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THE EFFECTS OF CEREBELLAR LESIONS UPON SKILLED MOVEMENTS AND INSTRUMENTAL CONDITIONED REFLEXES

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Abstract. Eight cats were trained in reaching for food with their forelegs in cylinders 19–21.6 cm long of various diameters (3.9–10.1 cm). When the pre-operative training was completed, in six cats the interposite and dentate intracerebellar nuclei were destroyed, whereas in two cats the paravermal cortex was ablated. Interposite animals displayed big oscillatory movements around the entrance to the cylinder and overshooting in reaching for food with occasional forced grasping. Paravermal cats displayed overflexion leading to missing the entrance of the cylinder and wild batting movements observed in the large cylinder. The physiological mechanism of these disorders is discussed.

INTRODUCTION

The extensive research work devoted to the problem of cerebellar functions has been mainly developing along two lines: one line concerns the electrophysiological and anatomical studies of the connections both inside the cerebellum and between the cerebellum and other structures (*see* Eccles et al. 1967); the other line has been concerned with the effects of cerebellar lesions upon reflex activity, postures, and general motor behavior (Dow and Moruzzi 1958). Only a few studies have been done on the effects of cerebellar lesions upon learned motor responses established in instrumental conditioning training. This gap should be filled up for the following reasons.

It is generally agreed that the cerebellum is a structure interposed between the proprioceptors situated in muscles and tendons on the one hand, and the cerebral cortex on the other. Its role consists, among other things, in mediation of messages delivered to the brain by muscles and tendons during particular functional states of these organs. Since the tendon organs and spindles give information to the central nervous system only about tensions, and the brain is rather interested in muscular activity, we may reasonably assume that this change of coding is due precisely to the cerebellar function. If this assumption is true, the animal deprived of the cerebellum should develop a particular form of ataxia, due to the fact that information from the periphery about the performed motor acts does not reach the brain.

It is well known that the impulses reaching the cerebellum from the periphery impinge through granule and inferior olivary cells upon the Purkinje cells which send their axons to the intracerebellar nuclei. Beside this there is growing evidence to show that the intracerebellar nuclei also receive more direct messages from the periphery which are believed by most authors to consist of collaterals of pathways going to the cerebellar cortex (*see* Eccles et al. 1967).

Moreover, the recent electrophysiological data indicate that Purkinje cells are inhibitory with regard to the neurons of these nuclei (Ito et al. 1964, 1970). Therefore, when experimenting on the effects of cerebellar lesions upon instrumental motor acts we should separately remove either the cerebellar cortical fields related to these acts, or corresponding intracerebellar nuclei.

The present paper deals with the problem of what are the effects of cortical and nuclear cerebellar lesions upon instrumental responses which require little effort for their execution.

MATERIAL AND METHODS

Pre-operative training. A total of eight young adult cats were trained to take food with the forepaw from horizontally mounted transparent leucite cylinders, 19–21.6 cm long and of five different inside diameters (cylinder 1, 10.1 cm; cylinder 2, 7.6 cm; cylinder 3, 6.3 cm; cylinder 4, 5.1 cm; cylinder 5, 3.9 cm). The test chamber was adapted from a sound damped box, 137.2 cm long, 76.2 cm wide, and 106.7 cm high. The sound dampened door was left open and a 76.2 cm × 76.2 cm transparent leucite plate was mounted to block the lower part of the door opening. The leucite plate had a 10.1 cm circular opening the center of which was 21 cm from the floor level and centered in the left and right dimensions. Runners and a stop were fixed to the leucite plate so that anyone of the five cylinders mounted on a leucite plate (15.2 cm × 15.2 cm) could be readily interchanged (Fig. 1).

All cats were tractable animals kept for a few days on reduced rations of milk and cat chow and then placed in the test chamber, and offered small pieces of bovine spleen placed in the largest cylinder. At first the spleen was placed on the floor of the cylinder near its chamber entrance. The cat grasped the food with its teeth when the piece of spleen was near the cylinder entrance. However, after a few rewards the food was placed deeper in the cylinder and the animal now used one or the other forelimb to grasp the food in its claws and usually took it to his mouth. At other times the cat might drop the food from its forepaw and he would then take food from the floor by his mouth. After learning to take food from cylinder 1, the cats were then found to be able to enter and take food from all of the cylinders without any further training.

For the forelimb to enter the cylinder without error and take food from its far end, the cat had to pay attention to the task at hand and position his body so the forelimb could be extended into the cylinder up to the shoulder joint. All cats were able to perform the tasks of manually taking food with well coordinated delicate and rapid movements. When the smallest cylinders were used, vision of the food was partially obscured by the entering limb and the leucite interfaces; and the animals located the exact position of the food by delicate and rapid palpation. The palpation movements were chiefly movements occurring at the wrist.

