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INHIBITION OF AFFERENT TRANSMISSION IN CUNEATE NUCLEUS DURING VOLUNTARY MOVEMENT IN THE CAT

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It is well established that transmission of afferent volleys through the dorsal column nuclei may be modified by peripheral and by central influences¹⁵. Nevertheless the physiological circumstances under which these mechanisms operate are only beginning to be investigated. Inhibitory changes have been seen during particular phases of sleep⁶, periods of motor activity^{1,16} and during attention to novel stimuli⁸.

Any change in the transmission properties of the dorsal column–lemniscal system in relation to voluntary movement might be of some consequence with respect to the possible role of somatosensory feedback in controlling the ongoing motor output. For these reasons we have undertaken a series of studies aimed at determining the changes in transmission of afferent volleys through the dorsal column nuclei during the course of a standard voluntary movement.

In an initial study^{10,11} we trained cats to respond to a tone by lifting their forepaw from the ground and depress a lever in order to obtain a food reward. The animals were to maintain the bar depressed for several seconds before replacing their paw on the ground. Circuits, shorted by contact with the animal's paw, provided signals indicating the different phases of movement. The response evoked in the contralateral medial lemniscus by an electrical stimulus applied to the superficial radial nerve was studied during the various phases of movement. In all animals the amplitude of the lemniscal response was reduced by an average of 20% (15–35%) throughout the course of both lifting and releasing phases of movement. This reduction started regularly in excess of 100 msec prior to displacement of the limb, as indicated by the opening of the circuit placed on the ground where the animal rested its paw. The changes in the lemniscal responses was not related to the tone nor to any change in effective stimulus due to electrode displacement. These observations have since been confirmed independently by Coulter and Thies⁹.

In the present study we have directed our attention to two main questions. First, to identify the parameters of movement to which the change in lemniscal transmission might be related, *i.e.*, the direction of movement, the force exerted and the velocity of movement. Secondly to determine if pre- and/or postsynaptic inhibitory influences within the cuneate nucleus might underlie the changes in lemniscal potentials.

Modulation of lemniscal responses in relation to force and velocity of movement. Three adult cats were trained in a similar paradigm as that described above. The main

difference was that a different bar operandum was used. In these cases downward motion of the lever was opposed by a torsion bar. This was arranged so the experimenter could vary the amount of torsion, so changing the force necessary to depress the lever. The animals were rewarded with food when they responded to the tone by lowering the bar and maintaining it at a given angle which was not to be exceeded.

Once the animals responded to the tone and their performance was reliable, stimulating and recording electrodes were implanted under barbiturate anesthesia. These included sleeve and cuff electrodes around the proximal portion of the superficial radial nerve which was divided, and pairs of stainless steel hook electrodes in the biceps and triceps muscles all in the limb performing the movement. A bipolar stainless steel (100 μ m diameter wire, 1 mm interelectrode distance) electrode was stereotaxically placed in the contralateral medial lemniscus.

During the recording sessions following recovery from anesthesia we monitored the electromyograms of biceps and triceps muscles, the angle of the bar and the signals of the circuits indicating contact with bar or ground where the animal rested its paw. Stimuli were delivered at set angles of the bar as well as once the animal assumed a stable posture either with its paw resting on the ground or following delivery of the food reward while maintaining the bar depressed. In order to sample the changes occurring immediately prior to movement, stimuli were triggered at intervals following the onset of the tone.

The findings reported previously^{10,11} were confirmed in the present experiments in which stimuli were triggered at set angles in the course of movement of the bar. Both flexor and extensor movements were associated with equal depression of the lemniscal volley, amounting on the average to 20%.

In all cases there was a statistically significant negative linear correlation between the amplitude of the lemniscal response and the logarithm of the velocity of the bar determined at the instant the stimulus was delivered (Fig. 1).

The effect of increasing loads was investigated by having the extensor movement oppose different forces from 75 to 300 g. No significant difference was observed

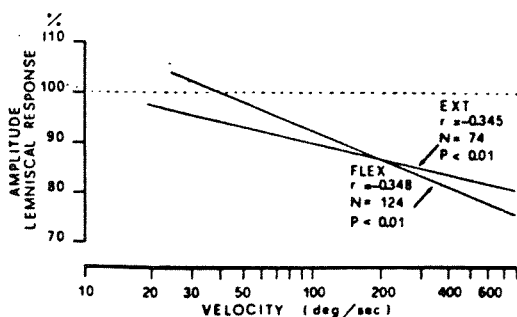


Fig. 1. Least square regression lines showing negative relation between the amplitude of the lemniscal response and velocity of movement. In the ordinate, lemniscal responses during flexor and extensor movements are expressed as percentages of control values obtained when the animal was still with both paws on the ground. The abscissa represents the velocity of the bar calculated at the instant the stimulus was delivered. Data from 4 recording sessions were grouped.

by analysis of variance between the responses obtained under different load conditions. Analysis of the regression lines of the various velocities of movement failed to reveal differences for lower and higher forces, either in terms of correlation coefficients (Fisher's Z transformation) or with respect to *t*-tests applied to either parameter of the regression line.

