AN EXPERIMENTAL STUDY OF THE FORNIX IN THE RABBIT

By JAMES M. SPRAGUE* and MARGARET MEYER
Department of Human Anatomy, University Museum, Oxford

The extrinsic connexions of the hippocampus have been studied in a number of vertebrate types, and the complexity of the system has been described by many workers (cf. von Kölliker, 1894, 1896; Elliot Smith, 1896; Cajal, 1911; Johnston, 1913; Kappers, Huber & Crosby, 1936; Young, 1936). The voluminous and controversial literature based on normal material has been reviewed by these authors and will not be repeated here. The experimental papers are few (cf. Edinger & Wallenberg, 1902; Gudden, 1881; Probst, 1901; Allen, 1944; Fox, 1943; Gerebtzoff, 1941–2), and these are based chiefly upon the Marchi method and, to a lesser extent, upon studies of retrograde cell degeneration. The information thus gained, however, is incomplete and contradictory, and there is thus need to undertake a re-examination of this system with modern methods.

The present study reports the results of experiments in rabbits in which small lesions have been placed in various parts of the fornix system (Text-fig. 1), the brains being subsequently prepared by a modification of the silver method of Glees (1946). This technique demonstrates in very satisfactory fashion the degenerative fragmentation of nerve fibres and their terminals, whether the latter consist of boutons terminaux or a pericellular plexus (free endings). The terminals may show marked degenerative changes as early as the third day following section of the axons, though in the case of the larger fibres these may not be apparent until the fifth day. During this period the degeneration is wholly distal to the site of the lesion with the exception only of retraction bulbs which are developed at the cut ends of the fibres. The method forms, without question, the most reliable, sensitive and precise technique for the study of fibre degeneration following axonal interruption within the central nervous system which is available at present, although isolated fibre connexions of minor significance are difficult to follow and may be overlooked.

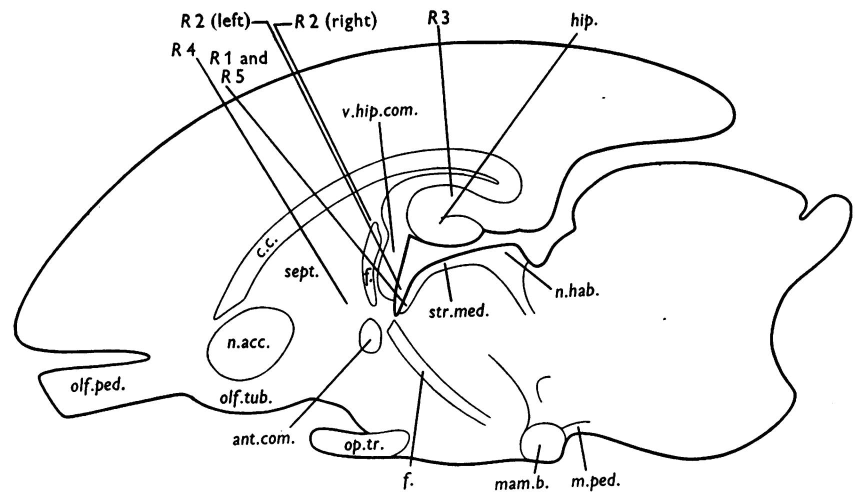
The fornix represents the only known efferent pathway of the hippocampus. It arises, according to Allen (1944), from all the pyramidal cells of the hippocampus and also from isolated pyramidal cells of the polymorph layer of the dentate gyrus. Fibres leaving the hippocampus collect in the alveus to form the large tract known as the fimbria, and the latter splits into two components, commissural and projection. The projection fibres have been divided into those which pass in front of the anterior commissure into the septum (precommissural fornix), and those which form the descending column of the fornix (or postcommissural fornix) and terminate mainly in the mammillary body. In normal, and in some experimental studies it has also been stated that fornix fibres have been traced to other centres such as the preoptic

* John Simon Guggenheim Memorial Foundation Fellow. On leave of absence from the Department of Anatomy, The Johns Hopkins University, Baltimore, Maryland, U.S.A.

region, to hypothalamic nuclei other than the mammillary body, to the habenula, and even into the tegmental region.

