JOURNAL OF NEUROPHYSIOLOGY
Vol. 40. No. 5. September 1977. *Printed in U.S.A.*

Effects of Changes in Mechanical State of Limb on Cerebellar Intention Tremor

T. VILIS AND J. HORE

Department of Physiology, University of Western Ontario, London, Ontario, Canada N6A 5C1

SUMMARY AND CONCLUSIONS

1. An animal model for the study of cerebellar intention tremor was produced by implanting cryoprobe sheaths alongside the dentate and interpositus nuclei of the cerebellum in three *Cebus* monkeys. These monkeys were trained to make fast flexion and extension elbow movements by moving a handle in a horizontal arc and to resist perturbations applied to the handle as it was held within target regions.

2. Cooling through both sheaths simultaneously (to 10°C sheath reference temperature) resulted in a 3- to 5-Hz tremor in the ipsilateral forelimb, which was especially evident during rapid movements and following perturbations applied to the handle.

3. The character of the tremor was altered by mechanical loads applied to the limb: the frequency was increased by addition of spring stiffness and by an increase in constant torque and decreased by addition of mass. The amplitude of the tremor was decreased by an increase in viscous resistance. In addition, randomly timed perturbations applied to the forearm resynchronized the phase of the tremor.

4. The frequency of the tremor was also dependent on the position of the forelimb, being higher in flexion than in extension.

5. During cerebellar nuclear cooling the EMG responses to limb perturbations sometimes showed an increase in the segmental response (20 ms), while later responses (35–100 ms), which may reflect activity in suprasegmental pathways, exhibited little change. There was no apparent relationship between changes in these early EMG responses and the tendency toward oscillation.

6. The fact that changes in the mechanical state of the limb can affect the character of cerebellar intention tremor supports the view that this tremor originates from instability in one or more reflex pathways. However, the lack of increase of the late EMG responses during cerebellar cooling suggests that the tremor is not due simply to an increase in gain in these reflex pathways, as tested by sudden limb perturbations. An alternative possibility, whereby changes in the characteristics of reflex pathways could produce cerebellar intention tremor, is discussed.

Received for publication December 28, 1976.

INTRODUCTION

The function of reflex loops in motor control has frequently been compared to the operation of a servomechanism. In this mechanism, commands are generated on the basis of a comparison of actual performance as determined by feedback from the periphery, with some internally generated measure of desired performance. The advantage of a servomechanism is a rapid and automatic response to errors in performance. The disadvantage of a servo is that once the commands are locked into this system a malfunction in the feedback signal will automatically generate incorrect commands, which in some cases will result in uncontrollable oscillations. One of the first reflex loops to be considered as a servomechanism was the spinal stretch reflex. This loop provides a rapid response to muscle stretch; however, inappropriate feedback in the loop has been suggested to cause physiological tremor (16, 19).

Recently, evidence has been found for the participation of longer suprasegmental loops in motor responses to sudden limb perturbations (8, 11, 27, 29), and it has been suggested that excessive gain in these loops may be the cause of pathological tremors such as cerebellar intention tremor (28). The possibility to test this suggestion in an animal model arose from the finding that cerebellar tremor of humans could be produced in the monkey by lesions of (7, 12) or by cooling (9, 22) cerebellar nuclei. If tremor is due to instability in reflex loops, then changes at the periphery will, by means of feedback, affect the character of the tremor. This has been investigated in the present experiments by studying the effects of changes in the mechanical state of the forelimb on cerebellar tremor produced by cooling the cerebellar nuclei in monkeys. Such experiments have revealed that changes in the mechanical load affect the frequency and amplitude

of the oscillations and that perturbations applied to the limb resynchronize the phase of the tremor. However, analysis of EMG responses following sudden limb perturbations suggests that cerebellar intention tremor cannot be explained by excessive gain in long-loop reflexes.

METHODS

Three *Cebus* monkeys (*M28L, M26L, M24L*) were trained to rotate a freely moving handle, pivoted at the elbow, in a horizontal arc. The instructions to the monkeys were first, to move the handle on a visual command from one target position to another and, second, to resist a torque perturbation applied at random times to the handle while the handle was held stationary within a target region. Unless otherwise specified, perturbations consisted of a torque pulse, 10 ms duration and 300-g magnitude, as measured at the end of the 10.5-cm handle. The position of the handle was indicated to the monkey as either being in or out of target by sound and light cues. The width of the target region was adjusted between 10 and 30° to accommodate the extent of tremor oscillations.

The handle, which the animals were trained to rotate, constituted primarily an inertial load. This was altered in the experiments by adding *1*) constant torque through the torque motor, *2*) viscosity by means of velocity feedback through the torque motor, *3*) spring stiffness by feedback of position, and *4*) greater inertia by the addition of mass to the handle. Details of the torque motor through which these loads were applied have been described previously (4).

Reversible lesions

Two cryoprobe sheaths (1.3 mm in diameter) were implanted stereotaxically under pentobarbital anesthesia (35 mg/kg ip), one lateral to the dentate nucleus and the other through the region of the interpositus nucleus ipsilateral to the forearm tested. These will be referred to as the lateral and medial probe sheath, respectively. Temperatures referred to in this paper are those of the outside of the probe sheath, measured by a thermocouple, 4 mm from the sheath tip.

Histological confirmation of sheath positions was obtained after sacrificing the animal by intraperitoneal injection of Nembutal and perfusing with 10% formalin. Figure 1 shows the location of the sheaths and the extent of the estimated 20°C isotherms (6), the temperature at which synaptic transmission is first impaired (2, 5). The isotherms indicate that when the lateral sheath was cooled to 10°C the lateral portion of the dentate nucleus was affected in all three monkeys. Cooling the medial sheath to 10°C affected the medial portion of the dentate and a major part of the interpositus. In addition, in *M26L* and *M24L*, cooling the medial probe may have affected transmission in the fastigial and lateral vestibular nuclei.

