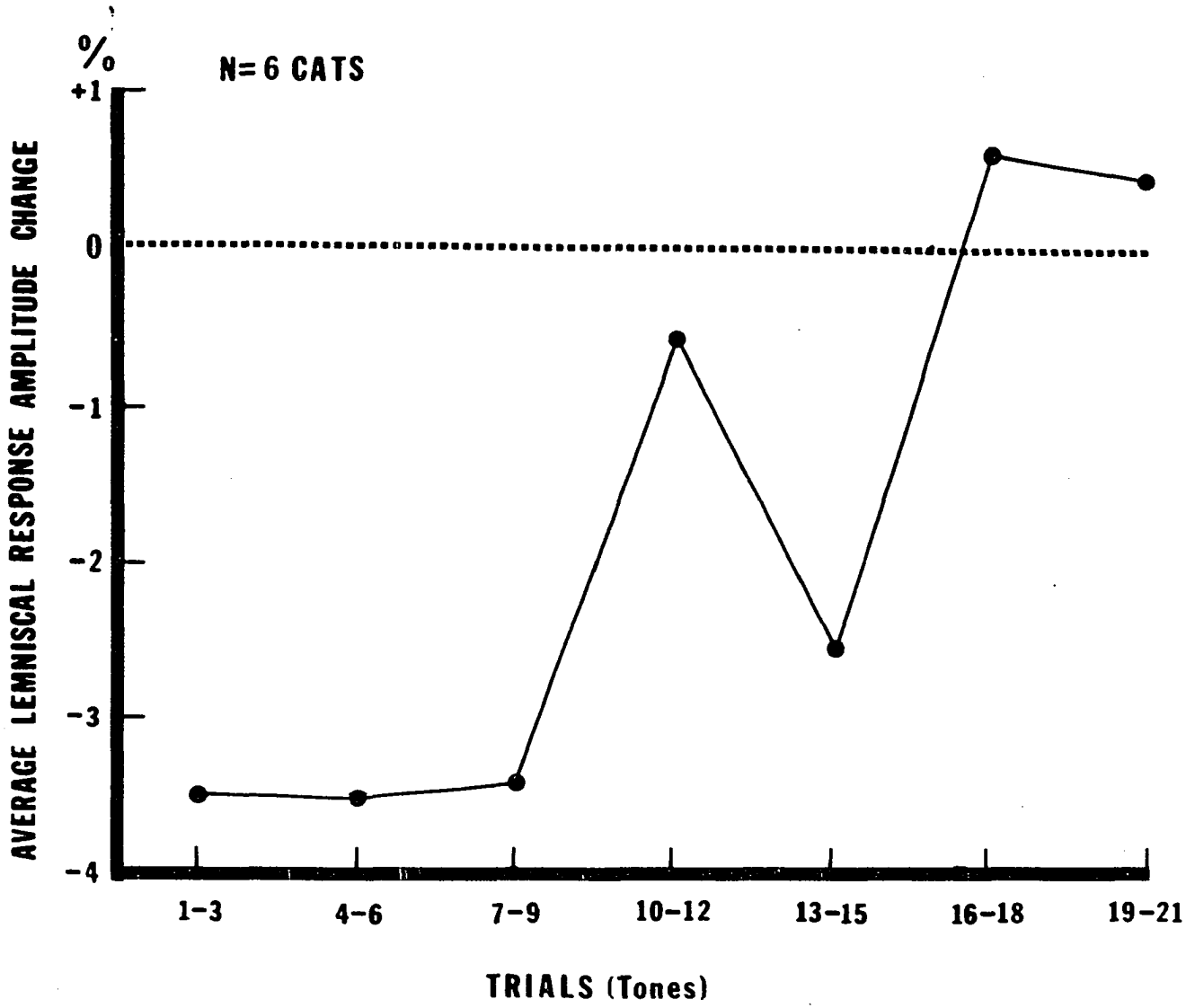
with a decrease in the evoked response, being combined over the three sessions for each animal. In agreement with the previous experiments, the amount of reduction in the lemniscal response amplitude over the first 11 tone trials ranged from 1.5 to 4.5 percent and averaged almost 3 percent ($p<.01$, $\underline{t}_{ou}$) for the 6 animals. Similarly, the probability of observing a decrease in the evoked response on a given tone trial ranged from 55 to 70 percent, the average being 63 percent ($p<.01$, $\underline{t}_{u=50\%}$).

In Figure 8 the average percent amplitude reduction in the lemniscal response is plotted in blocks of three trials across a total of 21 presentations of the tone. For both blocks of trials one through three and seven through nine, the average decrease in lemniscal response amplitude amounted to 3.5 percent across animals, but these values were statistically significant only at $p<.10$ level ($\underline{t}_{ou}$). While these results are rather meager, from a statistical standpoint, the overall group data do support the following hypothesis. The effect of the tone on the evoked lemniscal response may show a process of habituation as the novelty of the auditory stimulus is diminished with repeated presentations. Thus, the amount of reduction in lemniscal response amplitudes as well as the probability of observing such a decrease is greatest following the first few presentations of the tone, but becomes progressively smaller as a function of trials. This hypothesis can be evaluated statistically using the average Spearman Rank-Order Correlation Coefficient (57, 58) which tests the extent to which several sets of ranked scores, in this case the scores across trials for each animal, conform to a predicted rank order; the predicted set of ranks are that

Figure 8. Effect of repeated presentations of a novel auditory stimulus on the evoked lemniscal response amplitude; three combined sessions.

The average value of the evoked lemniscal response amplitude across three separate sessions for 6 animals is calculated as a percentage of the pre-tone control value and plotted in blocks of 3 trails (tones) for 21 trials.

The initial presentations of the tone are associated with the greatest decrease of the evoked lemniscal response amplitude, while with further tone trials there is a progressive diminution of the effect.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N= 6 CATS
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-2
-3
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AVERAGE LEMNISCAL RESPONSE AMPLITUDE CHANGE
1-3
4-6
7-9
10-12
13-15
16-18
19-21
TRIALS (Tones)

trial block 1 through 3 will be associated with the greatest decrease in the evoked response and be ranked one, trial block 4-6 have the next greatest decrease and be ranked two, and so on. Calculation of this statistic (Lubin's K) for the average percent amplitude change, yields a value of 0.41 which is significant beyond the $p<.01$ level (two-tailed test). Thus, these results confirm the hypothesis that the magnitude of reduction of the lemniscal response amplitude observed with the tones is inversely related to the number of presentations of the auditory stimulus.

Time Course of Evoked Lemniscal Response Suppression from Novel Stimulus Onset

In the preceding analyses, the average amplitude of the first two evoked lemniscal responses following the tone were compared to the average amplitude of the two evoked responses just preceding the tone. In this section the first and second evoked responses following the tone are examined separately.

It will be recalled that the lemniscal potential was being evoked once every two seconds. For three of the 7 animals tested in the first experiment, the tone was presented randomly with respect to the evoked response. Therefore, on the average, the first lemniscal response would fall at one second after tone onset while the second evoked response would occur two seconds later and correspond to 3 seconds after the tone. In the four remaining animals, the first evoked response was set to occur at 0.23 seconds after tone onset (one animal), 0.90 seconds (two animals), and 1.57 seconds (one animal) with the second evoked response occurring respectively two seconds after the first.

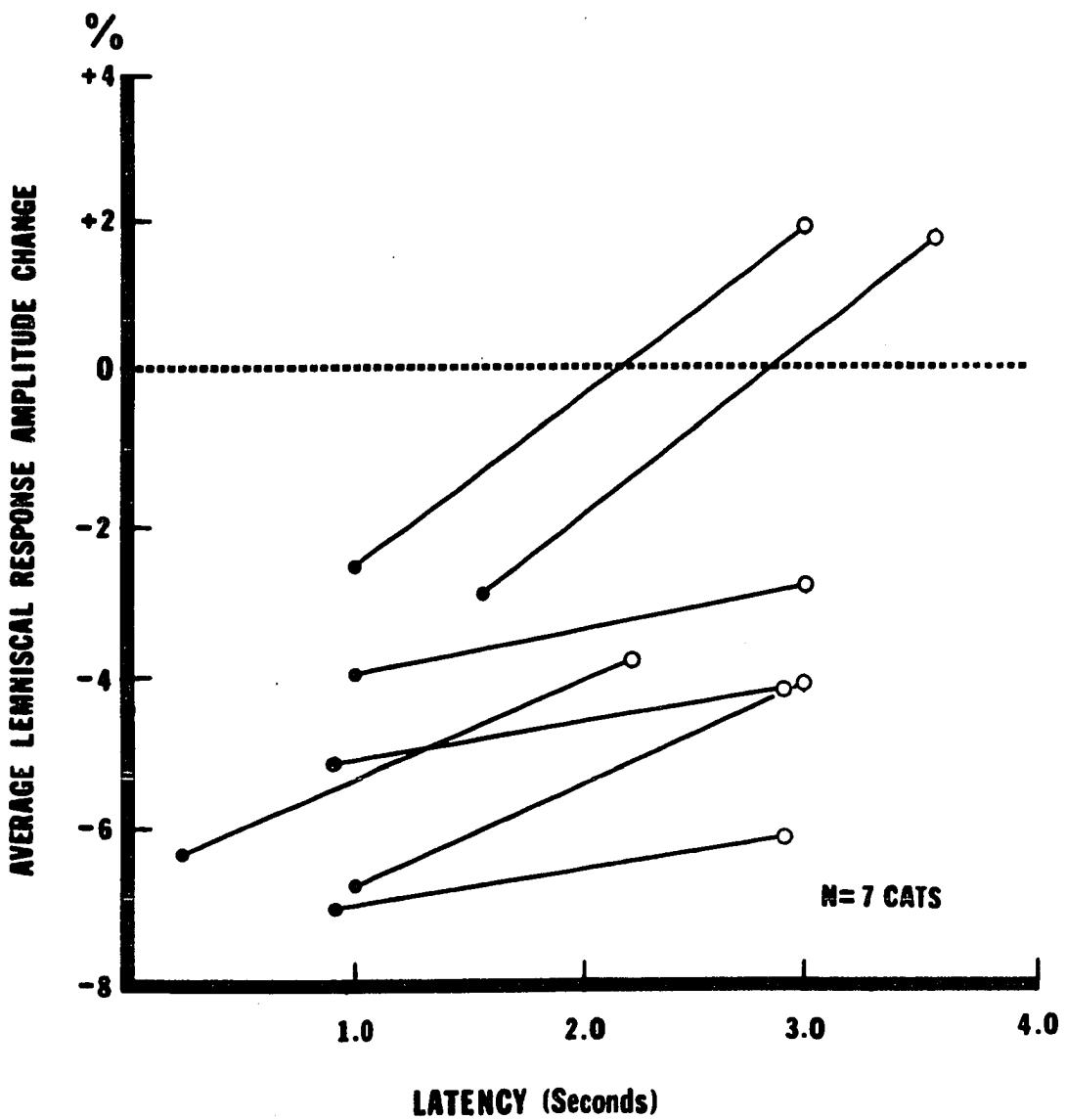
In Figure 9 the average percent amplitude change for the first and second evoked responses is plotted, with respect to latency from tone onset, for the first 11 tones for each of the 7 animals. The figure is based upon the same experiments as the data shown in Table 1. It will be noticed that for every animal the amplitude of the first evoked potential following the tone is depressed more than the second evoked response which occurs two seconds later. The first lemniscal potential following the tone was reduced on the average by 5% ($p<.001$, $\underline{t}_{ou}$) compared to an average of 2.4 percent ($p<.10$, $\underline{t}_{ou}$) for the second evoked response. The average difference between the first and second evoked response was 2.6 percent (range: 0.83 to 4.89 percent), this value being statistically significant beyond $p<.01$ level (t-test, correlated means). Since this difference occurred over a span of 2 seconds, the average rate of return of the lemniscal response to normal, pre-tone amplitude is about 1.3 percent per second (range 0.42 to 2.45 percent per second).