The commissural fibres connect the hippocampi of the two hemispheres. In the rabbit a differentiation into dorsal and ventral hippocampal commissures exists, described as the dorsal and ventral psalterium by von Kölliker (1896). According to Cajal (1911) the dorsal psalterium consists chiefly of the crossed temporo-ammonic tract and is therefore not primarily interhippocampal in its connexion. The ventral psalterium, on the other hand, is supposed to be a true commissure, though its exact terminations have not so far been determined experimentally.

Longitudinally orientated fibres which lie between the corpus callosum and the dorsal part of the hippocampus constitute another component of the fornix system.



Text-fig. 1. Outline of sagittal section through a rabbit's brain indicating the different positions of the lesions in the experiments described.

Considerable confusion in the terminology of this subcallosal part of the fornix exists in the literature, and it does not appear profitable to review the different usages of terms such as 'fornix of Forel', 'fornix longus', 'superior fornix' or 'dorsal fornix'. The term dorsal fornix is used here to designate the whole of this longitudinal system consisting, as Cajal suggested, of a variety of afferent and efferent pathways, including the fibres penetrating the corpus callosum, possibly fibres running forward from the dorsal psalterium, and afferent fibres said to arise in the nucleus of the diagonal band of Broca.

The experiments here recorded are intended to give a conclusive answer to a number of disputed points: (1) the termination of the fornix in respect of the different nuclei of the mammillary body; (2) the existence and relative importance of fornix fibres which end in other parts of the hypothalamus; (3) the existence and composition of fornix fibres which pass beyond the mammillary body into the tegmentum; (4) the possible contribution of any part of the fornix system to the habenula by way of the stria medullaris; (5) the septal termination of any part of the fornix system; (6) the composition of the hippocampal commissures; and (7) the origin and termination of fibres of the dorsal fornix.

In all the cases described, fibres of the cingulum were severed and show degeneration. Since the origin and termination of the cingulum is outside the scope of this report, they will be the subject of a special study.

MATERIAL

Eight young rabbits were operated upon under the usual aseptic conditions with the use of pentobarbital sodium (Abbot) or of Dial (Ciba), administered intraperitoneally. A burr hole was made in the superior aspect of the parietal bone and slightly enlarged, the dura incised and the underlying cortex exposed. A narrow scalpel was then inserted vertically close to the median fissure and moved laterally through a distance of approximately 5 mm. in order to sever the fornix. The animals were killed 3–5 days after the operation by intravascular perfusion, under anaesthesia, of normal saline, followed by 10% formol-saline. The lesions were in each case checked histologically. It was found that in all cases the cingulum and the supracallosal striae had been cut by the incision, as well as the fornix. Cortical injury was practically confined to the immediately adjacent part of the cingulate gyrus. Interference with the vascular supply had, in some cases, resulted in an area of necrosis in the ventral hippocampal commissure, and this has been referred to in the description of the individual experiments. Frozen sections were cut and treated with silver, cresyl violet and Weil's stain. Selected sections were traced with a microprojector and the distribution of the degeneration plotted under a 2 mm. oil-immersion lens. Only the most representative sections from each case are recorded in the diagrams; many other levels were examined, and each case was studied independently by both authors. Five of the eight experimental animals are described; the remaining cases were used for confirmation of the results obtained.

RESULTS

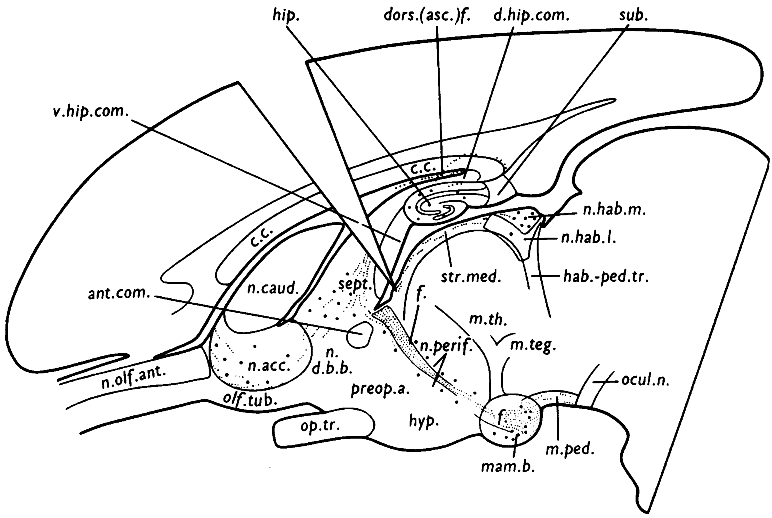
R.1, survival time 5 days (Text-fig. 2)*

