THE TERMINATION OF ASCENDING TRACTS IN THE THALAMUS OF THE MACAQUE MONKEY

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It is well known that a large part of the elaborate cerebral cortex of the mammalian brain is concerned with the reception and interpretation of sensory impulses which are relayed to it by the thalamus. The progressive evolution of this cortical structure has formed the main theme of many classical studies by Sir Grafton Elliot Smith, and so far back as the beginning of this century(8) he designated it by the term "neopallium", a term which has now passed into the common language of neurologists. In his Arris and Gale Lectures in 1910(9), Sir Grafton[1] summarized the implications of his earlier researches, and showed how the original mapping out of the neopallium into different morphological and functional areas was determined primarily by the topographical arrangement of the various thalamic nuclei which gave rise to cortical projection fibres. The present problem forms part of a general enquiry into the relation of the thalamus to the cortex in the Primates. In some recent papers(4, 5, 18) the precise arrangement of various thalamo-cortical projection systems has been studied in the macaque monkey by defining the cell atrophy in the thalamic nuclei which follows local cortical ablations. It has now become necessary to determine the source of the afferent fibres which reach these nuclear elements from lower functional levels, with the object of analysing the nature of the impulses which are relayed by them to the neopallial cortex. In the present study, attention has been directed to the precise locus of termination of various ascending tracts from the spinal cord and the brain stem in regard to different nuclei of the thalamus. This question has been partially discussed in the case of lower mammals by Probst(13), Wallenberg(19, 20), Cajal(2), Ranson & Ingram(14), etc., and to a limited extent in the monkey by Vogt(15). In making use of the Marchi method for the study of this problem it may be mentioned that the limitations of this technique are fully realized. Nevertheless it is desirable to ascertain what information it can provide even if some of the conclusions to which it leads may require to be corroborated by other experimental methods.

[1] The stimulus provided by this eminent anatomist in his work as an original investigator, as a teacher, and as an exponent of the problems of Primate evolution, has been justly recognized as a potent factor in the development of neurological anatomy in this country. It would be difficult for the present writer to express how much he owes to this stimulus—it is sufficient to say that he derived the original inspiration for his enquiries into anatomical problems from the lectures and writings of Sir Grafton Elliot Smith, and that he feels it to be a signal honour to contribute to this dedication volume of the *Journal of Anatomy*.

MATERIAL AND METHODS

The ordinary macaque monkey, *Macaca mulatta*, was used for the experimental lesions. The observations recorded here are based on eight experiments, in some of which lesions were made on either side involving different afferent elements. The lesions were distributed over the spinal cord, the medulla, and the mid-brain. The animals were anaesthetized by an intraperitoneal injection of sodium ethyl barbiturate (nembutal), using 0·7 c.c. of a 5 per cent solution per kg. of body weight. Following the operations, the animals were allowed to survive for approximately 12–14 days. They were killed by chloroform anaesthesia followed by an injection through the aorta of 10 per cent formol saline. After 2 hours the brain was removed and cut into slices 2 or 3 mm. in thickness. These were washed for several hours in running water and stained for Marchi degeneration in the usual way. The site of the lesion was in every case serially sectioned and stained either with haematoxylin and eosin or by the Marchi method. Serial sections were prepared through the whole length of the thalamus, every fourth section being preserved and mounted. In the study of these sections, the distribution of osmic-stained degenerating fibres in relation to the different thalamic nuclei was carefully mapped out. In all cases the identification of these fibres as truly undergoing Marchi degeneration could be established beyond doubt, for they were usually cut slightly obliquely and in each section they could thus be traced for a short distance along their length. In some instances the sections were quite free of pseudo-Marchi reaction, and here the fine stippling of certain elements of the thalamus with Marchi granules made it possible to define the actual site of the terminal breaking up of degenerating tracts with considerable assurance. In other experiments there was a certain degree of pseudo-Marchi deposit which obscured this stippling. In these cases the degenerating fibres were traced as far as they could be certainly identified, and the precise area of their termination was approximately judged to be in the region where they finally disappeared. In the diagrams illustrating the experiments, the distribution of recognizable degenerating fibres is indicated by interrupted lines, while in those cases in which the sections were sufficiently excellent to allow areas of terminal stippling to be defined, these areas are indicated by dots. The sections illustrated were traced out with a projection apparatus. In Marchi material the outlines of many of the thalamic nuclei (though faintly marked) could be readily detected, as, for instance, the dorso-medial, centre median, arcuate and anterior nuclei, and element *La* of the lateral nucleus. On the other hand, the boundary between the main part of the lateral nucleus (element *Lb*) and the pars externa of the ventral nucleus could not be accurately defined. In any case these nuclei merge into each other with no intervening medullary lamina though their limits can be approximately determined by cyto-architectural and myelo-architectural features. As has been recently shown, also, they can be differentiated by their cortical connexions, for while the pars externa of the ventral

nucleus projects entirely on to the area postcentralis, the lateral nucleus (in its caudal part) projects on to the parietal association areas of the cortex (5, 18). In the diagrams in this paper, the approximate boundary between the pars externa of the ventral nucleus and the lateral nucleus has been estimated by comparison with large numbers of Nissl sections cut at equivalent transverse levels (which are available in this laboratory), and by comparison with various atlases of the thalamus of the monkey which have been published. Of these atlases, by far the best is to be found in the magnificent series of microphotographs of Nissl sections reproduced in a paper by Friedemann (10), and this has been extensively used in the present study. The myelo-architecture of the cercopitheque thalamus has been illustrated in a similar way by Vogt. More recently the cyto-architecture of the macaque thalamus has been figured photographically by Grünthal (11) who, however, uses an unfamiliar nomenclature and has made the confusing error of mistaking the centre median nucleus for the arcuate nucleus. Descriptions of the nuclear configuration of the macaque thalamus have been published in America by Crouch (7) and Aronson & Papez (1), but these are illustrated by hand-drawn diagrams which, however excellent in themselves, are much less useful for purposes of reference and comparison.

EXPERIMENTAL RESULTS

Experiment A. O.M. 83. Operation 13 September 1935, killed 27 September 1935.

A local lesion was made in the right gracile nucleus of this monkey. The medulla was exposed by a laminectomy of the first three cervical vertebrae and a partial removal of the occipital bone behind the foramen magnum. The gracile tubercle was readily identified and the lesion produced by a fine ophthalmic knife. The animal made an uninterrupted recovery.

Histological examination of the lesion

Serial sections were cut through the whole extent of the lesion and stained with haematoxylin and eosin. At the level of the upper limit of the pyramidal decussation, the lesion can be seen extending into the right gracile nucleus, cutting off approximately the medial half of the nucleus (Fig. 1 A). Further up, at the level of the lower end of the fourth ventricle, the lesion extends ventro-medially as far as the lateral margin of the dorsal vagal nucleus and the dorsal margin of the fasciculus solitarius, but if there is any involvement of these structures, it is so slight as to be practically insignificant. At the level of the vascular area postrema, the lesion begins rapidly to diminish and in a few sections disappears entirely. The cuneate nucleus or the arcuate fibres which arise in it are not touched by the lesion.

Course of degenerating fibres

Sections through the pons show marked degeneration localized to the fibres in the lateral half of the medial fillet of the left side. At the level of the mid-brain, the degenerating fibres can be traced up in the lateral end of the fillet, and form a conspicuous bundle lying immediately medial to the medial

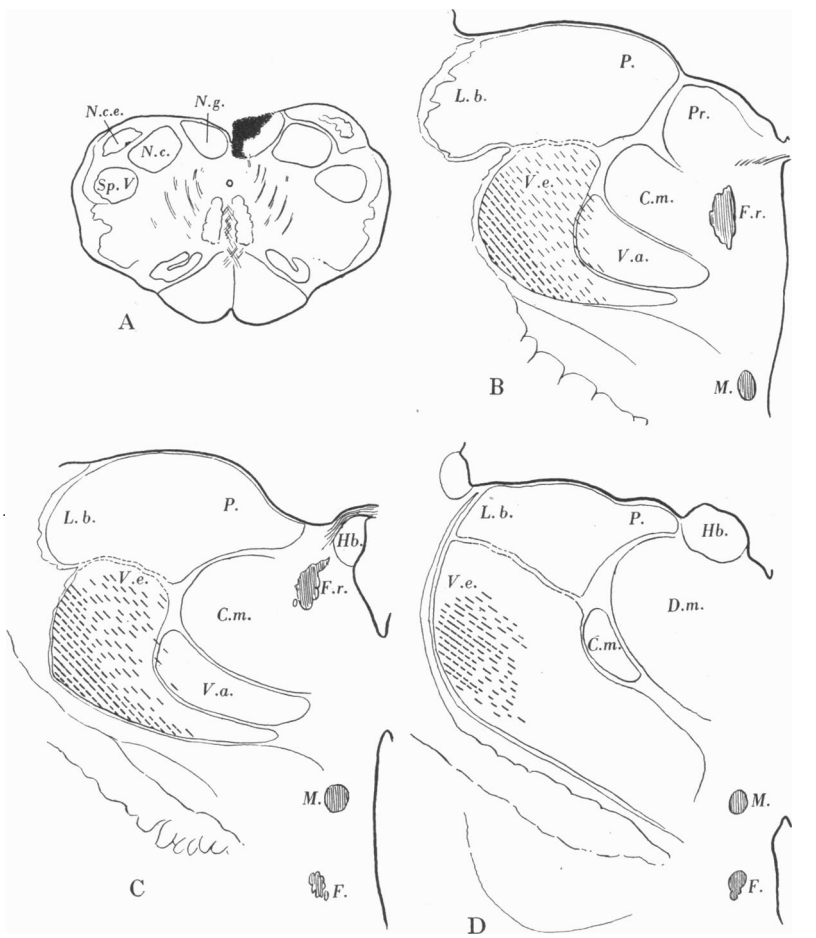

Fig. 1. The lesion and the distribution of degenerating fibres in the thalamus in experiment A (O.M. 83). In this and the following illustrations, the drawings have been made from sections by means of a projection apparatus.

geniculate body. The fibres, which here are cut obliquely, all stream in a lateral direction as they run forwards to reach the caudal limit of the thalamus. No degenerating fibres pass dorsally along the line of the nucleus limitans as they do to some extent after lesions involving the cuneate nucleus or its

arcuate fibres. Degenerating fibres are also completely absent in the medial geniculate body, pulvinar, or in the superior colliculus and its commissure.

In the main part of the thalamus, there is a certain amount of pseudo-Marchi deposit in this specimen. This can be readily distinguished in the sections from the true Marchi degeneration shown by dense osmic staining of fibres which are cut obliquely in their course, but it raises some difficulty in delimiting the zone in which the diffuse sprinkling of osmic granules usually defines the site of actual termination of degenerating fibres. In tracing the course of the affected fibres in the thalamus, therefore, attention has been confined to the fibres themselves, up to the point where they disappear as recognizable fibres. However, the area of actual termination is in fact indicated fairly strongly by the rich network which the degenerating fibres make in the ventral nucleus of the thalamus.

At the caudal end of the thalamus (Fig. 1 B), the degenerating fibres are seen crowding into the lateral half of the pars externa of the ventral nucleus. They are also present throughout this nucleus, but in the medial half they are scattered and appear to be fibres of passage making their way laterally. The arcuate nucleus (pars arcuata of the ventral nucleus) is quite free of degenerating fibres except at its lateral margin, and here the few isolated fibres showing osmic staining which are present are clearly fibres of passage. No degenerating fibres run over the arcuate nucleus in the intermediate medullary lamina as is the case with some of the fillet fibres which take origin from the cuneate nucleus. The lateral nucleus, centre median nucleus, and the dorso-medial nucleus are all entirely free of degenerating fibres. Traced forwards, the fibres gradually disappear from the medial half of the pars externa of the ventral nucleus. The lateral half of the nucleus becomes more crowded with a network of osmic-stained fibres, scattered in among which are numerous coarse Marchi granules. At the level of the rostral end of the centre median nucleus, degenerating fibres are only to be found in the lateral part of the ventral nucleus where they are limited to an area lying close against the lateral medullary lamina (Fig. 1 D). In front of the anterior end of the centre median nucleus, no more Marchi degeneration is to be seen.