In summary, in the unrestrained, unanesthetized cat, the presentation of a novel auditory stimulus was accompanied by a slight, but statistically significant decrease in amplitude of the evoked potentials recorded from the medial lemniscus in response to single shock stimulation of the contralateral superficial radial nerve. The depression of the lemniscal response was found to persist for several seconds after each tone stimulus. While the effect of the tone was observed in every animal tested, the magnitude of the reduction never amounted to more than 7 percent. Similarly, on the average, only two out of every three presentations of the tone were associated with a decrease in the evoked

Figure 9. Time course of the evoked lemniscal response suppression from novel stimulus onset.

The average evoked lemniscal response amplitude is calculated as a percentage of the pre-tone control value for the first (filled circles) and second (open circles) evoked responses for each animal and plotted with respect to latency following onset of the novel stimulus (tone). The tone is 500 msec in duration. The average lemniscal response amplitudes are computed over the first 11 trials for each animal, the figure being based upon the same data as shown in Table 1.

The lemniscal responses evoked nearest the onset of the tone are reduced more than the responses evoked 2 seconds later. The difference between the amount of reduction in the first and second lemniscal responses evoked following the tone ranged from 0.83 to 4.89 percent and averaged 2.6 percent for the 7 animals. This difference occurred over a span of 2 seconds. Therefore the average rate of return of the lemniscal response to normal amplitude following the onset of the tone stimulus is about 1.3 percent per second (range: 0.42 to 2.45 percent per second).


%
+4
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-2
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AVERAGE LEMNISCAL RESPONSE AMPLITUDE CHANGE
N= 7 CATS
1.0
2.0
3.0
4.0
LATENCY (Seconds)

lemniscal response amplitude. However, it was found that repeated presentations of the tone resulted in a progressive diminution of the effect such that finally the tone produced no change in the evoked response whatsoever. Whether this phenomenon represents a process of fatigue or habituation is not clear. On the other hand, the reduction of the lemniscal response did occur in the absence of overt motor activity. Taken together, these findings suggest a central mechanism to be responsible for modulating sensory transmission over the lemniscal pathway during the induced arousal evoked by a novel auditory signal.

CHAPTER V

EVOKED LEMNISCAL RESPONSES DURING VOLUNTARY MOVEMENTS

In a second series of experiments, potentials evoked in the left medial lemniscus to single shocks applied to the right superficial radial nerve were used to study changes in cutaneous sensory transmission through the lemniscal pathway during spontaneous, voluntary flexion movements of the right forelimb. The procedures used in these experiments have mostly been described in previous sections. The lemniscal responses were evoked repetitively once per two seconds by single shock stimulation of the superficial radial nerve at a stimulus intensity just sufficient to produce maximal amplitude evoked potentials in the contralateral medial lemniscus. All 7 animals were unanesthetized and completely mobile throughout these experiments.

In order to obtain movements it was often necessary to gently place the animal on its feet. A period of several seconds was then allowed before recording began. Phasic bursts of muscle activity from the right forelimb biceps were taken as an accurate measure of the occurrence and duration of voluntary flexion movements of the right forelimb. While direct visual observation indicated that the bursts of EMG activity were indeed correlated with movements of the right forelimb, the following points are worth noting.

Although the EMG is a direct measure of muscle activity, it does not necessarily reflect the degree of tension, velocity of movement, or even the amount of displacement, if any, of the limb in space. Since isometric contractions cannot be accurately differentiated from isotonic contractions, reference to the EMG activity in the biceps muscle as representing actual movements of the forelimb may be something of a misnomer. However, for the sake of economy and consistency, the bursts of EMG activity recorded from the biceps muscle will continue to be referred to as reflecting actual flexion movements of the forelimb.

In order to compare the lemniscal response evoked during movements to those evoked when the animal was not moving, the following procedure was used. The occurrence of discharges in the recordings from the biceps muscle during movements were clearly identifiable above the very low level of background muscle activity observed when the animal remained immobile. Since the bursts of EMG activity associated with movements tended to have an all-or-nothing character, no amplitude criterion was imposed and thus lemniscal responses evoked during even very small movements were included in the analysis. On the other hand, the measurement of lemniscal responses was restricted to those responses which occurred during bursts of muscle activity which had a duration of not less than 20 msec nor longer than 2.0 seconds. No distinction was made, however, between lemniscal responses which were evoked at different times with respect to the beginning or end of the burst of muscle activity. When an evoked response was found to occur during a movement, the nearest evoked response preceding the movement, as well as the nearest evoked response following the movement, were selected for comparison,

with the added stipulation that neither of these two responses could occur closer than 200 msec to any muscle activity. In cases where several discrete movements occurred in close succession, several evoked responses sometimes occurred during the movements. Each such response was compared to the pair of no-movement evoked responses occurring before and after the movement. For the purpose of quantitative analysis, the average amplitude of the two evoked lemniscal responses obtained before and after the movement were subtracted from the amplitude(s) of the individual evoked response(s) which occurred during movements. These difference scores, usually expressed as percent change scores, were then submitted to a variety of statistical tests and analysis.

Evoked Lemniscal Responses during Voluntary Movements of the Right Forelimb in Unrestrained, Unanesthetized Cats

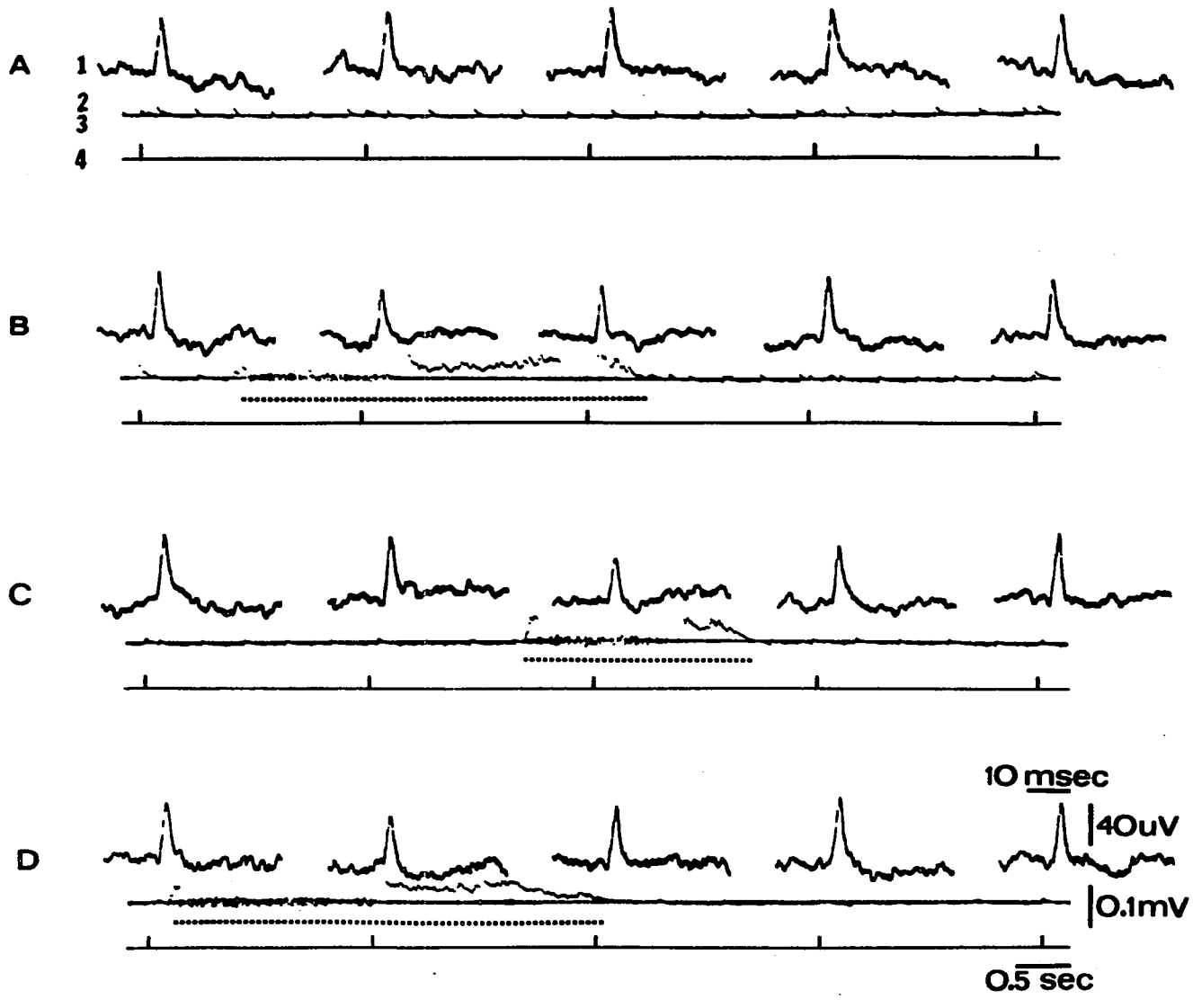
Figure 10 shows the reduction of the evoked lemniscal potential during the phasic bursts of EMG activity recorded from the biceps muscle during movements of the right forelimb. In the absence of movements, the evoked lemniscal response amplitude remains quite stable, whereas those responses evoked during the movements are substantially reduced regardless of whether they occur in the middle, or towards the end, of the movement.

Table 2 summarizes the results of the statistical analyses comparing the evoked lemniscal responses, which occurred during right forelimb movements, to those evoked responses obtained in the adjoining periods of no movement. Mean amplitudes (in microvolts) appear in the first columns for the evoked lemniscal responses obtained under the two

Figure 10. Reduction of the evoked lemniscal response amplitude during voluntary movements.

Unrestrained, unanesthetized cat, 2 days after chronic implantation of electrodes. 1: lemniscal responses recorded in the left medial lemniscus to single shock stimulation of the right superficial radial nerve; 2: integrated EMG from right forelimb biceps muscle, upper range of the output not shown; 3: EMG activity from the right forelimb biceps muscle; 4: signal marker of the shocks to the superficial radial nerve, once per 2 seconds, 0.05 msec duration pulse, 1.9 x T stimulus intensity. The lemniscal responses are aligned with respect to the occurrence of the shocks to the superficial radial nerve.

A: a series of 5 successive lemniscal responses shows the stability of the evoked potential amplitude during quiet waking in the absence of movement. The small inflections in the integrated EMG output are electrocardiographic artifact. In B, C and D the lemniscal responses evoked during the bursts of EMG activity (broken line) recorded from the right forelimb biceps muscle are reduced in amplitude compared to the lemniscal responses both before and after the muscle activity. In B and D even the lemniscal responses evoked during very small amounts of muscle activity, as indicated by the integrated EMG, are reduced although the magnitude of the suppression is not large.