There was no consistent or significant difference between the regression lines corresponding to flexor as opposed to extensor movements. Since only extensor movements were opposed by the force of the torsion bar, this further indicates that the force exerted during the movement was not important in determining the degree of attenuation of the lemniscal response.

Mechanisms involved in the modulation of the lemniscal response during movement; pre- and postsynaptic inhibition in the cuneate nucleus. Excitability changes in the afferent terminals of the cuneate nucleus were studied using Wall's technique²¹ in 3 animals trained to accomplish the movement described above. In these animals, a tungsten microelectrode was implanted in the cuneate nucleus 1-2 mm below the obex on the side of the limb performing the movement. The antidromic volley evoked by microstimulation of the cuneate nucleus was recorded monophasically by a distal pair of electrodes around the superficial radial nerve. Peripherally evoked primary afferent depolarization (PAD) was obtained by means of conditioning stimuli delivered via a second electrode pair placed proximally around the superficial radial

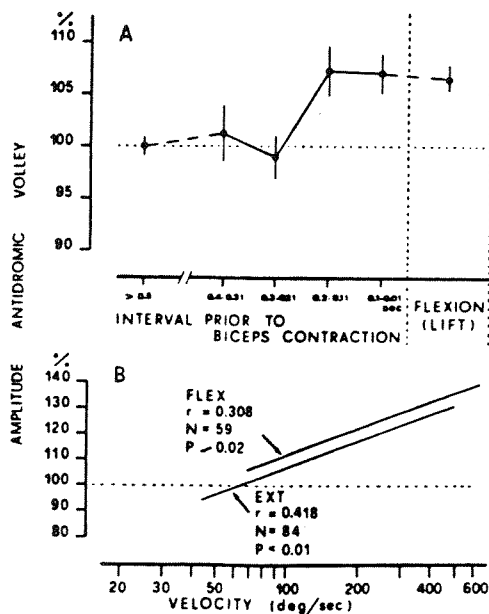


Fig. 2. A, Time course of primary afferent depolarization in relation to movement. The results obtained from 8 experimental sessions in one animal were grouped. Stimuli were triggered following the onset of the tone. Responses were expressed as percentages of control values obtained with the animal immobile, both paws on the ground and more than 0.5 sec prior to movement. B, Mean square regression lines showing direct relation between the amplitude of the antidromic volley and the velocity of movement of the bar. Data from 4 recording sessions were grouped.

nerve. The depth of the stimulating electrode in the cuneate nucleus, generally of the order of 1.5 mm, was determined on the basis of the optimal facilitation of the antidromic volley elicited by a conditioning stimulus.

During both flexor and extensor movements facilitation of the antidromic volley occurred. This facilitation preceded the onset of the biceps contraction associated with the 'lift' phase of movement (Fig. 2A) by over 100 msec (100–200 msec).

The degree of facilitation of the antidromic volley showed a statistically significant linear correlation with the logarithm of the velocity of movement (Fig. 2B). With the higher velocities of movement, the facilitation reached 140–150% of control values obtained when the animal was still. On occasion, the facilitation during the more rapid movements was more marked than that produced by a near maximal conditioning peripheral stimulus. Again, no significant difference was observed between flexor and extensor movements.

It must be noted that after 2–4 days, progressive deterioration of the preparation invariably occurred. In these instances, facilitation of the antidromic volley during movement and following conditioning stimuli diminished and eventually disappeared.

Unfortunately we were not able to adequately compare the velocity thresholds for the occurrence of depression in lemniscal response with those of facilitation of the antidromic volleys. Indeed only in a few instances were sufficient numbers of responses obtained in the lower velocity range (below 50°/sec) and extrapolation of regression lines to a hypothetical threshold is not a valid procedure. Nevertheless, in some cases it could be ascertained that the slower movements were not associated with changes in either lemniscal evoked potentials or with primary afferent depolarization.