It is clear from this experiment that fillet fibres from the gracile nucleus are destined for the most lateral part of the pars externa of the ventral nucleus. Many of these fibres reach this area from below by running laterally in the ventral medullary lamina of the thalamus, while others approach it from the medial aspect by running through the medial half of the pars externa.

Experiment B. O.M. 86. Operation 19 September 1935, killed 2 October 1935.

In this experiment a lesion was made in the cuneate nucleus on the left side, and the spinal nucleus of the fifth nerve on the right side. The medulla was exposed by a laminectomy of the upper three cervical vertebrae, and removal of part of the occipital bone. The animal made a rapid recovery.

Histological examination of the lesions

Right side. At the level of the lower margin of the pyramidal decussation the lesion can be seen entering the superficial aspect of the spinal nucleus of the fifth nerve. It cuts through the middle of the nucleus in a ventro-medial direction to reach its ventro-medial angle (Fig. 2 A). The lesion thus interrupts the fibres which run medially from the ventro-lateral half of the lower part of the nucleus. The lesion extends up to the level of the lower angle of the fourth ventricle, where it extends ventrally as far as the margin of the dorsal spino-cerebellar tract.

Left side. As the sections are traced rostrally, the lesion on this side is first seen entering the termination of the fasciculus cuneatus at the level of the lower extremity of the fourth ventricle. Further up it extends ventro-medially, involving the dorsal part of the external cuneate nucleus (Fig. 2 B). Still more rostrally (Fig. 2 C), the lesion extends inwards to involve the cuneate nucleus proper (the pars triangularis as defined by Ferraro and Barrera).

On both sides, the lesions are strictly localized.

Course of degenerating fibres

Right side. Sections through the medulla, pons, and mid-brain stained with osmic acid show numerous coarse degenerating fibres scattered throughout the right medial fillet, the result of the lesion involving the left cuneate nucleus. At the caudal end of the thalamus, the majority of these fibres turn dorso-laterally and stream into the pars externa of the ventral nucleus in this direction. A few run dorsally along the line of the nucleus limitans (Fig. 3 A). At the level of the caudal extremity of the arcuate nucleus, the fibres mainly skirt the margin of this nucleus on their way dorso-laterally; some, however, can be seen as separate and isolated fibres running through the nucleus. It seems certain that these are fibres of passage only, for they can be traced laterally in the serial sections into the pars externa of the ventral nucleus, and, unlike the latter, the groundwork of the arcuate nucleus is free of osmic sprinkling. At the caudal end of the pars externa degenerating fibres are already breaking up into a terminal network in this nucleus (Fig. 3 A). It may be noted that no Marchi degeneration is present in the pulvinar, in the lateral nucleus, or in the posterior commissure. At the transverse level of the maximum development of the centre median nucleus, most of the medial half of the pars externa is filled with numerous degenerating fibres. Along the medial border of the nucleus and at its ventro-medial extremity, these appear to be fibres of passage only. The actual site of termination is indicated by a rich deposit of Marchi granules concentrated in a vertical zone in the middle of the nucleus (Fig. 3 B). At this level the arcuate nucleus is devoid of osmic staining except at its margins and its dorso-lateral extremity, where isolated fibres of passage are present in small numbers. Further rostrally, the dorso-lateral extremity of the arcuate nucleus becomes free of degenerating fibres which have by this level passed into the

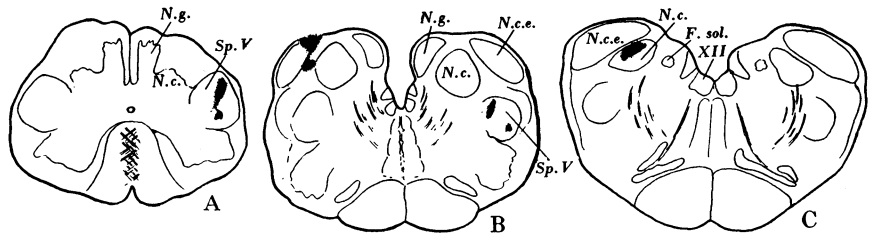

Fig. 2. The lesions in the medulla in experiment B (O.M. 86).

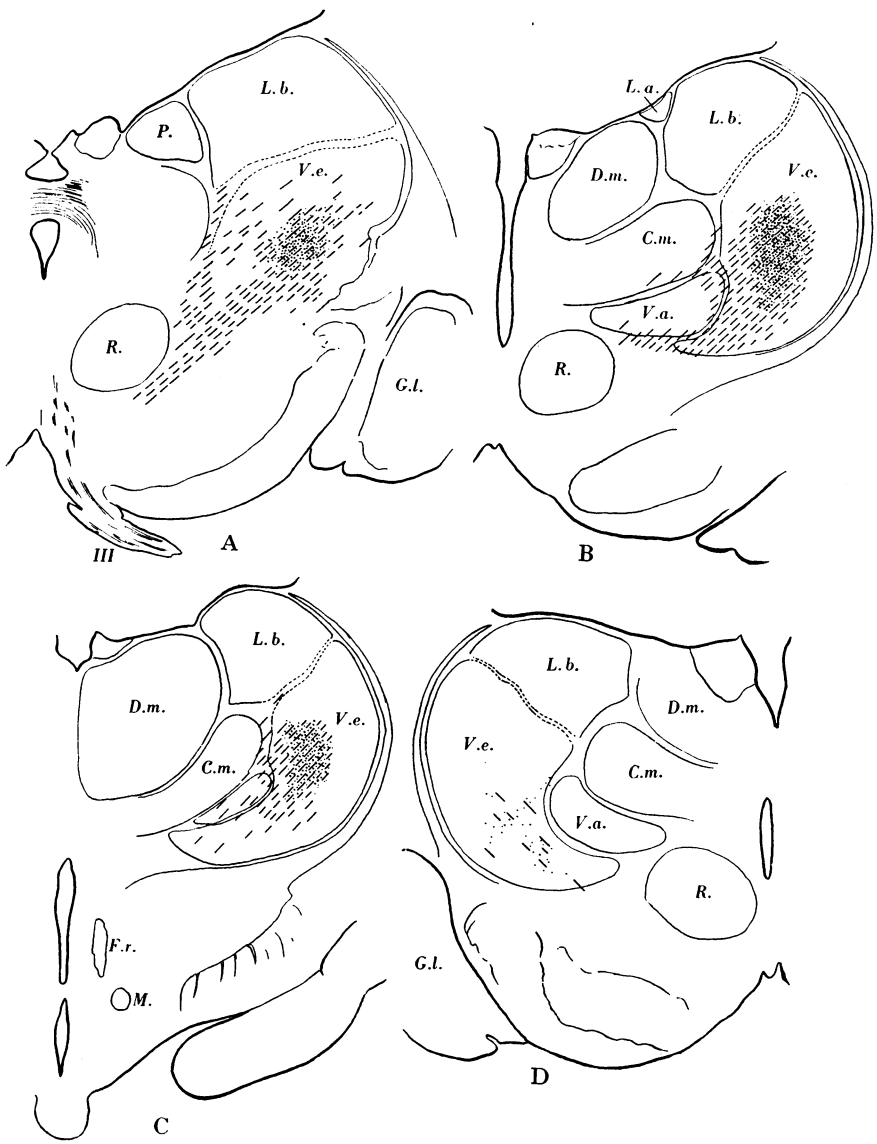

Fig. 3. The distribution of degenerating fibres in the thalamus in experiment B (O.M. 86).

medial aspect of the pars externa. The centre median nucleus is also free of degenerating fibres, though a few may be seen skirting its lateral and ventral margins in the intermediate medullary lamina. In sections through the middle of the thalamus, degenerating fibres are confined to the medial half of the pars externa (Fig. 3 C). Again, the area of termination appears to be a zone near the middle of the nucleus, the medial margin and ventral extremity containing fibres of passage only. At the level of the rostral end of the centre median nucleus, that is, approximately mid-way between the posterior commissure and the anterior limit of the thalamus, no Marchi-stained fibres are present on the right side.

Left side. Although it is certain from a study of serial sections that the lesion on the right side must have interrupted a considerable proportion of secondary neurones arising in the lower half of the spinal nucleus of the trigeminal nerve, it has produced extremely little degeneration in the sensory tracts which ascend to the thalamus on the left side. There are indeed a few Marchi granules scattered in the medial fillet of this side, and also a few in the central tegmental fasciculi, which certainly indicate in these sections degenerating fibres. In sections through the mid-brain, where the fibres of the medial fillet are cut somewhat obliquely as they begin to turn dorso-laterally, a few of them seem definitely to be undergoing degeneration, and here, also, one or two fibres stained with osmic acid can be seen running into the deeper layers of the superior colliculus. At the caudal end of the thalamus, a few isolated and fine degnerating fibres are present in the ventro-medial end of the pars externa of the ventral nucleus (extending laterally from the position of the nucleus limitans), and over a small area here there is a diffuse scattering of Marchi granules which is sufficiently distinct to suggest the termination in this region of a small number of degenerating fibres (Fig. 3 D). This area of slight osmic staining can be traced forwards in serial sections to the level of the rostral extremity of the centre median nucleus. There is no Marchi deposit in the arcuate nucleus, centre median nucleus or dorso-medial nucleus, nor are any degenerating fibres present in the periventricular grey matter.

The results of this experiment indicate that the cuneate nucleus (which receives impulses from the upper extremity and the upper part of the trunk), projects on to a zone extending along the middle of the pars externa of the ventral nucleus. On the other hand, the projection of the spinal nucleus of the fifth nerve on to the thalamus appears to be very slight indeed, and is confined to the medio-ventral end of the pars externa (i.e. to an area lying medio-ventral to the area of termination of the cuneate fibres).

Experiment C. O.M. 104. Operation 15 October 1935, killed 29 October 1935.

In this experiment the intention was to make a circumscribed lesion in the spinal nucleus of the trigeminal nerve on the right side, and in the medullary nucleus on the left side. The medulla was exposed by removing the laminae

of the first three cervical vertebrae and also the lower part of the occipital bone. On opening the spinal theca, the tubercle of Rolando was identified and provided a landmark for the spinal nucleus. A lesion was produced with a small curved ophthalmic knife. The vermis of the cerebellum was then retracted upwards and the cavity of the fourth ventricle exposed. The knife was passed up towards the lateral recess and allowed here to penetrate the medulla in a direction which was judged to reach the medullary nucleus of the trigeminal nerve.

The animal made a rapid and uneventful recovery, and showed no ascertainable effect of the lesions.

Histological examination of the lesions

Sections through the lower part of the medulla, at the level of the pyramidal decussation, show the site of the lesion marked by two small patches of fibrosis in the spinal nucleus of the fifth nerve on the right side (Fig. 4 A).

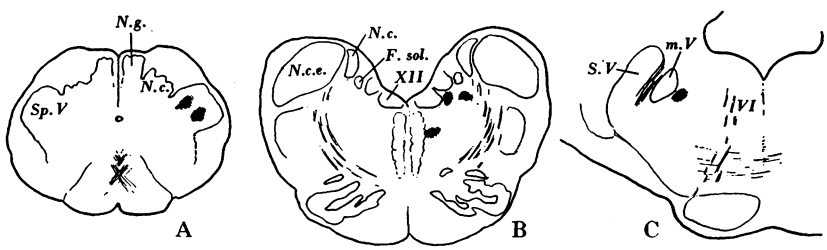

Fig. 4. The lesions in the medulla in experiment C (O.M. 104).

