AN OSCILLOGRAPHIC STUDY OF THE CEREBELLO-CEREBRAL RELATIONSHIPS*

A. EARL WALKER†
Division of Neurology and Neurosurgery, University of Chicago
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I. INTRODUCTION

RECENTLY the relationship of the cerebellum to the activity of the cerebral cortex has been stressed by experimental and clinical (Walshe, 8) studies. Rossi (6) (confirmed by Bremer, 2) showed that simultaneous stimulation of a lateral lobe of the cerebellum rendered a previously infraliminal stimulus capable of producing a motor response from the contralateral cerebral cortex. Fulton and his associates (1, 5) have shown experimentally the importance of the cortex in the genesis of the cerebellar disturbances. Anatomical studies have indicated the structural basis for these physiological phenomena by demonstrating that the main efferent connection of the cerebellum of primates is with the contralateral motor and premotor areas through thalamic relays. In view of these advances, it seemed probable that, if the cerebellum played an active rôle in the functioning of the cerebral cortex, changes should occur in the action potentials of the motor areas with cerebellar stimulation.

II. METHODS OF INVESTIGATION

The isolated encephalon of the cat, a preparation introduced by Bremer (3), has been used for all the experimental procedures. The preparation is simply made, and once established, no further anaesthetic is necessary. Under ether anaesthesia the posterior neck muscles are scraped from their insertions on the occipital bone to expose the arch of the atlas and the foramen magnum. The intervertebral ligaments and dura between these are incised, bringing into view the lower part of the medulla. With a blunt spatula the exposed medulla is completely transected at approximately the obex. At the time of transection the animal should be deeply anaesthetized to prevent undue shock. Artificial respiration is maintained for the remainder of the operation. A small dose of ephedrine (0.01 gm. per kilo) increases the blood pressure, depressed as the result of lowered vasoconstrictor tone, and insures a good encephalic circulation. The cerebellum, on one or both sides, and the cerebral cortex are exposed in the usual manner and cortical potentials led off by one or two pairs of electrodes (5-6 mm. apart) placed indirectly upon the cortex and recorded after amplification by the Matthews or Dubois oscillograph. Small electrodes connected to the secondary coil of an inductorium, the primary of which is in series with a two volt battery and a key, are used for

* From the Laboratoire de Pathologie Générale, Université de Bruxelles, Bruxelles, Belgium (Prof. Fr. Bremer).
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‡ Fellow of the Rockefeller Foundation.
bipolar stimulation of the cerebellar cortex. The frequency of stimulation varies from 12 to 25 break shocks per second. The strength of excitation is generally about that necessary to obtain a motor response from stimulation of the cerebral cortex. Both the stimulating and receiving electrodes are firmly attached to the calvarium by wax, so that slight movements of the head do not introduce an artefact. All experiments were carried out in a completely shielded room; the inductorium was separately shielded.

III. Experimental Results

Faradic stimulation of the cerebellum, especially the cerebellar hemispheres, produces changes in the cortical potentials obtained from the motor areas and to a lesser extent from the parietal and temporal regions. These alterations consist of an increased frequency and amplitude of the cortical waves. Usually the change is striking and not at all to be confused with the unavoidable artefact introduced by spread of potential from the stimulating electrodes. The response usually is initiated by a wave which at times so closely follows the artefact that they seem to be almost synchronous, but which reaches its acme much slower than the spike of the artefact. It is of greater amplitude than the normal cortical waves. Usually smaller secondary waves are present. Their frequency is definitely greater than that of the normal cortical activity, the increase varying between 25-50 per cent. These effects appear immediately without a delay. In some cases they may augment during the first second of stimulation. Following the stimulation the large waves cease immediately, but the cortical activity may not regain its normal rhythm for a half or one second. During this interval the waves are of greater frequency and smaller amplitude than normal. Another feature may superimpose upon this response. During spontaneous sleep, which was frequently the state of the animal, the cortical rhythm is punctuated every few seconds by spontaneous bursts of activity. Cerebellar stimulation may augment the number, intensity and duration of such bursts (Fig. 2 A). Auditory stimuli give rise to similar changes of the cortical potentials led from the temporal lobe (Bremer, 4).

It has not been possible to facilitate the response by repeated stimulation of the cerebellar cortex at small intervals, nor has it been possible to tire or fatigue the response similarly.

