ELECTRICAL STIMULATION OF THE INTERIOR OF THE CEREBELLUM IN THE MONKEY

H. W. MAGOUN, W. K. HARE AND S. W. RANSON

From the Institute of Neurology, Northwestern University Medical School

Received for publication March 11, 1935

Investigations of the cerebellar nuclei and the white matter adjacent to them have been very few in number as compared with many studies of cerebellar function based upon gross extirpation of this organ or upon destruction or stimulation of its cortex. It is well known, however, that the nuclei constitute at least the major source of all efferent cerebellar connections, and the small amount of attention which they have received is by no means commensurate with their importance in cerebellar activity. The difficulty of approaching these nuclei, situated as they are within the interior of the cerebellum, has doubtless been the primary obstacle to their study, but this difficulty has been overcome by several investigators.

With the immediate object of investigating the reactivity of the cerebellar nuclei to electrical stimulation, Horsley and Clarke (1) devised their stereotaxic instrument for accurately orienting an electrode within the interior of the brain. Unfortunately their study of the cerebellar nuclei was never completed, and we have only brief and incidental mention of their results (1, 2). At Horsley's invitation this work was continued by Sachs and Fincher (3) but only a preliminary report was made, in which again but brief mention of the results appeared. Some observations of the effect of electrical stimulation of the medial cerebellar nuclei, with the aid of the Horsley-Clarke instrument, have been reported by Mussen (4). In the work of Miller and Laughton (5, 6) on the decerebrate animal, the cerebellar nuclei were electrically stimulated after their exposure by ablat- ing the over-lying cerebellar parts.

In the present investigation, the Horsley-Clarke stereotaxic instrument has been employed in the electrical stimulation of the cerebellar nuclei and the territory adjacent to them in the rhesus monkey (Macaca mulatta).

METHOD. Stimulation of the cerebellum was performed under light nembutal anesthesia (10–19 mgm. per kgm. of body weight) plus supplemental ether added when necessary by means of a tracheal cannula and ether bottle. The animal was suspended untied in a hammock with the limbs hanging free and the head in the freely swinging stereotaxic instru-

1 Aided by a grant from the Rockefeller Foundation.
ment supported from above. In some of the experiments, the body was supported from above by strings under the supraspinous ligament at the shoulder and pelvis. The technique of electrical stimulation used has been described in detail by Ranson (7), and need be only briefly referred to here.

Using the Horsley-Clarke stereotaxic instrument and a bipolar needle-like electrode, less than 1 mm. in diameter, with the tips of the two wires separated by a distance of 1 mm. along the axis of the electrode, the interior of the cerebellum was systematically explored by electrically stimulating in orderly succession every cubic millimeter of its substance. The current was supplied by a single dry cell registering 1.5 amp. attached to a Harvard inductorium, the secondary coil of which was set at 9 cm.

In eight monkeys stimulation was performed along punctures in a vertical plane, the electrode being inserted through the overlying cerebral hemisphere, after removal of a part of the calvarium and dura, and retraction of the superior sagittal sinus. In four of these animals, stimulation was begun on the left side and extended to the midline and onto the right side. In the other four, stimulation was begun to the right of the midline and extended onto the left side. In two cases the exposure was made through the occipital bone above the foramen magnum, and stimulation of the left side was performed along punctures in a horizontal plane, the electrode being introduced through the caudal, rather than the dorsal, surface of the cerebellum. In every case, stimulation was begun in the caudal portion of the cerebellum and continued rostrally through the cerebellar nuclei to the cerebellar peduncles. The intact efferent cerebellar pathways, therefore, always lay ahead of every point of stimulation.

Subsequent microscopic examination of serial sections of the explored area enabled the localization of each point stimulated. A correlation between the location of these points and the responses obtained from their stimulation, as represented by appropriately situated symbols on a series of eight transverse sections at millimeter intervals through the interior of the cerebellum, gave a composite and graphic picture of the results obtained.