A
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2
3
4
B
C
D
10 msec
40uV
0.1mV
0.5 sec

Table 2

EFFECT OF RIGHT FORELIMB MOVEMENT ON EVOKED LEMNISCAL RESPONSE AMPLITUDE

Cat		No Movement (μV)	Right Forelimb Movement (μV)	Amplitude Reduction (%)	t value[1]	Number of Lemniscal Responses Reduced (%)
3772*	$\bar{x}$	28.3	24.6	13.1	-4.43	78.0
	S	3.9	4.6		(p<.001)	
4702*	$\bar{x}$	61.2	56.3	8.0	-4.23	87.0
	S	5.5	5.5		(p<.001)	
4852	$\bar{x}$	20.9	14.7	29.7	-2.50	75.0
	S	4.0	5.2		(p<.05)	
1589*	$\bar{x}$	44.9	40.9	8.9	-2.66	71.0
	S	5.2	5.1		(p<.05)	
4849	$\bar{x}$	21.8	18.7	14.2	-2.97	83.0
	S	3.8	4.1		(p<.01)	
4853	$\bar{x}$	51.0	46.9	8.0	-2.54	74.0
	S	6.9	8.4		(p < .05)	
5044*	$\bar{x}$	21.7	18.3	15.8	-4.90	92.0
	S	1.5	2.3		(p<.001)	
				13.9		80.0
				t_{ou} 4.84 (p<.01)		$t_{u=50\%}$ 10.42 (p<.001)

*Superficial radial nerve tied-off distal to stimulating electrode.

[1] t-test for correlated means computed from percent difference scores.

conditions for the 7 animals on the first recording session. The percent amplitude reduction with right forelimb movements as well as the number of movements associated with a decrease in the evoked response, expressed as a percent, appear in the third and fifth columns respectively. An average of 20 movements per animal was analyzed.

The data shown in Table 2 indicate that the amplitude of the evoked lemniscal response recorded during movements of the right forelimb was reduced by 8 to 30 percent compared to no-movement controls, with all animals showing a statistically significant decline in the evoked response amplitude during movement at the $p<.05$ level or better (t test, correlated means). Similarly, between 71 and 92 percent of all right forelimb movements were associated with a depression of the evoked response.

In the lower part of Table 2 appear the overall averages and statistical tests indicating that the evoked lemniscal response was reduced on the average by about 14 percent ($p<.01$, t_{ou}) and that the average number of movements associated with a decrease in the evoked response was 80 percent ($p<.001$, $t_{u=50\%}$).

Similar results were found for the 5 animals from which recordings were obtained on additional sessions. Combining the results of all the sessions, each animal showed a reduction of the evoked lemniscal response which was statistically significant beyond $p<.02$ level or better in every case (t test, correlated means). The amplitude of the evoked response was decreased on the average by 10 percent ($p<.01$, t_{ou}) and the number of movements associated with a depression of the lemniscal potential averaged 72 percent ($p<.01$, $t_{u=50\%}$). A total of 231 movements were included in this analysis.

Relation between EMG Activity and the Evoked Lemniscal Response Amplitude

In Figure 11 the amplitude of the lemniscal response is plotted as a function of EMG activity level for one animal. From this illustration it is clear that there is a negative correlation between the two measures such that the greater the amount of EMG activity recorded during movement, the smaller the amplitude of the associated evoked lemniscal response. All of the animals showed a similar negative correlation between EMG activity level and evoked response amplitudes with the value of r (Pearson's r) ranging from -0.08 to -0.57. The average Pearson r for the 7 animals was -0.36 which is statistically significant ($p<.01$, t_{ou} on z scores converted from r).

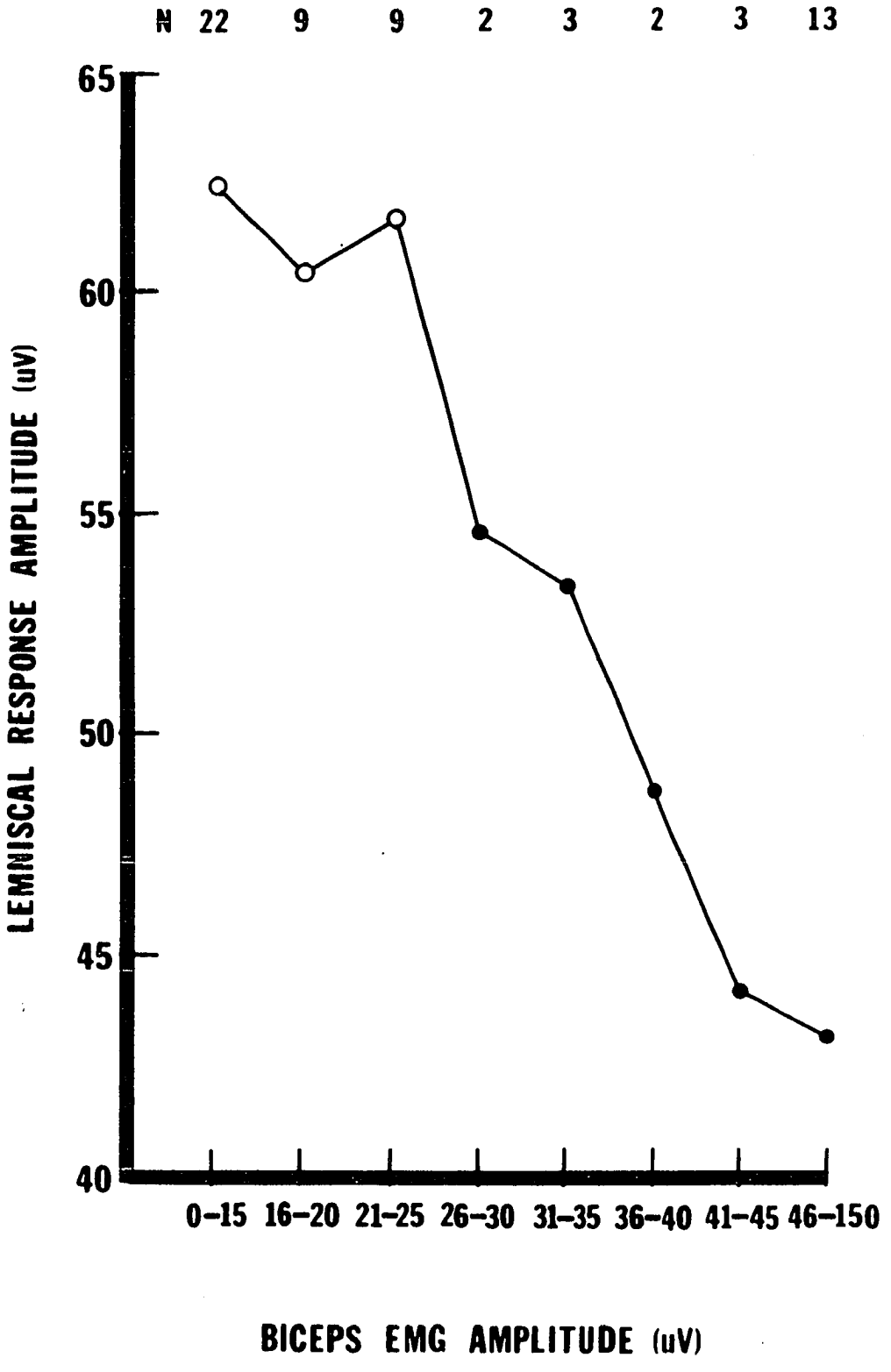
It will be noticed that none of the 7 animals studied here produced a correlation as large as that shown in Figure 11. This may have resulted from the use, in the present study, of the continuously integrated EMG which takes into account both the average frequency and amplitude of the recorded muscle activity. On the other hand, the data shown in Figure 11 were obtained from single oscilloscope sweeps at sufficient speed for direct measurement of the muscle potentials in microvolts over the short interval during which the lemniscal response was evoked.

In summary the results of these experiments in unrestrained, unanesthetized cats indicate that spontaneous voluntary movements of the right forelimb are associated with a consistent and significant reduction in amplitude of the potentials evoked in the left medial lemniscus to single shock stimulation of the right superficial radial nerve. Furthermore, there tends to be a relationship between the effect

Figure 11. Relation between evoked lemniscal response amplitude and amplitude of EMG activity in the biceps muscle during movement.

The figure represents data obtained from one animal on a single recording session. The average amplitude of the lemniscal responses, evoked by stimulation of the right superficial radial nerve, are plotted with respect to the amplitude of the EMG activity recorded from the right forelimb biceps muscle. The unfilled circles represent the average amplitude of the lemniscal responses which occurred in the presence of EMG activity considered, for this experiment, to be below the amplitude criterion established for movement. These responses occurred in the adjacent intervals both before and after the lemniscal responses obtained during the larger bursts of EMG activity defined as movements (filled circles). The number (N) of evoked lemniscal responses averaged together for each of the plotted points is indicated at the top of the graph. Over the entire recording session all lemniscal responses occurring in the presence of EMG activity which exceeded 25 μv amplitude have been included.

The depression of the evoked lemniscal response amplitude is greater, the larger the amount of EMG activity observed during movement. This relationship is indicated by a negative correlation of -0.66 (Pearson's r) which is statistically significant beyond $p<.001$ level.


N 22 9 9 2 3 2 3 13
65
60
55
50
45
40
LEMNISCAL RESPONSE AMPLITUDE (uV)
0-15 16-20 21-25 26-30 31-35 36-40 41-45 46-150
BICEPS EMG AMPLITUDE (uV)

on the evoked responses and the movements such that the amount of decrease seen in the evoked potential is roughly proportional to the magnitude of the muscle activity recorded during the movement. In view of these findings, another set of experiments was undertaken in order to determine whether the effect was specific with respect to laterality, and, furthermore, to what extent arousal and orienting behavior might be involved.

Evoked Lemniscal Responses during Movements of the Left and Right Forelimbs

Earlier it was shown that the presentation of a novel auditory stimulus which presumably aroused the animal, was associated with a reduction in the amplitude of the evoked lemniscal response. Although this effect was observed to occur in the absence of movements it could reasonably be hypothesized that movements may themselves represent spontaneous activation and arousal of the organism. Thus, the decrease in the evoked lemniscal response amplitude during movements of right forelimb might actually be attributable to the same influence which mediated the reduction of the evoked response during induced arousal. One way of testing this hypothesis would be to record responses in the left medial lemniscus to stimulation of the right superficial radial nerve while simultaneously recording muscle activity in both the right and left forelimbs. If movements *per se* are associated with arousal, as predicted from the above hypothesis, then the evoked response should be reduced during movements of the left as well as the right forelimb.