These responses to cerebellar excitation may be readily obtained from the motor cortex surrounding the cruciate sulcus and extending posteriorly along the midline. In only three of twenty-one experiments was cerebellar stimulation ineffective, probably due to the poor general condition of the animal. Responses may be obtained to a lesser degree from the parietal and temporal cortex. Although less distinct and requiring a slightly greater strength of stimulation, such responses present the same characteristics as those obtained from the motor area. Cerebellar stimulation caused no alteration in the po-

* The differences in the resting or normal cortical rhythms of the frontal, parietal and temporal cortex, as pointed out by Kornmüller have been constantly a striking feature.
FIG. 1. A and B (cat No. 10) Stimulation of right cerebellar hemisphere with secondary coil of the inductorium at 22.5 cm.
A. Leads from the left cruciate sulcus (point 2).
B. Leads from left parietal cortex (point 3).
C, D and E. (cat No. 11) lead I (upper) from right cruciate sulcus: lead II from left cruciate (points 1, and 2).
C. Stimulation of the right cerebellar hemisphere along the intercrural fissure (secondary coil at 23 cm.).
D. Stimulation of same point as C, but right superior cerebellar peduncle sectioned 15 min. previously (secondary coil at 23 cm.).
E. Stimulation of left cerebellar hemisphere along the intercrural fissure (secondary coil at 25 cm.).
F and G. (cat No. 5) Cortical lead from the left cruciate sulcus (point 2).
F. Stimulation of the lateral portion of the right inferior ansiform lobe (point 6).
G. Stimulation of the right inferior ansiform lobe 3 mm. medial to the point stimulated in A and near the vermis. Secondary coil of the inductorium was set at 26 cm. for F and G, which were taken within 1 min. of each other. (Cont. on p. 19.)
tentials led from the cortex of the occipital lobe other than the spike produced by the spread from the exciting electrodes in the only two cases so studied.

The changes may be markedly diminished or abolished by local application of novocaine or ice to the cerebellar cortex. Under such circumstances although the cortical activity remains normal, cerebellar excitation produces very slight, if any, alteration in the cortical rhythm. The influence of the artefact alone may thus be seen (Fig. 2 B). If the effect of these depressing agents is allowed to pass off, stimulation of the cerebellum once more produces marked alterations in the cortical activity (Fig. 2). Following application of 2 per cent novocaine to the cerebellar cortex, strengths of stimulation formerly producing a good response are no longer effective, but stronger excitation may give rise to changes in the cortical potentials. This is not un-

In all records the sensibility of the oscillograph was 20 mm. for 100 uv. The time marker signalled 1 sec. intervals. In a few of the earlier experiments owing to mechanical difficulties, there was a slight delay between the signalling of the closure of the secondary circuit of the inductorium and the onset of excitation. This gives the false impression of a latent period (Fig. 1 F).
expected for such strong stimuli must reach the deep cerebellar nuclei which are not affected by the local anaesthetic.

Abolition of the cortical activity by asphyxiation, readily carried out in the isolated encephalon by discontinuing artificial respiration, prevents a response to cerebellar stimulation. The only effect of such excitation is a series of spikes produced by the spread of potentials from the stimulating electrodes. If artificial respiration is resumed the activity of the cerebral cortex rapidly returns and cerebellar stimulation will again produce a response (Fig. 3).

The application of strychnine to the cerebellar cortex has failed in two instances to produce alterations in the cortical activity.

Section of the superior cerebellar peduncle in the two experiments studied has abolished the response obtained from stimulation of the same side of the cerebellum without altering the effect of exciting the opposite hemisphere. In these cases leads were taken simultaneously from both motor areas along the cruciate sulcus. The effect of cerebellar stimulation is thus shown to be not strictly unilateral, a weak response being present in the ipsilateral motor cortex (Fig. 1, C, D, and E).
The response varies with the point of the cerebellar cortex stimulated. Excitation of the vermis does not give any response at times, and at best, it does not give rise to nearly so pronounced changes in the cortical activity as excitation of the cerebellar hemispheres. Within the latter are optimal places for producing a response in any particular point of the cerebral cortex. However, the results of such studies have not been sufficiently constant to warrant a statement regarding cerebellar localization. In general better responses are obtained when the exciting electrodes span the small sulcus between the superior and inferior ansiform lobes (fissura intercruralis) than when either the superior or inferior lobe is stimulated alone.

The method of preparing the animal does not allow coincidental observations on the effect of cerebellar stimulation on the posture of the extremities. Changes in the cortical potentials may occur quite independent of eye movements, which are readily elicited from the anterior part of the cerebellum in this preparation.