At this level no other parts of the medulla are involved. Further rostrally, the lesion extends medially, reaching the margin of the cuneate nucleus and involving some of the fibres of the sensory decussation which issue from it. At the level of the lower end of the fourth ventricle the lesion extends medially immediately below the hypoglossal nucleus, severing here the lemniscus fibres from the upper end of the gracile and cuneate nuclei. Still further rostrally, the lesion is marked by three separate patches of fibrosis, of which one lies immediately below the hypoglossal nucleus and close against the lateral margin of the medial lemniscus and the posterior longitudinal bundle, involving a few fibres of these tracts (Fig. 4 B). The other patches lie immediately below the dorsal vagal nucleus and the solitary bundle.

The serial sections show that the lesion on the left side was situated too medially to reach the main sensory nucleus of the fifth nerve, and a little too dorsally to involve the arcuate fibres from either the spinal or the main sensory nucleus. At its lower extremity, the lesion lies immediately below the position of the medial vestibular nucleus, here interrupting fibres running medially from this nucleus to the posterior longitudinal bundle. Further rostrally it cuts through the ascending limb of the intramedullary root of the facial nerve.

At its extreme upper end the lesion reaches to the level of the central origin of the sixth nerve, here lying medial to the motor nucleus of the fifth nerve, but unfortunately a little dorsal to the arcuate fibres from the main sensory nucleus (Fig. 4 C).

On the right side, then, the lesion involves the lower end of the spinal nucleus of the fifth nerve, a proportion of the lemniscus fibres coming from the upper end of the cuneate nucleus, and, to a lesser extent, of the gracile nucleus, and also a few of the crossed fibres of the medial lemniscus of this side. On the left side, the lesion unfortunately misses any part of the lemniscus system.

Course of degenerating fibres

Left side. Sections through the mid-brain, at the level of the upper border of the pons, the superior colliculus and the medial geniculate body, show well-marked degeneration throughout the medial fillet which arises from the lesions in the right side of the medulla. Scattered degeneration is also present in the central tegmental fasciculi close to the central grey matter around the aqueduct. This degeneration occupies the position of the dorsal secondary trigeminal path described by Wallenberg, but in this experiment it may be derived from interruption of fibres lower down by the lesion in the left half of the medulla. Isolated fibres showing marked degeneration run dorsally from the central tegmental fasciculi to course round the central grey matter, and a few of these fibres enter this grey matter. On both sides, and especially on the right, there is scattered degeneration in the posterior longitudinal bundle (probably resulting from interruption by the lesion of fibres from the medial vestibular nucleus), and a fine network of degenerating fibres extends from the bundle into the oculomotor nucleus. A few isolated degenerating fibres are definitely present in the commissure of the superior colliculus, apparently derived from the central tegmental fasciculi of the left side. Further rostrally, the degenerating fibres of the medial fillet may be divided into two main groups, of which the more medial now begin to stream dorso-laterally along the line of the nucleus limitans, while the more lateral and denser part forms a fairly compact bundle immediately medial to the medial geniculate body. At least some of the more medial fibres run dorsally into the deeper layers of the superior colliculus. There is complete absence of osmic staining in the pulvinar, medial geniculate body and posterior commissure. Sections through the caudal part of the thalamus show numerous degenerating fibres ending in the greater part of the pars externa of the ventral nucleus, except for its most dorsal part (Fig. 5 A). The degeneration is rather less dense in the lateral margin of the nucleus. Not only are abundant fibres showing the osmic staining, and cut obliquely, seen coursing dorso-laterally in the pars externa, but the ground substance of this nucleus is richly sprinkled with osmic granules, indicating the actual termination of degenerated fibres therein. Some of the more medial fibres of the medial fillet enter the intermediate medullary lamina which forms the lateral boundary of the centre median nucleus, and a few run through the

caudo-lateral extremity of this nucleus. By tracing the serial sections forwards, these fibres can be followed laterally eventually to end in the dorso-medial part of the pars externa of the ventral nucleus. Moreover, the centre median nucleus contains no sprinkling of osmic granules which might indicate a terminal breaking up of degenerating fasciculi, and the greater part of the nucleus

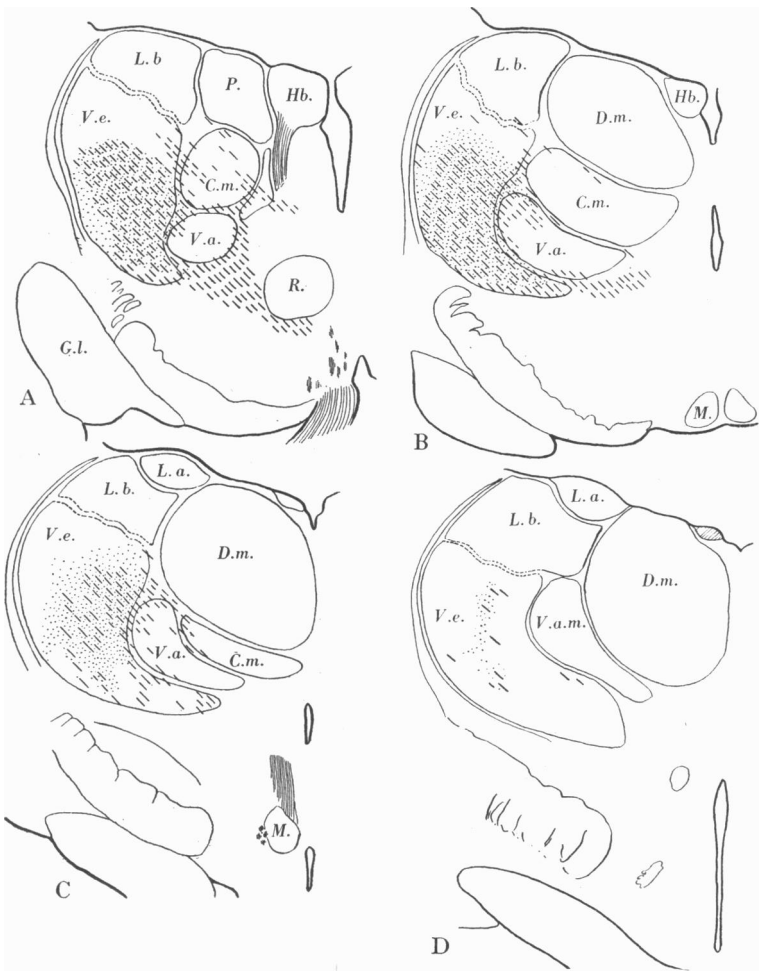

Fig. 5. The distribution of degenerating fibres in the thalamus in experiment C (O.M. 104).

is quite free even of degenerating fibres of passage. At the caudal part of the thalamus, the pars arcuata of the ventral nucleus appears. Again, isolated fibres showing osmic staining are evident, passing through the caudal extremity of this nucleus, but a careful study indicates that they are fibres of passage only, running dorso-laterally to reach the pars externa of the ventral nucleus.

As the sections are traced forwards, the medio-ventral part of the arcuate nucleus becomes free of degenerating fibres.

Towards the middle of the thalamus, the degenerating fibres in the pars externa of the ventral nucleus diminish rapidly, and at this level the lateral part of the nucleus is free of osmic deposit (Fig. 5 C). Finally, at the level of the caudal border of the optic chiasma, only very few isolated fibres are evident, and osmic granules in the groundwork of the nucleus are very inconspicuous (Fig. 5 D). Further rostrally, no degenerating fibres are to be seen.

It may be noted that no Marchi degeneration is present in the lateral nucleus, the dorso-medial nucleus, the nuclei of the mid-line or in the hypothalamus. The medial medullary lamina (circumscribing the dorso-medial nucleus) contains no degenerated fibres except at its posterior end, where one or two isolated fibres of passage are passing laterally between the caudal extremities of the dorso-medial and centre median nuclei to reach the intermediate medullary lamina.

On the left side, then, the degenerating fibres which arise from the lesions involving the spinal nucleus of the fifth nerve and a part of the medial lemniscus fibres appear to end entirely in the pars externa of the ventral nucleus. If any terminate in the centre median or arcuate nuclei, they are very few and are confined to the caudal extremity of the former and the dorso-lateral extremity of the latter. But, as pointed out, the sections indicate that these are almost certainly fibres of passage only. The fact that the dorsal part and most of the lateral margin of the pars externa of the ventral nucleus are also free of degenerating fibres, is perhaps related to the fact that the lesion involves predominantly the fifth nucleus and fibres from the cuneate nucleus, whereas only very few of the lemniscus fibres from the gracile nucleus (bringing impulses from the caudal end of the body) could have been interrupted.

Right side. A few scattered fibres showing Marchi staining are present in the most lateral part of the medial fillet, and these can be traced rostrally to terminate in the most lateral part of the pars externa of the ventral nucleus. This degeneration probably results from the slight involvement of the crossed fibres at the lateral margin of the medial fillet of the right side as already described. No other elements of the thalamus on this side show any degenerating fibres.

In no sections could degenerating fibres be found in the periventricular grey matter of the third ventricle on either side.

Experiment D. O.M. 59. Operation 1 October 1935, killed 15 October 1935.

A lesion was made in the floor of the fourth ventricle on the left side in an attempt to reach the medullary nucleus of the fifth nerve. The fourth ventricle was approached by the sub-occipital route, the cerebellum being raised in order to expose the lower part of its floor.

Serial sections were taken through the medulla, but unfortunately they only show the rostral end of the lesion, for the latter had not reached so far

forwards as had been intended. Thus it is not possible in this experiment to state the precise extent of the medullary lesion. Since the Marchi sections show abundant degeneration throughout the medial fillet of the right side, it is quite evident that the decussating fibres from the rostral ends of the cuneate or gracile nuclei (or both) must have been involved. The lowest of the serial sections shows the anterior end of the lesion extending ventrally and slightly medially into the medulla to reach a point approximately mid-way between the ventral border of the descending nucleus of the fifth nerve and the medial plane (Fig. 6 A). Thus this part of the lesion interrupts some of the arcuate fibres of the trigeminal fillet from the descending nucleus, and also some of the fibres forming the central tegmental fasciculi. The rostral end of the lesion is at the level of the lower end of the facial nucleus. The medullary nucleus of the fifth nerve is intact.

Course of degenerating fibres

Sections through the mid-brain at the level of the anterior colliculus show degenerating fibres strewn throughout the width of the medial fillet on the right side, rather more densely in the lateral half. There is no osmic staining in the fibres of the left medial fillet. There is also scattered degeneration in the central tegmental fasciculi of both sides. This is quite definite, and some of the affected fibres may be seen, cut obliquely along their length, radiating dorsally from the fasciculi towards the colliculus. The degenerating fibres in the tegmental fasciculi of the right side are evidently the result of the interruption of the arcuate fibres from the descending nucleus of the fifth nerve on the left side, and mark the course of the secondary trigeminal path in the tegmental region which was originally described by Wallenberg. On the left side the degeneration is due to the interruption of these tegmental fibres on the same side at a lower level by the lesion.

Degenerating fibres from the central tegmental fasciculi can be traced on both sides in among the cells of the mesencephalic nucleus of the fifth nerve, a few also extending into the central grey matter around the cerebral aqueduct. Others run dorsally into the commissure of the anterior colliculus, where they cross the mid-line, or into the deeper layers of the colliculus. Further rostrally, some extend upwards and forwards along the line of the nucleus limitans.