Some cats were initially distracted in the test chambers by the observer and/or the odor of other cats and one cat was too hyperactive at times. The above behavior caused some initial difficulty in entering the smallest cylinders and reaching for food placed in the far end of the cylinders. Before surgery, the performances of most animals were recorded cinematographically and all animals were clinically tested (tone, posture, supporting reactions, gait, placing and hopping reactions). No attempt was made to train a specific limb to perform the task of reaching for and taking food from the cylinder.

After the animals ran through training involving all the cylinders, an additional test was applied. Six 1.3 cm holes were symmetrically drilled on the both sides of cylinder 2 (*see* Fig. 1) through which the pieces of food were inserted. Thus the cats had to take the food not only from the bottom of the cylinder, but also from various points on its walls. It has been found that the cats trained in taking food from the bottom of the cylinders easily mastered the task of taking it from its walls. This task required not only extension of the limb but also its inversion when the food was placed on the wall oposite to the limb used, or its eversion when the animal used the ipsilateral limb.

Surgery. After the pre-operative training was completed, which took in average less than a week, the cats were operated upon. In six animals denoted as IP1 to IP6, the interposite and interposite-dentate intracerebellar nuclei were destroyed, whereas in the two remaining animals, PV1 and PV2 the paravermal cortex was ablated.

All surgical procedures were performed under Nembutal anesthesia (36 mg/kg) with strict asepsis. The intracerebellar lesions were produced by electrocoagulation. The lesion electrode, oriented stereotaxically, entered the posterior cerebellum via the paramedian lobules and was passed horizontally through the nuclei. The unilateral paravermal cortical ablations required extensive removal of bone overlying one side of the cerebellum and occipital lobe. The occipital lobe was then gently elevated and part of the bony tentorium overlying the anterior lobe of the cerebellum was removed. The dura was then excised and paravermal cortex of the anterior and posterior lobes was gently aspirated.

Anatomy. All animals were anesthetized and sacrificed by intravascular perfusion (Koenig et al. 1945). The calvarium was removed and the head mounted in the stereotaxic instrument. The brain was sectioned coronally into two blocks. The block containing the brainstem and cerebellum was imbedded in celloidin and serially sectioned along the coronal planes of the stereotaxic instrument. Alternate sections were stained by the cresyl violet and Mahon techniques and the lesions were plotted on projection drawings.

RESULTS

1. *Interposite-dentate lesions*

Bilateral interposite or interposite-dentate lesions were made in six cats (denoted as IP1 to IP6).

Cats IP1 to IP4 with lesions primarily confined to the interposite nuclei (Fig. 3*AB*) showed increased extensor tone all four limbs. However, supporting responses were weaker than normal. The hopping reactions were slow and hypermetric and the hopping limb had a tendency to collapse on placement. Tactile placement to hair touch was initially absent in all four limbs; but recovered in IP1 in the right fore and right hindlimb on the fourth post-operative day, and in the left fore and right hindlimb in IP3 by the 14th post-operative day. The recovered tactile placement of these limbs required facilitation for their elicitation (i.e., by threatening to drop the animal or holding him in a precarious tilted position). Even with this facilitation the recovered limbs frequently failed to place. Proprioceptive, visual and abduction placing responses and the extension of limb and spreading of the toes to suddenly lowering the animal were never lost but were performed with ataxia. Proprioceptive placing was initially of high threshold, requiring considerable bending of the limb joint for placement. The proprioceptive placing recovered rapidly, and by 7 days required only the slightest joint displacement in IP1 for the right limbs and for all limbs in IP3. All placing reactions were hypermetric