To confirm that the effects of cooling described in RESULTS were due to a reversible lesion of the nuclei and not of the overlying cerebellar tissue, tests were performed in which the cooling probe was withdrawn approximately 5 mm within the implanted sheath while a constant cooling rate was maintained. During this procedure the temperature of the probe sheath at the approximate location of the nuclei returned to 33°C, and the EMG responses and the movement parameters were equivalent to those obtained under control conditions.

As part of other experiments (23) a metal chamber was implanted over the forearm area of the precentral gyrus for single-unit recording of extracellular activity, and concentric stimulating electrodes for antidromic identification of corticofugal neurons were implanted in the right cerebral peduncles.

Data acquisition and analysis

Three parameters were monitored: *1*) handle position by means of a thin-film potentiometer, *2*) handle velocity by means of electronic differentiation of position, and *3*) EMG activity by means of a pair of Teflon-coated wires inserted into the muscle during each experiment. The EMG data was amplified, filtered (bandwidth, 30–300 Hz), and full-wave rectified. The three parameters were then digitized on-line (sampling rate, 1,000 Hz) by a PDP-12 digital computer. Block averaging the data in 5-ms bins resulted in digital integration of the EMG. The velocity data was subsequently digitally differentiated to provide acceleration. The data were stored in digital form on magnetic tape for later off-line analysis.

Fourier analysis was performed, off-line, on selected segments of data by means of an IBM subroutine. The real and imaginary values of each frequency component were obtained. Subsequently, an average of each component was calculated for repetitive trials. From this averaged transform, the averaged magnitude and phase were calculated (18).

RESULTS

General effects of cooling cerebellar nuclei

After implantation of the cryoprobe sheaths, one lateral and one medial to the dentate nucleus (Fig. 1), no deficit was observed in any of the three monkeys during such tasks as moving about the cage or feeding. Limbs on both sides appeared to be used with equal dexterity and without signs of tremor. The general effects of cooling the medial and lateral probes to 10°C

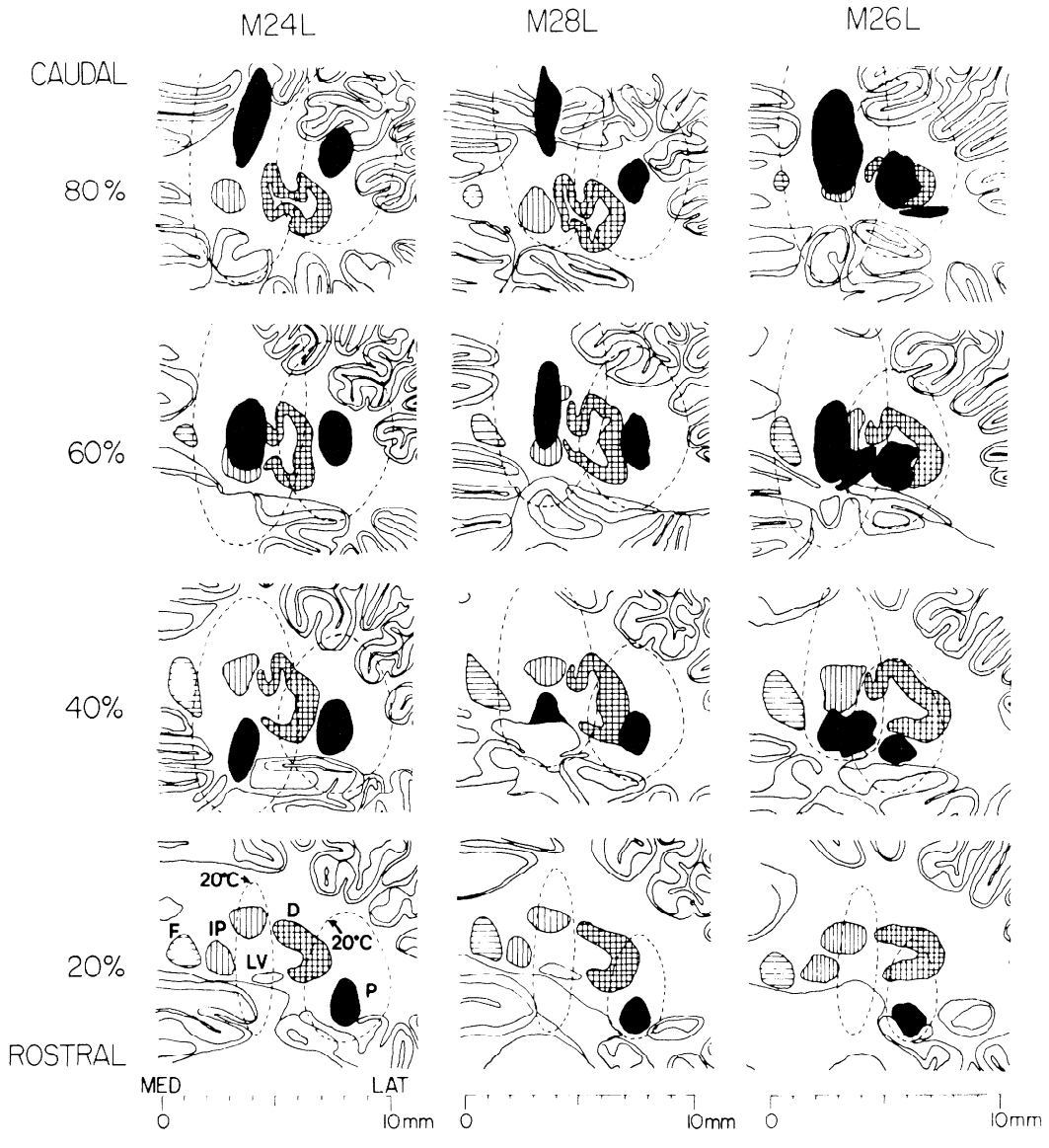

FIG. 1. Positions of medial and lateral cooling probe sheaths in *M24L*, *M28L*, and *M26L*. Frontal sections are shown for each monkey at 20, 40, 60, and 80% of the rostral-caudal extent of the dentate nucleus. Dotted lines are estimated isotherms for tissue temperature of 20°C when sheath reference temperature was 10°C. Midline is at the left border of each section. D, dentate nucleus (cross hatched); IP, interpositus nucleus (vertical hatching); F, fastigial nucleus (horizontal hatching); LV, lateral vestibular nucleus (unshaded); P, sheath probe position (black).

were examined while the animal attempted to reach for a piece of apple and while the animal executed the paradigm. In the former case a normal animal would grab the apple promptly, even when it was moved about, and place it in his mouth with no apparent difficulty. During cooling, the animal frequently missed the apple, especially if it was moved about, and the forearm exhibited an irregular oscillation (ataxia) when the animal attempted to place the apple in his mouth. No oscillations were observed when the arm was at rest at his side.