As the affected fibres of the right medial fillet are traced rostrally, they are seen to run in well-defined fasciculi in a dorso-lateral direction on the lateral aspect of the red nucleus—between it and the anterior end of the medial geniculate body. From here, they stream laterally into the caudal end of the pars externa of the ventral nucleus, the medial portion of which they fill (Fig. 6 C). Immediately adjacent to the anterior end of the medial geniculate body the network of degenerating fibres is particularly dense, and here the groundwork is scattered with osmic granules indicating the termination in this area of the fillet fibres. Further dorsally, on the right side, there is a slight concentration of degenerating fibres in the intermediate medullary lamina at

the caudal pole of the centre median nucleus, while a few isolated fibres are also to be seen penetrating the nucleus parafascicularis close alongside the fasciculus retroflexus. Where the posterior pole of the arcuate nucleus first

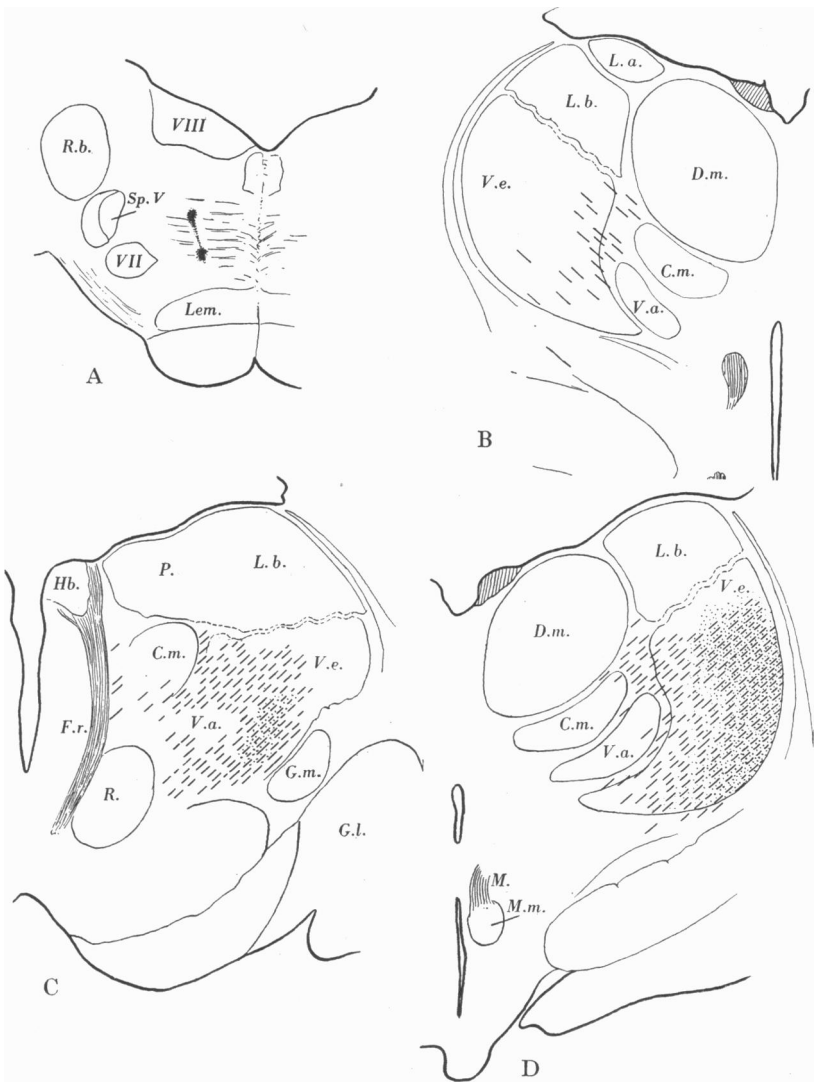

Fig. 6. The rostral end of the lesion, and the distribution of degenerating fibres in the thalamus in experiment D (O.M. 59).

becomes recognizable, the degenerating fillet fibres for the most part skirt its margins on their way to more rostral levels of the pars externa of the ventral nucleus. Further forwards, at the level of the mammillary bodies and the tuber cinereum, the pars externa is practically filled throughout its extent in coronal

section by Marchi-stained fibres (Fig. 6 D). This network is more dense towards the lateral and dorsal parts of the nucleus, and in these regions the profuse sprinkling with osmic granules suggests that most of the fibres terminate. The lateral nucleus throughout is quite free of osmic staining. These sections are particularly instructive in showing an abrupt transition between the clear zone of the lateral nucleus above and the Marchi-sprinkled area of the ventral nucleus below. On the right side most of the degenerating fibres enter the pars externa of the ventral nucleus from the ventral medullary lamina below. Some, however, which are probably mainly derived from the central tegmental fasciculi of the brain stem, run through the ventral part of the medial medullary lamina, and the intermediate medullary lamina, to enter the pars externa from the medial aspect. The degeneration in the pars externa of the right side extends forward as far approximately as the middle of the thalamus. It may be noted that, on the right side, the centre median and arcuate nuclei are free of Marchi staining except for isolated fibres of passage at their posterior extremities, while the dorso-medial nucleus is entirely clear throughout its extent.

On the left side a moderate number of degenerating fibres can be seen extending into the pars externa of the ventral nucleus, the result of the involvement by the lesion of the secondary trigeminal paths in the central tegmental fasciculi of the same side (Fig. 6 B). They reach the caudal part of the thalamus by passing for the most part through the parafascicular nucleus. From here they radiate laterally into the ventro-medial extremity of the caudal end of the pars externa, while others run forwards into the ventral part of the medial medullary lamina and the capsule of the centre median nucleus to reach the medial margin of the pars externa further rostrally. In this relative position, the degenerating fibres reach forwards to the level of sections passing through the caudal margin of the optic chiasma. No degenerating fibres on the left side are found to end in the centre median, arcuate, dorso-medial or lateral nuclei.

Experiment E. O.M. 80. Operation 11 September 1935, killed 23 September 1935.

In this case a hemisection of the spinal cord was made on the left side between the fourth and fifth cervical nerve roots. The animal made a rapid recovery from the immediate effects of the operation, showing complete paralysis of the left arm and leg. Following the operation, it remained very quiet and huddled up, and could only be persuaded to take nourishment with difficulty. The post-mortem examination showed that the lesion was entirely local and uncomplicated by sepsis or haemorrhage. Serial sections were taken through the site of the lesion, demonstrating that the hemisection was complete and did not extend across the mid-line.

Course of degenerating fibres

Sections through the spinal cord above the level of the lesion show complete Marchi degeneration of the posterior columns, and considerable degeneration in the more superficial parts of the lateral and ventral funiculi. In the medulla,

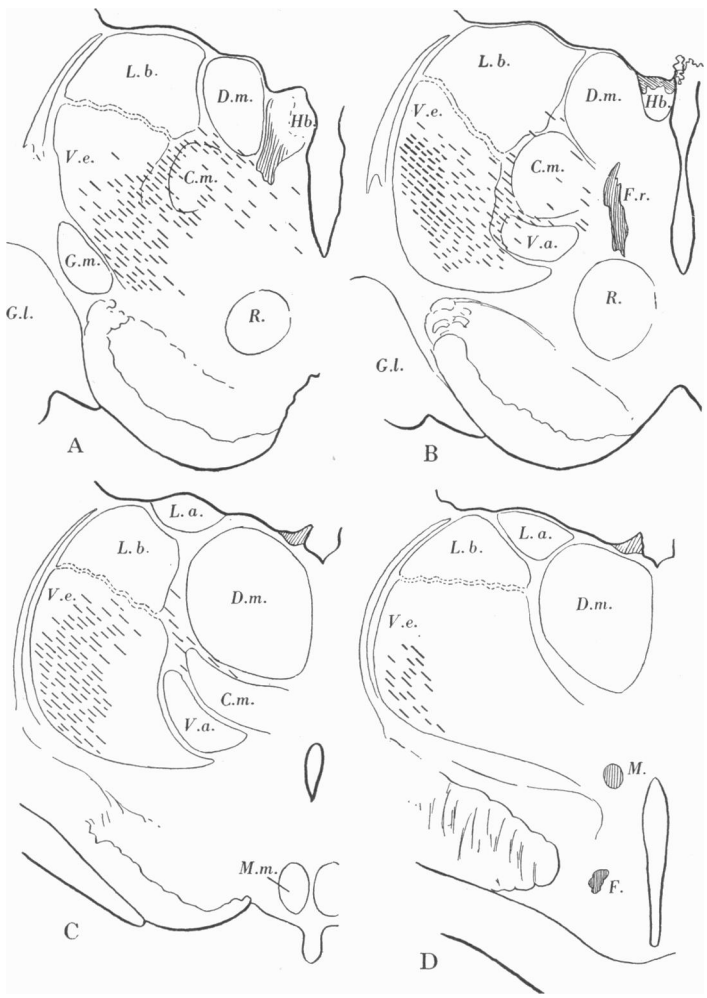

Fig. 7. The distribution of degenerating fibres in the thalamus following hemisection of the spinal cord in experiment E (O.M. 80).

the termination of the posterior column fibres in the cuneate and gracile nuclei is to be observed, the spino-cerebellar tracts are clearly marked out, while the spino-tectal and spino-thalamic tracts (whose identity can be determined by tracing their subsequent course in the serial sections) lie on a deeper plane, ventral to the spinal nucleus of the fifth nerve. At the lower end of the medulla

degenerating fibres, well-stained with osmic acid, occasionally leave these tracts and run dorso-medially to reach the grey matter around the central canal. At a slightly higher level, the spino-thalamic and spino-tectal fibres lie latero-dorsal to the inferior olive, between it and the spinal nucleus of the fifth nerve. They are not sharply separated here from the ventral spino-cerebellar tract. Some fibres penetrate into the inferior olive from its latero-dorsal aspect, while others are observed running at intervals dorso-medially to reach the central grey matter, some of these passing transversely through the medial fillet and crossing over the mid-line. At the level of sections through the pons and upper part of the fourth ventricle, the ventral spino-cerebellar tract is a very conspicuous structure as its degenerating fibres run up over the surface of the brachium conjunctivum. Immediately deep to it and dorsal to the lateral extremity of the medial fillet are the spino-thalamic and spino-tectal fibres. There is no certain evidence of Marchi degeneration in the central tegmental fasciculi, nor is there any degeneration in the medial fillet. At the level of the posterior colliculus many degenerating fibres of the spino-thalamic and spino-tectal tracts run upwards and forwards among and deep to the fibres of the lateral fillet, reaching from a point dorsal to the lateral end of the medial fillet as far as the ventro-lateral margin of the nucleus of the posterior colliculus. Immediately below the latter, a number of well-stained fibres run medially, penetrating the mesencephalic tract and nucleus of the fifth nerve, to reach the central grey matter round the cerebral aqueduct. Some of these degenerating fibres can be traced very distinctly into a sub-ependymal position, where their termination is apparently indicated by a copious sprinkling of Marchi granules on the left side. A considerable number of fibres also skirt the caudal margin of the posterior colliculus, and cross over the mid-line above the aqueduct in the commissure of the posterior colliculus. At the level of the anterior colliculus the spino-thalamic tract is seen as a conspicuous bundle of Marchi-stained fibres lying under cover of the caudo-lateral margin of the colliculus and immediately deep to the inferior brachium. A few degenerating fibres (comprising the spino-tectal component) run dorsally into the deeper layers of the colliculus, and some of these cross over the aqueduct in the commissure of the anterior colliculus.