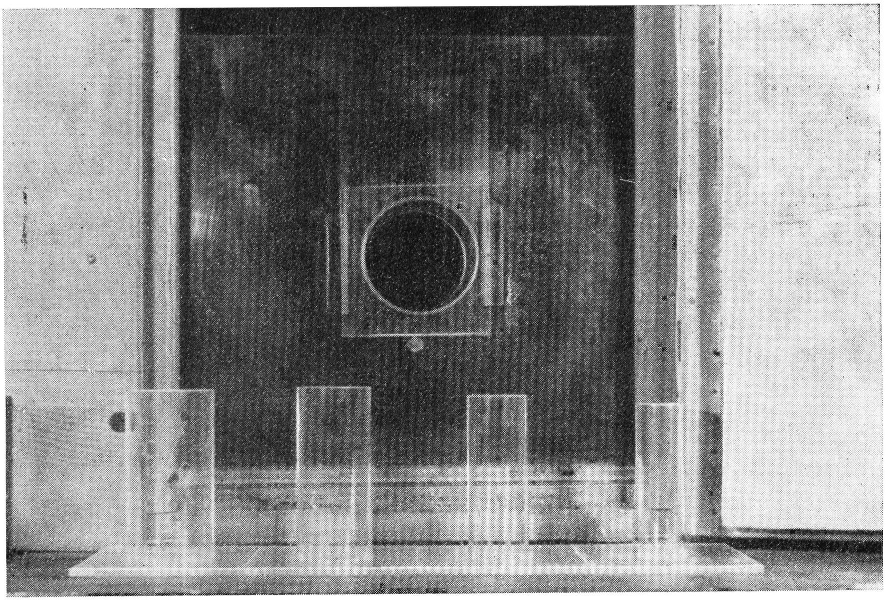

Fig. 1. Photograph of front test chamber showing cylinder 1 in place and the other four cylinders displayed in front of the chamber.

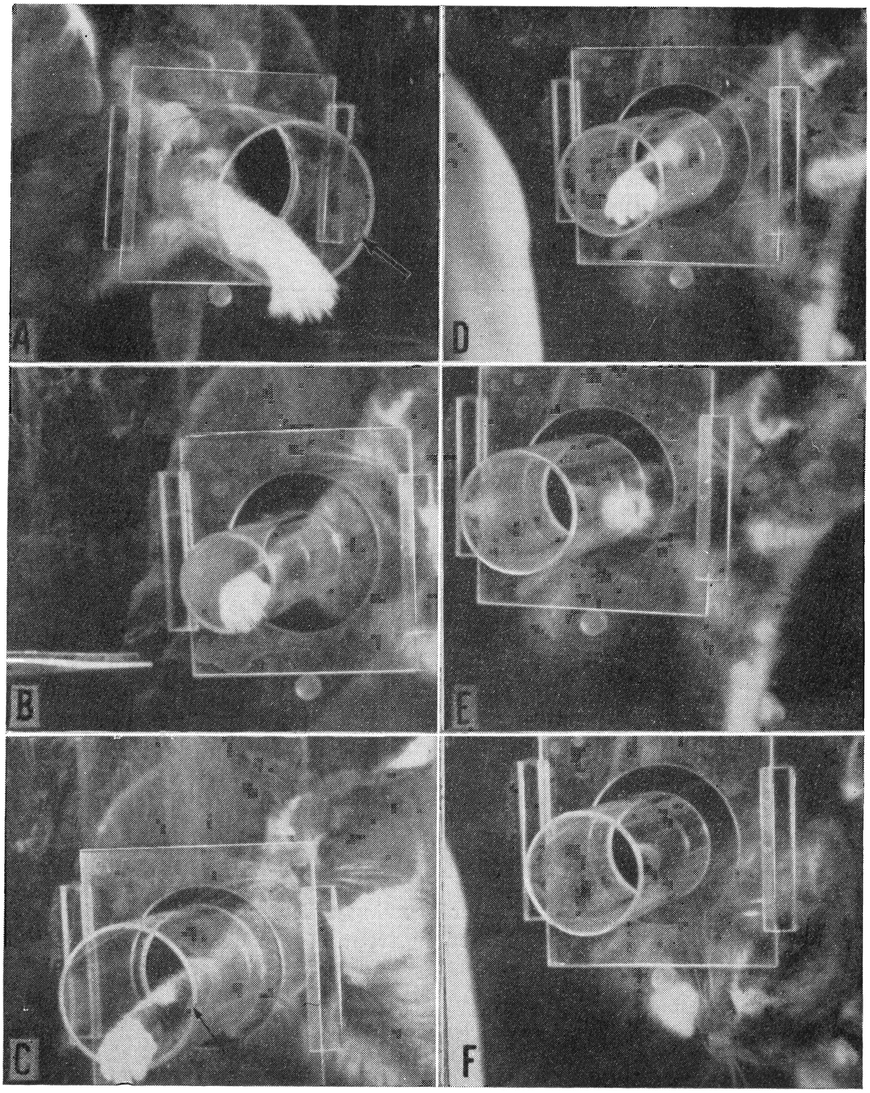

Fig. 2. Frames taken from a movie to illustrate the motor performance of cat IP3, 2 weeks after bilateral interposite nuclear lesions. *A,* overshooting beyond the place of food (arrow); *B,* forced grasping of the far end of the cylinder; *C,* lack of directional movement; *D* and *E,* retrieval of food from cylinder; and *F,* taking food held in foot.