When executing the paradigm under control conditions, the animal responded quickly to the move instruction and performed a rapid movement with little or no overshoot (Fig. 2). Similarly, the response to an unexpected perturbation exhibited little or no oscillations. In the few trials where oscillations occurred, these were of a small amplitude, quickly damped out, and at 5–7 Hz. On combined cooling of the medial and lateral probes, prominent oscillations at 3–5 Hz appeared both after the initiation of a rapid movement and after a perturbation (Fig. 2).

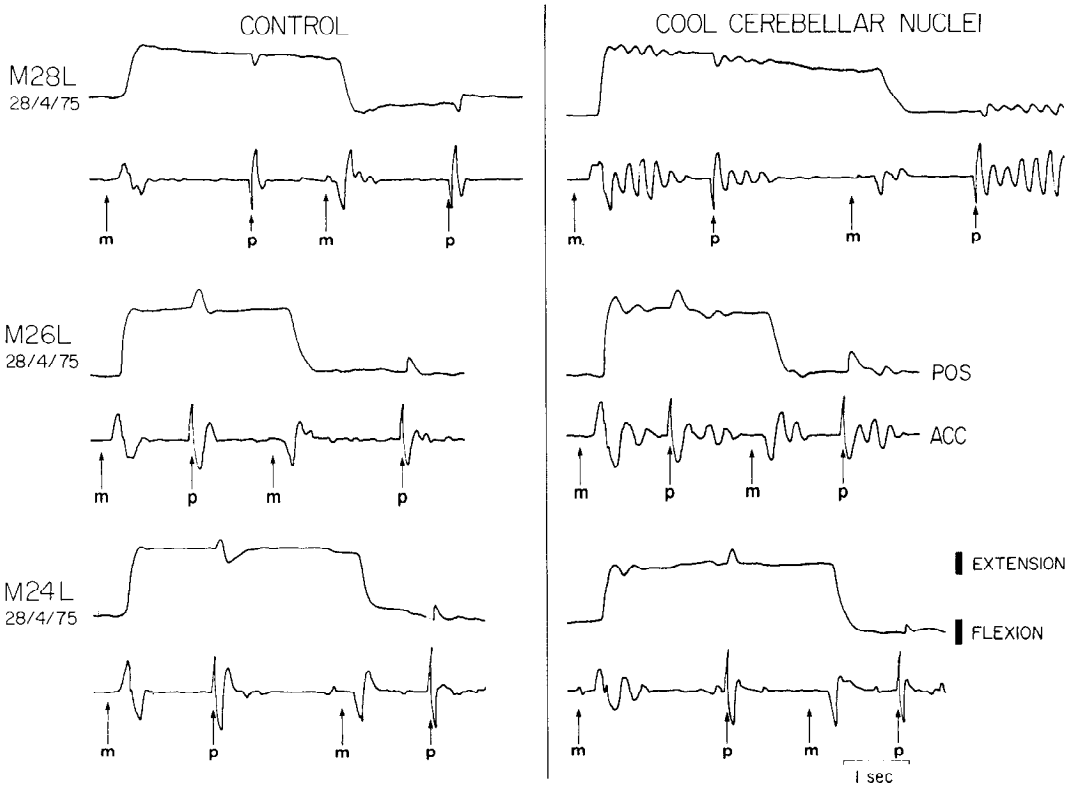

FIG. 2. Effect of cooling cerebellar nuclei on oscillations that occur following arm movements and following perturbations applied to the arm. Left column: position (upper of each pair) and acceleration (lower) traces of individual trials in monkeys *M28L*, *M26L*, and *M24L* under control conditions (normal brain temperature). Right column: position and acceleration records during cerebellar nuclei cooling produced by combined cooling through medial and lateral cryoprobes (sheath reference temperatures, 10°C). Extension and flexion target position (20° width) are shown at the bottom right. *M28L*: extension load pulse; *M26L*, *M24L*: flexion load pulse; m: move command; p: perturbation.

These oscillations were more regular in appearance than during apple reaching when the forearm was unsupported. The magnitude of the oscillations and the number of cycles varied between the three monkeys: *M28L* showed large oscillations which often continued as a tremor for many seconds, *M26L* had moderate oscillations, and *M24L* had little or no oscillations. Only *M28L* and *M26L*, the animals which exhibited consistent oscillations, were studied in detail.

Synchronizing effect of a torque perturbation on tremor

Perturbations applied to the limb during cerebellar nuclear cooling initiated oscillations of the limb. These triggered oscillations always had the same starting phase for perturbations in the same direction. Randomly timed torque pulses were also applied during ongoing oscillations, such as those that occurred following a movement (Fig. 3). For reasons which will be dealt with in the next section, only oscillations which occurred at approximately the same elbow angle were included. On averaging the movements with respect to the torque pulse (Fig. 3, bottom trace), the averaged response showed well-defined oscillations after the perturbation of the same frequency as the ongoing oscillations seen in individual trials both prior to and after the perturbation. No oscillations were apparent in the averaged response prior to the torque pulse, confirming the fact that the perturbations were randomly timed. Thus, the perturbation not only triggered oscillations but also resynchronized the phase of ongoing oscillations. However, from the individual trials it can be seen that, because of the small size of the torque pulse, resynchronization was not always complete. In trace 3, the change in phase produced by the perturbation resulted in an oscillation which was approximately 180° out of phase with respect to the average. In addition, perturbations timed so that they opposed the direction of a particular movement cycle reduced the tremor amplitude

