EXPERIMENTAL STUDIES ON FRONTAL LOBE FUNCTIONS IN MONKEYS IN RELATION TO LEUCOTOMY.*

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Introduction.

Prefrontal leucotomy as an operative method of treatment for mental disease greatly stimulated research into the functions of the frontal lobes. The operation was a direct result of the observation of Fulton and Jacobsen (1935) that rage reactions seen in monkeys in the course of increasingly difficult experimental tasks do not occur after extirpation of the frontal lobes.

Most investigations on behavioural changes in animals are based on material where the whole prefrontal cortex was extirpated. Fulton (1943) states that after such extirpation monkeys and chimpanzees are more restless and distractible, exhibit a fatuous equanimity of spirit, their capacity for recall is impaired and their reactions are largely influenced by immediate sensory experiences. The animals are described as "living in a perpetual present." Bard and Mountcastle (1948) were able to produce a state of apathy in cats by bilateral removal of the frontal areas. They point out that for the production of this state it is necessary to spare certain areas of the orbital cortex and rhinencephalic structures near this region. Similar changes are not found after removal of other cortical areas, Jacobsen and Elder (1936).

Our knowledge of the functions of the different areas of the prefrontal cortex is still incomplete. Ruch and Shenkin (1943) showed that the hypermotility previously reported after bilateral frontal lobectomy occurs only when area 13 is injured. Richter and Hines (1938) and Mettler (1945) believe, however, that hyperactivity occurs only when the prefrontal cortex lesions are combined with damage to the striatum. Meyer and McLardy (1948) found that cases with striatal and without orbital damage showed the same incidence of restlessness. Fulton, Livingston and Davies (1947) indicate that fibres projecting to area 13 pass through the caudate nucleus, which might explain this phenomenon.

Prefrontal leucotomy, as carried out in man, is a blind operation and the lesions, therefore, can be much less precisely located than in previous experimental studies. Most techniques, such as that of Freeman and Watts (1942),

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lead to extensive separation of the prefrontal cortex from lower structures. More limited lesions were suggested by Dax and Radley Smith (1943) and others. Their experience taught them to avoid lower and posterior cuts in very excited and restless patients. The first object of the present investigation was an attempt to show any possible correlation between the type of cut and the resulting behavioural changes.

The present state of our knowledge of the anatomy of the prefrontal cortex and its connections was recently reviewed by Le Gros Clark (1948). He states that the prefrontal lobes should be regarded, not as association areas, but primarily as afferent projection areas. Le Gros Clark and Boggon (1933) had already observed after experimental studies that a large part of the frontal lobe is a projection area for the dorsomedial nucleus (D.M.N.) of the thalamus. Meyer and McLardy (1947) and Freeman and Watts (1947) showed that the areas of the prefrontal cortex are connected with certain sub-divisions of the D.M.N. in the thalamus. The central part of the D.M.N. was found to be connected with the frontal pole, the lateral portion with the convexity, and the medial portion with the orbital surface.

The second object of our investigations was to discover whether the same behavioural changes result from lesions of the D.M.N. as result from lesions of the prefrontal lobe.

Material and Methods.

Monkeys of the Rhesus macaque type were used for all experiments. Anaesthesia was carried out with Nembutal 0·6 mg. per kilo body weight. A large exposure was always performed by a frontal osteoplastic flap. After removal of the dura, the motor area was located by electrical stimulation in each case.

The leucotomies were performed with a blunt leucotome penetrating the cortex at the posterior and lower end of the sulcus rectus in front of the sulcus arcuatus, that is to say, at the rostral border of area 8. There were three types of subcortical leucotomy :—

1. A complete leucotomy in the coronal plane to a depth of 1·5 to 2 cm., covering the whole area of the frontal lobe. (See Fig. 1) (M.Th.L. 9, 13.)