Sections through the caudal end of the thalamus show that most of the spino-thalamic fibres enter the thalamus in the position of the nucleus parafascicularis and in the area between the latter and the medial geniculate body, somewhat dorsal, therefore, to the entry of the majority of medial lemniscus fibres. The parafascicular nucleus is richly strewn with degenerating fibres, and from this position they radiate in different directions. The bulk of the fibres course laterally, dorso-laterally or ventro-laterally, in order to enter the pars externa of the ventral nucleus (Fig. 7 A). Others run into the intermediate medullary lamina surrounding the centre median nucleus; a few run through the caudal end of this nucleus, but it is doubtful whether they end here. A few fibres also extend into the medial medullary lamina, lateral to the ventral

half of the dorso-medial nucleus. Lastly, at the caudal end of the thalamus, a small number of quite distinct fibres undergoing Marchi degeneration are to be seen in the periventricular grey matter medial to the plane of Meynert's bundle, and they apparently reach this region by running dorso-medially from a more lateral position. In front of the plane of the habenulo-peduncular tract, no degenerating fibres are to be seen near the ventricle. Further forwards, almost the whole of the pars externa of the ventral nucleus is permeated with coarsely degenerating fibres. They are rather more conspicuous towards the lateral half of this nucleus and, in this position, mainly run dorsally and laterally. At the level of the mammillary bodies, they are almost entirely collected in the lateral half of the pars externa (Fig. 7 C). At the level of infundibulum and the caudal margin of the optic chiasma they are limited to its ventro-lateral angle, and they can be traced forward in this position almost as far as the transverse plane of the caudal margin of the anterior nucleus of the thalamus.

It is evident that the great bulk of the degenerating fibres of the spino-thalamic tract terminate in the pars externa of the ventral nucleus, probably ending in all parts (as far forwards as approximately the rostral border of the centre median nucleus) except the medio-ventral region. Unfortunately, in this specimen, there is some pseudo-Marchi staining in the thalamus which makes it too difficult to determine the precise site of the breaking up of fibres of termination by reference to diffuse osmic stippling. However, fibres undergoing true Marchi degeneration can be distinguished readily enough, and the appearance of the network of these fibres does give some indication of the site of their termination. It has been noted that some degenerating fibres enter the medial and intermediate medullary lamina. These can be traced forwards as far as the level of the anterior extremity of the centre median nucleus. Many of them run forwards through the nucleus centralis lateralis. Those in the ventral half of the medial medullary lamina are cut obliquely, and they are seen to be directed dorso-laterally. Their destination is uncertain, for they lie too far dorsally to be aiming for the ventral nucleus, and they certainly cannot be traced into the lateral or dorso-medial nucleus. The impression is gained that these fibres probably end in the intra-laminar nuclei corresponding to the medial and intermediate medullary lamina, and including the nucleus centralis lateralis.

The pars arcuata of the ventral nucleus is empty of degenerating fibres except for the lateral part of its caudal extremity, and here the fibres are probably passing through on their way to the pars externa and the intermediate medullary lamina. The same applies to the centre median nucleus which is also clear of degenerating fibres for the most part. Further, it may be noted that no fibres undergoing Marchi degeneration can be found in the pulvinar, the lateral nucleus, or the dorso-medial nucleus.

Experiment F. O.M. 127. Operation 26 February 1936, killed 10 March 1936.

In this experiment a hemisection of the spinal cord was made between the third and fourth thoracic segments. The animal made a good recovery. Serial

sections were taken through the lesion and showed that the hemisection was complete and limited strictly to the left side of the cord.

Course of degenerating fibres

Sections through the cervical part of the spinal cord show that the fibres of Goll's tract on the left side have undergone well-marked Marchi degenera-

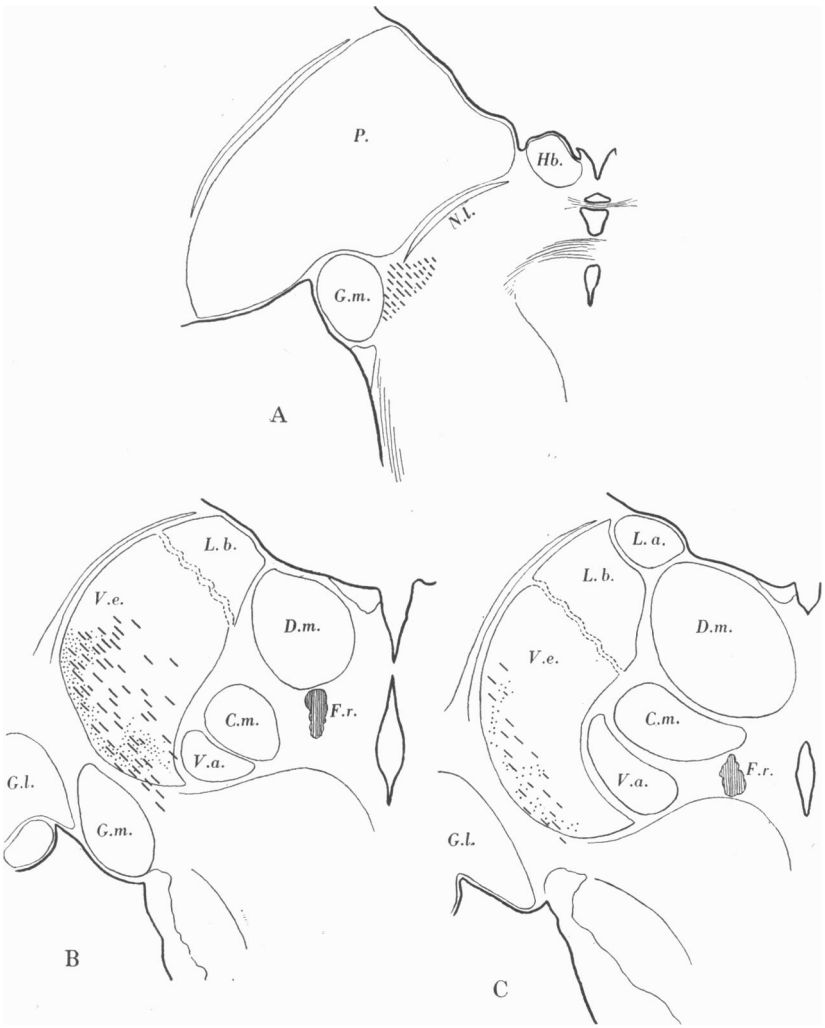

Fig. 8. The distribution of degenerating fibres in the thalamus following hemisection of the cord in experiment F (O.M. 127).

tion. Degeneration also extends over the peripheral part of the lateral and ventral funiculi, involving the spino-cerebellar and the spino-thalamic and spino-tectal tracts. On the right side there are scattered degenerating fibres

in the same regions, but these are very few and inconspicuous. Sections through the medulla at the level of the pyramidal decussation show degenerating fibres ramifying in the gracile nucleus and in the extreme medial corner of the cuneate nucleus on the left side. At the level of the middle of the inferior olive, the fibres of the dorsal spino-cerebellar tract are seen running into the restiform body. The spino-tectal and spino-thalamic fibres here lie near the surface of the medulla immediately dorsal to the lateral part of the olive, and cannot at this level be distinguished from the ventral spino-cerebellar tract. In sections through the mid-brain, a mass of degenerating fibres can be seen coursing up in the lateral fillet. These are spino-thalamic and spino-tectal fibres. While a few of them evidently terminate in the nucleus of the posterior colliculus, the great majority skirt the ventro-lateral margin of this nucleus, and continue rostrally as a fairly compact bundle immediately medial and slightly dorsal to the inferior brachium. One or two osmic-stained fibres run medially below the anterior margin of the posterior colliculus and can be traced into the margin of the central grey matter of the aqueduct. Others extend into the deeper layers of the anterior colliculus.

The spino-thalamic fibres which have been interrupted in this experiment enter the thalamus from a position immediately medial to the medial geniculate body (Fig. 8 A). From here they extend up slightly alongside the lower end of the nucleus limitans, and then turn laterally over the rostral pole of the medial geniculate body to enter the caudal extremity of the pars externa of the ventral nucleus by way of the ventral medullary lamina. Thus they appear all to enter this nucleus from the ventral aspect. The pars arcuata of the ventral nucleus and the centre median nucleus are free of osmic deposit, nor is there any certain evidence of degenerating fibres in the parafascicular nucleus or in the periventricular grey matter. At the level of sections passing through the caudal end of the lateral geniculate body and the middle of the medial geniculate body, degenerating fibres are scattered through the ventral half of the pars externa, but they are mainly concentrated here along its ventral and lateral borders (Fig. 8 B). In this region of the pars externa there is a pronounced stippling of the groundwork with Marchi granules, which indicates the terminal breaking up of the spino-thalamic fibres. On the other hand, the isolated degenerating fibres found in the medial part of the pars externa appear to be fibres of passage directed towards the lateral border of the nucleus. Further rostrally, in sections through the middle of the lateral geniculate body and in front of the level of the medial geniculate body, very few osmic-stained fibres are to be seen. However, there are a few very distinct degenerating fibres here along the ventral part of the lateral border of the pars externa of the ventral nucleus, and in the same area there is a scattered deposit of Marchi granules among the cells of the nucleus (Fig. 8 C). Tracing the sections forwards, an occasional degenerating fibre may be seen in the pars externa as far forwards as the level of the rostral extremity of the centre median nucleus. Here, however, they are extremely scattered, and only one or two can be identified in

each section. On the right side of the thalamus (the opposite side to the lesion) occasional degenerating fibres are seen limited to the same area as those on the left side.

Nowhere in the thalamus is there any Marchi staining in the pulvinar, lateral nucleus (elements *a* and *b*), pars arcuata of the ventral nucleus, centre median nucleus or dorso-medial nucleus.

Experiment G. O.M. 119. Operation 10 January 1936, killed 22 January 1936.

The object of this experiment was to interrupt as many of the ascending tract fibres as possible on one side immediately behind the caudal level of the thalamus. In this way the maximum extent of the terminal distribution in the thalamus of afferent fibres from the mid-brain, hind-brain and spinal cord (so far as they are shown by the Marchi technique) would be determined. A large osteoplastic flap was raised in the posterior parietal and occipital region of one side of the skull. The occipital pole of the hemisphere was mobilized by severing its venous connexions with the sagittal and transverse sinuses by means of the endothermy apparatus, and retracted upwards. The tentorium cerebelli was thus fully exposed. Working forwards along its upper surface, the splenium of the corpus callosum and the anterior colliculi were brought into view. A fine ophthalmic knife with a blunted tip was introduced in a vertical position close to the mid-line at the rostral border of the anterior colliculus, and pushed ventrally until it reached the base of the skull. The knife was then carried laterally in order to cut through the mid-brain transversely on one side at this level. Very little haemorrhage ensued and was quickly checked by slight pressure. The animal made a rapid recovery.

Histological examination of the lesion

Serial sections were made through the mid-brain and stained by the Marchi method. They show that dorsally the lesion penetrates through the caudal margin of the splenium and the rostral margin of the anterior colliculus close to the mid-line. It enters the mid-brain almost vertically, involving the most caudal fibres of the posterior commissure, and penetrating the central grey matter immediately to the right of the cerebral aqueduct (Fig. 9 A). Further down it cuts across the mesencephalic tract of the fifth nerve, and interrupts a considerable proportion of the central tegmental fasciculi (which here contain secondary trigeminal fibres). The central tegmental fasciculi are thickly strewn with degenerating fibres which can be traced up to the thalamus. The right brachium conjunctivum is cut through just caudal to its decussation, and its fibres, stained deeply with osmic acid, can be traced in continuity across the mid-line to the red nucleus of the left side. On the other hand, the red nucleus of the right side is free of osmic staining, the fibres of the left brachium conjunctivum having escaped injury. Further ventrally, the lesion cuts right across the fillet system as it is running dorso-laterally to enter the caudal pole of the thalamus. It appears from the sections that all the elements of the

fillet system are thus involved (Fig. 9 B). Finally, the lesion penetrates the substantia nigra of the right side and pierces the middle third of the cerebral peduncle to reach the basal surface of the mid-brain (Figs. 10 A, 10 B).