Results. It is interesting to note that in the order of frequency of response to cerebellar stimulation, the parts of the body have been represented in this series of experiments as follows: eyes, ipsilateral forelimb, head, contralateral forelimb, hind limbs, trunk and tail. In our opinion no particular significance should be attached to this sequence, beyond the suggestion that the anterior part of the body has a greater representation than the posterior.

The responses of the eyes, head, trunk and tail have consisted of deviations from the longitudinal axis of the body and may be grouped together as reactions of the eyes, head and axial musculature. The responses of
the limbs form a second group manifest as reactions of the musculature of the extremities. For convenience in presenting the results, the responses of the two groups may be taken up separately, but reactions of both groups have occurred together from stimulation of certain regions of the cerebellum.

The responses obtained from cerebellar stimulation have been definitely postural reactions, as distinct from the quick reactions produced by stimulation of the cortico-spinal system or peripheral nerves, and from the usually phasic responses obtained through reflex activation of the motor system. Such cerebellar responses take a number of forms. They may consist of a slow movement during stimulation to a posture which is maintained throughout stimulation. On the other hand, an inhibition or relaxation of a previously existing muscular contraction often occurs during stimulation. After stimulation, there follows either a sudden rebound to a posture usually representing the opposite of that produced by stimulation, or a slow assumption of an attitude, usually after repeated stimulation, which may persist as a postural background throughout the experiment.

Eyes, head and axial musculature. The reactions of the eyes, head and axial musculature to electrical stimulation varied with the region stimulated and consisted: first, of a marked conjugate deviation of the eyes and a slight turning of the head (not always present) to the side stimulated, or secondly, of a movement of the eyes and usually the head to a position of forward gaze, each from a position of contralateral deviation existing as a posture slowly assumed during the course of the experiment. In every case these reactions of the first and second type were confined to the eyes and head. Responses of these types have been very widespread throughout the interior of the cerebellum, being obtained from the stimulation of points within the extent of all of the cerebellar nuclei, and the white matter adjacent to them.

Reactions of a third type have concerned not only the eyes and head, but in some instances the trunk and tail also. In the latter case, they represent responses of the entire length of the body axis. These reactions of the third type were made up of two phases, the first occurring during the period of stimulation, and the second occurring as a rebound at the end of stimulation. During the period of stimulation, the eyes and head moved to a position of forward gaze or deviated to the side of stimulation, as before. Immediately following the cessation of the stimulus, the eyes and head briskly and actively deviated to the contralateral side.

Such responses of the head are shown in some of the photographs of figures 1 and 2. In figure 1, A and B, the head was turned slightly to the left during stimulation of the left side of the cerebellum (A), and at the end of stimulation exhibited a rebound deviation to the right (B). In figure
Fig. 1 is made up of three pairs of photographs, each pair showing the responses to stimulation of a single point within the interior of the cerebellum. In each case, the photograph on the left shows the phase of the reaction occurring during stimulation, the photograph on the right the rebound after stimulation. Photographs A and B show a response of the head, stimulation being on the left side of the cerebellum. Photographs C and D show a response of the ipsilateral forelimb, stimulation being on the left side of the cerebellum. Photographs E and F show a response of the ipsilateral forelimb, stimulation being on the right side of the cerebellum. The animals were under nembutal anesthesia and did not experience pain.
2, E and F, the head was turned to the right during stimulation of the right side of the cerebellum (E), and exhibited a rebound deviation to the left at the end of stimulation (F). In figure 2, C and D, the head took a position of forward gaze during stimulation of the right side of the cerebellum (C), and exhibited a rebound deviation to the left at the end of stimulation (D). In the photographs movements of the head can be gauged best by noting changes in the long axis of the stereotaxic instrument.

Responses of the trunk and tail, when present, occurred in two phases. The first phase appeared during stimulation and consisted either of a relaxation of a preexisting concavity of the body axis to the opposite side, or of the production of a concavity of the trunk and deviation of the tail to the side of cerebellar stimulus. The second phase appeared as a rebound at the end of stimulation and consisted of the production of a concavity of the trunk and a deviation of the tail to the side opposite cerebellar stimulus.