2. A leucotomy in the horizontal plane. (See Fig. 2) (M.Th.L. 11.)

3. A leucotomy of only the lower orbital part in the coronal plane. (See Fig. 3) (M.Th.L. 12.)

4. A leucotomy in the coronal plane further posterior (M.D.M.2).

5. For attempted lesions of the thalamus, the Souttar-Beattie stereotaxic instrument was employed (M.D.M.1, M.D.M. 3, 4). The instrument consists of a suitable length of hypodermic needle tubing of diameter 1½ mm. in which is concealed a spring-loaded steel knife. When the needle has been inserted to the required depth the spring-loaded steel knife is pushed out and the centre point of the knife can be moved laterally. In the present experiments the knife was pushed in at right-angles to the Rolandic fissure to a total depth of 2·5 cm. ; when right in the knife was rotated. The cortex was gently withdrawn from the midline to allow insertion of the knife about 2 mm. from the midline. This was repeated on the other side. (Glees, Wall and Bright, 1947.)

6. A bilateral thalamic lesion by surgical exposure of the thalamus.

M.Th.L.10.—In this monkey an attempt was made to make an extensive lesion of the medial region of the thalamus by direct exposure. The corpus callosum was opened and the motor area identified by electrical stimulation. Finally, the medial portions of the thalamus were destroyed by suction.

The animal unfortunately died after 24 hours without recovering consciousness.

This was the only attempt to cause a thalamic lesion by visual control. The difficulties of this extensive surgical approach are too great to follow up the effects of chronic lesions necessary for this study.

The neuro-histological investigation of the brains was carried out by using the Marchi technique (Swank-Davenport modification), the Nissl stain for retrograde cell changes, and the Heidenhain technique for normal myelinated nerve fibres. The Marchi (Swank-Davenport modification) proved of great use, not only for following degenerating fibre tracts, but also for observing retrograde cell changes. (Glees, 1947).

In each animal behavioural changes were recorded and special psychological tests were given to some animals. Delayed reaction tests were made on the four monkeys: M.Th.L.13, M.D.M.1 and M.D.M.2; in M.D.M.3 tests were started only after the operation, while in the other three cases a measure of "immediate memory span" was made before and after the operation. The test consisted simply in placing food under one of three identical mugs within view of the subject, lowering a screen for varying periods of time, then noting which mug the monkey lifted when the screen was raised. In working out the results, a correction was made for chance right solutions, then a "limen of immediate memory" calculated, representing the period of time after which 50 per cent. correct responses would be made. The value varied from day to day for individual monkeys, also; immediate-memory span appeared to be twice as good when the bait was ripe pear instead of apple. These tests could, unfortunately, not be given to every operated animal and only tentative conclusions can therefore be drawn.

Results.

Complete Bilateral Leucotomy in Coronal Plane. M.Th.L.9 (Fig. 1).

(*a*) *Behavioural Changes.*—For the first experiment a very aggressive female monkey was used. She had to be separated from the others because of continual fighting.

On the day following the operation, her behaviour was markedly changed; the animal was very quiet and inactive, allowed herself to be touched, and took sugar from the observer's hand; there was some piloerection along the trunk. Eye movements were preserved. The animal continued to be indifferent and inactive on the following day. She made frequent circling movements in both directions; the left hand was not used at all and appeared definitely weaker. Eight days later she was still apathetic. When the cage was tapped the animal turned her head slowly and showed no fear reaction. She was taken out on lead and made no attempt to escape. Ten days after the operation the monkey was still very apathetic, although on one occasion she chased a cat. As time went on the animal gradually became more active, and reacted more to her environment, but continued to show much less fear than before the leucotomy. The animal was killed 77 days after the operation.

(*b*) *Neuro-histological Findings.*—Although a complete leucotomy was attempted, it was found from sections in a more posterior plane that the orbital surfaces were less involved than had been expected.

A considerable loss of cells was found on both sides in the dorso-medial nucleus of the thalamus. However, the degeneration of cells in the thalamus was limited mainly to the lateral portion of the D.M.N. (c.f. M.Th.11). As the injury of the dorsal portions of the frontal lobes had extended back into the motor area, through post-operative necrosis, both pyramidal tracts showed Marchi degeneration in the spinal cord, more concentrated on the left than on the right. The involvement of the motor area explains the slight degeneration which is observable in the nucleus ventralis lateralis.

Complete Bilateral Leucotomy in Coronal Plane. M.Th.L13 (Fig. 1).