Course of degenerating fibres

On the right side there is profuse and conspicuous Marchi degeneration in the whole of the fillet system as it enters the thalamus, while the crossed brachium conjunctival fibres on this side are quite unstained.

On the left the opposite is the case, for here the fillet system is free of Marchi degeneration, while the crossed brachium conjunctivum fibres are heavily stained. The latter run up to the red nucleus of the left side, some of the fibres leaving the main bundle to reach the oculomotor nucleus of the left side by penetrating among the fasciculi of the medial longitudinal bundle.

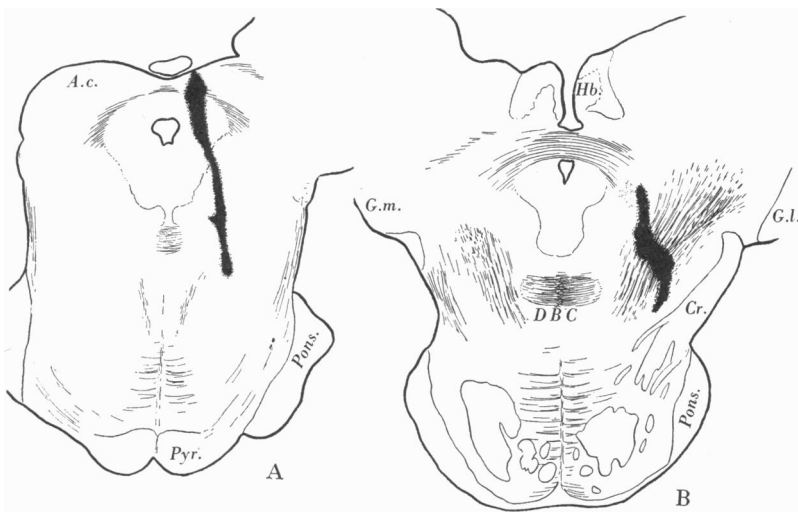

Fig. 9. The lesion in the mid-brain in experiment G (O.M. 119).

The oculomotor nucleus of the left side is strewn fairly thickly with Marchi granules. On the right side it is free of osmic deposit. In addition, degeneration is present in the tectospinal tract from the right anterior colliculus and can be followed through the dorsal tegmental decussation to the left side of the brain-stem. There are many degenerating fibres in the commissure of the anterior colliculus which extend into the colliculus of the left side, while a few scattered Marchi-stained fibres are also present in the posterior commissure. The course of degenerating fibres into the thalamus may most conveniently be dealt with separately on each side.

On the right side the fibres which reach the thalamus run in two main streams—in the fillet and in the central tegmental fasciculi, though where they enter the thalamus these two systems are not sharply separated from each

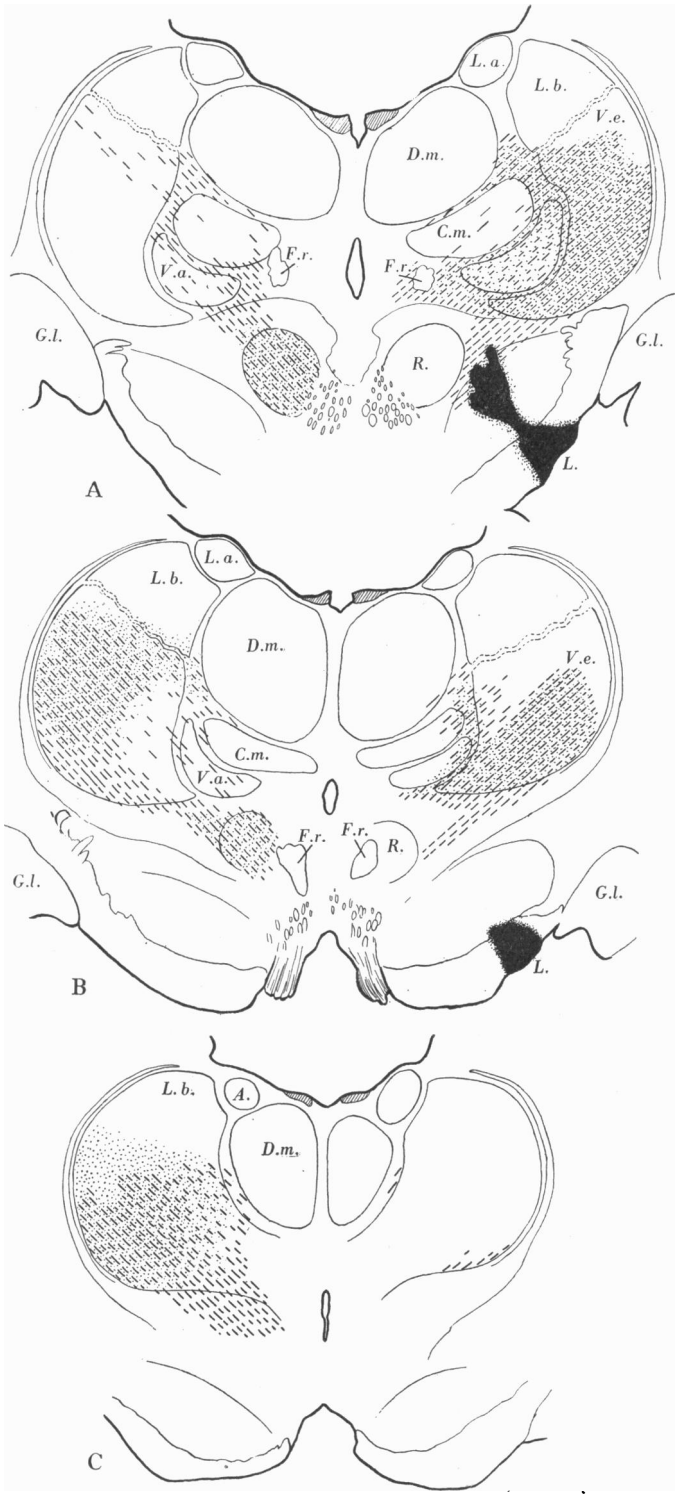

Fig. 10. The distribution of degenerating fibres in the thalamus in experiment G (O.M. 119).

other. The degenerating fibres of the fillet system course dorso-laterally from a position immediately lateral to the red nucleus (Fig. 10 A). The great majority of them form a conspicuous stream of interlacing osmic-stained fibres permeating the pars externa of the ventral nucleus at its posterior extremity. At this level the whole of this nuclear element is filled with degenerating fibres, while among these fibres the interstitial substance is sprinkled with Marchi granules. Towards the level of the rostral border of the centre median nucleus, the upper part of the pars externa of the ventral nucleus becomes clear of degenerating fibres (Fig. 10 B), and the latter, as the sections are traced forwards, rapidly disappear in a dorsi-ventral direction. When the level of the caudal margin of the anterior nucleus is reached, degenerating fibres have completely disappeared from the ventral nucleus, except for a very few which are still to be seen for a few sections at its extreme ventro-lateral margin (Fig. 10 C). The degenerating fibres in the pars externa of the ventral nucleus enter it mainly from the ventral medullary lamina. Some, however, run forwards and enter its medial aspect from the intermediate and medial medullary laminae. In the latter, a few can be followed as far rostrally as the transverse level of the anterior nucleus (Fig. 10 C), but these cannot be traced from the medial lamina into any of the adjacent thalamic nuclei. Possibly they end in the interstitial cells of the lamina (nucleus centralis lateralis of some authors).

The pars arcuata of the ventral nucleus is also filled with degenerating fibres throughout most of its extent, and on this side it is sprinkled with a deposit of Marchi granules, which, however, is not so dense as in the pars externa except at its dorso-lateral extremity. The fibres which permeate the arcuate nucleus are also very distinctly finer than those of the main part of the fillet which reach the pars externa of the ventral nucleus. The sections suggest that the degenerating fibres in the arcuate nucleus are derived from the medial fasciculi of the fillet system or from the central tegmental fasciculi, or both. Certainly the great majority of the lemniscal fibres skirt the lower margin of the arcuate nucleus and sweep round it to reach the pars externa of the ventral nucleus. It has been noted that the dorso-lateral extremity of the arcuate nucleus is more densely occupied by degenerating fibres. At the rostral end of the nucleus this is the only part which shows Marchi staining (Fig. 10 B).

The degenerating fibres in the central tegmental fasciculi run into and through the nucleus parafascicularis, and it seems probable that a proportion of them end here. Others turn antero-laterally at this level and appear to end in the arcuate nucleus. It is not possible, however, to be certain of this.

There is a complete absence of osmic-stained fibres in the substance of the dorso-medial nucleus, though a number may be followed forwards in the ventral part of the medial medullary lamina which forms a capsule for this nucleus. Further, no degenerating fibres are present in the elements of the lateral nucleus (*L. a.* or *L. b.*), in the nuclei of the pulvinar, in the medial and lateral geniculate bodies, or in the anterior nucleus. The centre median nucleus contains isolated Marchi-stained fibres which are running in a dorso-lateral

direction. They are more numerous near the posterior margin of the nucleus, but even here they are not very conspicuous. There is no sprinkling of osmic granules in the nucleus, which might indicate the breaking up of terminal fibres here, and the serial sections suggest strongly that the few degenerating fibres which are to be seen in the centre median nucleus are fibres of passage only.

On the left side, the Marchi degeneration is confined to the fibres of the brachium conjunctivum. The red nucleus of this side is filled with osmic deposit, and from its rostral aspect degenerating fibres are continued in an anterior and dorsi-lateral direction to reach the thalamus. At the caudal end of the thalamus these fibres enter it from the region of the medial part of the subthalamus, and at this level the ventral medullary lamina contains no degenerating fibres (Fig. 10 A). The brachium conjunctivum fibres can here be traced partly through the pars arcuata of the ventral nucleus, but mainly run in the intermediate and medial medullary laminae. From the latter, a few enter the most dorsal part of the pars externa of the ventral nucleus (Fig. 10 A). As the sections are traced forwards, degenerating fibres begin to enter the pars externa from below by way of the ventral medullary lamina, and, at the level of the rostral margin of the centre median nucleus, most of the pars externa (except for its ventro-medial part) shows Marchi degeneration (Fig. 10 B). Further forwards, at the level of the caudal margin of the anterior nucleus, these degenerating fibres are strewn throughout the ventral nucleus. As the sections are traced forwards from here, they become gradually restricted to the more ventro-lateral parts of the nucleus, and in this region a few Marchi-stained fibres may be seen close to the anterior extremity of the ventral nucleus.

As on the right side, there is no evidence of Marchi degeneration in the dorso-medial nucleus or in the elements of the lateral nucleus and pulvinar. A few degenerating fibres are to be seen in the arcuate nucleus and in the caudal part of the centre median nucleus, but it seems probable that these are fibres of passage only. The degenerating fibres on the left side are all of a finer calibre than those of the fillet system on the right side.

Experiment H. O.M. 122. Operation 17 January 1936, killed 29 January 1936.

In this animal a lesion was made involving both superior cerebellar peduncles. As in the previous experiment, the occipital lobe was exposed on one side by raising an osteoplastic flap, and was retracted upwards. The tentorium cerebelli was then incised so as to expose the superior vermis of the cerebellum. An ophthalmic knife was passed through the vermis and carried laterally on either side in order to sever the peduncles. The animal made a good recovery, but showed a characteristic cerebellar tremor and ataxia until its death.