Responses of the body axis do not stand out clearly in the accompanying photographs, but were present in each of the responses shown in figure 2. In figure 2, A and B, the body axis was straightened during stimulation of the left side of the cerebellum (A), and exhibited a rebound concavity to the right at the end of stimulation (B). In figure 2, C and D, the body axis was straightened during stimulation of the right side of the cerebellum (C), and exhibited a rebound concavity to the left at the end of stimulation (D). In figure 2, E and F, the body axis exhibited a concavity to the right during stimulation of the right side of the cerebellum (E), and a rebound concavity to the left at the end of stimulation (F).

These responses of the third type were obtained only from the medial part of the interior of the cerebellum, i.e., from the stimulation of points in the white matter bordering on the roof nuclei, and in some instances also from points on the medial edge of the emboliform nucleus.

Limbs. Postural reactions of the limbs have been obtained both as responses during stimulation and as rebound contractions at the end of stimulation. Two groups of such responses may be differentiated.

Group 1 of the limb responses includes a number of reactions, usually slight in excursion and confined to parts of the ipsilateral forelimb, or rarely to the ipsilateral hind paw. These responses consisted of two phases and usually made their appearance as a brisk, short-lasting assumption of posture at the end of the period of stimulation. A second stimulation, immediately following, relaxed this posture, but at the conclusion of the stimulus, the attitude was once more assumed. Because of its appearance at the end of stimulation, the assumption of posture appeared to be of the nature of a rebound contraction following inhibition. As a common variation, an attitude was often assumed as a result of a contraction of one muscle group during the period of stimulation, while a brisk rebound con-
Fig. 2 is made up of three pairs of photographs, each pair showing the response to stimulation of a single point within the interior of the cerebellum. In each case, the photograph on the left shows the phase of the reaction occurring during stimulation, the photograph on the right the rebound after stimulation. Photographs A and B show responses of the limbs and body axis, stimulation being on the left side of the cerebellum. Photographs C and D show responses of the limbs and body axis, stimulation being on the right side of the cerebellum close to the midline. Photographs E and F show responses of the limbs and body axis, stimulation being on the right side of the cerebellum. The animals were under nembutal anesthesia and did not experience pain.
traction of the respective antagonistic muscles at the end of stimulus reversed the attitude in the part concerned. In none of these cases was there a rebound rigidity or resistance to passive manipulation.

Responses of this nature consisted: a, of a flexion or relaxation from extension of the forearm, hand, or fingers during the period of stimulation, followed at the end of stimulation by a rebound extension of these parts of the limb; b, of a relaxation from flexion during stimulation followed by a rebound flexion of these parts at the end of stimulus; c, of a relaxation from pronation or of an active supination of the forearm and hand during the period of stimulation, followed by a rebound pronation at the end of stimulus; d, of a relaxation from abduction or an active adduction of the arm during the period of stimulation, followed at the end of stimulus by a rebound abduction. These responses appeared of a diverse nature from the point of view of the muscles and joints involved, but they could be associated in that they were all concerned with postures of parts of the ipsilateral anterior extremity.

Photographs of two reactions belonging to this group are shown in figure 1. In figure 1, C and D, a response is shown of the left forelimb, stimulation being on the left side of the cerebellum. During stimulation the left forelimb was relaxed (C), while at the end of stimulation it exhibited a rebound flexion of the elbow and wrist (D). In figure 1, E and F, a response is shown of the right forelimb, stimulation being on the right side of the cerebellum. During stimulation the right forelimb was flexed at the elbow and slightly supinated (E), while at the end of stimulation it exhibited a rebound extension of the elbow and some pronation of the forearm (F).

Responses of group I were obtained from the buried cerebellar cortex of the anterior lobe both caudal to and overlying the fastigial, globose, and emboliform nuclei. The reactive points converged laterally in the underlying white matter, so that many responses were obtained from the stimulation of points in the region occupied by the emboliform and globose nuclei, while no responses of this nature were obtained from the dentate or fastigial nuclei.