(*a*) *Behavioural Changes.*—Before the operation this monkey was very nervous ; when stared at he would make exaggerated ear, scalp and lip movements, with continued mouth gaping, and jerky movements of the whole body about once a second ; this pattern of behaviour might last several minutes before gradually disappearing. It was a highly exaggerated form of the startle reaction seen in most rhesus monkeys. Twelve days before the operation the monkey escaped, and subsequently developed a "neurotic" tendency to avoid the front of the cage. If offered food from the front, his behaviour appeared typical of an approach-avoidance conflict, resulting in vacillation.

Immediately after the operation the animal was slow (but with no obvious motor impairments), tame and gentle. There were no jerky mouth, eye or body movements. On the whole the animal showed eagerness when being experimented on, but there were sudden losses of interest, of increasing frequency. After four weeks the animal was gentle and unexcited, but occasionally made sudden "irritable" snatches at the experimental apparatus. At this time, walking in circles (mostly clockwise), which had been seen frequently just after the operation, was seen only occasionally.

After five weeks there was a sudden increase in excitability and activity, including a backward and forward dash every two seconds. After six weeks, just before the animal was killed, excitability and fear reactions were nearly back to the pre-operative level, with occasional mouth-gaping, but without the specific jerky movements. The "phobic" attitude to the front of the cage did not return.

At three weeks after the operation there had been a measurable "immediate memory span," but this was lost after a week, largely through the tendency to perseverate on one response. (See Discussion.)

(*b*) *Neuro-histological Findings.*—The lesion involved, on the left side : the corpus callosum, caudate nucleus, anterior limb of internal capsule and putamen ; on the right side the damage to the corpus striatum was only slight. The lesion reached the orbital cortex. The dorso-medial nucleus of the thalamus

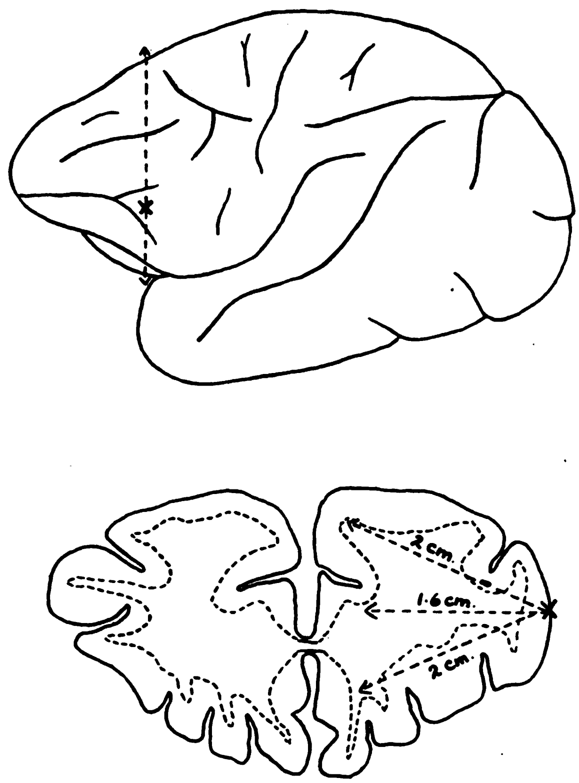

FIG. 1.—A diagrammatic representation of the plane of leucotomy and depth of incision in the monkeys M.Th.L.9 and 13.

in both sides showed gross signs of nerve cell degeneration in its medial and lateral parts and the beginnings of proliferation of glia cells. Cell changes were found also in the N. ventralis anterior and in the antero-medial nucleus.

Leucotomy in the Horizontal Plane. M.Th.L.11 (Fig. 2).

(*a*) *Behavioural Changes.*—A rather apprehensive female animal was selected for operation. On the day following the operation the animal was hyperactive, and restless, walking up and down the cage. When it passed the gate it grasped it and jumped up and down. The behaviour seemed somewhat stereotyped; the animal over-reacted to external stimuli. Three days after the operation the animal continued to show this hyperactivity together with piloerection.

After about 16 days the hyperactivity had more or less subsided and the monkey continued to be much quieter until it had to be killed 68 days after the operation, because an oedema had developed from the waist downwards. Post mortem examination showed a severe interstitial hepatitis with destruction of the liver parenchyma.