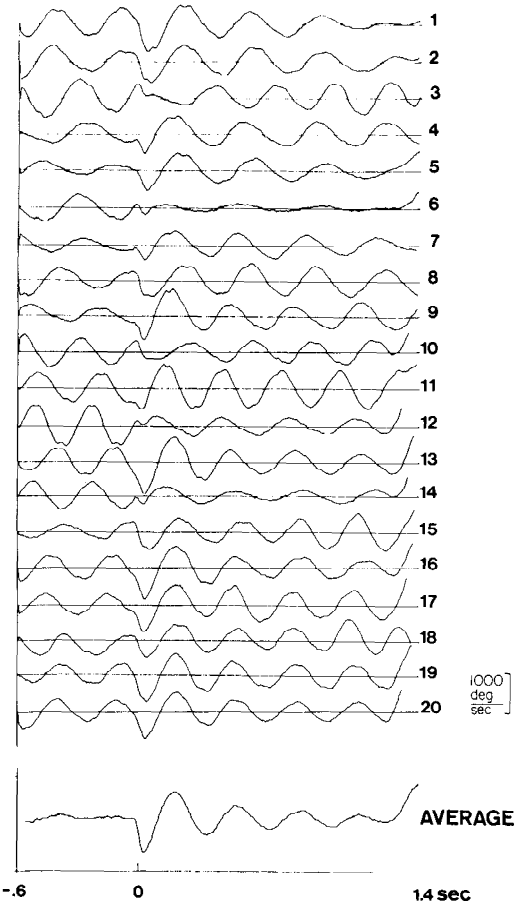

FIG. 3. Resynchronizing effect of a randomly timed flexion-load torque pulse on forearm oscillations occurring during combined cooling of the medial and lateral cryoprobes (10°C) (*M28L*, 5/3/75). Upper 20 traces: individual velocity records. Lower trace: average of the same 20 velocity records.

(traces 6 and 14). This indicates that the force present in the oscillating limb and that of the perturbation summate to produce subsequent oscillations.

Effect of forearm angle on tremor characteristics

The averaged response in Fig. 3 shows a progressive decline in the magnitude of the oscillations which is not obvious in the individual trials. This results from slight variations in the frequency of the individual trials. One factor responsible for this variation is forearm angle. When oscillations, which occurred when the mean forearm position was in flexion, were compared to those in extension (Fig. 4), the former were found to be higher in frequency, smaller in amplitude (in degrees of arc), and stabilized in a shorter time.

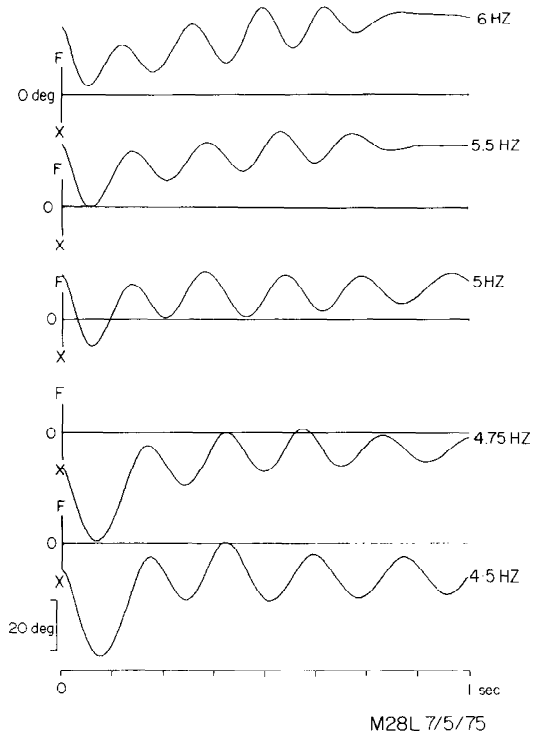

FIG. 4. Effect of arm position on the frequency of cerebellar tremor. Oscillations of the arm were produced by applying flexion-load torque pulses at time zero to the stationary limb during combined cooling of both cryoprobes (sheath reference temperatures, 10°C). Single traces of handle position are shown in five different positions, three in flexion (upper records) and two in extensions (lower records). Moving from flexion to extension produces a progressive decrease in the frequency of tremor (the frequency of the individual traces are shown on the right). Zero-degrees handle position (horizontal straight line) occurred when the elbow was approximately at right angles. F: toward flexion; X: toward extension.

To quantify the change in frequency, Fourier analysis was performed on individual segments of data that followed a perturbation (Fig. 5). The position of the largest amplitude component on the frequency axis corresponds to the dominant frequency in the tremor record.

Effect of changes in mechanical load on tremor characteristics

If the oscillations that occur during cerebellar cooling are the result of an unstable reflex loop, then changes in the dynamics of any portion of the loop should alter the character of the tremor. To test this hypothesis, the mechanical characteristics of the handle which the animal rotated were varied (Fig. 6). When additional mass was attached to the handle to increase its inertia, the frequency of oscillations following a torque

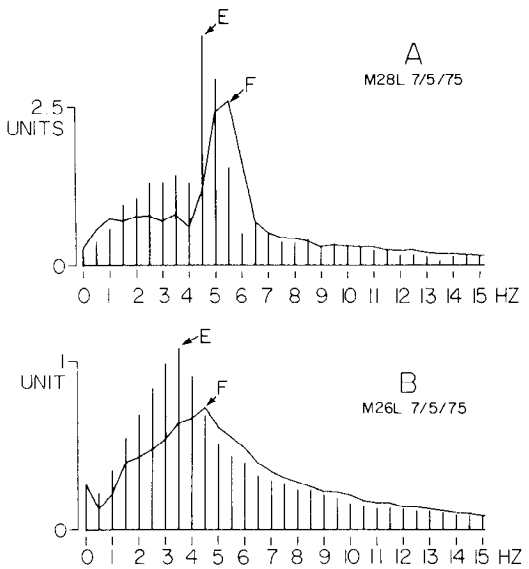

FIG. 5. Magnitude of the frequency components of handle velocity obtained during combined cooling of the medial and lateral cryoprobes (10°C). *A*: average of the Fourier transforms of 10 velocity records (2 s duration) following a torque-pulse perturbation in monkey *M28L*. Vertical bars represent the averaged transform when the mean forearm position was in extension (E). The solid line envelope is for a mean flexion position (F). *B*: the same for monkey *M26L*.

pulse decreased. When the load of the handle behaved as a linear spring the frequency of oscillation increased. Little change in the frequency was noted with the addition of viscous resistance (friction). However, in this case, the amplitude of the oscillation was reduced. The amplitude of the oscillations was also reduced with the addition of inertia and generally increased with a spring load. Similar changes in the frequency and amplitude were observed in the oscillations which were initiated during a rapid voluntary movement and in the continuous tremor seen in *M28L*.