Group II consisted of responses of all four limbs. These reactions were similar to those just described in that the reaction occurred in two phases, and was usually first seen as a rebound assumption of posture at the end of the period of stimulation. A second stimulus relaxed this posture, which was briskly assumed once more as the stimulus was concluded. While a number of variations were observed in the postures involved in the responses of this group, very commonly the reactions consisted of a relaxation of the limbs during stimulation, followed, at the end of stimulus, by a brisk and gross rebound extension of the limbs on the ipsilateral side and a flexion of those on the contralateral side. The rebound was usually
greater in the forelimbs than in the hind and was often most marked in the ipsilateral forelimb. In the marked responses of this nature, the rebound posture was maintained for a period of minutes, as a strong rigidity and resistance to passive manipulation, chiefly of the forelimbs and greatest in the ipsilateral forelimb. In a number of cases such rebound postures were timed and were still undiminished at the end of five minutes. The cycle of inhibition and rebound could be continued indefinitely with repeated stimulation, the responses becoming augmented on repetition.

In some cases, instead of a relaxation of a pre-existing posture during stimulation, an actual contraction occurred in the muscle groups antagonistic to those contracting in the rebound at the end of stimulation. That is, during stimulation there was a flexion of the ipsilateral limbs and an extension of the contralateral limbs, while after stimulation there followed, as before, a rebound extension of the ipsilateral limbs and a flexion of the contralateral limbs. In reactions obtained from stimuli close to the midline, the limbs of the two sides often assumed similar rather than contrary postures, either during or after stimulation.

In whatever form they were manifest the reactions of group II appeared to be concerned not so much with the attitudes seen in small movements of specific parts of a single anterior extremity, as with those involved in the gross postures of all four limbs.

Photographs of reactions belonging to this group are shown in figure 2. In figure 2, A and B, a response is shown to stimulation on the left side of the cerebellum. During stimulation there was a relaxation of all limbs (A), which was followed at the end of stimulation by a rebound extension of the left limbs and a rebound flexion of the right limbs (B). This rebound posture (B) was timed, and at the end of five minutes showed no appreciable relaxation.

Figure 2, C and D, shows a response to stimulation of the right side of the cerebellum, close to the midline. During stimulation both forelimbs were retracted and flexed (C). At the end of stimulation there was a rebound extension of the right limbs and a rebound flexion of the left limbs (D).

Figure 2, E and F, shows a response to stimulation of the right side of the cerebellum. During stimulation the right limbs were flexed and the left limbs were extended (E). At the end of stimulation the right limbs exhibited a rebound extension and the left limbs a rebound flexion (F). The photograph of the rebound posture (F) was taken two minutes after the cessation of the stimulus. A comparison of the rebound postures shown in figure 2, D and F, with that obtained from the opposite side of the cerebellum (fig. 2, B) will demonstrate the striking reversal of response encountered in passing from one side of the midline to the other, reactions of contrary sides being mirror images of one another. A similar reversal
on crossing the midline is seen in the movements of the head. During stimulation of appropriate points on the left side, the head turns to the left and after stimulation rebounds to the right (fig. 1, A and B). Conversely, stimulation on the right side produces a turning of the head to the right during stimulation followed by rebound to the left (fig. 2, E and F).

Reactions of group II were obtained from the buried cerebellar cortex of the anterior lobe, both caudal to and overlying the globose and fastigial nuclei. The reactive points appeared to converge slightly medially in the underlying white matter, so that many responses were obtained from the stimulation of points in the vicinity of and within the substance of the fastigial nucleus, while at least the caudal part of the globose nucleus appeared definitely lateralward of the responsive region. No responses of this nature were obtained from the emboliform or dentate nuclei.