(*b*) *Neuro-histological Findings.*—The sections of the frontal lobes showed that it was mainly the fibres to and from the dorsal aspects of the frontal cortex which had been severed, while the connections of the orbital cortex were not interrupted. Sections of the thalamus stained with the Nissl method

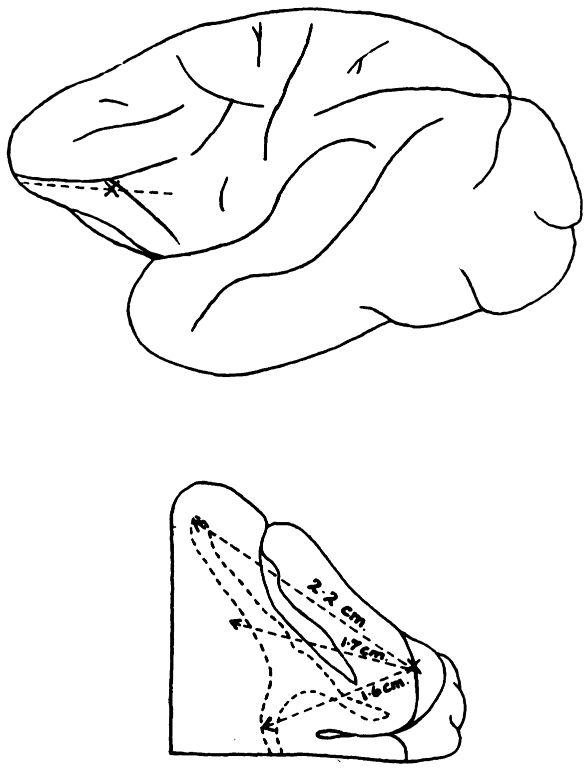

Fig. 2.—Plane of leucotomy and depth of incision in M.Th.L. 11.

revealed that the lateral portions of the D.M.N. had undergone retrograde changes.

Bilateral Leucotomy. M.Th.L.12. (Fig. 3.) Lesion of the lower orbital part in the coronal plane.

(*a*) *Behavioural Changes.*—A male monkey was used for this operation. On the day following the operation the animal appeared lively and alert. It showed some hyperactivity with continuous circling movements clockwise and anti-clockwise. This became even more marked three days later. The hyperactivity with circling remained present throughout the period of observation; it did, however, gradually become less marked. The animal always remained fearful and alert, and was killed 83 days after the operation.

(*b*) *Neuro-histological Findings.*—The degeneration of fibres and cells in the Marchi preparations was very well marked in this monkey and retrograde degeneration could be clearly followed.

Sections of the frontal lobe showed that the lesion involved the orbital part of the frontal lobes, and also the genu and anterior limb of the internal capsule, so that fibres other than those coming from the frontal lobe were intercepted; damage to the anterior portions of the striatum on the left side was observed.

The fibres from the frontal lobe enter the D.M. nucleus by passing through the thalamus, leaving the internal capsule at the level of the genu to enter the thalamus.

Marchi material of the thalamus showed degenerating cells in the anterior portion of the dorso-medial nucleus, the pars magnocellularis or medial part being most heavily affected. (These cells show up because of the fatty