Both Marsden et al. (21) and Newsom Davis and Sears (25) have shown that the gain of reflex loops is roughly proportional to the initial or mean force exerted by a muscle. To study the effect of gain on cerebellar intention tremor, the degree of tonic muscular activity was varied by the addition of constant loads opposing flexion. Increased constant loads increased the frequency of oscillation (Fig. 7). This increase in frequency was usually accompanied by a small decrease in the amplitude of the oscillations.

Effect of cerebellar cooling on muscle activity

When tremor in the monkey's forearm was elicited by cerebellar cooling, rhythmic bursts of activity were observed in all the muscles involved in the movement, i.e., those acting at shoulder, elbow, and wrist, and were of the same frequency as oscillations in the movement. This rhythmic activity was most distinct in muscles that acted about the elbow joint. The phase, or timing, of the burst in the movement cycle depended on muscle function. For example, the peak of biceps activity preceded the peak of acceleration by 50–60 ms. This was the same latency as in the control situation, indicating that muscle activity is the driving force behind each oscillation. The activity of other synergists such as brachioradialis and pectoralis major were approximately in phase with biceps activity, while the activity of antagonist (e.g., triceps) was 180° out of phase.

The fact that changes in the mechanical state of the limb can affect the characteristics of tremor (shown in previous sections) suggests that afferent feedback as part of reflex loops may be the driving force for cerebellar tremor. If this is the case, the next question to consider is: what changes in these loops could cause oscillatory behavior? One possibility is that cerebellar cooling produces changes in the gain of reflex loops. Some measure of the efficacy or gain of reflex loops can be obtained from the magnitude of the reflex EMG responses, which are elicited by a torque pulse perturbation.

Three peaks were observed in the EMG response of the stretched muscle in the first 100 ms following the perturbation. The latency of these peaks, designated as M1, M2, and M3 (29), was 20, 40, and 75 ms, respectively, in the present experiments. The magnitude of M3 was consistently smaller than that of either M1 or M2. In *M28L*, the monkey with the greatest tendency for oscillations, cerebellar cooling produced little effect on these early EMG responses (Fig. 8). In over a dozen experiments, the averaged M1 response was either unaffected or slightly increased, while the M2 and M3 responses were either unaffected or slightly decreased. The effect of cooling on *M26L*, the monkey with moderate oscillations, was a marked increase in M1. The EMG activity at 40 ms was often reduced and a larger response was sometimes observed starting at 60 ms. It is not possible to say whether these later changes were the direct effect of cerebellar dysfunction or a result of the increased M1 response. The only change observed in *M24L*, the monkey with the least tendency for oscillation, was a slight increase in the size of the M1 response. Thus, there appears to be no apparent correlation between the magnitude of tremor and changes in the early EMG responses (0–100 ms).

Changes, or lack of changes, observed in the EMG responses with cerebellar cooling should also be reflected in the position and acceleration trajectories. Since the muscles are acting mainly

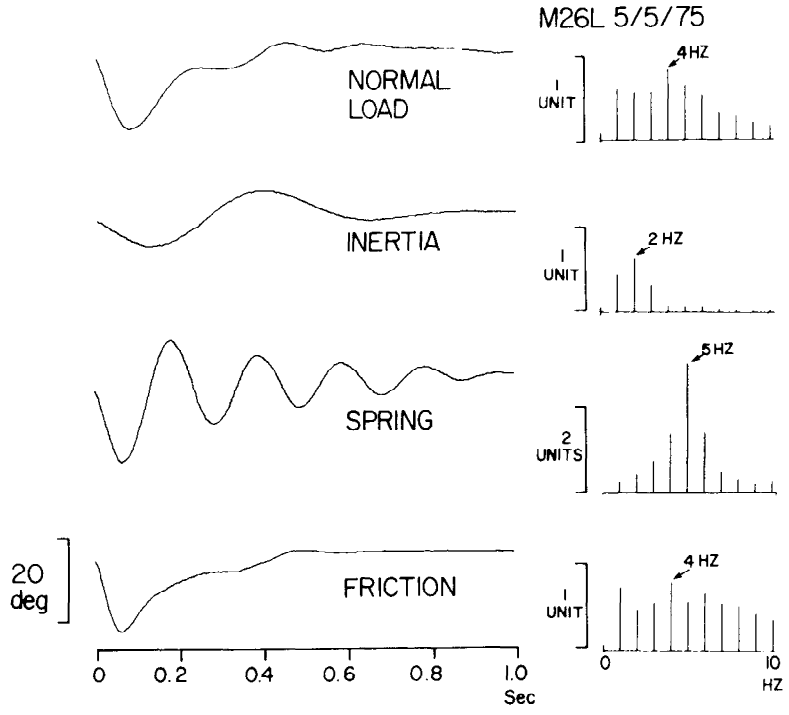

FIG. 6. Effect of inertial, elastic (spring), and viscous (friction) loads on the frequency and amplitude of the forearm oscillations during cerebellar nuclear cooling (lateral and medial probes 10°C). Left side: individual traces of position following a torque-pulse perturbation at time zero. From top to bottom; normal load, added inertia, added spring, and added friction. Right side: averaged magnitude of the frequency components obtained by Fourier analysis from 10 corresponding velocity records synchronized to a torque pulse.