The reactions which have been reported above, from stimulation of the interior of the cerebellum, disappeared as the electrode emerged from the lower surface of the cerebellum into the fourth ventricle. Stimulation of points in the underlying brain stem never has yielded responses of the types described above, but chiefly contractions of isolated groups of muscles supplied by the fifth, sixth, seventh or eleventh cranial nerves.

Discussion. The results just reported indicate the extent to which this method of electrical stimulation may be employed in an investigation of the interior of the cerebellum. The technique does not appear to be applicable to a study of all parts of this region. For example, stimulation of points within the substance of the dentate nucleus, under the conditions of these experiments, has yielded no consistent response specific to this nucleus. There are, however, two regions of the interior of the cerebellum which, in these experiments, have been regularly associated with a consistent type of reaction pattern.

The first of these is the region of the emboliform and globose nuclei and the neighboring white matter, which appears to be closely associated with the limb responses of group I, concerned with small and short-lasting postures of parts of the ipsilateral anterior extremity. The second is the region of the fastigial nucleus and the neighboring white matter, which appears to be closely associated with the limb responses of group II, concerned with gross and long-lasting postures of all four limbs, and probably also with the eye, head, and trunk responses of type III, concerned with lateral deviations from the longitudinal body axis.

The biphasic nature of these responses, consisting usually of an inhibition during stimulation and a rebound contraction after stimulation, suggests their relationship to similar responses obtained by a series of workers from stimulation of the cerebellar cortex in the decerebrate preparation. Reference has been made to a number of these studies in the most recent
report on this subject, that by Denny-Brown, Eccles, and Liddell (8). There are many points of similarity between the results obtained by these authors and our observations on the limb responses of group II, which in this series of experiments have been followed from the buried cortex of the anterior lobe through the underlying white matter to the region of the fastigial nucleus.

This similarity suggests that we are dealing here with one and the same reaction, obtained by Denny-Brown, Eccles, and Liddell from stimulation of the surface of the cerebellar cortex, and obtained in the present investigation from stimulation of the underlying cortex and white matter, and region of the fastigial nucleus. If this be true, the presence or absence of a decerebrate rigidity in the animal would appear to be an indifferent factor, possibly serving only to quantitatively augment the normal reaction of this cerebellar system to the point at which it might be elicited by surface stimulation of the cerebellar cortex.

This suggestion receives support from the fact that the results of the present study are in agreement, in some general features, with the observations of Miller and Laughton (5, 6) obtained from stimulation of the cerebellar nuclei in the decerebrate cat.

SUMMARY

Electrical stimulation of the interior of the cerebellum in the monkey, employing the Horsley-Clarke stereotaxic instrument, has yielded responses of the eyes, head, and axial musculature, and responses of the limbs.

With the possible exception of some reactions of conjugate deviation of the eyes and head to the side of stimulation, these responses have been biphasic in nature, and have consisted of one effect during the period of stimulation, followed by a second effect occurring as a rebound at the end of stimulation.

Such responses have consisted either of an inhibition of a muscle group during stimulation followed by a rebound contraction of this muscle group at the end of stimulus, or of a contraction of one muscle group during stimulation followed at the end of stimulus by a rebound contraction of its antagonist.

Reactions of this nature involving small and short-lasting postures of parts of the ipsilateral anterior extremity have been traced from the buried cortex of the anterior lobe through the underlying white matter to the region of the emboliform and globose nuclei.

Other reactions of this nature involving pronounced and long-lasting postures of all four limbs, the rebound contractions usually persisting for a period of minutes, have been traced from the buried cortex of the anterior lobe through the underlying white matter to the region of the fastigial nucleus. Similar responses of the eyes, head, and axial musculature, in-
volving lateral deviations from the longitudinal body axis, have been ob-
tained from the white matter in the vicinity of the fastigial nucleus.

Somewhat comparable reactions have been observed from cerebellar
stimulation in the decerebrate preparation by a series of workers. The
suggestion is made that such reactions simply represent normal cerebellar
responses, the presence of a decerebrate rigidity being an incidental factor.

REFERENCES

(2) Clarke, R. H. Brain 49: 557, 1926.