Out of the 7 animals studied in the previous experiment, 4 animals carried implanted EMG electrodes in the biceps muscles of both

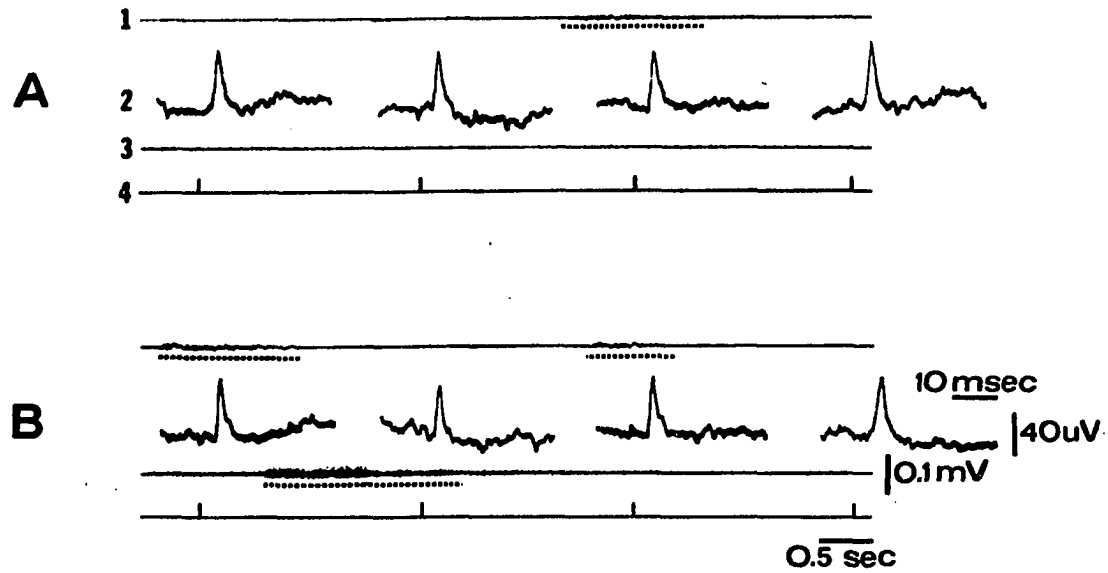
forelimbs. Procedures for eliciting the responses recorded in the left medial lemniscus were the same as described previously, as were the criteria for selection of the movements. The data comprising the results of the present experiments are, however, completely independent of the previous experiments, except that 4 of the same subjects were used and the recordings were obtained on the same days as in the other experiments.

Figure 12 shows a short continuous recording in one animal of EMG activity from the biceps muscles of the left (upper trace) and right (lower trace) forelimbs. As can be seen clearly, bursts of muscle activity occurring in conjunction with movements of the left forelimb are not associated with any change in the lemniscal response amplitude. On the other hand, compared to times during which there is movement in neither limb, a burst of EMG activity recorded from the right forelimb flexor muscles is accompanied by a significant reduction in the evoked response amplitude.

In the lower part of Figure 12 the average lemniscal response amplitude change, for all 4 animals, is plotted for three movement conditions. Movements of the left forelimb resulted in only a small decrease (average less than 2%) with one animal showing an increase and another no change in average lemniscal response amplitude. Furthermore, compared to evoked responses recorded when the animal was immobile, none of the statistical tests revealed any significant differences in the lemniscal response amplitudes during movements of the left forelimb in any of the animals ($\underline{t}$ test for correlated means), nor across the animals as a group ($\underline{t}_{ou}$).

Figure 12. Evoked lemniscal responses during movements of the left and right forelimbs.

The upper portion of the figure shows two short segments of recording obtained from an unrestrained, unanesthetized cat, 2 days following chronic implantation of the electrodes. 1: EMG activity in the left forelimb biceps muscle; 2: evoked responses in the left medial lemniscus to stimulation of the right superficial radial nerve; 3: EMG activity in the biceps muscle of the right forelimb; 4: signal marker of the shocks of the superficial radial nerve, once per 2 seconds, 0.05 msec duration pulse, 1.9 x T stimulus intensity. A: The stability of the evoked lemniscal response amplitude is shown during a burst of EMG activity in the left forelimb biceps (dashed line). B: In comparison to the responses evoked in the absence of EMG activity, the lemniscal response evoked during activity in the right forelimb biceps is reduced. Lemniscal responses evoked during EMG activity in the opposite forelimb remain unmodified. C: The average value of the evoked lemniscal response amplitude is calculated as a percentage of the no-movement control value for each of the 4 animals (filled circles) under the conditions of left forelimb movement, right forelimb movement, and simultaneous left and right forelimb movements. The unfilled circles represent the averages across the 4 animals in each condition. Only during movements of the right forelimb is the evoked lemniscal response significantly reduced. Movements of the left forelimb alone are not associated with a systematic effect on the lemniscal response amplitude.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4
B
10 msec
40uV
0.1mV
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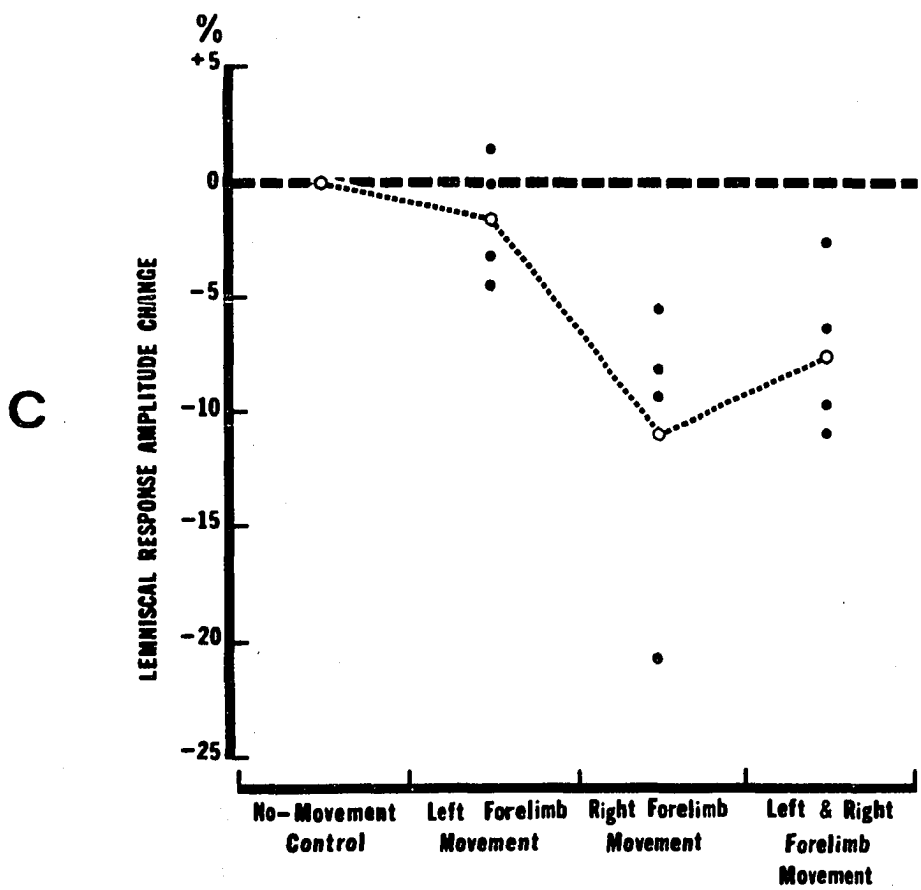
C
%
+5
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-5
-10
-15
-20
-25
LEMNISCAL RESPONSE AMPLITUDE CHANGE
No-Movement Control
Left Forelimb Movement
Right Forelimb Movement
Left & Right Forelimb Movement

In contrast, movements of the right forelimb, as observed in previous experiments, were associated with a consistent decrease in lemniscal response amplitudes with two subjects showing a highly significant effect ($p<.001$; t test correlated means) and the remaining two animals showing a reduction significant beyond $p<.05$ and $p<.10$ levels, respectively. The amplitude of the evoked response was reduced on the average by 11 percent ($p<.05$, t_{ou}) while the number of responses reduced during right forelimb movements averaged 75 percent ($p<.05$, $t_u = 50\%$). Approximately 20 right forelimb movements and an equal number of left forelimb movements were analyzed for each animal. Analysis of an additional 83 right and left forelimb movements obtained on subsequent recording sessions yielded comparable results.

In a limited number of cases, movements occurred simultaneously in both the right and left forelimbs (in one animal only 2 such instances were recorded). However, because of the small sample size most statistical analyses are inappropriate. Nevertheless, across animals the evoked response showed an average amplitude reduction of a little over 7.5%, while the percentage of evoked responses showing a decrease during movements of both forelimbs averaged 70%.

In summary, movements of the left forelimb alone were not associated with changes in the evoked potential recorded from the left medial lemniscus in response to stimulation of the right superficial radial nerve. Thus, the hypothesis that movements *per se* may be accompanied by arousal and hence lead to decreased evoked lemniscal responses can be rejected as an explanation of the effects observed in previous experiments. In the present experiments only during the bursts of EMG

activity recorded from the right forelimb were the potentials evoked over the ascending pathways from this limb ever modified. Therefore, whatever the mechanism responsible for modulating the amplitude of the evoked response in conjunction with movements, the distribution of the effect appears limited to the actively moved region. In other words, the modulation of sensory transmission over the lemniscal system which occurs during voluntary movement appears to specifically involve the pathways which carry afferent impulses originating in the limb which was actually moved.

Influences Responsible for the Reduction of the Evoked Lemniscal Response

The rest of the experiments to be reported here were aimed at determining whether the reduction of the lemniscal response recorded during right forelimb movements could be attributed to either a central or peripheral influence or both. It will be recalled that discharges in a particular set of peripheral afferent nerves are capable of inhibiting evoked activity in response to stimulation of other nerves, this effect being especially strong when the two sets of nerves have overlapping, mutually inhibitory receptive fields. This phenomenon is generally referred to as "afferent" or "surround" inhibition and is known to influence sensory transmission through the dorsal column nuclei by the mechanisms of both pre- and post-synaptic inhibition (see 7).

On the other hand, among the central structures capable of modulating sensory transmission in the lemniscal system are the sensorimotor cortex and pyramidal tract, both of which are presumably concerned with the genesis of voluntary movements. Since activity in this system

is likely to be correlated with movements and motor behavior, changes in the evoked lemniscal response during these times may be attributable to such a central influence and not to a peripherally induced process. Therefore, the problem under investigation in the following experiments concerns whether the influences which produce the reduction in the lemniscal response amplitudes, observed during voluntary movements, originate mainly in the peripheral nerves or instead have as their source the central mechanisms which may actually generate the movements.

While there are a number of possible approaches to this problem, no single experiment, which can be performed in intact, free-moving animals, is capable of giving an unqualified result. Therefore, a series of experiments, each involving a different approach with independent manipulation of the several variables involved, was necessary.

The Effect of Restricting Afferent Feedback on Evoked Lemniscal Responses during Movement

The superficial radial nerve is an obvious potential source of afferent inhibition and/or occlusion, and the presence of activity in its constituant fibers would conceivably have a significant effect on responses evoked in the medial lemniscus by its stimulation. Since movements of the forelimb undoubtedly do produce impulses which ascend by this pathway, it might be expected that by blocking this peripherally generated activity the reduction of the lemniscal responses seen during movement would be lessened or might not even occur.