Histological examination of the lesion

Serial Marchi sections were cut throughout the extent of the lesion. The latter was found to penetrate the superior vermis in the median plane, and to involve the brachia conjunctiva on both sides at the level where they emerge

from the cerebellar hemispheres. It also involves the roof nuclei. On the right side it reaches as far as the lateral margin of the fourth ventricle in its upper part, reaching here some of the fibres of the tegmental fasciculi which, as Wallenberg has shown, comprise a portion of the secondary trigeminal path, and extending partly into the vestibular nuclei. Further rostrally on this side the lesion reaches the rostral border of the brachium pontis, involving here also a portion of the lateral fillet system immediately in front of the pons. At this level spino-thalamic and spino-tectal fibres are running up among the fibres of the lateral fillet system, and some of these have been interrupted by the lesion. The lesion, therefore, was rather more extensive than had been intended. There is abundant Marchi degeneration in the medulla among fibres of the vestibulo-spinal tract, the posterior longitudinal bundle and the central tegmental fasciculi. In the following description, however, attention will be confined to the degenerating fibres which extend to the thalamus.

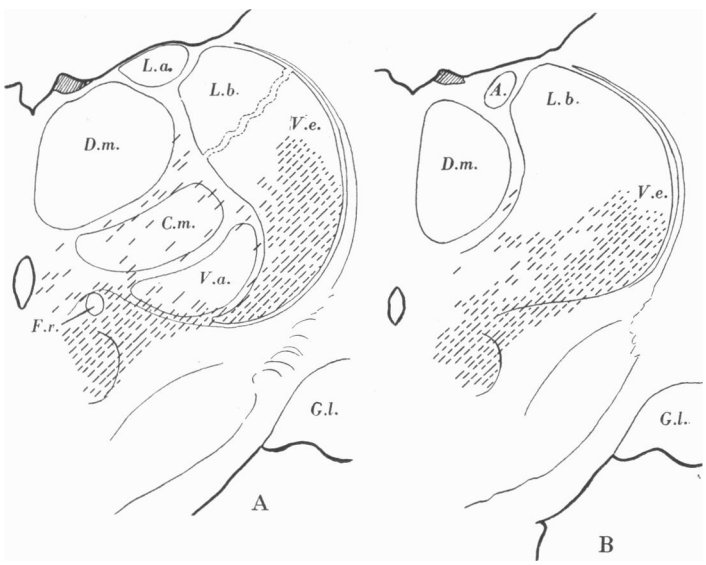

Fig. 11. The distribution of degenerating fibres in the thalamus in experiment H (O.M. 122).

Course of degenerating fibres

Immediately above the level of the lesion the fibres of both brachia conjunctiva are extensively stained with osmic acid. These degenerating fibres can be traced through the decussation of the brachia to the red nuclei of the opposite sides, whence many of them extend into the thalamus. Scattered degenerating fibres are also to be seen among the fibres of the lateral fillet. The subsequent course of the latter show them to belong to the spino-tectal and spino-thalamic tracts. At the level of anterior colliculi, scattered degenerating fibres are fairly numerous in the grey matter immediately surround-

ing the cerebral aqueduct, and quite a number of fibres in the central tegmental fasciculi of both sides also show Marchi staining. The origin of this latter degeneration is evidently the result of the fact that the lesion on the right side involved part of the secondary path of the trigeminal nerve which—as Wallenberg has shown in the rabbit—lies immediately under the brachium conjunctivum at the lateral margin of the 4th ventricle (see Fig. 10 of his paper, 1895). A few degenerating fibres extend into the anterior colliculus and across the commissure of the anterior colliculus to the opposite side. The medial longitudinal fasciculus, especially of the right side, is extensively degenerated, and from this numerous fibres extend into the nuclei of the third and fourth cranial nerves. The degenerating spino-thalamic fibres can be traced up in a position immediately deep to the inferior brachium. From here they pass medial to the medial geniculate body through the region of the nucleus limitans, where they splay out in a lateral and dorsal direction to enter the caudal extremity of the pars externa of the ventral nucleus.

On the right side, the degenerating fibres which enter the thalamus run in the spino-thalamic tract, the central tegmental fasciculi and the brachium conjunctivum. As they reach the thalamus these systems are distinct, but they rapidly come into such close relation with each other that their subsequent course in the thalamus cannot be followed separately. The more dorsal fibres run through the region of the parafascicular nucleus and many of them through the capsule of the centre median nucleus. Scattered degenerating fibres penetrate the substance of the centre median nucleus, especially in its caudal part, but there is no certain evidence that they end here. This nucleus contains no Marchi deposit among its cells which might indicate the breaking up of fibres of termination. Above and in front of the centre median nucleus, these degenerating fibres are seen to enter the medial medullary lamina in which they can be traced forwards as far as the transverse level of the anterior nucleus of the thalamus. The ventral medullary lamina contains numerous degenerating fibres at caudal levels of the thalamus, which in general course dorsally and laterally to enter the pars externa of the ventral nucleus. This nuclear element is almost completely filled with Marchi-stained fibres in its caudal part, though not so densely as in cases of lesions involving the medial fillet system (Fig. 11 A). In front of the level of the centre median nucleus, degenerating fibres can only be found in the lower part of the ventral nucleus (Fig. 11 B). They can be traced in this position as far forwards as the level of the middle of the anterior nucleus, beyond which they are no more evident. Comparison with previous experiments in which the tracts were separately involved indicates that the degenerating fibres in the caudal part of the pars externa of the ventral nucleus are derived from the spino-thalamic system, while those more rostrally are fibres of the brachium conjunctivum. The latter, however, are not so extensive anteriorly as on the left side of the thalamus or in experiment G, possibly because the left brachium conjunctivum was in the present case not completely involved. Most of the degenerating fibres which

enter the pars externa of the ventral nucleus from the ventral medullary lamina skirt the lower margin of the pars arcuata. Isolated fibres showing Marchi staining do penetrate the nucleus, however, and run through its medullary capsule. These seem mainly to be derived from the brachium conjunctivum. The sections suggest that these few fibres do not end in the arcuate nucleus, but are fibres of passage merely. Further medially, a number of degenerating fibres are to be seen in the periventricular grey matter on the medial aspect of the fasciculus retroflexus and close to the ventricle (Fig. 11 A).

On the left side of the thalamus the distribution of degenerating fibres is practically identical with that of the left side of the thalamus in experiment G, in which degeneration was confined to the brachium conjunctivum.

DISCUSSION OF RESULTS

In discussing the results of the experiments which have been recorded in this paper, it is convenient first to consider separately the various afferent fibre systems which have been involved by the lesions.

The termination of the medial fillet

As is well known, the fibres of the medial fillet take origin in the cuneate and gracile nuclei in the medulla. In the first two experiments localized lesions were produced in the gracile and cuneate nuclei respectively, while in experiments C and D the fillet fibres were interrupted in part soon after their origin from these nuclei. The Marchi degeneration following these lesions indicates that the medial fillet probably ends entirely in the pars externa of the ventral nucleus, reaching in its extent as far forwards as approximately the level of the rostral border of the centre median nucleus. The majority of the fibres enter the ventral nucleus from below by way of the ventral medullary lamina of the thalamus. Some, however, especially those from the cuneate nucleus, penetrate the caudal extremities of the centre median nucleus and the arcuate nucleus and, running in the intermediate and the ventral part of the medial medullary lamina, pass into the pars externa of the ventral nucleus from its medial aspect. No sure evidence was found of the actual termination of medial fillet fibres in the pars arcuata of the ventral nucleus or in the centre median nucleus, the scattered degenerating fibres found in the posterior ends of these elements being probably fibres of passage only. In all the experiments the lateral nucleus (both elements *a* and *b*) was quite free of Marchi degeneration. In many sections the contrast between the osmic-filled ventral nucleus and the clear groundwork of the lateral nucleus along their line of junction is very striking. The contrast is sufficiently abrupt to permit considerable assurance in the statement that no medial fillet fibres end in the lateral nucleus of the thalamus. It has been shown experimentally that the pars externa of the ventral nucleus, but not the lateral nucleus, projects on to the area postcentralis of the cortex (5). It may be inferred, therefore, on the basis of experi-

ments recorded here, that the afferent impulses conveyed by the medial fillet must be projected on to this area. With regard to the topographical relation in the ventral nucleus of terminal fibres conveying impulses from different levels of the body, these experiments indicate that those from lower levels reach the more lateral parts of the ventral nucleus, and those from higher levels the more medial parts. Thus, in experiment A the nucleus gracilis was injured, and it is known that this nucleus receives the fibres of Goll's tract which conveys impulses from the lower half of the trunk and the lower extremity. In this case, the degenerating fibres were concentrated along the ventro-lateral margin of the pars externa. In experiment B the lesion involved the cuneate nucleus which receives impulses by way of Burdach's column from the upper half of the trunk and the upper extremity, and here the degenerating fibres end predominantly in the central portion of the pars externa of the ventral nucleus, the lateral part remaining free of Marchi staining (Fig. 3 B). These conclusions confirm the impression gained by Wallenberg (20) from his observations on lower mammals that, in general, a more caudal origin of afferent impulses corresponds to a more latero-ventral position in the thalamus. They also fall into line with recent experiments which have demonstrated that the more lateral part of the pars externa of the ventral nucleus projects on to the upper end of the post central gyrus, while the more medial part projects on to the lower end (5, 16). While the Marchi technique does not permit of a very precise definition of the several areas of termination in the ventral nucleus of different groups of fillet fibres, the study of cell atrophy following cortical ablations in the experiments just quoted suggests that there is probably quite a sharply defined topographical representation in this nucleus of different sensory regions of the body.

The observation that medial fillet fibres terminate probably exclusively in the pars externa of the ventral nucleus in the monkey is in accord with the results of previous studies. In 1895 Mott (12) made an experimental enquiry on the afferent tracts of the central nervous system of the monkey. Although he did not concern himself with a detailed study of their thalamic termination, his figures indicate that in experiments in which the gracile and cuneate nuclei were destroyed, degenerating fibres all ended in the pars externa of the ventral nucleus. Vogt (15) found that fibres from the cuneate nucleus pass to the caudal end of this nuclear element, and though some of the more medially situated fibres were also seen to enter the capsule of the centre median nucleus and to penetrate the arcuate nucleus, it is probable that they all eventually terminated in the pars externa. Wallenberg (20) found in the rabbit that degenerating fibres following lesions in the posterior column nuclei extend into a region of the ventral nucleus of the thalamus, which, from his descriptions and figures, evidently corresponds to the pars externa of the macaque thalamus. Similar observations were made by Probst (13) in 1900. Recently Ranson & Ingram (14) defined very clearly the precise termination of the medial fillet in the cat, and demonstrated that it ends in the greater part of the pars externa of the

ventral nucleus except for its rostral end. Observations on the rat (3) similarly show the relation of the medial fillet to the pars externa of the ventral nucleus.

It is worth while emphasizing the fact that the experiments recorded in this paper show that the terminal fibres of the medial fillet in the thalamus are distributed over precisely that part of the ventral nucleus whose cells undergo complete atrophy after lesions confined to the postcentral gyrus (area post-centralis).

Spino-thalamic tracts

In two experiments (E and F) a hemisection of the spinal cord was made in order to interrupt on one side the spino-thalamic tracts. In one case the lesion was in the cervical region, between the fourth and fifth cervical nerve roots, and, in the other, in the thoracic region between the third and fourth thoracic nerve roots. These cases show that proportionately many more degenerating spino-thalamic fibres follow the cervical lesion. This corroborates the statement of Collier & Buzzard on human material that "the number of spino-tectal and spino-thalamic fibres was considerably greater in lesions of the cervical enlargement than in lesions at lower levels". In the rabbit, according to Wallenberg (20), spino-thalamic fibres take origin only from the cervical part of the spinal cord.