The lesion on the right side cuts the fimbria and the dorsal fornix, injuring the septum and the stria medullaris; much of the ventral hippocampal commissure is destroyed. The lesion is similar but less complete on the left side. The brain was sectioned sagittally.

Anterior to the lesion on the right side, fibres of the fornix are degenerated. Some can be traced into the septal region; they terminate in the lateral and medial septal nuclei, but mainly in the antero-ventral part of the nucleus accumbens. All the remaining fibres of the fornix form the descending column which is completely degenerated. In traversing the hypothalamus, fibres terminate along the whole length of the perifornical nucleus surrounding the fornix. The other hypothalamic nuclei anterior to the mammillary body, and also the preoptic region, are normal. Within the mammillary body the degenerating fibres of the fornix form most of the posterior part of the capsule surrounding it, and they appear to spread anteriorly in

* In all the text-figures degenerating fibres are indicated by fine dotted lines and degenerating terminals by coarse dots.

the fibre capsule to terminate in the basal and intermediate parts of the medial mammillary nucleus (Pl. 1, fig. 2). Terminal degeneration is particularly severe in the basal area (Pl. 1, fig. 1), which is situated in the ventral and posterior part of the mammillary body.* Some fascicles of degenerating fibres overshoot the mammillary body and can be traced into the mammillary peduncle as far as the point of exit of the oculomotor nerve. The fine fornix fibres are easily distinguished among the heavy fibres of the peduncle. The more superficial fibres of the stria medullaris are degenerated and can be followed into the habenular nuclei. Terminal degeneration is chiefly confined to the medial habenular nucleus. Since the lesion in the ventral hippocampal commissure is extensive, there is severe fibre and terminal degeneration in all layers of the hippocampus, and also in the dentate gyrus.



Text-fig. 2. Diagram of sagittal section of brain in experiment R. 1, right side, indicating the lesion and the resultant fibre and terminal degeneration.

Some of the fibres of the dorsal fornix show fragmentation; they appear to penetrate the corpus callosum and, after joining the deep layers of the cingulum, curve round the splenium of the corpus callosum and apparently terminate in the hippocampus. Most of the fibres penetrating the corpus callosum are normal.

R. 2, *survival time* 5 *days* (Text-figs. 3, 4)

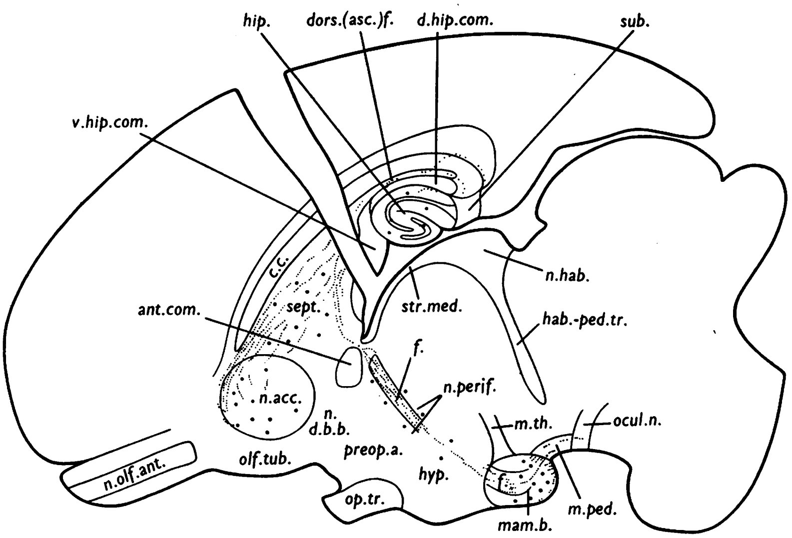
On the right side the fimbria is almost spared, the dorsal fornix has been cut and the posterior part of the septum is injured. On the left side the lesion is more extensive, apparently cutting the fimbria entirely. Injury to the ventral hippocampal commissure is slight, being confined to a local, clean-cut, incision in the medial part of the left side only. The stria medullaris has remained uninjured on both sides.