In order to test this hypothesis, in 4 of the original 7 animals, the superficial radial nerve was crushed and tied-off about 3-4 mm distal to the stimulating electrode. At the end of all the

experiments, gross histological examination indicated the distal part of the nerve to have a shrunken, segmented appearance as well as showing other signs of degeneration, thus confirming that the surgical treatment would have effectively destroyed the nerve's ability to transmit impulses from peripheral receptors. On the other hand, the proximal end had only a slightly swollen appearance just next to the suture, but otherwise appeared entirely normal. Also the evoked response in the medial lemniscus to stimulation of the nerve as well as the stimulus strengths sufficient to obtain it did not appear different from the evoked responses and stimulus threshold values observed in the remaining intact control animals.

The results of these experiments are summarized for the two groups in Table 3 and for the individual animals in Table 2. On the whole, there was little difference between the intact animals and the animals which had tied-off superficial radial nerves. The latter group appeared to show a somewhat more consistent reduction of the lemniscal response amplitudes during movements of the right forelimb; 82% of the responses evoked during movements were reduced, in comparison to 77% for the intact group. On the other hand, the intact subjects showed, on the average, an almost 5% greater reduction of the evoked lemniscal response occurring during movement, but this result was not statistically significant.

In summary, there appears to be little, if any, systematic effect of tying off the superficial radial nerve on the reduction of the evoked lemniscal response observed to occur during voluntary movement. The tendency for there to be a greater decrease in the evoked

Table 3

EFFECT OF TIED-OFF SUPERFICIAL RADIAL NERVE ON LEMNISCAL RESPONSES DURING RIGHT FORELIMB MOVEMENTS[1]

Measures		Superficial Radial Nerve Tied-Off (N=4)	Intact (N=3)	t-test[3]
Percent Amplitude Reduction with Movement	$\bar{x}$	11.5	17.3	
	S	3.7	11.2	0.87
Percent Lemniscal Responses Reduced with Movement	$\bar{x}$	82.0	77.3	
	S	9.3	4.9	-0.85
Correlation between Lemniscal Response Amplitude and EMG Activity[2]	r	- 0.38	- 0.34	-0.29

[1]Based on data in Table 2.

[2]Pearson r, average computed after conversion to z scores.

[3]t-test, uncorrelated means, Intact versus Superficial Radial Nerve Tied-Off.

response in intact animals might favor the interpretation that afferent activity may indeed be generated in the superficial radial nerve in conjunction with movements. However, the presence of these hypothetical discharges would seem to have only a limited influence, since in their complete absence the evoked responses continue to be significantly depressed. Therefore, it can be concluded that any peripherally induced afferent inhibition or occlusion produced by impulses carried over the superficial radial nerve, while they may contribute to the effect, cannot account for the overall reduction of the evoked lemniscal response which occurs during voluntary movements.

Although these experiments have ruled out what is likely the most potent potential source of a peripherally induced modification of the evoked lemniscal response, there remain several other possibilities. Activity in other cutaneous nerves besides the superficial radial, in addition to the activity which must occur in muscle afferents, might also mediate a reduction in the evoked response via the afferent inhibition mechanism. Obviously, however, the technique of deafferentiation cannot be extended to all the sensory nerves of the forelimb. In particular the afferent fibers innervating the muscles travel together in the same nerves containing the efferent motor fibers. Therefore, another completely different approach was developed.

Effect of Passive Movements on Evoked Lemniscal Responses

In the following experiments, the effect of passive movements of the right forelimb on the evoked lemniscal response was investigated in 6 animals. These experiments sought to determine whether movements

of the forelimb cause any systematic modification of the lemniscal response in the complete absence of the central mechanisms responsible for generating voluntary movements. However, there is one substantial difference in the procedures employed in the present study as opposed to the previously reported experiments.

As shown earlier, arousal and orienting behavior may be associated with a reduction in the evoked lemniscal response, an effect which can occur without any apparent signs of peripheral motor activity. Furthermore, it is extremely doubtful whether passive manipulation of the forelimb in the unanesthetized cat could ever be accomplished without some active movement as well as general behavioral arousal taking place. Thus, any change in the lemniscal response found to occur during passive movement under such conditions could as easily be attributed to a central arousal mechanism as it could be to any peripheral process evoked by the movements. Therefore, in order to rule out all possible central influences, it was necessary that the effect of passive movement on the evoked lemniscal response be studied in the acutely anesthetized animal. This is in contrast to all the previous experiments in which the animals were completely unrestrained and unanesthetized.

The procedural details and the method used for recording passive movements in the anesthetized cat have been described previously. Briefly, the lemniscal response was evoked repetitively at once per 2 seconds while both passive flexion and extension movements were carried out. The output of a specially constructed device for indicating the direction as well as relative speed of the movements was recorded on

film along with the lemniscal potentials, EMG and time marker. For the purposes of analysis, the lemniscal responses in each animal were separated into three groups corresponding to no movement, flexion movement, and extension movement conditions. The differences between the three sets of scores were then statistically evaluated for each animal, using the *t*-test for uncorrelated means.

The statistical analysis carried out in all 6 animals indicated that on the average, passive flexion movements were associated with less than a 3% increase in the lemniscal response amplitude with 3 of the 6 animals showing decreases and the remainder being increased, all non-significant differences except for one animal. Similarly, in none of the animals were any significant effects observed with passive extension movements, the average change for the group amounting to less than 1% of the average no-movement control value. Therefore, despite a rather substantial increase in two cases, there was no overall systematic effect of either passive flexion or extension movements of the right forelimb on the amplitude of the evoked lemniscal response in anesthetized cats. Furthermore, these results rule out the possibility that physical displacement of the stimulating electrode with respect to the superficial radial nerve would have been responsible for the systematic reduction of the lemniscal responses, evoked during normal voluntary movements of the forelimb.

While passive movements have only the crudest resemblance to normal voluntary movement, the present experiments do suggest that such activity as may be generated in joint and muscle afferents does not modify the lemniscal response evoked by cutaneous nerve stimulation.

This conclusion is consistent with evidence that afferent inhibition is limited almost exclusively to fibers originating from skin receptors sensitive to the displacement of hairs (see 32, 67) rather than to receptors located in the muscles. Specifically, stimulation of the large IA muscle afferents does not produce inhibition of cutaneous evoked responses in the cuneate nucleus of anesthetized cats (74). In summary, in the absence of the central mechanisms responsible for the initiation and control of voluntary movements, passive movements of the forelimb are not associated with reduction of the evoked lemniscal response amplitudes.

Evoked Lemniscal Responses Prior to Movements

While results of the previous experiments continue to favor a central influence to account for the reduction of the lemniscal response during voluntary movements, a final approach was developed which tested this hypothesis more directly. If a central mechanism were indeed responsible for modulating sensory transmission over the lemniscal pathway, it might be expected that this influence would actually be exerted prior to the onset of movements. The basis for such a prediction is fairly simple. The conduction time from higher motor centers to the synaptic relays of the dorsal columns, on which a descending discharge would presumably operate, is considerably shorter than to the conduction time required for the transmission of an efferent volley through the spinal cord and peripheral nerves to the musculature. Thus, modulation of synaptic activity in the lemniscal pathway would occur before the muscular contractions leading to movements were even initiated. Such a prediction assumes that efferent discharges destined

for the sensory relays of the lemniscal system originate simultaneously with the efferent volleys responsible for generating movements. Furthermore, it assumes that conduction speed and synaptic delay in the descending pathway(s) are comparable. While there may be some evidence in support of these assumptions, the actual existence and operation of such a precisely organized system remain speculative. Nevertheless, it appeared useful to test the hypothesis that sensory transmission over the lemniscal pathway is modified not only during movement but also in the brief interval just before the movement begins.

A separate set of experiments was not needed to evaluate this question, since from the 7 animals previously studied there were a sufficient number of instances where the lemniscal response was evoked within 150 msec of the onset of voluntary movements. However, as might be expected, the probability of obtaining such examples was relatively low. As previously described, the lemniscal responses were evoked repetitively once per 2 seconds by single shock stimulation of the right superficial radial nerve in unrestrained, unanesthetized cats. Recordings obtained from the biceps muscles of the right forelimb along with the integrated EMG signal were used to determine the onset and termination of movements, but these measures, it should be recognized, are accurate only to within 10 to 20 msec. Since the onset of voluntary muscular contraction represents a process of recruitment in increasingly greater numbers of motor units, the beginning of muscle activity could not be resolved beyond these specified limits. Therefore, intervals from zero to 25 msec, 26 to 50 msec, and so on out to the interval 126 to 150 msec were used to categorize the latencies of the evoked responses

which could definitely be identified as occurring before movement began. Across the 7 animals a total of 99 evoked responses occurred in the 150 msec interval before movement and were analysed in the same manner as described for the analysis of evoked responses during voluntary movement.

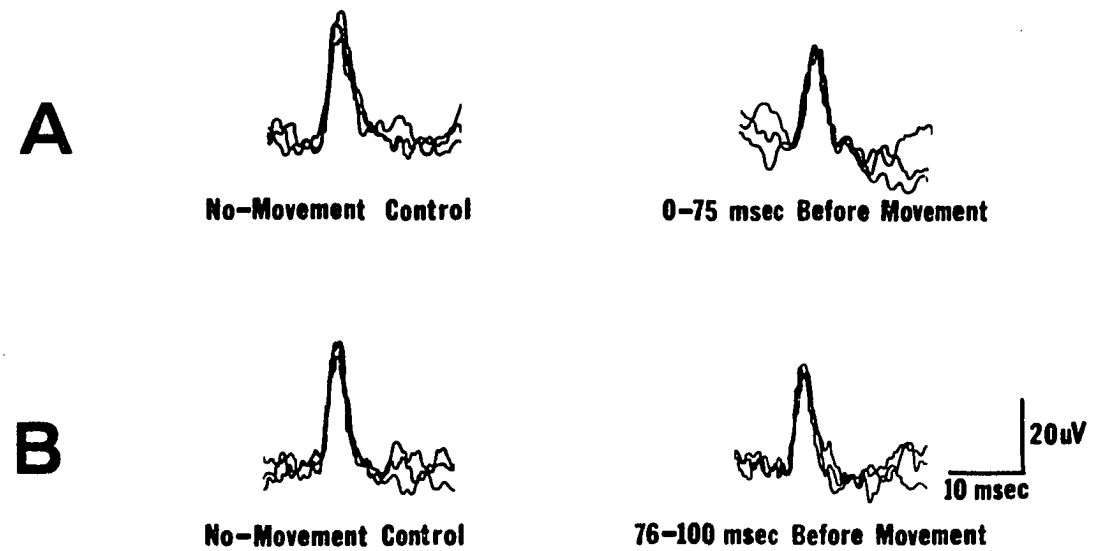
Figure 13 shows 4 sets of 3 superimposed sweeps taken for a single recording session during voluntary right forelimb movement in an unrestrained, unanesthetized cat. Compared to the three no-movement control responses, the three evoked responses which occurred within the 75 msec interval before movement are depressed by about 15%. Furthermore, the two lower sets of traces indicate that the three evoked responses occurring in the interval of 75 to 100 msec before movement are also decreased compared to the no-movement control responses, but the effect is diminished at this latency. From these examples it appears that sensory transmission through the lemniscal pathway is indeed modified prior to the onset of movements and further that the depression of evoked activity in this system can be observed as much as 100 msec before the movement begins. These results were substantially confirmed when the reduction of the evoked lemniscal response was plotted against the latency of the response from the onset of movements. The lower part of Figure 13 shows a small reduction in the evoked response amplitude as much as 150 msec before the movement, but more importantly the amount of reduction of the response approached that seen during actual movement well before (75 to 50 msec) the movements themselves occurred.