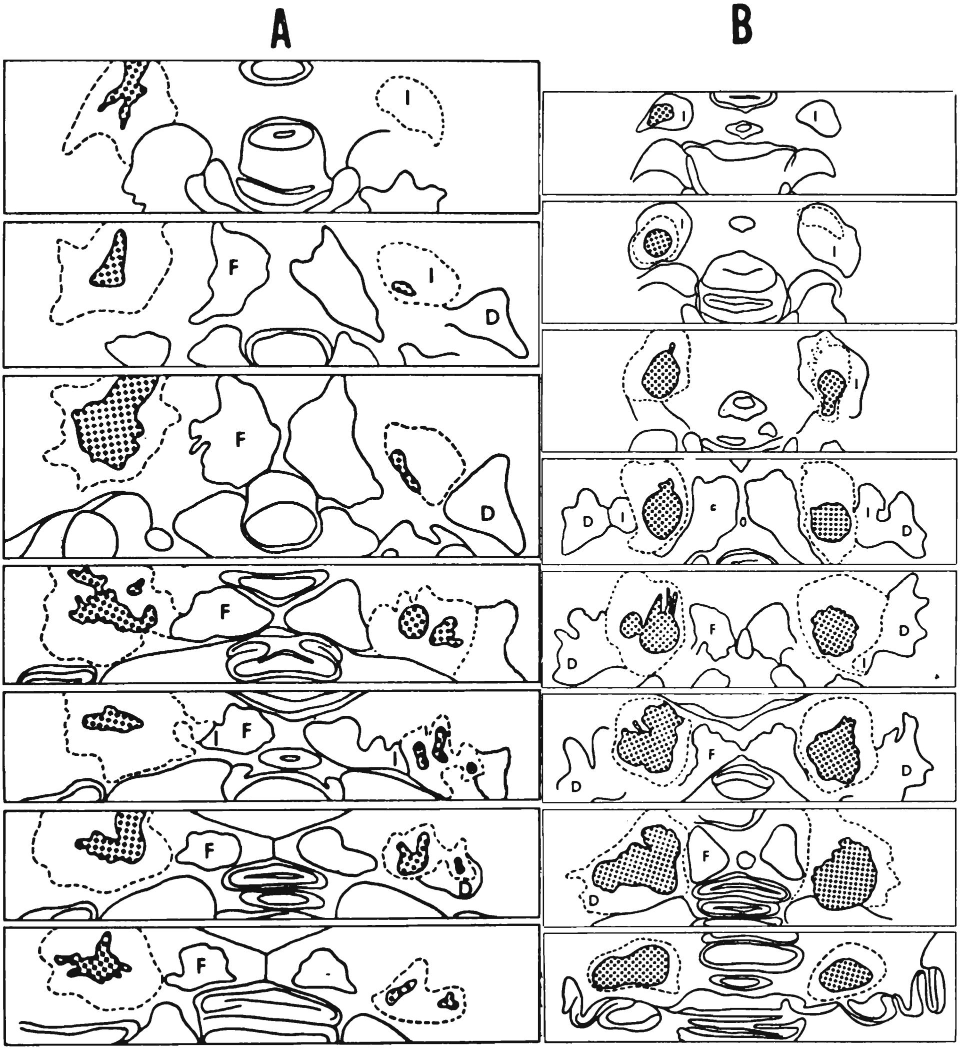

Fig. 3. Projection drawing of the cerebellar nuclear lesion in IP1 (*A*) and IP3 (*B*). Lesion cavity, checkered area; area of gliosis and neuronal destruction, outlined by dashed lines; *D*, dentate nucleus; *F*, fastigial nucleus; *I*, interposite nucleus.

and were performed with ataxia and repeated over and undershooting when the placement was on a narrow bar. These cats were able to stand and walk on the floor by the second or third post-operative day. There was a marked goose step in the forelimbs and circumduction and hyper-protraction of the hindlimbs. Yet the coordination between limbs in the stepping sequence was normal. All of these cats were lethargic during the first week and would not eat until the fifth or sixth day. These cats would turn away from food during this time and expelled food placed in their mouths, unless it was placed at the back of the tongue.

The cats were fit to experiments on fifth or sixth post-operative day, except IP5 and IP6 who sustained more extensive lesions (*see* below) and manifested postural and equilibrating disorders preventing them from regular manipulatory activity.

Already during the first experimental session all the animals had their chain instrumental reflex fully preserved. However, particular segments of this reflex were impaired in particular ways, described below.

Entering the cylinder. This motor act is composed of raising the foreleg and placing it in the entrance of the cylinder. This movement was performed relatively easily when the larger cylinders were used, but was strongly impaired in regard to C4 and C5. Before entering these cylinders the cats made wild oscillatory movements both vertical and horizontal and they banged the wrist against the anterior wall of the box. The poor entering into the cylinder was also due to the inadequate alignment of the animals with its axis.