IV. DISCUSSION

The increase in the cortical activity subsequent to excitation of the cerebellar hemispheres probably represents a normal function of the cerebellum. Certainly the fact that the changes are abolished when the activity of the cerebellum is arrested by novocainization, or the local application of ice, or its main efferent pathway interrupted by section of the superior cerebellar peduncle is ample evidence that they do not represent artefacts introduced by the potentials of the stimulating electrodes. Because the cortical activity does not appear to be altered by removal of the cerebellar influence by any of these methods it may be assumed that in the cat the cerebellum, while physiologically at rest, does not add a perceptible factor to the cortical rhythm. It is possible that this may be correlated with the fact that hypotonia is not a prominent sign following removal of the cerebellum in this animal. The fact that the cerebellum is able to increase the activity of the motor areas leads to the supposition that the former is exerting a stimulating influence on the cerebral cortex. There is, however, no reason to suppose that this influence is sufficient to produce the specific response of the motor cortex, rather it would appear merely to sensitize the cortex so that it might be activated by a minimal stimulus. In other words it serves to lower the threshold of excitation of the cerebral cortex. Thus one would expect that subthreshold stimuli would produce motor responses when the cerebellum was simultaneously stimulated. This Rossi (6) has shown is precisely what happens.

The fact that the effect is most pronounced in the motor cortex is not surprising in view of previous anatomical (Walker, 7) and physiological (Aring and Fulton, 1) studies. It is possible that the response may be entirely confined to the motor cortex in animals in which the cerebral cytoarchitecture is better differentiated, such as in the monkey, ape and man.

It is probable that both the cerebellar cortex and deep nuclei of the cerebellum take part in the production of this stimulating influence, for although
local application of novocaine abolishes the effect of weak stimuli, stronger ones produce a response. It is likely that this latter effect is due to excitation of the deep cerebellar nuclei. The efferent pathway is by way of the superior cerebellar peduncle to the thalamus. Another neurone then projects to the motor areas of the cerebral cortex. This pathway has been clearly demonstrated anatomically in cat, monkey and anthropoid ape.

That the effect is mainly obtained from stimulation of the neocerebellar parts is not unexpected in view of the anatomical, physiological and clinical evidence that neocerebellar function is largely dependent upon the integrity of the cerebral cortex. Comparative anatomy has taught that the cerebellar hemispheres develop pari passu with the elaboration of the cerebral cortex. Fulton, Liddell and Rioch (5) and Aring and Fulton (1) have shown that cerebellar tremor, essentially a sign of neocerebellar dysfunction is greatly diminished or absent following ablation of the motor cortex.

The neocerebellum is not entirely concerned with the cerebral cortex. Undoubtedly it plays an important role in association with the parvocellular part of the red nucleus and the rubroreticular tracts. In ascending phylogeny, however, the neocerebellum is more and more functionally related to the cerebral cortex, especially to the motor and premotor areas.

The significance of this cerebellocerebral relationship is to be found in an analysis of the disturbances resulting from lesions of the cerebellum. Bremer in a recent excellent survey of the subject concludes as follows (2, p. 126): "L'analyse du syndrome de déficit néo-cérébelleux et la considération des connexions cérébello-cérébrales nous amène donc à formuler l'hypothèse que les trois éléments de ce syndrome, l'asthénie volontaire, l'hypotonie musculaire et les anomalies des temps de réaction volontaire, sont l'expression d'une seule et même perturbation fondamentale: le défaut de tonus, l'asthénie, des mécanismes moteurs cortico-bulbaires et cortico-spinaux privés d'une action dynamogénique cérébelleuse." Such a cerebellar action is well confirmed by the present investigation.

The absence of this cerebellar dynamic influence increases the threshold of the cerebral cortex, and in higher primates at the same time releases the peripheral musculature from that slight cortical stimulation which is probably the basis of normal tone. In these circumstances the cerebral cortex must be set into action by an abnormally strong excitation, one which on account of its abnormal strength is apt to produce a response of too great or too little intensity. The lack of tone of the peripheral musculature introduces another disturbing factor. When this is summated by the same abnormal reaction of the antagonists which normally modulate the activity of the agonists, a physiological basis for the ataxia, tremor and dysmetria seen in cerebellar lesions is apparent.

V. Summary

1. Excitation of the cerebellar hemispheres produces a marked increase in the amplitude and frequency of the cortical action potentials from the motor areas of the cat.
2. Section of the superior cerebellar peduncle abolishes the response of the contralateral motor cortex but a slight change in the potentials of the ipsilateral motor cortex may still be elicited.

3. From these experiments it is concluded that the cerebellum especially the neocerebellum exerts a stimulating influence upon the cerebral cortex, which may be the mechanism through which the cerebellum normally maintains a coordinating influence upon volitional movement.

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