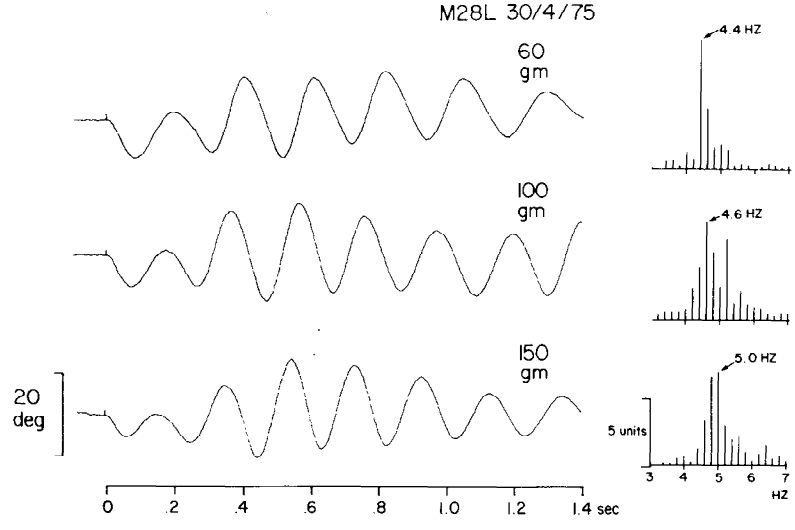

FIG. 7. Effect of the magnitude of a constant external load on the frequency and amplitude of forearm oscillations during cerebellar cooling (lateral and medial probes, 10°C). Left side: individual traces of position for constant torque loads of 60, 100, and 150 g following a torque-pulse perturbation at time zero. Vertical calibration: 20° of arc. Right side: averaged magnitude of the frequency components obtained by Fourier analysis from 10 corresponding velocity records synchronized to the torque pulse.

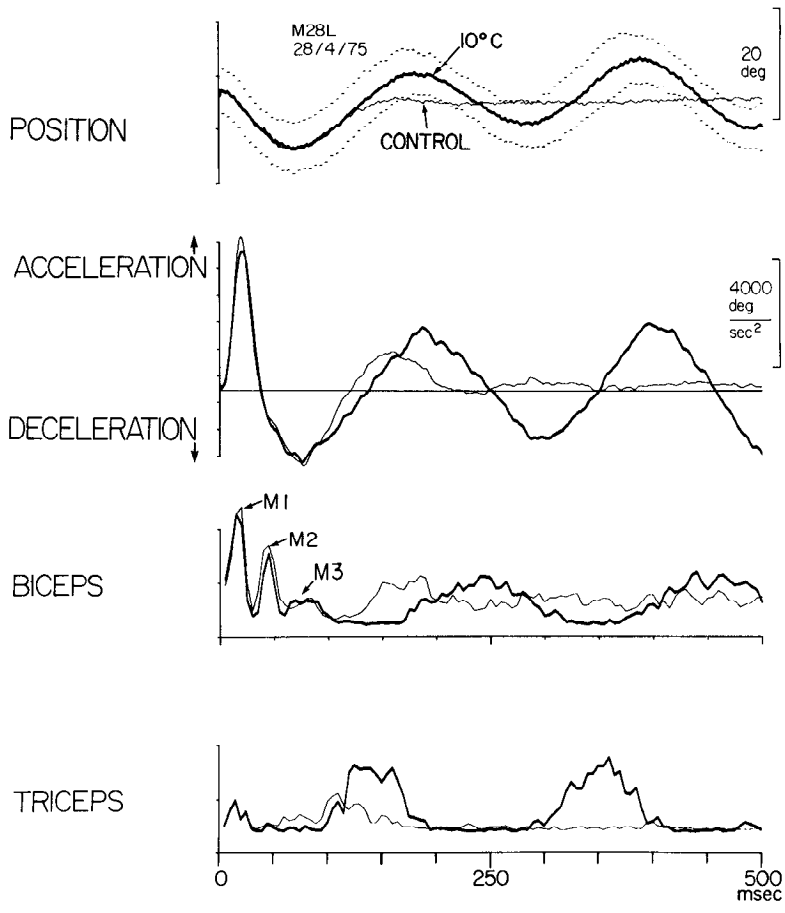

FIG. 8. Effect of cerebellar nuclear cooling on the position, acceleration, and EMG responses in biceps and triceps following a torque-pulse perturbation applied to the stationary limb. Each trace represents the averaged response of 20 trials. Thin line: control; thick line: cerebellar nuclear cooling (medial and lateral sheaths, 10°C). Dotted lines on position trace during cooling represent 1 SD. Initial peak on triceps traces is a movement artifact.

against the inertial load of the forearm and handle, the force generated by these muscles is primarily related to handle acceleration. The first peak in the acceleration trace corresponds to the external torque pulse applied to the handle. The subsequent deceleration in part reflects the M1, M2, and M3 responses of the biceps and its synergists. During cerebellar cooling little change was observed in the shape of this deceleration except for a slightly larger initial decline in *M26L*, which reflected the increased M1 response. In *M28L*, the acceleration trace during cerebellar cooling began to differ from the normal response only at the second acceleration peak (Fig. 8). The larger acceleration peak observed during cerebellar cooling was reflected in an increased and prolonged triceps activity (100–200 ms). In this case, instead of terminating the return trajectory in the target region, excess acceleration initiated another cycle of oscillation. In *M26L*, in which the second cycle of oscillation was greatly attenuated, only a smaller increase in triceps activity (150–250 ms) was observed with cerebellar cooling.

DISCUSSION

The 3- to 6-Hz forelimb tremor observed during simultaneous cooling through sheaths located medial and lateral to the dentate nucleus appears to be an exaggerated form of the oscillations previously observed in movements (6, 9, 22) and following torque pulses (22) during cooling of the lateral part of dentate nucleus. This tremor is apparently the same as cerebellar intention tremor which occurs following lesions of the cerebellar nuclei in humans (13, 14) and in monkeys (7, 12). One of the characteristics of this cerebellar intention tremor is that the affected limb has to be involved in goal-directed behavior: for example, rapid repetition of the finger-to-nose test in patients and reaching for food in monkeys. Similarly, the tremor was evi-

dent as monkeys made goal-directed movements such as moving a handle from target to target or returning the handle to a target following a limb perturbation. In these handle movements in which arm displacement was largely restricted to the elbow joint, the ataxia seen in reaching movements was evident as rhythmic oscillations of the limb. No tremor was seen when the monkey's limb was at rest by his side.