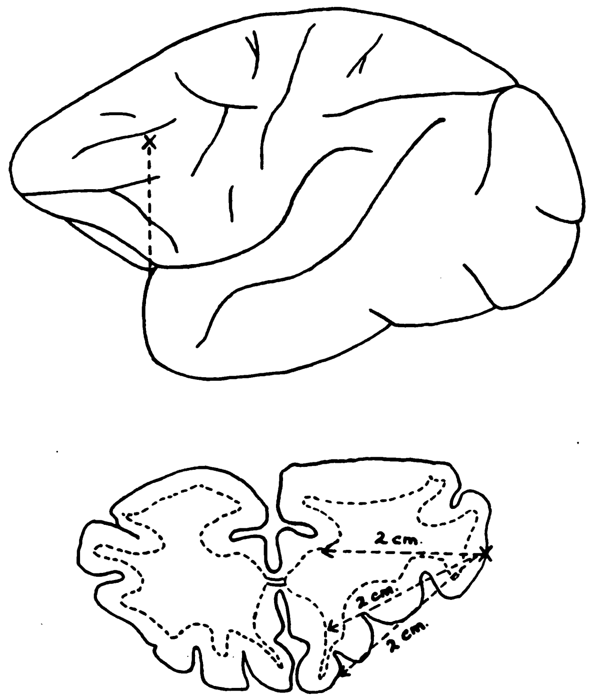

FIG. 3.—Plane of leucotomy and depth of incision in M.Th.L. 12.

degeneration which is Marchi positive.) As the internal capsule was damaged, degeneration in various other fields was seen, namely in the middle peduncle, the A.V. nucleus of the thalamus and in Forel's field. Fibres were also seen tracking towards the centre median nucleus of the thalamus on the right side.

Posterior Leucotomy in the Coronal Plane. M.D.M.2.

A bilateral lesion of the medial nuclei of the thalamus was attempted but histological examination showed that the lesions were mainly anterior to the thalamus and because of this the case is grouped under bilateral leucotomy, the type of injury being similar to a very posterior leucotomy.

(*a*) *Behavioural Changes.*—Before the operation this female rhesus was very tame, gentle and co-operative, compared with the majority of the monkeys reported here, none of whom were given time to become acclimatised to rigorous experimental treatment. She was not easily distractible, but occasionally lost interest.

After the operation, for the first five weeks, she was even less distractible, showed great eagerness in all experiments, attempting to manipulate the apparatus herself. Towards the end of this period she showed frequent violent

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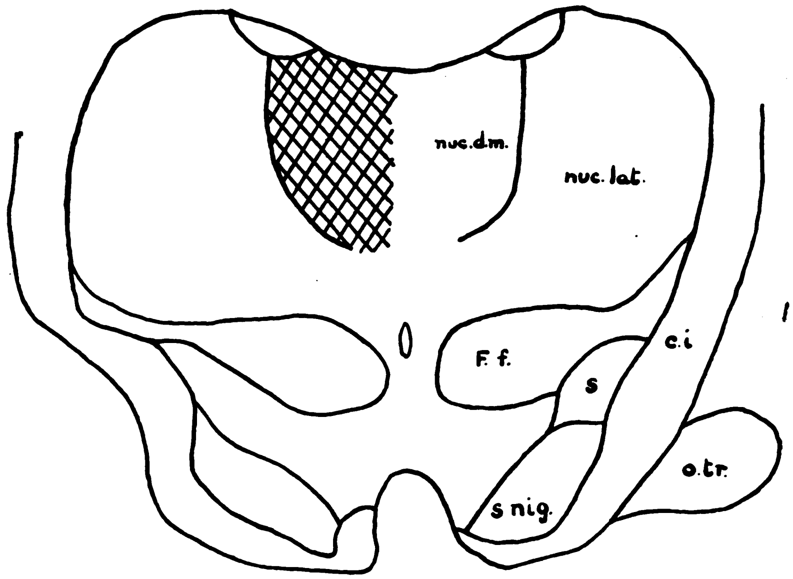

FIG. 4.—Diagrammatic representation of the unilateral lesion of the dorso-medial nucleus in M.D.M. 1.

agitations, and in the experimental situation was "too eager to stop and think." She was highly excited by novel stimuli.

After five weeks there was a sudden change. She reverted to very gentle and tame behaviour, but became more distractible in experiments than previously. She was killed at six weeks.

(*b*) *Neuro-histological Findings*.—Many of the sections were studied successfully using Heidenhain's myelin stain. The right lesion extended more posteriorly than the left. Knife damage was seen in both sides of the corpus callosum, reaching the hypothalamic region on the right by cutting between the anterior nucleus and the nucleus ventralis anterior, damaging the mammillo-thalamic tract and entering the right paraventricular region. On the left the internal capsule, the globus pallidus and the left anterior nucleus were damaged. Both medial portions of the dorso-medial nucleus were heavily degenerated, particularly on the right side of the ventro-medial portion. This may have been partly due to connections with the damaged paraventricular region of the hypothalamus.