On the left side (Text-fig. 3), terminal degeneration in the septal nuclei is severe, and fascicles of degenerating fibres pass through the septum to collect in a compact

* Diagrams of transverse sections are shown in text-fig. 7 *a–c* to illustrate the distribution of degenerating fibres in the mammillary nuclei after interruption of the fornix.

subcallosal tract which is completely degenerated. This tract borders the superior and rostral surface of the nucleus accumbens, and many of its fibres terminate in this nucleus. It appears that some of these degenerating fibres turn laterally when reaching the medial forebrain bundle, but they could not be traced beyond this point. The olfactory tubercle, the nucleus of the diagonal band of Broca, the anterior olfactory nucleus and the preoptic region are intact. The descending column of the fornix passing through the septum is degenerated, while fibres which lie between the ventral hippocampal commissure and the descending column are normal.

Traversing the hypothalamus, the descending fornix column and the mammillary body present the same picture as that described for R.1. As in the latter case, a considerable number of degenerated fascicles overshoot the mammillary body into



Text-fig. 3. Diagram of sagittal section of brain in experiment R.2, left side.

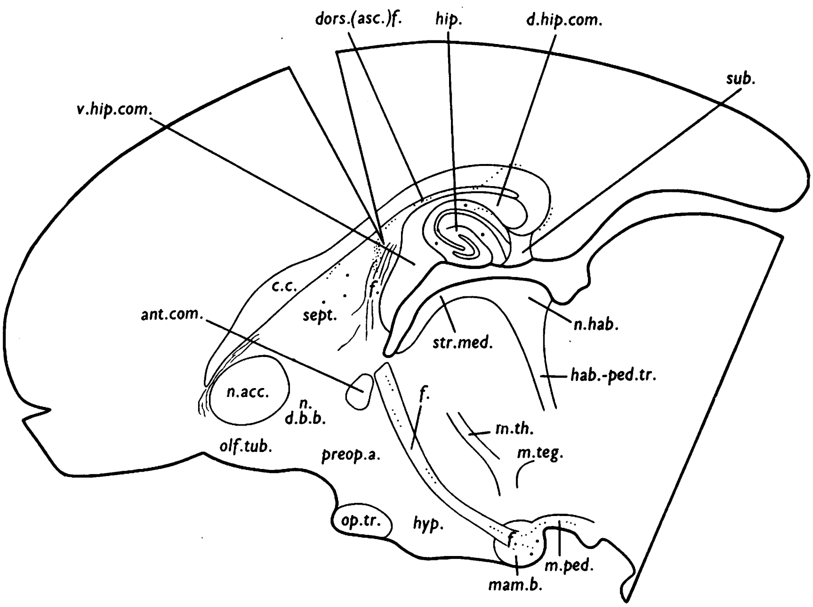
the tegmental region and can be traced among the fibres of the oculomotor nerve. The stria medullaris and the nuclei of the habenula are intact.

The area posterior to the lesion shows essentially the same degenerative changes as R.1, except for much less degeneration in the hippocampus which is explained by the small extent of the lesion in the ventral hippocampal commissure.