Reaching for food. The most characteristic feature of this act was overshooting due to overextension of the foreleg till the far end of the cylinder, or even further, irrespectively of where the food was placed (Fig. 2*A*). Quite often the animals used to catch the far edge of the cylinder with claws, and for a few seconds could not get rid of this forced grasping (Fig. 2*B*). In large cylinders the clear impairment of the directional character of the extension movement was observed. If the piece of food was placed on the side of the cylinder, the animal always missed it extending his foreleg forward (Fig. 2*C*).

Grasping food. Although the crude palpation of food was preserved, the paucity of wrist and digital movements was manifest. Usually the cat simply "raked" the food when withdrawing his limb. Withdrawing movement was smooth and rapid (Fig. 2*DE*). The tests with placing the food on the sides of cylinder 2 revealed that inversion of the wrist is impaired and eversion abolished.

Bringing food to the mouth was relatively skillful and no oscillatory movements around the target observed. However, impairment in feeding was seen for the limb was brought into a flexed posture nearer the floor than normal and with the paw less supinated than normal. This posture required the animal to lower and tilt his head in order to take the food (Fig. 2*F*). Frequently, the animal dropped the food from his foot and ate it on the floor.

Gradually some of these disorders were compensated. The animals learned to better align with the cylinder and the oscillatory movements around its entrance became smaller. Accordingly the latency of entering the small cylinder was shortened. However, the main symptom — extension overshooting — was preserved till the end of observation.

Below we present some additional observations concerning particular cats.

Cat IP1 revealed typical disorders of the responses of the left foreleg, whereas the responses of the right foreleg were much better. And the animal preferred to use this limb for instrumental responses.

As shown in Fig. 3*A* these results are in good agreement with anatom-

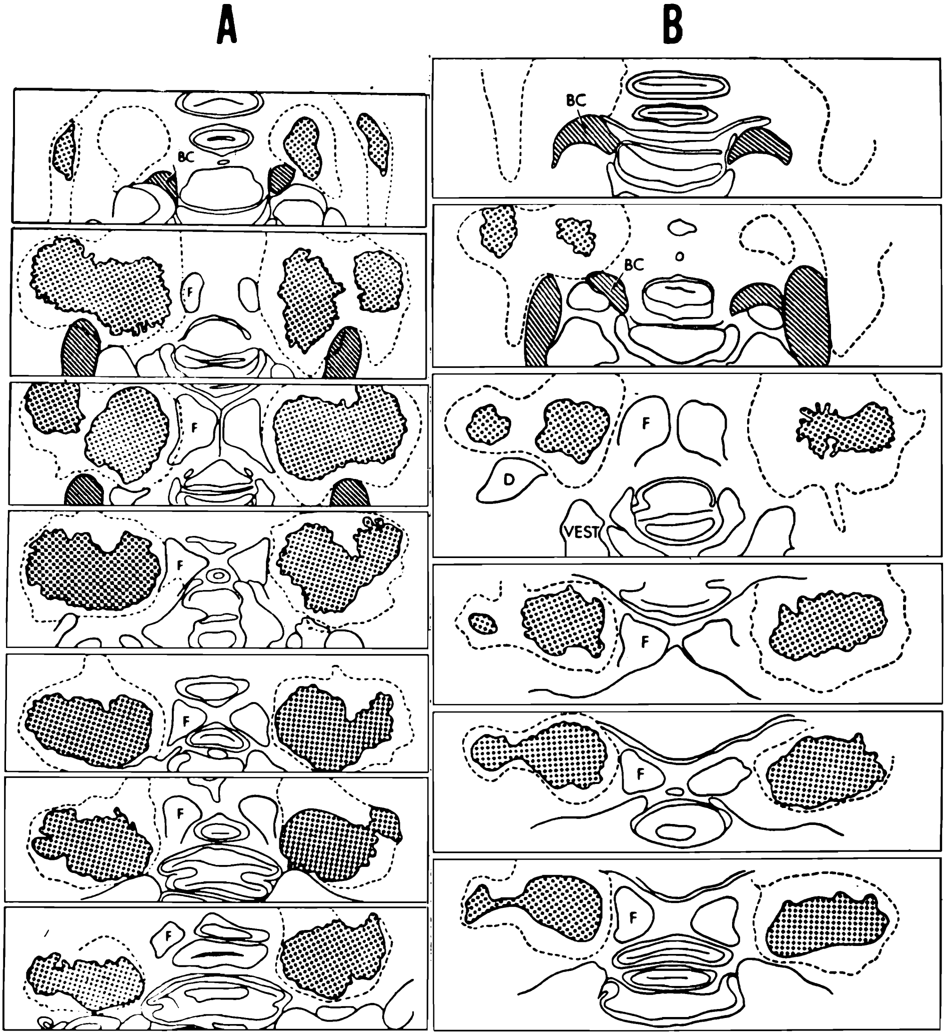

Fig. 4. Projection drawing of cerebellar lesions in IP5 (*A*) and IP6 (*B*). Lesion and cerebellar nuclei are designated the same as for Fig. 3. BC, brachium conjuctivum; VEST, lateral vestibular nucleus.

ical data showing that on the right side the lesion is much less severe than on the left side.