In several experiments conducted on one animal we were able to satisfactorily record the orthodromic potential in medial lemniscus to stimulation of the cuneate nucleus. This potential conformed with the description given by Andersen *et al.*^{2,4}. An initial, or alpha wave with a latency of 0.6 msec followed by a later beta wave at 1.5–1.7 msec. The former is attributed to the direct excitation of the cuneothalamic cells and its modulation is a reflection of postsynaptic changes. The latter is due to transsynaptic excitation of these neurons and interpretation of any change in its amplitude is complex² and of limited value. Consequently we confined our analysis to the changes in the alpha wave. As noted by Andersen *et al.*² we also observed that only the alpha wave was depressed by the application of a peripheral conditioning stimulus to the superficial radial nerve.

During voluntary flexor and extensor movements the alpha wave was slightly (10%) though significantly ($P < 0.02$) depressed. Furthermore, the onset of this depression preceded the onset of the biceps contraction associated with movement ($P < 0.01$ for the responses occurring in the 200 msec interval prior to movement).

Stimulus current was monitored and the changes in the antidromic and orthodromic responses could not be ascribed to changes in effective stimulus resulting from electrode movement with consequent possible shifts in electrode impedance.

These observations show that transmission of cutaneous volleys to the medial lemniscus may be diminished both prior to and during voluntary movement in the cat. Our findings are in accord with those of O'Keefe and Gaffan^{1,16} who observed de-

creased unit responses of cuneate neurons to peripheral stimuli during periods of motor activity in the rat.

The finding of primary afferent depolarization (PAD) with a similar time course and relation to velocity of movement, as well as the decrease in alpha cuneothalamic response indicates that pre- and postsynaptic inhibition in the cuneate nucleus contribute to the attenuation of the lemniscal response. Indeed, only a minor part of the lemniscal potential derives from the spinocervico-thalamic projection to the medial lemniscus^{4,5}.

Both pre- and postsynaptic inhibition of cuneate neurons are known to result from both central and peripheral influences impinging upon the dorsal column nuclei³. With a sustained stimulus to the hairy skin of the dorsal surface of the forepaw, the PAD although conspicuous is of short duration⁴. On the other hand, while muscle afferents are recipients of PAD in the cuneate nucleus, they are poor donors of PAD to other terminals^{17,18}.

The attenuation of lemniscal potentials, the PAD and depression of alpha cuneo-thalamic responsiveness prior to the onset of movement is more readily attributable to central influences impinging upon the cuneate nucleus. On the other hand it is difficult to determine the relative contribution of central and peripheral factors to the changes observed during the course of the movement itself.

We also have observed brief decreases in lemniscal responses as well as PAD in cuneate nucleus when applying pressure to the forepaw especially with movement of the hair on its dorsal surface. This effect was less pronounced when stimulating the more proximal portions of the foreleg. Vigorous passive movement of the upper extremity did not produce noticeable changes in lemniscal responses, as noted also by Coulter and Thies⁸, nor PAD. Additional, albeit indirect evidence in favor of a central contribution during movement itself is that increases in the force and pressure applied did not *per se* influence lemniscal transmission.

The absence of apparent relation between these inhibitory events in the cuneate nucleus and the force exerted is interesting in view of the strong relation between pyramidal output and force of movement⁹. Velocity is however represented in the cortical output¹³ and several central structures other than the cerebral cortex are capable of influencing transmission through the cuneate nucleus^{12,19}.

There is ground to suppose that similar pre- and postsynaptic inhibitory effects might affect proprioceptive and muscle afferent transmission in the cuneate nucleus. Indeed, Carli *et al.*⁶ found that during the bursts of rapid eye movements of desynchronized sleep, PAD occurred in both muscle and cutaneous afferent terminals of the cuneate nucleus.

While a reduction of 20% in amplitude of the lemniscal response might seem modest, the underlying deterioration in signal to noise ratio could be more substantial¹⁴. This assumption fits well with the finding of Coquery⁷ that perception of an electrical stimulus to the fingers is decreased or abolished prior to and during voluntary finger flexion.

These observations lend support to the hypothesis that rapid or ballistic movements might to a large extent be centrally pre-programmed²⁰. The inhibitory processes

described undoubtedly alter the transmission of somatosensory volleys through the lemniscal system particularly during the execution of more rapid movements. Thus, information carried by this system would not represent a faithful indicator of peripheral events. Since our evidence does favor a central origin of the changes in transmission, it seems likely that they represent an expression of a central program in some way related to velocity. It cannot be excluded however that the need for a central program is rather a consequence of the alterations in transmission.

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