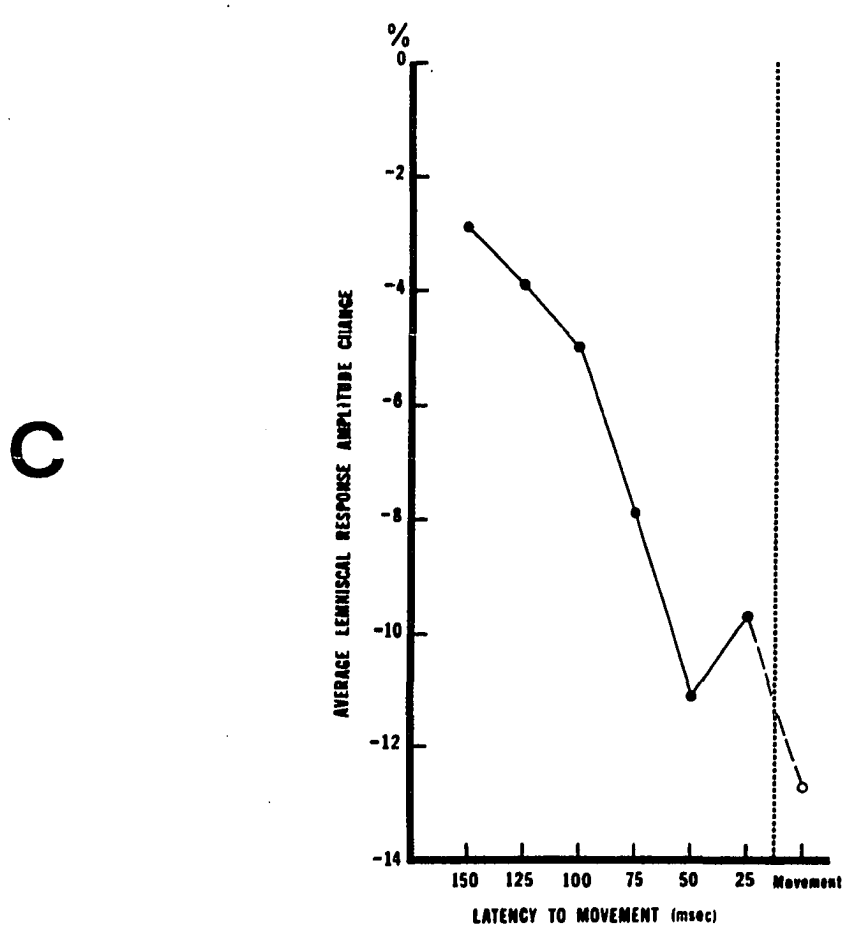
Over the interval from 0 to 100 msec, every animal showed a reduction of the evoked lemniscal response (ranging from 2 to 24%) with the overall decrease averaging 9%. This effect was statistically

Figure 13. Evoked lemniscal responses prior to movements.

A: Sets of 3 superimposed lemniscal responses (traced from the film at the camera lucida) are shown for the interval 0 to 75 msec prior to movement along with the respective no-movement control responses. B: Sets of lemniscal responses for the interval 76 to 100 msec prior to movement are shown along with corresponding no-movement control responses. The responses were recorded in the left medial lemniscus to single shock stimulation (once per 2 seconds, 0.05 msec pulse, 2.2 x T stimulus intensity) of the right superficial radial nerve in one experiment on an unrestrained, unanesthetized cat 3 days following chronic implantation of the electrodes.

C: The average value of the evoked lemniscal response amplitude, calculated as a percentage of the no-movement control value, is plotted with respect to latency prior to onset of movements of the right forelimb. Each of the filled circles represents the value of the lemniscal response amplitude computed from the averages of all animals having lemniscal responses which occurred in the respective latency intervals. The unfilled circle similarly represents the average lemniscal response amplitude decrease across all animals for all movements of the right forelimb on all recording sessions. The figure indicates that the reduction of the evoked lemniscal response during movements begins well before the EMG activity responsible for the movements can be observed. The amount of reduction approaches the value seen during movements in the interval of 0 to 50 msec before movement onset (broken line).


A
No-Movement Control
0-75 msec Before Movement
B
No-Movement Control
76-100 msec Before Movement
20uV
10 msec


C
%
0
-2
-4
-6
-8
-10
-12
-14
AVERAGE LEMNISCAL RESPONSE AMPLITUDE CHANGE
150
125
100
75
50
25
Movement
LATENCY TO MOVEMENT (msec)

significant beyond the $p<.05$ level (t_{ou}). Similarly, across animals, 75% (range 61 to 100%) of the lemniscal responses which occurred within this interval were reduced. This result was also statistically significant ($p<.01$, $t_u = 50\%$).

In summary, it was observed that the amplitudes of lemniscal responses evoked just prior to the onset of voluntary movements in unrestrained, unanesthetized cats were decreased. The magnitude of this effect was nearly as great as that observed during actual movements. Furthermore, the reduction of the evoked response appeared to begin almost 150 msec before the movement. These findings are particularly significant since the depression of lemniscal potentials in this instance cannot be accounted for by any movement-induced afferent inhibition because the movements themselves had not yet occurred at this time.

In conclusion, the hypothesis was confirmed that modulation of evoked activity in the lemniscal pathway which occurs during voluntary movements actually anticipates the onset of movements themselves. Although only circumstantial, this evidence would implicate a centrally originating descending influence on the synaptic relays of the dorsal column-medial lemniscal system to be responsible for the reduction of evoked lemniscal response which occurs during voluntary movement.

CHAPTER VI

DISCUSSION

In the Introduction, several theories are described which implicate the active control of sensory processes as an important factor in certain perceptual constancies, selective attention and postural-motor coordination. Also reviewed is complimentary evidence from physiological and anatomical studies indicating that mechanisms do exist in the brain which are capable of modulating afferent input transmitted over ascending sensory pathways. On the basis of these two approaches, the present series of experiments was developed. These studies sought to determine to what extent the modification of sensory input inferred to occur under certain behavioral conditions might actually be represented at the neural level. Further, these experiments attempted, indirectly, to define the functional significance of the efferent pathways known to project from certain motor centers of the brain to the relay nuclei of the sensory input systems.

Sensory Transmission through the Lemniscal Pathway during Induced Arousal

Responses evoked in the medial lemniscus to single shock stimulation of the contralateral superficial radial nerve were used to study changes in sensory transmission through the lemniscal pathway

during induced arousal in the unrestrained, unanesthetized cat. In association with a novel auditory stimulus (tone) the amplitude of the evoked lemniscal response was reduced, an effect which occurred in the apparent absence of overt motor activity. After repeated presentations of the novel stimulus, the lemniscal responses were no longer modified. Since no movements were observed, a peripherally induced phenomenon, such as afferent inhibition, or occlusion, would not appear to have contributed to the changes in the lemniscal potentials. Therefore, the reduction of the evoked lemniscal response amplitude during the tones may be attributable to a central mechanism which is subject to a process of either fatigue or habituation. These findings are relevant to the postulated existence of mechanisms for modulating sensory input in conjunction with attentive arousal and selective perception.

Beginning with the fundamental observations of Hagbarth and Kerr (35) it is now well known that sensory impulses passing through even the lowest levels of the ascending afferent pathways are under the direct control of central descending influences. Subsequently, it has been suggested that the depression of sensory transmission by activity in cortical and subcortical structures may be correlated with different states of arousal and attentive wakefulness (40-44). For example, potentials evoked in the somatic afferent pathways are reported to be reduced when an animal is attentively sniffing a strong odor (43). Likewise, the monotonous repetition of an auditory stimulus is ultimately associated with a reduction of evoked responses recorded from the dorsal cochlear nucleus (40). These two instances of sensory suppression have been attributed to active inhibitory influences arising in particular

from the reticular formation, and interpreted to represent the neural basis of selective attention and habituation respectively (see 41). The hypothesis has been further extended to suggest that during the orienting or arousal reaction induced by a novel stimulus, irrelevant sensory information is inhibited while the receptivity of the organism to the new stimulus is correspondingly enhanced (41, 42).

The findings reported here showing a reduction of the lemniscal response following the presentation of a novel auditory signal appear consistent with this hypothesis. Other investigators also report that evoked potentials in the medial lemniscus are reduced during both spontaneous and induced arousal (9, 23). Since activation of the reticular formation may correspond with behavioral arousal, it has further been suggested that the depression of the lemniscal responses at these times may be attributable to this influence (23). While recent evidence shows that the reticular formation may directly modify sensory transmission through the dorsal column nuclei (14, 15), the possibility that the reticular formation contributed to the depression of the lemniscal response seen in the present study cannot be evaluated. It is of interest that the changes in the lemniscal potential produced by the tone stimulus were not accompanied by movements. On the other hand, compared to the depression which is found to occur during spontaneous voluntary movements, as shown here in the second set of experiments, the effect of the tones on the evoked lemniscal response is remarkably subtle. Control experiments do suggest that the reduction of the lemniscal response during movements does not represent the influence of a general arousal mechanism. Whether the converse is

true, namely, that the central influences operating during movement do not contribute to the changes in the lemniscal response during arousal, is less certain. It could be argued that had a stronger arousal stimulus been employed, the influence of the arousal system on the lemniscal pathway would have been greater. However, it must be recognized that strong arousal is almost by definition represented by overt motor behavior. Based upon the present evidence, the influences producing the reduction of the evoked lemniscal response during voluntary movements would largely supercede the small contribution of any so-called arousal mechanism.

In summary, the presentation of a novel auditory stimulus is associated with a small reduction of the lemniscal response evoked by cutaneous nerve stimulation in chronic cats. A central influence is suggested to produce the depression of the evoked response. However, the magnitude of the effect is so small as to make interpretation of its functional significance difficult. To the extent that sensory changes produced in association with voluntary movements can be ruled out as a contributing factor, the reduction of the lemniscal response may represent the inhibition of irrelevant sensory input during the attentive arousal induced by a novel stimulus.

Sensory Transmission through the Lemniscal Pathway During Voluntary Movements

In a second series of experiments, the amplitude of the lemniscal response evoked by stimulation of the superficial radial nerve was found to be reduced during active voluntary flexion movements of the forelimb. The effect appeared specific to the pathways originating

from the actively moved limb as shown by the absence of any change in the evoked response when the contralateral forelimb was moved. This particular finding also indicated that movements per se are not associated with activation of a general arousal mechanism conceivably capable of modifying the lemniscal potentials. It was further shown that the amount of reduction in the evoked response is roughly proportional to the magnitude of the muscle activity recorded during the movement. While all of these observations are consistent with the operation of a central influence on the lemniscal pathway during movements, further experiments were done to rule out other possibilities.