Cats IP2, IP3 and IP4 did not reveal this dissymetry of symptoms. Most prominent symptoms were observed in IP3, in whom anatomical analysis revealed nearly complete bilateral lesion of interposite nuclei with no other nuclei involved (Fig. 3*B*).

Finally cats IP5 and IP6 were subjected to combined lesions of the interposite and dentate nuclei (Fig. 4*AB*). Both cats, particularly IP5, exhibited strong extension of all limbs with frequent bouts of opisthotonus during the first two post-operative days. Proprioceptive placement in these cats showed greater impairment than in the cats with lesions chiefly confined to the interposite nuclei, and after 6 weeks they required joint displacement of from 15 to 45° to elicit placing reactions. Cats IP5 and IP6 were able to right and assume a low crouched posture and make some progression movements by the third post-operative day. These progression movements led to frequent falling to one side or the other, with marked trunkal ataxia; and the limbs were frequently displaced coming to rest in bizzar extended positions (i.e. scissoring, hyperadductions, abduction or retraction). Improvement in posture, equilibrium and gait was more rapid in IP6 than in IP5. IP6 could maintain a fairly stable posture by the 8 day and use his limbs to enter the largest cylinder, while IP5 took 43 days to attain a similar stage of recovery. IP5 and IP6 required forced feeding for 7 days. When they started to feed they had jerky pecking movements of the head when attempting to take food by their mouths. Despite the marked disturbance in posture tone and equilibrium and the severe head ataxia, there was no direct involvement of the fastigal nuclei by the electrolysis and only a slight destruction of the dorsal part of the right lateral vestibular nucleus in cat IP5 (Fig. 4*A*).

Cat IP6 was started in the test chamber on the ninth post-operative day and IP5 on the 43rd day.

In both these cats the deficits in chained instrumental responses were even more pronounced and longlasting than in other cats. It is difficult to say whether this effect was due to the involvement of the dentate nucleus, or rather to the more extensive lesion of the interposite nucleus involving its lateral part.

2. *Paravermal lesions*

Left paravermal cortical lesions were made in cats PV1 (Fig. 6*AB*) and PV2. For a few days after operation these cats, similarly to the IP cats, manifested a poor balance, posture and gait. For 2 days after the operation these animals were unable to stand, both ipsilateral limbs were flexed