This lesion could be classed as a very posterior leucotomy since it severed fibres connecting the frontal lobe and the dorso-medial nucleus of the thalamus (shown by heavy degeneration in the latter).

Attempted Lesions on the Thalamus.—Four monkeys were used for these experiments (M.D.M. 1, 2, 3 and 4) but owing to severe haemorrhage into the third ventricle positive results were not obtained from M.D.M.4, which died six days after the operation, while the lesion in M.D.M.2 proved to be too far anterior, and this case has been classed elsewhere.

*M.D.M.*1 (Fig. 4). (*a*) *Behavioural Changes*.—Before the operation, this male rhesus was rather more timid and jumpy than the average. He would never accept food from strangers.

Immediately after the operation he appeared tamer, but at the end of a week he was showing signs of a returning timidity at taking food from outside the cage. He became more distractible, and would suddenly lose interest in a food-reward experiment (even when very hungry), jumping around the cage and vocalising. In general the animal remained fairly tame but there were occasional spontaneous outbursts of motor activity, and, in particular, sudden snatches and biting at the experimental equipment, especially when waiting, or after making an incorrect response to a test. He frequently gave the appearance of "not stopping to think" in choice-reaction experiments. This sort of behaviour persisted until 25 days after the operation, when the animal was killed.

(*b*) *Neuro-histological Findings.*—A well marked lesion was found in the medial portion of the left dorso-medial nucleus, from which fibres were seen passing through the lateral nucleus to the internal capsule, via the anterior medullary lamina.

The lesion involved the left fornix and this degeneration could be followed into the hypothalamus; the posterior commissure and habenular commissure were cut and there was marked degeneration of heavily myelinated fibres descending into the pons. The corpus callosum, supra-optic commissure, cerebral peduncles and gyrus cinguli showed degeneration, probably through direct injury in the latter. There was further degeneration showing one bundle of the mammillo-thalamic tract entering the medial nucleus in the centre, the other bundle forming the capsule. There was incidental degeneration in the stria of Lancisi and fibre degeneration of a coarse nature in the septal cortex, corresponding to the coarse degeneration seen in a caudal section at fornix level.

M.D.M.3 (*a*) *Behavioural Changes.*—Before the operation this male rhesus was co-operative and lively, and would frequently "steal" food from an observer. Occasionally he became distractible, and his reactions to an observer saring at him were similar to those of M.Th.L.13—mouth gaping, jerky movements and vocalising. At one time a female monkey in the next cage died, and he became subdued for a fortnight, after which the old liveliness returned.

Immediately after the operation he was lively and tamer, but two days after the operation a paralysis developed. At this stage he would go out of his way to be stroked, responding sexually. He made no overt responses to painful stimuli. Twelve days after the operation, the monkey appeared to have recovered, and his general behaviour was indistinguishable from that pre-operatively, except that changes of mood were more sudden, and that he was rather more distractible.

(*b*) *Neuro-histological Findings.*—The lesions made in this monkey were unfortunately too far posterior, in spite of the use of an elaborate technique. The misplacement was probably due to excessive forward tilting of the head resulting in the lesion being placed just above and anterior to the posterior commissure on the left and in the medial portion of the pulvinar on the right. There was much operational damage in the parietal cortex. The needle tracts could be seen clearly on both sides and there were obvious lesions in the fornix and corpus callosum. A large number of cortico-pontine and cortico-spinal fibres degenerated, traceable in the internal capsule and in the region of the pons.

Within the thalamus the nuclei showing degeneration were the pulvinar, Forel's Field, and the n. ventralis lateralis; also several commissures showed clear fibre degeneration; the posterior commissure, the intercollicular commissure and the inter-thalamic commissure. An interesting fibre degeneration was seen in the hippocampus; such degeneration results from both frontal and angulate lesions. Particularly large fibres could be seen in the fasciculus thalamicus, passing into Forel's Field and from there reaching the posterior part of the hypothalamus. Owing to damage in the fornix, degeneration was found in the two mammillary bodies.

*M.D.M.*4.—Male rhesus. As the post-mortem examination showed that, apart from the ventricular haemorrhage, the operational procedure to produce a bilateral thalamic lesion was successful, a more detailed account of the operation will be given.