In several animals the superficial radial nerve was crushed and tied-off distal to the stimulating electrode, thus removing an obvious potential source of peripheral afferent inhibition or occlusion. All of these animals showed a reduction of the evoked response amplitude during active movements. On the other hand, passive movements of the forelimb in the anesthetized cat did not have any effect on the lemniscal response. Finally, it was observed that lemniscal responses evoked just prior to the onset of voluntary movements were reduced in amplitude by almost as much as the responses evoked during movements. This finding is particularly significant in that the depression of the lemniscal potential in this instance cannot be accounted for by any peripheral mechanism since the movement had not even occurred at this point. Taken together, these results recommend the conclusion that there exists a blockade of sensory transmission through the lemniscal pathway which is attributable to a central descending influence operating in conjunction with the mechanisms responsible for the generation of voluntary

movements. In view of the well-known relations of the pyramidal tract to the synaptic relays of the dorsal column-medial lemniscal pathway, it is further suggested that the depression of the evoked lemniscal response, and, to an extent, the occurrence of the movements themselves, arise from activity in the cortical-pyramidal tract system.

In agreement with these findings is a recent report that lemniscal responses evoked during a conditioned limb movement in the cat are also reduced (28). The depression of the evoked response was similarly observed to occur before the onset of movement, suggesting a central influence on the lemniscal system. However, no other experiments were done to test this hypothesis. The conditioned stimulus (tone) reportedly did not affect the lemniscal responses, this finding being in contradiction to the results reported here using a similar stimulus.

The depression of evoked lemniscal responses in association with voluntary movements in awake animals is relevant to investigations of sensory transmission over the lemniscal pathway during different stages of sleep in cats. During the bursts of rapid eye movements (REMs) of desynchronized sleep there occurs a phasic reduction of the evoked lemniscal response (9) which can be attributed to the mechanisms of both pre- and post-synaptic inhibition operating at the level of the dorsal column nuclei (10). It is of interest that these changes in the sensory pathway are simultaneously accompanied by high frequency discharges in descending motor systems such as the pyramidal tract (61). These motor discharges, however, are manifested only as brief muscular twitches which occur together with the motor activity producing the

eye movements (25). Even so, bilateral ablation of the sensorimotor cortex which prevents the appearance of the phasic increases in pyramidal tract activity also prevents the inhibition of the evoked lemniscal response (11). These observations led to the conclusion that afferent impulses ascending over the lemniscal pathway are directly modulated by the efferent pyramidal tract discharges which contribute to the phasic motor patterns occurring during the REM (11).

The results of the present study, indicating a reduction of evoked lemniscal response amplitude during voluntary movements in awake animals, appear to correspond with the changes observed in lemniscal responses recorded during the REMs of desynchronized sleep. In particular during sleep, the evoked response is reduced in association with spontaneous bursts of activity occurring in descending motor systems which are likewise correlated with short lasting muscular contractions and movements of the limbs. The influence of the cortex and pyramidal tract, suggested here to account for the depression of the lemniscal response during voluntary movements in the awake animal, is shown to be the actual mechanism responsible for the inhibition of sensory transmission over the lemniscal pathway under the physiological conditions of sleep. Presumably the generation and control of movement as well as the concurrent modulation of afferent activity in the lemniscal system are mediated similarly in both the awake and sleeping animal. It is of interest that sensory changes which occur during voluntary movement in the waking animal are also found during REM sleep which, in man, is characterized by vivid visual hallucinations and dreaming (20).

In a recent review, Wall (87), has reinterpreted the sensory functions of the dorsal column system to suggest the important role of this pathway in communicating sensory information produced by exploratory movements. Specifically, he suggests that when information is inadequate for the identification of a particular stimulus, an "external search" is initiated involving exploratory movements. He assumes that the afferent input thus generated in the dorsal columns controls the analysis of input occurring in other cutaneous sensory pathways which are ultimately responsible for the recognition and discrimination of the stimulus. Wall further postulates that in association with movements, the cortex exerts descending influences on the afferent systems which set these systems to detect particular events (87).

While it is unclear from this theory whether descending controls also influence activity in the lemniscal pathway, the results of the present experiments indicate that sensory modulation does occur in this system during movement. Perhaps, through an inhibitory interaction operating at the level of dorsal column nuclei, excitatory afferent input originating from the periphery is subjected to a preset bias which allows only certain patterns of excitation to ascend to higher levels. Since this mechanism would be linked with the systems responsible for the generation and control of movements, the dorsal column-medial lemniscal system seems particularly well suited to evaluate sensory stimulation during exploratory motor activity. While this interpretation may go beyond the proposed theory, it nevertheless is consistent with Wall's conclusion that dorsal column function "...is related to some crucial aspect of action" (87).

The interaction between motor activities and sensory processes in the lemniscal system has also been implicated in studies of motor control in monkeys with deafferented forelimbs. In the absence of visual cues, animals, in which all the appropriate dorsal roots have been cut, are still able to learn a discrete motor response with the affected limb (see 80). Even total deafferentiation of the spinal cord is not incompatible with accurate performance on a motor task. While these findings cast considerable doubt on traditional reflex interpretations of movement control, they raise the obvious question of what central mechanism could allow the animal to learn to use a deafferented limb. The concept of "central efferent monitoring" has been introduced as a possible explanation (80). It is postulated that the relation of the pyramidal tract to the dorsal column nuclei may enable movement-induced motor impulses generated in the cortex to be fed back via the lemniscal system to the thalamus and thence returned to the cortex. Such a mechanism would be capable of providing information to higher centers concerning the performance of movements in the absence of peripheral feedback (80).

While certain crucial evidence for this hypothesis is lacking, the results of the present study are not necessarily inconsistent with this notion. Assuming that during movements lemniscal (cuneothalamic) neurones are directly excited by descending impulses carried over the pyramidal tract, the lemniscal response evoked by peripheral nerve stimulation might conceivably be reduced, due to a process of occlusion. Other alternatives are possible, however, including a facilitation of the peripheral evoked response under these same basic conditions. As

has been emphasized, however, evidence (11) has yet to be provided showing that cuneothalamic neurons are actually activated by descending volleys from the sensorimotor cortex. As noted by others (6, 11) and mentioned before here, stimulation of the cortex apparently excites only interneurons mainly responsible for presynaptic inhibition in the dorsal column nuclei. These observations could argue against the view that, in the absence of peripheral input, descending motor impulses can be rerouted via the medial lemniscus, to be evaluated at higher centers. Nevertheless, a feedback loop involving the cortex and thalamus is not ruled out. On the contrary, recent evidence would favor the role of such a system in the production of central feedback accompanying movements (21, see 22, 27).

In summary, physiological, anatomical and behavioral studies point to the existence of an interaction between the central mechanisms of movement and the mechanisms of sensory transmission in the lemniscal pathway. However, there remains considerable confusion about the nature of this interaction. Neurophysiological investigations of sleep suggest that during movements descending motor influences inhibit the sensory input carried over the lemniscal system. On the other hand, the interpretation of deficits following lesions of ascending spinal tracts emphasizes the importance of afferent impulses transmitted through the dorsal columns for the analysis of somatosensory stimulation obtained during exploratory motor activity. Finally, it is postulated that the lemniscal system is somehow capable of sensing the motor outflow generated by higher centers in association with movements, thus serving as part of a central feedback control circuit. Although the results of

the present study by no means contradict any of these interpretations, there is yet another approach which may be more consistent with the findings reported here.

Corollary Discharge Theory and the Modulation of Sensory Transmission in the Lemniscal System during Voluntary Movement

The postulated existence of a corollary discharge from motor centers into sensory relays has proven to be a useful concept in the analysis of perceptual stability and feedback control during voluntary movements (see 81, 22). It is suggested that with the initiation of an efferent discharge towards the peripheral musculature there simultaneously occurs a central (corollary) discharge into the appropriate sensory pathway which counteracts or cancels out those changes which are produced as a result of intended movement. Afferency caused by movement of an external stimulus is assumed to be perceived directly, whereas afferency caused by movement of the organism is thought to be inhibited. Such a system would allow the organism to differentiate changes in sensory stimulation originating in the environment from self-produced sensory input generated by the organism's own movements.

With regard to the control of sensory information transmitted through the lemniscal system, the concept of a corollary discharge mechanism recommends the following hypothesis: During voluntary movement the descending influences, exerted on the dorsal column-medial lemniscal system, represent a predetermined, internal pattern of nervous activity which anticipates and predicts the pattern of sensory stimulation produced by movement. The incoming excitatory pattern is compared and evaluated against the internally generated pattern via an

inhibitory interaction. Afferent impulses which correspond to the internal pattern are suppressed, while other sensory impulses, which do not match the internal pattern, remain unmodified. The organization and development of the internal pattern is determined primarily by the relations between the location and type of peripheral receptors and the actions of muscles which may cause these receptors to be stimulated. Information from muscular and cutaneous sources as well as from the other sensory modalities may also contribute to the organization of the internal pattern. The operation of this mechanism is proposed to be of importance for discriminating between changes in sensory stimulation arising from external sources and changes in sensory stimulation caused by voluntary movements.

The results obtained in the present study are in agreement with several of the essential aspects of this hypothesis. Specifically, the depression of the evoked activity in the medial lemniscus seen during movements is restricted to the pathways leading from the forelimb which actively moves. In other words, the sensory pathways over which movement-produced afferent input would be expected to be transmitted are the same pathways over which evoked sensory input is suppressed. Thus lemniscal responses evoked by stimulation of the superficial radial nerve of the right forelimb are reduced during flexion movements of the same forelimb but are not modified by movements of the contralateral limb. Similarly, others have reported that a conditioned flexion movement is associated with a greater reduction of the lemniscal response evoked by stimulation of the superficial radial nerve than is a conditioned extension movement of the same limb (28). Since the

superficial radial innervates the dorsal aspect of the paw, this region would be predisposed towards receiving greater sensory stimulation during a flexion movement of the paw than during an extension movement. Thus, these findings are consistent with the principle that the topographic organization of the internal inhibitory pattern exerted on the transmission of ascending sensory input during movements is determined by the relations between the location of peripheral receptors and the actions of muscles which may cause these receptors to be stimulated. The central inhibitory influence is assumed to be directed exclusively to those sensory channels over which a given voluntary movement is potentially capable of generating afferent input.

It was also shown here that the reduction of the evoked lemniscal response which accompanies movement begins well before the movement itself occurs. Furthermore, the suppression of the evoked response appears almost completely developed by the time the muscular contractions leading to movement have started. Presumably this represents the creation of the postulated internal pattern which anticipates the activity to be produced in the ascending afferent system by the movement. Thus by the time the afferency caused by movement begins to be transmitted centrally, the mechanisms responsible for correlating this input with the motor output are already available and in operation.

On the other hand, passive movements of the limb do not result in any systematic modification of the evoked activity in the lemniscal pathway. This finding is consistent with the idea that only self-produced sensory stimulation brought about through the organism's own voluntary actions is subject to modification at the central level.

Finally, it was found that the amount of depression of evoked sensory input during movement is limited. Whereas approximately 80 percent of all movements are associated with a reduction of the evoked lemniscal response, the magnitude of this effect varies considerably and only rarely exceeds 30 to 40 percent of normal amplitude. Presumably this reflects on underlying organization and restriction of the central suppressive influence operating on the afferent pathway during movement. The observation that the amplitude of the evoked lemniscal response is reduced roughly in proportion to the amount of muscle activity recorded during movement supports this notion. Clearly, not all sensory input is blocked during movement, nor is there evidence that the internal inhibitory influence is exerted in a constant arbitrary fashion. On the contrary, the amplitude of the evoked response is reduced on the average by no more than 10 to 20 percent, with the greatest amount of suppression being related to movements associated with the largest amounts of muscle activity. Perhaps the larger bursts of muscle activity represent more vigorous movements and hence result in more self-produced afferent input which in turn requires greater suppression at the central level.