What is the physiological basis of tremors resulting from lesions in the central nervous sytem? One view is that they arise from central neural networks, which because of pathological damage, behave as oscillators (17). Evidence in support of this view is that a Parkinson-like tremor produced by lesions of the ventromedial tegmentum of the brain stem and the lateral cerebellar system is not abolished by extensive dorsal rhizotomy (15). However, in the case of cerebellar intention tremor, the situation is not clear. On the one hand, Denny-Brown (10) reported that peripheral deafferentation abolished cerebellar intention tremor. On the other hand, Liu and Chambers (20) concluded that if a cerebellar-lesioned, deafferented monkey was forced to make goal-directed movements, then a tremor could be seen. However, inspection of their figures leaves some doubt as to whether the tremor of these monkeys had the same characteristics as cerebellar intention tremor seen in monkeys with only cerebellar lesions.

An alternative view, though not mutually exclusive, is that cerebellar intention tremor results from an inability to make appropriate correctional movements following a movement error. These inappropriate corrections lead, in turn, to further errors and thus, to a series of oscillations. This view implies: first, that there is a central structure which provides a goal for the movement and, second, that some feedback of peripheral information occurs on which to base corrections. Although some authors (e.g., ref 12) have argued that recognition and correction of the error is voluntary in nature, an alternative explanation is that corrections normally occur in reflex fashion via a servo loop through motor cortex or brain stem. Tremor may then result when improper corrections in this servo loop occur as a result of cerebellar lesions.

The dynamics of a feedback loop are determined by the dynamic nature of each component in the loop (26). Thus, strong evidence in favor of a servomechanism for cerebellar tremor is that changes in the tremor were observed with the addition of external loads to the limb; for example, the addition of mass decreased the frequency, while the addition of spring stiffness increased frequency.[1] These effects were observed in oscillations that were damped and in those that continued undamped for many seconds. These latter oscillations, in particular, could not have been maintained by the mechanical characteristics of muscle and its load (28). Thus, cerebellar tremor shows many similarities to physiological tremor (cf. Figs. 3 and 4, ref 16). This similarity is not surprising if it is assumed that both are reflex driven.

What is the reflex loop that is involved in cerebellar tremor? Joyce and Rack (16) have demonstrated that instability in the segmental stretch reflex results in oscillations of 8–12 Hz in the forearm of man. Stein and Oğuztöreli (28), by modeling this system, have found that when the latency of the feedback pathway is increased to one which allows feedback through the motor cortex, the frequency of oscillations shifts from 8–12 Hz to 4–6 Hz. Since the delay of the suprasegmental pathway, as measured by the latency of M2 and M3 transients, appears to be shorter in monkeys than in man (29), and since central delay appears to be the most significant factor in determining tremor frequency (28), the rapidly damped oscillations at 5–7 Hz observed in the present control situation could correspond to oscillations arising from suprasegmental pathways such as one that projects through the motor cortex (1, 3, 8, 11, 22, 24, 29, 30). This is supported by the observation that, in the control situation, neurons of the motor cortex have cyclic activity at this same frequency and have a phase appropriate to produce oscillations in the limb (8). It was subsequently proposed (22) that the larger and slower oscillations observed during cerebellar dysfunction resulted from inappropriate feedback of corrections to the motor cortex.

How could cerebellar dysfunction render this suprasegmental loop unstable? One possibility is excess loop gain. Joyce and Rack (16) have demonstrated that when the gain of the segmental loop is increased by increasing the tonic background activity in the muscle, the amplitude of physiological tremor also increases. By modeling, Stein and Oğuztöreli (28) have suggested that the stability of suprasegmental loops can, likewise, be degraded by an excess in loop gain.

Could cerebellar intention tremor be caused by excess gain? This is unlikely for two reasons. First, if one assumes that stable oscillations at 5–7 Hz are suprasegmental in origin, it is difficult to postulate a mechanism whereby an increase in

It should be noted, however, that an absence of change in tremor frequency with the addition of peripheral loads does not necessarily imply that the oscillations are not reflex mediated. In fact, Joyce and Rack (16), in their study of physiological tremor, demonstrated that with very stiff springs, oscillations in the arm of some subjects contained two frequencies; one frequency was largely determined by the mechanical properties of the arm and its imposed load, and the other was more dependent on the latency of the stretch reflex.

gain in this path would reduce the frequency of oscillations. As noted in RESULTS, increase in gain by increasing tonic activity increases the frequency of cerebellar intention tremor (Fig. 7) as it does for physiological tremor (16). Second, if the gain of suprasegmental loops has increased, one might expect to observe an increase in the size of the M2 and M3 EMG transients, because it has been suggested that responses at these latencies correspond to activity over suprasegmental pathways (1, 3, 8, 11, 29). In fact, our experiments demonstrate no correlation between changes in these responses and the amplitude of tremor.

One further way in which instability in a reflex loop can occur is if the reflex response is delayed by an increase in phase lag (cf. ref 24). Such an increase in phase lag could account for the decrease in frequency of oscillations from 5 to 7 Hz in the normal monkey to 3–5 Hz with cerebellar dysfunction. An increase in phase lag would result if transmission through the shortest suprasegmental pathway was blocked by cerebellar nuclear cooling and corrections during cerebellar dysfunction were forced through a pathway with a longer latency. However, if as suggested above, the M2 and M3 EMG components do represent reflex activity over suprasegmental pathways, then the failure to block these responses by cerebellar nuclear cooling would apparently rule out this hypothesis. Alternatively, phase lag could arise if the phasic nature of the feedback response over some range of frequencies was reduced by cerebellar cooling. This second suggestion can be tested by examining quantitatively the changes in the frequency content of the reflex responses with cerebellar cooling. It remains for further experiments and analyses to test this possibility.