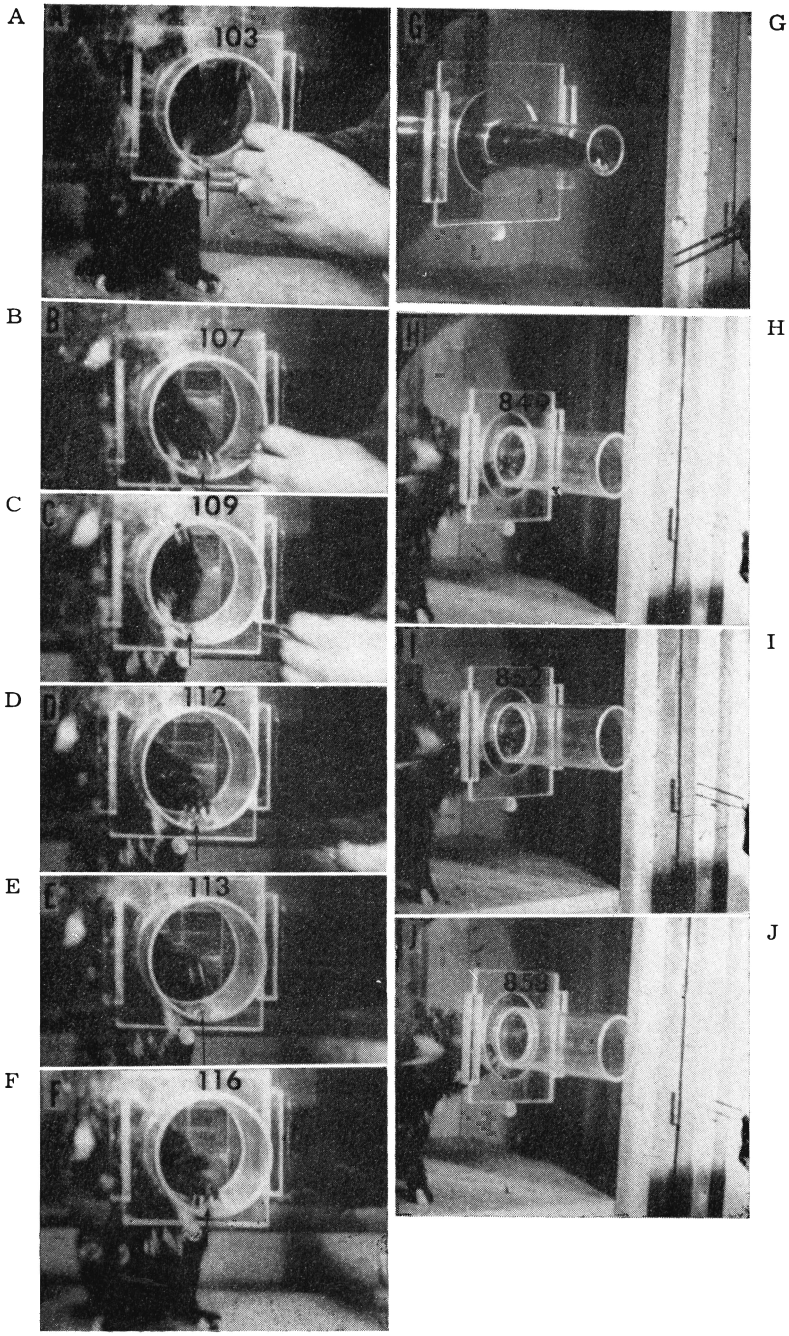

Fig. 5. Frames taken from a movie to illustrate the motor performance of cat PV2, 8 days after left paravermal cortical ablation. *A–F,* repeated hyperflexion and undershooting in a single attempt to retrieve food with the left fore; *G,* full extension of limb in smallest cylinder; *H–J,* retrieving and taking food to mouth. Frames selected for *A–F* and *H–J* are numbered (24 frames/sec); position of food is indicated in *A–F* by arrows; paw position in *C* indicated by asterisk.

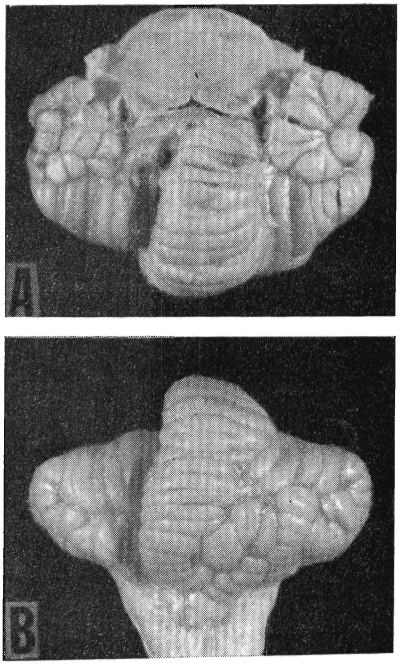

Fig. 6. Photographs showing the paravermal (cortical) lesion in PV1. *A*, anterior view; *B*, dorsal view: Note incomplete lesion of lobulus centralis with some encroachment on its vermal area. Scale: 1 division = 1 mm.

and at times were rhythmically flexed at 1–2/sec. The supporting responses were inadequate to sustain good hopping reactions. Visual placing and vestibular drop responses led to further flexion of the involved forelimb rather than the usual extensor movements elicited pre-operatively and in the contralateral limbs post-operatively. When the animals were able to stand by the third or fourth post-operative day the flexor posture and rhytmicity was reduced but the animal hyperflexed his ipsilateral limbs with each step (salute steps) and on placement of the limbs there was a marked tendency for the limbs to collapse. They also refused to take food for 5 days.

Testing in both cats began on the sixth post-operative day. In spite of the fact that the right forelimbs were in these animals virtually unimpaired, they preferred to respond with the left forelimbs. One reason for this limb preference was the poor supporting response of the left limbs, for example, when the animal tried to lift his right foreleg, he often fell down and could not perform the task.

In the first few days getting into the cylinder with the affected leg was simply impossible because, when lifting the left foreleg to place it in the cylinder, the animal overflexed it in a salute manner, raising it over the ear and head.

By seven days this over-flexion was reduced so that the animals were able to enter the cylinder. The tendency to overflex remained and was clearly seen when the largest cylinder was used. The cat, instead of extending the foreleg in order to reach the food placed on the far end of the cylinder, made wild flexor movements, missing the food a number of times (Fig. 5*A–F*). These marked flexor movements were impossible in the smallest cylinder and therefore the animals reached for food with the limb fully extended in the cylinder (Fig. 5*G*). Palpation movements were better preserved than in the interposite animals.

Although withdrawal of the leg from the cylinder was good, the limb showed an impairment in taking the food to the mouth. The limb was flexed near the chest and the paw supinated and the head was then lowered to take the food (Fig. 5*HIJ*).