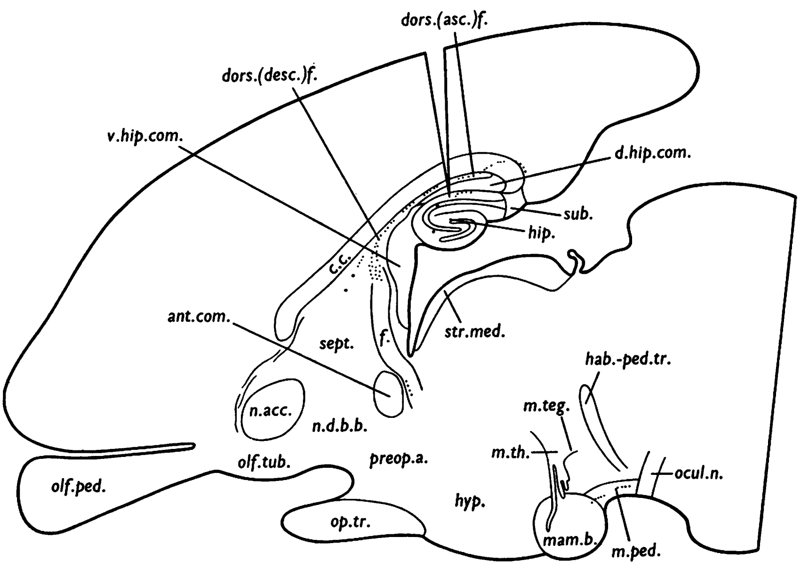
On the right side (Text-fig. 4), the septal degeneration is limited to a small amount in the lateral septal nucleus. Degenerating fascicles join the otherwise normal pillars of the fornix dorsally as it passes through the septum. There is little degeneration in the descending column of the fornix and in the mammillary body, but the fascicles passing into the tegmentum show quite severe degenerative change.

R.3, survival time 5 days (Text-fig. 5)

The lesion is entirely limited to the right side, cutting the dorsal fornix and only at one point penetrating into the hippocampus. There is no injury to the septum, fimbria or stria medullaris. Rostral to the lesion the fine fibre fascicles of the dorsal



Text-fig. 4. Diagram of sagittal section of brain in experiment R. 2, right side.



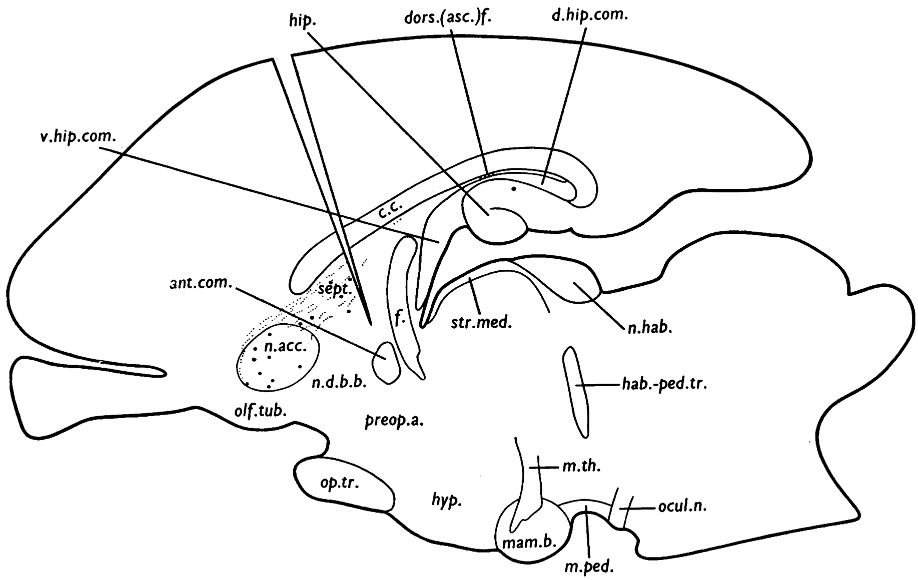
Text-fig. 5. Diagram of sagittal section of brain in experiment R. 3, right side.

fornix are completely degenerated. They are observed to turn ventrally into the upper part of the descending column of the fornix. Septal degeneration is very slight and confined to the lateral septal nucleus. There is slight degeneration in the lower part of the descending column of the fornix. In the mammillary body no change could be detected; on the other hand, a number of the fibres passing into the tegmentum are degenerated.

The degeneration in the dorsal fornix posterior to the lesion is similar to that already recorded for the other cases. The hippocampus shows little change.

*R.*4, *survival time* 5 *days* (Text-fig. 6)

The lesion is limited to the right septum, passing deeply into the lateral septal nucleus. Secondary degeneration in the septal nuclei and in the nucleus accumbens is severe and is similar to that in R. 1 and on the left side of R. 2. The descending column of the fornix, the mammillary body, the olfactory tubercle and the preoptic region are normal. The dorsal fornix posterior to the lesion and the hippocampus show very little change in this case.