While the results of the present experiments appear consistent with the stated hypothesis, many of the interpretations put forward here must remain speculative until further evidence is available. Of crucial importance would be the identification of those afferents which are inhibited during movements. Whether they constitute a specifically organized population with both distinct topographic and functional properties needs to be determined. An analysis of single units recorded

from the dorsal column nuclei during voluntary movements, with localization of the receptive fields and classification of receptor characteristics of the units, remains to be done in chronic animals. However, it is of interest that in acute preparations, those afferents having small receptive fields and giving a rapidly adapting response to bending of hairs are reported to be preferentially inhibited by cortical stimulation (36). Of all cutaneous receptors, these same "hair" units also appear to have the lowest thresholds to natural stimulation (32, 52, 67). It is no less significant that when these afferents were originally identified, the adequate stimulus for their excitation was determined to be movement (1). These observations suggest that those afferent units specifically inhibited by cortical stimulation are the same set of afferents responsible for transmitting sensory information concerning the occurrence of movements over the skin. Support for this conclusion, however, awaits further investigations into the neural processes which code movement stimulation in the cutaneous sensory pathways.

Corollary Discharge Theory and Cutaneous Sensibility during Voluntary Movements

Although the findings of the present study may be taken as evidence for the existence of a corollary discharge mechanism operating on the lemniscal system during movement, there remains an important question concerning the theory itself. In particular, it is difficult to understand why, during active exploratory behavior the cutaneous feedback generated by voluntary movements would be inhibited. As Mackay has pointed out (59), just the opposite would be expected.

He suggests that the cancellation of movement-produced stimulation may be the very last thing the system needs for perceptual stability. Similarly, Wall's (87) recent analysis of dorsal column function stresses the importance of afferent impulses transmitted over the lemniscal pathway during movement rather than the modulation of this activity by higher centers. Both of these positions appear in direct contradiction to the notion put forward here, namely, that there exists a central suppression of cutaneous input during voluntary movement. However, it must be emphasized that the inhibition of ascending afferent impulses during movements may not necessarily represent a loss of sensory information. On the contrary, the phenomenon of afferent or surround inhibition is a clear example of how inhibitory mechanisms enhance rather than diminish the ability to detect changes in peripheral stimulation. Likewise, the modulation of afferent activity in the lemniscal pathway may represent a mechanism which facilitates sensory discrimination during voluntary movements by suppressing certain patterns of afferent input.

There appear at least two essentially different processes by which the postulated internal inhibitory pattern may augment cutaneous sensibility during voluntary movement. One mechanism could involve the selective suppression of certain predictable patterns of afferent input which normally accompany movements. A second process may possibly allow for an enhancement of contrast in the cutaneous sensory inflow resulting from voluntary movements.

With regard to the first mechanism, the existence of a direct relation between patterns of motor activity and the resultant patterns

of sensory stimulation which accompany movements must be recognized. If the palm of the hand is in contact with a stable surface the actions of the arm and wrist muscles which move the hand from right to left always result in displacement of the sensory image in a direction opposite to the movement. Furthermore, the rate of displacement of the image is normally a function of the speed of movement. These relations are constant and thus serve to illustrate that at least part of the sensory input which results from movement can be directly predicted from the pattern of motor activity which gives rise to movement. According to the hypothesis stated earlier, only the sensory consequences resulting from movement which are directly predictable from the movement itself are canceled out by the internal inhibitory pattern. Therefore, if part of the sensory input accompanying movements can be known from the motor output, then given the motor output, inhibition of the predicted sensory input would not result in a loss of internal information. However, since all or part of the information contained in the motor discharge is assumed to be removed from the sensory input by the internal inhibitory pattern, the information ultimately transmitted to higher centers would be derived mainly or exclusively from external sources of stimulation.

Thus it can be seen that the inhibition of certain patterns of afferent impulses during movement may not necessarily imply a reduction of cutaneous sensitivity to external stimulation at these times. On the contrary, the modulation of sensory activity in the lemniscal pathway may represent a mechanism which, through an inhibitory interaction, allows for the sensory consequences resulting from voluntary

movement to be evaluated with respect to the information contained in the motor discharge originally responsible for the movement.

There may also be another function of the internal inhibitory pattern presumed to be exerted on the lemniscal system during movement. While more prosaic than the mechanism just described, it may make no less an important contribution to the discrimination of sensory changes occurring during voluntary movement. If the inhibition of afferent impulses which is assumed to occur at the dorsal column level were to be accompanied by a simultaneous facilitation at the thalamic level there could result a large enhancement of sensory contrast in the incoming afferent barrage. A central inhibitory influence operating at the first sensory relay would act in concert with the mechanisms of afferent inhibition to suppress low level signals contained in the afferent volleys generated by movements. Any overall loss in intensity of the resulting sensory patterns would be compensated by amplification at subsequent synaptic relays. Such a process might serve as an effective mechanism for eliminating "blur" in the sensory input caused by rapid movement of stimulus over the skin.

It is of interest that during the bursts of REM of desynchronized sleep there is reported to be a facilitation of somatic afferent transmission at the thalamic level which may be simultaneously accompanied by inhibition at the level of the dorsal column nuclei (27). There also appears at these times a phasic excitation of the motoneurons which leads to short lasting muscular twitches and movements (25, 61). It has therefore been postulated that part of the central motor discharge giving rise to the muscular contractions is fed into the

somatic sensory pathway at the thalamus, thus to interact with the afferent volleys which have been filtered at the level of the dorsal column nuclei. The result is that part of the external sensory feedback produced in conjunction with movements is substituted for internal stimulation which may become further elaborated at the cortical level (27, 70).

It has been emphasized here and previously by Pompeiano (see 70) that the neural events which take place during REM sleep may partially correspond with changes occurring in the sensory and motor pathways during voluntary movements in awake animals. Therefore, it would be expected that the facilitation of sensory transmission which occurs at the thalamic level during REM sleep would likewise be observed in waking animals during voluntary movements. Were such evidence available, it would support the suggestion made here that the suppression of afferent input at the level of the dorsal column nuclei could result, by way of subsequent amplification at the thalamic level, in an enhancement of sensory contrast in the incoming afferent barrage. This conclusion would not rule out the postulated partial substitution of external sensory feedback by an internal motor discharge into the somatic afferent pathway during movements. However, it must be emphasized that regardless of any modifications which may subsequently occur along the sensory pathway, the neural representation of any peripherally initiated stimulation at higher levels is crucially dependent upon the activity passing through the first synaptic relays of the dorsal column-medial lemniscal system.

CHAPTER VII

SUMMARY

The active control of sensory processes has been implicated as an important factor in certain perceptual constancies, selective attention, and the integration of sensory feedback during movements. In spite of the well documented existence of mechanisms for sensory control in the fast-conducting cutaneous pathways (lemniscal system), a review of the literature reveals that a systematic study of these processes during normal, waking behavior in intact animals is yet to be reported. Therefore, experiments were undertaken to study changes in sensory transmission through the lemniscal pathway during induced arousal and during voluntary movements in unrestrained, unanesthetized cats bearing chronically implanted electrodes for stimulation and recording.

The first set of experiments tested the effect of presenting a novel auditory stimulus on the size of the lemniscal potentials evoked in response to stimulation of the contralateral superficial radial nerve (a pure cutaneous nerve). In association with the novel stimulus (tone) the evoked lemniscal response was found to be reduced in amplitude, an effect which occurred in the apparent absence of overt motor activity. After repeated presentations of the novel stimulus,

the lemniscal responses were no longer modified. Since no movements were observed, a peripherally induced phenomenon, such as afferent inhibition, or occlusion, would not appear to have contributed to the changes in the lemniscal potentials. Therefore, the reduction of the evoked lemniscal response amplitude during the early tones may be attributable to a central mechanism which is subject to a process of fatigue or habituation. These findings are relevant to the postulated existence of mechanisms for modulating sensory input in conjunction with attentive arousal and selective perception. In particular, the reduced responsiveness of the lemniscal pathway during presentation of the tone is consistent with the hypothesis that irrelevant sensory information is inhibited during the orienting or arousal reaction induced by a novel stimulus.

In a second series of experiments, the amplitude of the lemniscal response evoked by stimulation of the superficial radial nerve was found to be reduced during active voluntary flexion movements of the forelimb. The effect appeared specific to the pathways originating from the actively moved limb as shown by the absence of any change in the evoked response when the contralateral forelimb was moved. This particular finding also indicated that movements <u>per se</u> are not associated with activation of a general arousal mechanism conceivably capable of modifying the lemniscal potentials. It was further shown that the amount of reduction in the evoked response is roughly proportional to the magnitude of the muscle activity recorded during the movement. While all these observations are consistent with the operation of a central influence on the lemniscal pathway during movements,

further experiments were done to rule out other possibilities.

In several animals the superficial radial nerve was crushed and tied-off distal to the stimulating electrode, thus removing an obvious potential source of peripheral afferent inhibition or occlusion. All these animals showed a reduction of the evoked response amplitude during active movements. On the other hand, passive movements of the forelimb in the anesthetized cat did not have any effect on the lemniscal response. Finally, it was observed that lemniscal responses evoked in the interval just prior to the onset of voluntary movements were reduced in amplitude by almost as much as the responses evoked during the movements. This finding is particularly significant in that the depression of the lemniscal potential in this instance cannot be accounted for by any peripheral mechanism because the movement itself had not yet even occurred. Taken together these results recommend the conclusion that there exists a partial blockade of sensory transmission through the lemniscal pathway which is attributable to a central influence operating in conjunction with the mechanisms responsible for the generation of voluntary movements.

Other studies have also suggested an interaction between the central mechanisms of movement and the mechanisms controlling sensory transmission in the lemniscal system. However, the nature of this interaction as well as its functional significance have remained unclear. It has been postulated here that the descending influences, exerted on the dorsal column-medial lemniscal system, represent a per-determined, internal pattern of nervous activity which anticipates and predicts the pattern of sensory stimulation produced by movement. The

incoming excitatory pattern is compared and evaluated against the internally generated pattern via an inhibitory interaction. Afferent impulses which correspond to the internal pattern are suppressed, while other sensory impulses, which do not match the internal pattern, remain unmodified. The organization and development of the internal pattern is determined primarily by the relations between the location and type of peripheral receptors and the actions of muscles which may cause these receptors to be stimulated. Information from muscular and cutaneous sources as well as from the other sensory modalities may also contribute to the organization of the internal pattern. The operation of this mechanism is proposed to be of importance for discriminating between changes in sensory stimulation arising from external sources and changes in sensory stimulation caused by voluntary movements.

While the results of the present study are consistent with this hypothesis, further investigations are required in order to more directly determine its validity. The suggestion that central motor influences contribute to the integration of sensory information is in agreement with the conceptions, expressed by others, that the active control of afferent input is an important factor in sensory discrimination and the maintenance of perceptual stability during voluntary movements.

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