A rectangular bone flap was turned and the dura on both sides turned back to the mid-line. On either side four veins entering the superior sagittal sulcus were coagulated. After identifying the motor cortex the rotating knife was inserted on the left side 3 mm. in front of the central sulcus and the lesion effected. A similar procedure was used on the right side. The knife was moved further frontally after the first and second lesions and additional lesions on either side 5 mm. in front of the central sulcus were made. Unfortunately, after the fourth lesion a vessel of the choroid plexus of the third ventricle was cut, causing the interventricular haemorrhage.

The effects of the lesions and the haemorrhage proved to be so severe that the animal was killed after six days as he was unable to feed himself and had great difficulty in breathing.

When the brain was sliced extensive bilateral damage to both anterior and medial nuclei was found, so from this point of view the lesions were successful. Further attempts at using this procedure could not be made because of lack of material.

Psychological Test Results.

M.D.M.1 (Thalamotomy, extensive lesion of left D.M.N.) had a measurable memory-span 15 days after operation, but this disappeared by the 20th day; M.Th.L.13 (complete bilateral leucotomy) had a measurable span at 21 days after the operation (of the same order as the pre-operational span), but this had disappeared by the 35th day; M.D.M.2 (posterior leucotomy) had a measurable span at 15 days after the operation (of the same order again as the pre-operational span), and in this case the subject continued successfully to solve this test until its death. M.D.M.3 (no thalamic nor prefrontal lobe damage) had a measurable memory span of a pre-operational order from 13 days after this operation until observation ceased four weeks later.

It is difficult to point to anything in the neuro-histological findings in M.D.M.2 which might parallel this differentiation in behaviour from M.Th.L.13 and M.D.M.1, except that only the medial parts of the D.M.N. were unequally

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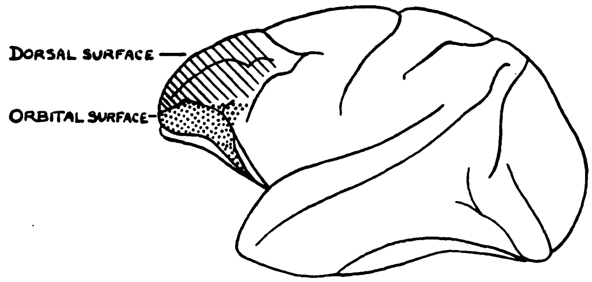

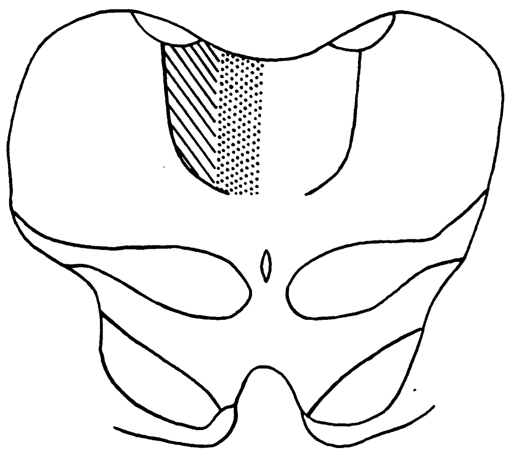

FIG. 5.—A composite diagram to illustrate the projection of the dorso-medial nucleus onto the dorsal and orbital surface of the frontal lobe.

involved in M.D.M.2. In the subject M.D.M.3 there was no involvement of frontal areas and no degeneration of the D.M.N.

The final deterioration of performance of M.D.M.1 and M.Th.L.13, and the occasional deterioration of M.D.M.2 all took the form of the persistent taking of one mug, despite continued lack of reward; in the cases of M.D.M.2 and M.Th.L.13, it was a mug for which preference had been shown also before operation, and the preference did not appear to depend on handedness. Before the operation M.D.M.3 tended to perseverate on the right-hand mug. After the operation this was the one mug he tended to avoid.

These results indicate that:—

1. The inability after leucotomy or thalamotomy to perform delayed-reaction tests may not result directly from damage caused by the knife, but may depend more on subsequent degeneration.