After several days the animals performance gradually improved, but the basic symptoms of overflexion in the large cylinder and missing the opening of the small cylinder remained.

DISCUSSION

Earlier studies on the effects of paravermal cortical vs. interposite lesions in the cerebellum have revealed that while the paravermal lesions produce the exaggeration of flexor tonus and flexor reflexes the interposite lesions led to the increase of the extensor tonus and extensor reflexes (Chambers and Sprague 1955*ab*, Sprague and Chambers 1959).

The problem arises as to how these particular disorders of motor activity and muscular tonus influenced the chain instrumental reflex trained in our animals, a reflex composed of several segments involving both flexions and extensions of the forelimbs.

It is clear that essential disorders are in fact closely related to facilitation of extensions in interposite animals and flexions in paravermal animals. Thus, the main symptom of the interposite animals — overshooting of the forelimb during the act of reaching the food — is due to the increased tendency to extend this limb, clearly manifested in the goose step. Another symptom — banging the wrist against the anterior wall of the box during the attempts to enter the small cylinder — is again manifestation of the tendency to extend the limb. On the contrary, such symptoms of the paravermal animals as salute movements and/or vertical oscillations at the attempts to enter the cylinder are manifestations of the hyperflexion tendency. Also the characteristic deficits in movements during the act of reaching food in a large cylinder belongs to the same type of disorders. Whereas in the small cylinder the cat must perform a regular extension of the forelimb to reach food, in the large cylinder he can make first flexion in shoulder lifting the limb upwards and then bringing it down in the direction of the food. The normal cat makes moderate upward movement of the foreleg allowing it to reach correctly the food, whereas the paravermal cat raises the leg very high and drops it haphazardly, failing to touch the food.

On the other hand, we may observe that the antagonistic movements to those facilitated by lesions — flexion in interposite cats and extension in paravermal cats — are much more normal. In fact, flexion movement during withdrawing the leg from the cylinder and bringing the food to the mouth in the interposite animal is practically unimpaired. Similarly, extension of the limb during taking food in the small cylinder is also correct and precise in the paravermal animal, although occasionally the animal fails to reach the far end of the cylinder.

The explanation of these facts is that when the animal has to perform a voluntary movement opposite to the exaggerated tonus of the limb, the cerebral cortex inhibits that tonus and gives way to the proper performance of the suppressed movement. This mechanism is, of course, not in operation when the voluntary movement is allied with the exaggerated tonus and it leads to overshooting in extension and undershooting in flexion.

Finally, we should briefly comment upon those disorders which are common for both lesions. Here belong the deficits of skillful manipulation with the distal parts of the limbs in taking food, in inversion, and particularly in eversion.

In some way these deficits are similar to those encountered after deafferentation of the limb, (Górska and Jankowska 1961) when, also, this limb is not fit for skilled manipulatory movements. Since lesions in both cerebellar cortex and intracerebellar nuclei are the important stations of the transmission of information from the proprioceptive organs to the brain, it may be concluded that this information is of particular importance for skilled movements. This conclusion, however, should be verified in special tests analyzing the movements of wrist and fingers in more detail.

To sum up the conclusion may be reached that the general pattern of the given instrumental task is preserved but its execution is maladaptive because of the lack of inhibitory mechanisms indispensable for the precision and skill of the movements performed.

SUMMARY

1. This paper is concerned with the analysis of disorders of an instrumental conditioned reflex of the forelimb in cat after unilateral paravermal lesions and bilateral interposite lesions. The reflex consisted of entering the horizontal cylinders of various diameters with the forelimb, grasping a piece of food placed in the cylinder, withdrawing the limb and bringing it to the mouth.

2. Raising the foreleg for entering a cylinder (in particular the small one) is characterized by big oscillations around the entrance in the interposite cats with banging against the wall of the box. In paravermal cats the difficulty in this stage of the instrumental reflex consists in overflexion leading to a "salute" response and missing the entrance of the cylinder.

3. Reaching for food leads in interposite cats to overshooting with occasional forced grasping the edge of the cylinder; directional aspect of the movement is impaired. In paravermal cats the extension movement in a small cylinder is virtually normal, but in the large cylinder the wild batting movements are observed.

4. Withdrawing of the limb after reaching the food is normal after both lesions. Bringing the food by the paw to the mouth is more impaired in interposite animals.

5. Movements of the wrist and fingers are impaired after both lesions, but the disorder is greater after interposite lesions. Palpation of food is present, but it is more crude in interposite cats. Retrieval of the food in these animals has a crude, raking character.

6. The physiological mechanism of these disorders is discussed in view of the role of cerebellum in controlling the motor activity. It is stressed that although the general program of the instrumental task is preserved, the precision and skill of the particular movements are impaired in different way after interposite and paravermal lesions.

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