ACKNOWLEDGMENTS

This research was supported in part by the Medical Research Council of Canada (MT-4465) and the Public Health Service (NS-10311).

REFERENCES

1. ADAM, J., MARSDEN, C. D., MERTON, P. A., AND MORTON, H. B. The effect of lesions in the internal capsule and the sensorimotor cortex on servo action in the human thumb. *J. Physiol., London* 254: 27–28P, 1975.
2. ANDERSEN, P., GJERSTAD, L., AND PASZTOR, E. Effect of cooling on synaptic transmission through the cuneate nucleus. *Acta Physiol., Scand.* 84: 433–447, 1972.
3. ANGEL, A. AND LEMON, R. N. Sensorimotor cortical representation in the rat and the role of the cortex in the production of sensory myoclonic jerks. *J. Physiol., London* 248: 465–488, 1975.
4. ATKIN, A., BROOKS, V. B., AND PISCHINGER, S. A torque device for studies of primate limb movements. *Physiol. Behav.* 12: 127–129, 1974.
5. BÉNITA, M. AND CONDÉ, H. Effects of local cooling upon conduction and synaptic transmission. *Brain Res.* 36: 133–151, 1972.
6. BROOKS, V. B., KOZLOVSKAYA, I. B., ATKIN, A., HORVATH, F. E., AND UNO, M. Effects of cooling dentate nucleus on tracking-task performance in monkeys. *J. Neurophysiol.* 36: 974–995, 1973.
7. CARPENTER, M. B. AND STEVENS, G. H. Structural and functional relationships between the deep cerebellar nuclei and the brachium conjunctivum in the rhesus monkey. *J. Comp. Neurol.* 107: 109–163, 1957.
8. CONRAD, B., MEYER-LOHMANN, J., MATSUNAMI, K., AND BROOKS, V. B. Precentral unit activity following torque pulse injections into elbow movements. *Brain Res.* 94: 219–236, 1975.
9. COOKE, J. D. AND THOMAS, J. S. Forearm oscillation during cooling of the dentate nucleus in the monkey. *Can. J. Physiol. Pharmacol.* 54: 430–436, 1976.
10. DENNY-BROWN, D. *The Cerebral Control of Movement.* Springfield: Thomas, 1966.
11. EVARTS, E. V. Motor cortex reflexes associated with learned movement. *Science* 179: 501–503, 1973.
12. GROWDON, J. H., CHAMBERS, W. W., AND LIU, C. N. An experimental study of cerebellar dyskinesia in the Rhesus monkey. *Brain* 90: 603–632, 1967.
13. HOLMES, G. The symptoms of acute cerebellar injuries due to gunshot injuries. *Brain* 40: 461–535, 1917.
14. HOLMES, G. The cerebellum of man. *Brain* 62: 1–30, 1939.
15. JOFFROY, A. J. AND LAMARRE, Y. Rhythmic unit firing in the precentral cortex in relation with postural tremor in a deafferented limb. *Brain Res.* 27: 386–389, 1971.
16. JOYCE, G. C. AND RACK, P. M. H. The effects of load and force on tremor at the normal human elbow joint. *J. Physiol., London* 240: 375–396, 1974.
17. LAMARRE, Y. Tremorgenic mechanisms in primates. In: *Advances in Neurology,* edited by B. S. Meldrum and C. D. Marsden. New York: Raven, 1975, vol. 10, p. 23–24.
18. LATHI, B. P. *Communication Systems.* New York: Wiley, 1968.
19. LIPPOLD, O. C. J. Oscillation in the stretch reflex arc and the origin of the rhythmical, 8–12 c/s component of physiological tremor. *J. Physiol., London* 206: 359–382, 1970.
20. LIU, C. N. AND CHAMBERS, W. W. A study of cerebellar dyskinesia in the bilaterally deafferented forelimbs of the monkey (*Macaca mulatta* and *Macaca speciosa*). *Acta Neurobiol. Exptl.* 31: 263–289, 1971.
21. MARSDEN, C. D., MERTON, P. A., AND MORTON, H. B. Servo action in human voluntary movement. *Nature* 238: 140–143, 1972.
22. MEYER-LOHMANN, J., CONRAD, B., MAT-

SUNAMI, K., AND BROOKS, V. B. Effects of dentate cooling on precentral unit activity following torque pulse injections into elbow movements. *Brain Res.* 94: 237–251, 1975.

23. MEYER-LOHMANN, J., HORE, J., AND BROOKS, V. B. Cerebellar participation in generation of prompt arm movements. 40: 1038–1050, 1977.
24. MURPHY, J. T., KWAN, H. C., MACKAY, W. A., AND WONG, Y. C. Physiological basis of cerebellar dysmetria. *Can. J. Neurol. Sci.* 2: 279–284, 1975.
25. NEWSOM DAVIS, J. AND SEARS, T. A. The proprioceptive reflex control of the intercostal muscles during their voluntary activation. *J. Physiol., London* 209: 711–738, 1970.
26. OGUZTÖRELI, M. N. AND STEIN, R. B. An analysis of oscillations in neuromuscular systems. *J. Math. Biol.* 2: 87–105, 1975.
27. PORTER, R. AND RACK, P. M. H. Timing of the responses in the motor cortex of monkeys to an unexpected disturbance of finger position. *Brain Res.* 103: 201–213, 1976.
28. STEIN, R. B. AND OGUZTÖRELI, M. N. Tremor and other oscillations in neuromuscular systems. *Biol. Cybernetics* 22: 147–157, 1976.
29. TATTON, W. G., FORNER, S. D., GERSTEIN, G. L., CHAMBERS, W. W., AND LIU, C. N. The effect of postcentral cortical lesions on motor responses to sudden upper limb displacements in monkeys. *Brain Res.* 96: 108–113, 1975.
30. VILIS, T., HORE, J., MEYER-LOHMANN, J., AND BROOKS, V. B. Dual nature of the precentral responses to limb perturbations revealed by cerebellar cooling. *Brain Res.* 117: 336–340, 1976.