2. A tendency to perseverative or stereotyped responses may be particularly characteristic of this period of deterioration.

Histological Findings.

See Fig. 5. They confirm previous observations by Le Gros Clark, Walker, Meyer, McLardy, and others.

Comments.

Behavioural Changes.

(*a*) *Following Leucotomies.*

The maximum taming effect was achieved by a complete leucotomy in the coronal plane (M.Th.L.9) where the neuro-histological findings revealed that the orbital surface had been spared and only the lateral portion of the D.M.N. was found to be degenerated.

In the second, complete leucotomy (M.Th.L.13) taming was also marked, though less pronounced than in M.Th.L.9. Histological examination in this monkey revealed an encroachment of the lesions towards the orbital surface and a more complete degeneration of the D.M.N.

In the horizontal leucotomy motor hyperactivity followed for only two weeks after the operation, the histological study showed that the connections from the orbital surface had not been interrupted and only the lateral portions of the D.M.N. had degenerated. Following the bilateral leucotomy (M.Th.L.12) involving the lower orbital part of the prefrontal lobe motor hyperactivity was more marked and persistent. With damage to the orbital part of the frontal lobes the medial portion of the D.M.N. especially the pars magnocellularis was severely degenerated. Behavioural changes followed the posterior leucotomy (M.D.M.2) were less definite, in spite of a certain amount of hyperactivity alternating with gentle and tame behaviour. Here both medial portions of the D.M.N. were heavily degenerated, particularly on the right side.

(*b*) *Following Thalamotomy.*

After an extensive lesion of the left dorso-medial nucleus (M.D.M.1) the animal was persistently less active, especially marked during the first week following the operation, but occasional outbursts of motor hyperactivity occurred. In M.D.M.3, where the dorso-medial nucleus remained undamaged, the behaviour was indistinguishable from that shown pre-operatively already 12 days after the operation.

(*c*) *Other Observations.*

Most animals showed a tendency to revert to pre-operational personality at from two to five weeks after the operation. The marked exception to this was M.Th.L.9. This monkey was the only one to be taken out of its cage and led about.

The three animals observed in detail (M.D.M.1, 2, M.Th.L.13) all developed certain tendencies at about the third week after operation ; these were (1) an " eager " attitude towards the tests, and the appearance of " not stopping to think." (2) Periodic outbursts of aggressive behaviour, usually directed at the experimental apparatus, and often occurring when the experimenter assumed the animal to be in a state of tension or suspense. (Not seen in M.D.M.3.)

There was some indication that these conditions became modified in time ; however, none of these subjects was kept longer than 45 days after operation, and further modifications might have occurred.

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Discussion and Conclusions.

In view of the fact that there were usually multiple lesions, only limited generalisations can be made.

The most marked state of apathy or taming having resulted from a complete leucotomy in the coronal plane where the orbital surface was spared confirms the results of Bard and Mountcastle (1947) in cats. Increased motor activity and aggressive behaviour following leucotomy was most marked when the orbital surface was involved in the lesion (thus confirming the work of Ruch and Shenkin on area 13), or when the medial parts of the thalamus, being the relay station of the orbital surface, were damaged in thalamotomy.

The psychological test results seem to indicate that the deterioration in memory span is dependent on the amount of white matter cut or the extent of the thalamic lesion. It was most marked following a complete leucotomy and absent where no involvement of the frontal areas and no degeneration of the D.M.N. was present. This confirms the view of Meyer and McLardy (1949) that there is a certain relationship between the degree of personality changes and the amount of prefrontal cortex cut. Whether it is of significance that deterioration was less marked when only the medial parts of the D.M.N. were involved as compared with the lateral ones remains to be confirmed.

The observation that deterioration in memory span and other behavioural changes like perseveration and stereotypies, tended to occur about three weeks following the operation may indicate that these changes do not result directly from damage by the knife but may depend on subsequent degeneration. Harlow et al. (1948) have reported a perseveration of a different kind following leucotomy. The observation that there is the same delay after leucotomy as after thalamotomy may suggest the prefrontal cortex or diencephalic structures as the seat of the degeneration necessary to produce these changes.

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