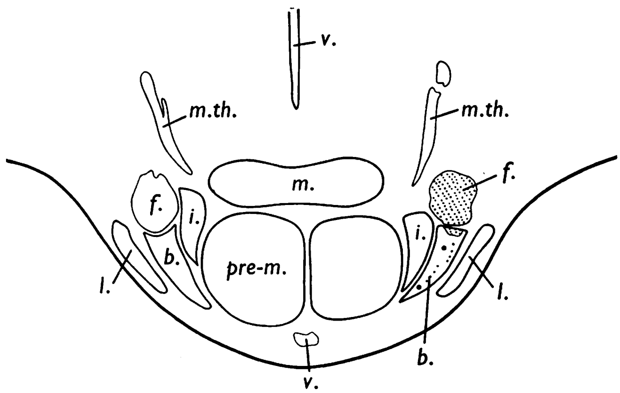


Text-fig. 6. Diagram of sagittal section of brain in experiment R. 4, right side.

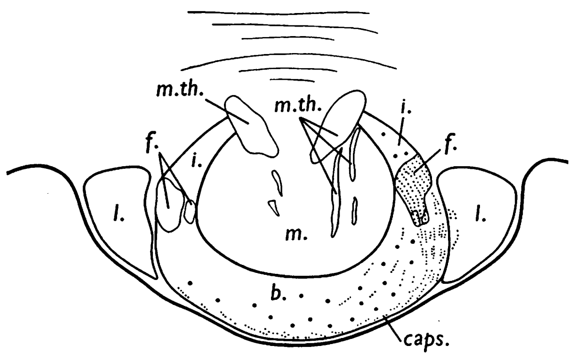
*R.*5, *survival time* 3 *days* (Text-figs. 7*a–c*)

The lesion is entirely confined to the right side, cutting the fimbria and destroying most of the right half of the ventral hippocampal commissure. The posterior part of the septum and the stria medullaris have also been injured. The brain was cut transversely, and only a series of diagrams through the mammillary body is given to indicate the course and termination of fornix fibres within the nuclei of the mammillary body. The results relevant to other areas are not described, except to clarify points which have remained doubtful from study of the sagittal sections of the other experiments.

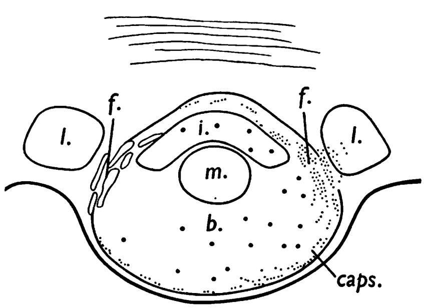
The right descending column of the fornix is degenerated. The contralateral side has been spared in this case, and the left descending column is entirely intact. The most medial fibres of the column of the fornix curving through the septum are normal on both sides, and are evidently ascending fibres.



Text-fig. 7*a*.



Text-fig. 7*b*.



Text-fig. 7*c*.

Text-figs. 7*a*–*c*. Series of diagrams of transverse sections through the mammillary body of experiment R. 5 to illustrate the distribution of degenerating fibres in the mammillary nuclei after interruption of the fornix.

In the anterior part of the mammillary body (Text-fig. 7*a*), there is no definite capsule. At this level the ventral part of the premammillary nucleus is seen and, superior to it, the anterior paired portion of the medial mammillary nucleus; the intermediate and basal parts are just beginning to appear. On the right very few degenerating fibres are seen in the basal part; the other nuclei on the right side and all those on the left are normal.

At the more caudal level shown in Text-fig. 7*b*, the degenerating fibres of the fornix are seen to contribute to the formation of the capsule of the mammillary body (fibres of the capsule which have other origins are intact). In the capsule degenerating fibres of the right fornix spread to the left side of the mammillary body. At this level there is terminal degeneration in the basal part of the medial nucleus, particularly in the proximity of the capsule; the intermediate part also shows a few degenerating terminals. Degenerating fascicles of the fornix spread out into the lateral nucleus, but they do not appear to end there; probably they rejoin the capsule more ventrally.