The spino-thalamic tract occupies quite a lateral position in the mid-brain, and its fibres run in a dorsal direction to form a component of the lateral fillet system. They approach the thalamus from a position immediately medial to the medial geniculate body (Fig. 8 A), extending from here dorso-medially to the nucleus parafascicularis. There is evidence from the two experiments that the fibres arising from more caudal levels occupy a more lateral position at their entry into the thalamus. In the cervical lesion many penetrated the parafascicular nucleus (which in this case was richly strewn with osmic granules), while in the thoracic lesion the degenerating fibres were concentrated close to the medial aspect of the medial geniculate body. In the thalamus at least the great majority of spino-thalamic fibres end in the pars externa of the ventral nucleus, the site of their termination corresponding closely with that of the medial fillet fibres. Those taking origin from the lower levels of the cord enter the ventral nucleus from below by way of the ventral medullary lamina, while those from higher levels mainly penetrate the nucleus from its medial aspect, approaching it by way of the intermediate medullary lamina and the ventral part of the medial medullary lamina. As in the case of the medial fillet, some of the latter fibres pass through the caudal extremities of the centre median and arcuate nuclei, but the evidence of the sections suggests that they do not end in these elements. Within the pars externa of the ventral nucleus the distribution of degenerating fibres suggests that those of a more caudal origin terminate in a more lateral position. The question arises whether the spino-thalamic fibres reach any other thalamic nuclei. It has already been noted that the few scattered fibres in the centre median and arcuate nuclei are probably fibres of passage only. No degenerating fibres were found in these

experiments (or in experiment G in which the whole fillet system was involved at its entry into the thalamus) in the dorso-medial nucleus, or in the lateral nucleus (except possibly for its extreme ventral border). In experiment E, and in experiment H in which the spino-thalamic tract was involved, a few degenerating fibres were found in the periventricular grey matter medial to the fasciculus retroflexus at the caudal end of the thalamus (Fig. 7 A), but they were absent from this region in experiment F. In experiment E, also (and in experiment G), the medial medullary lamina contained many Marchi-stained fibres, and it seems probable that some end in the nuclei of this lamina (nucleus paracentralis and nucleus centralis lateralis) since they could be traced forwards beyond the level at which they are found in the neighbouring region of the pars externa of the ventral nucleus (Figs. 7 C and 10 C). However, the Marchi technique is not adequate to decide this point, though it may be remarked that ablation experiments on the cortex indicate that neither the nuclei of the medial medullary lamina or the periventricular grey matter are connected to the cortex (17). Following lesions in the spinal cord of the monkey, Mott (12) followed ascending fibres by the Marchi method and found "a few *apparently* going on with the fibres of the fillet to the optic thalamus". His figure shows these fibres ending in what appears to be the medial part of the caudal extremity of the pars externa of the ventral nucleus, but the diagram is too crude to allow of any certainty on this point. In human material Collier & Buzzard (6) traced the spino-thalamic tract up to a point where it came "in contact with the mesial surface of the internal geniculate body", after which "it swung abruptly outwards—into the ventral nucleus of the thalamus". The fact that spino-thalamic fibres end preponderatingly in the same thalamic nucleus which receives the termination of the medial fillet fibres is worth emphasizing because of the generally accepted thesis that these two tracts serve to convey afferent impulses of different categories.

Dentato-thalamic fibres

It is well known that a considerable proportion of the efferent cerebellar fibres in the brachium conjunctivum pass by the opposite red nucleus and continue their way on to the thalamus. Their destination in the thalamus in the monkey has been studied experimentally by Vogt (15), who found that they terminated in the "intermediate ventral nucleus", dorsal and rostral to the ending of the medial fillet. It may be noted that the "intermediate ventral nucleus" of Vogt's terminology corresponds to the rostral part of the pars externa of the ventral nucleus. In the cat, Ranson & Ingram (14) traced brachium conjunctivum fibres into the rostral pole of the pars externa of the ventral nucleus, and also into the arcuate nucleus. In two experiments (G and H) recorded in this paper, a lesion had been made in the superior cerebellar peduncle. The distribution of Marchi degeneration subsequently showed that its thalamic fibres end almost entirely in the dorsal and rostral parts of the pars externa of the ventral nucleus from about the level of the

middle of the centre median nucleus as far forwards as the level of the anterior nucleus. This area of termination corresponds in a very striking way to the area of complete cell atrophy which follows cortical lesions involving the precentral gyrus. Whether there is any overlapping in the ventral nucleus of the areas of termination of the fillet fibres and the brachial fibres cannot, of course, be decided by the Marchi technique, but a comparison of the sections gives the impression that this is not so. Contrary to the findings of Ranson & Ingram, no certain evidence was found of the termination of cerebellar fibres in the pars arcuata of the ventral nucleus. In this nucleus (as well as in the centre median nucleus) only isolated fibres of passage were found at their caudal extremities. This discrepancy is due to the fact that the arcuate nucleus as described in the cat is evidently not entirely homologous with the arcuate nucleus of the macaque thalamus. A comparison of relevant figures shows that probably only the caudal end of the cat's arcuate nucleus is the equivalent of the macaque arcuate nucleus, and this region seems to have been comparatively free of Marchi degeneration in the experiment of Ranson & Ingram. On the other hand, the rostral part of the cat's arcuate nucleus as figured by these authors occupies the position of the rostral part of the pars externa of the ventral nucleus in the monkey.

Trigeminal fillet

In two experiments (B and C) local lesions were produced on one side in the spinal nucleus of the fifth cranial nerve. In experiment B the lesion was uncomplicated by injury to other elements on the same side. The sections of this case indicate that very few fibres from the spinal nucleus reach the thalamus. Scattered degenerating fibres were found in the medial fillet and in the central tegmental fasciculi of the opposite side, and some of these could be traced into the medio-ventral extremity of the pars externa of the ventral nucleus. In experiment C, injury to the spinal nucleus of the fifth nerve was also followed by some Marchi degeneration in the central tegmental fasciculi of the opposite side, but the termination of these fibres in the thalamus could not be determined because of their mingling with medial fillet fibres which were also involved in this case. In experiment D, the position of the secondary trigeminal path in the central tegmental fasciculi was involved by a lesion, and degenerating fibres could be followed into the medial border of the pars externa of the ventral nucleus, entering it from the region of the parafascicular nucleus. The dorsal path of secondary trigeminal fibres was also affected by the lesion in experiment H, but in this case Marchi degeneration of these fibres was obscured by the injury to the brachium conjunctivum. These experiments serve to indicate that trigeminal fibres arising in the spinal nucleus end in the medio-ventral part of the pars externa of the ventral nucleus. Some may end in the parafascicular nucleus and the nuclei of the medial medullary lamina through which they course, but there is no evidence that any terminate in the centre median, arcuate or dorso-medial nuclei.

Although the attempt was made, unfortunately in no case was a lesion placed in the main or medullary sensory nucleus of the fifth nerve. Thus no positive evidence has been obtained as to the thalamic termination of secondary fibres from this important element. On the analogy of the medial and spinal fillets, it might be supposed that the thalamic fibres of all parts of the trigeminal nucleus probably end in the same region, i.e. in the medio-ventral portion of the pars externa of the ventral nucleus. Another possibility, however, is the pars arcuata of the ventral nucleus which is known to project, at least in part, on to the face area of the pre- or post-central gyrus.[1] In only one experiment of this series was there definite evidence of the termination of degenerating fibres in the arcuate nucleus, and that is experiment G. In this experiment the lesion must have involved secondary trigeminal fibres from the main sensory nucleus, but, since it also cut across many other fibre systems at the caudal boundary of the thalamus, no certain conclusions can be drawn from such an observation. Wallenberg's Fig. 5 C, 6 E (20), and Fig. 5 (19), seem to show quite clearly that in the rabbit secondary trigeminal fibres end largely in the pars externa of the ventral nucleus, while that portion of the ventral nucleus which is apparently the equivalent of the macaque arcuate nucleus is left quite clear of Marchi degeneration in his experiments.

General relation of thalamic nuclei to ascending tracts

It is clear that at least the great majority of the fibres of the medial and spinal lemnisci and of the brachium conjunctivum, which reach the thalamus, end in the pars externa of the ventral nucleus, the first two ending in that region of the nucleus which projects on to the area post-centralis, and the last in the more dorso-rostral part which projects on to the motor cortex. The Marchi technique does not allow a decision whether any of these fibres end in the intra-laminar nuclei through which they run to their main destination, e.g. the parafascicular nucleus and the nuclei of the medial medullary lamina, but in the case of spino-thalamic fibres there is some positive evidence that this is so.

There is no evidence that the pars arcuata of the ventral nucleus receives terminal fibres of the medial and spinal fillets or of the brachium conjunctivum. That it receives some afferent fibres is indicated by experiment G, in which a large lesion involved ascending paths immediately behind their entry into the caudal end of the thalamus, but the source of these fibres is uncertain.

There is no evidence that the centre median nucleus receives any terminal fibres from more caudal levels of the brain stem. In several of the experiments

[1] My own experiments, some of which await publication, show that the arcuate nucleus projects on to the precentral gyrus. It was assumed, on the basis of Brodmann's charts, that it connects with the true motor cortex. However, it has been shown by Bucy (*J. comp. Neurol.* vol. LXII, 1935) that in the macaque monkey the sensory cortex of the area postcentralis extends across the lower end of the central sulcus and occupies the lower end of the precentral gyrus. It is possible, therefore, that the arcuate nucleus is related to this forward extension of the sensory cortex rather than to the lower extremity of the motor cortex.

isolated degenerating fibres were found penetrating its caudal extremity, but they appear to be fibres of passage only.

In no case could degenerating fibres be traced into the substance of the lateral or dorso-medial nuclei. The experiments indicate that these nuclei receive no contribution from any part of the fillet system or from the cerebellum. The same observation applies to the elements of the pulvinar and the anterior nucleus.

As regards nuclei of the mid-line, in only two cases in which spino-thalamic fibres had been involved by the lesion were isolated degenerating fibres found in the periventricular grey matter at the most caudal extremity of the thalamus.

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ABBREVIATIONS

A.	Anterior nucleus.	*m.V*	Motor nucleus of fifth nerve.
A.c.	Anterior colliculus.	*N.c.*	Nucleus cuneatus.
C.m.	Centre median nucleus.	*N.c.e.*	Nucleus cuneatus externus.
Cr.	Crus cerebri.	*N.g.*	Nucleus gracilis.
D.m.	Nucleus dorso-medialis.	*N.l.*	Nucleus limitans.
F.	Fornix.	*P.*	Pulvinar.
F.r.	Fasciculus retroflexus.		
F.sol.	Fasciculus solitarius.	*Pr.*	Pretectal nucleus.
G.l.	Lateral geniculate body.	*Pyr.*	Pyramid.
G.m.	Medial geniculate body.	*R.*	Red nucleus.
Hb.	Habenular ganglion.	*R.b.*	Restiform body.
L.	Lesion.	*S.V*	Sensory nucleus of fifth nerve.
L. a.	Element of lateral nucleus.	*Sp.V*	Spinal nucleus of fifth nerve.
L. b.	„ „ „	*V.a.*	Pars arcuata of ventral nucleus.
Lem.	Medial lemniscus.	*V.e.*	Pars externa of ventral nucleus.
M.	Mammillo-thalamic tract.	*V.a.m.*	Pars antero-medialis of ventral nucleus .
M.m.	Medial mammillary nucleus.		

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