At the next level (Text-fig. 7*c*), the fornix is reduced to narrow bands of fibres which form most of the lateral part of the capsule. The intermediate nuclei have become fused in the midline and enclose the much decreased medial part of the medial mammillary nucleus. The basal part has expanded and, at a still more caudal level, it occupies the entire mammillary body. The distribution of the secondary degeneration in the different nuclei of the mammillary body is illustrated in Text-fig. 7*c*.

The right stria medullaris has been injured in this experiment, and the right medial habenular nucleus is filled with clusters of swollen, argentophil annular boutons (Pl. 2, fig. 3); in the nucleus of the left side the fibre plexus is normal (Pl. 2, fig. 4).

DISCUSSION

The different positions and the varying extents of the lesions in the experiments described are graphically summarized in Text-fig. 1. It will be observed that the projection systems of the fornix have been severed selectively or in different combinations, and the relation of the distribution of the resulting fibre degeneration to these variations in the lesions becomes readily apparent. Summarizing the results of each experiment, it is convenient to discuss parts of the fornix system separately.

Descending column of the fornix. The degenerating fibres of the descending column of the fornix were followed to their termination in three cases (R. 1, R. 2, R. 5). These experiments provide no evidence that the hypothalamic nuclei which lie in front of the mammillary body receive any contribution from the fornix, with the exception of some fibres which leave the main bundle to terminate immediately in the perifornical nucleus. On the contrary, the experimental evidence shows that almost the entire descending column terminates in the latero-ventral and posterior parts of the medial mammillary nucleus. In lower mammals the medial mammillary nucleus is differentiated into a number of individual nuclei, which have been described in detail by M. Rose (1935) and J. Rose (1939–40). The silver method used in our experiments shows clearly that fibres of the fornix project only to the basal and intermediate parts of the medial mammillary nucleus* (J. Rose's terminology), and they terminate by means of a fine pericellular plexus which surrounds the nerve cells. The anterior and

* J. Rose finds that the basal and intermediate parts of the medial mammillary nuclei show the same cell type, and that both show a definite regression in higher mammals. However, it is not always possible to establish the homologies of these nuclei with accuracy in different mammalian groups.

medial parts of the medial mammillary nucleus which, according to the experimental work of van Valkenburg (1912), give rise to the mammillo-thalamic tract, have no direct connexion with the fornix.* Some fascicles of the fornix splay out into the lateral mammillary nucleus as has been described by Allen (1944) in Marchi material. Since we have found no evidence that fibres actually terminate in this nucleus, it is concluded that these fascicles may rejoin the capsule. The fornix enters the mammillary body at its dorso-lateral aspect, and much of the lateral and ventral, and almost the entire posterior, part of the capsule consists of fornix fibres. It may be noted that some authors (e.g. Allen, 1944) have held the view that the capsule is composed solely of fibres of the mammillo-thalamic tract.

It is confirmed in our material that fornix fibres do not cross the midline anterior to the mammillary body, which is in accordance with findings of Le Gros Clark (1938) and of Allen (1944). Only in the posterior part of the mammillary body is there a certain amount of overlap to the contralateral side by way of the capsule (Text-figs. 7*b*, *c*). Whether this can be interpreted as an illustration of bilateral representation is questionable, for in the rabbit's brain the mammillary bodies themselves are not bilateral as they are in higher mammals, and their nuclei in the posterior part are fused. It is probable, therefore, that this overlap does not exist in higher mammals where the two separate mammillary bodies are sharply divided by capsular fibres, and that in them the relationship between the hippocampus and the mammillary bodies is entirely unilateral.

A continuation of fornix fibres into the mesencephalon has been suggested by Edinger & Wallenberg (1902) and by von Kölliker (1896). In our experiments both the descending fibres of the fornix and the dorsal fornix contribute to a tract which descends in the fornix column and passes beyond the mammillary body into the mesencephalon, intermingling with fibres of the mammillary peduncle. These fibres are fine and can easily be distinguished from the coarse (undegenerated) fibres of the mammillary peduncle. In the material described they could not be followed farther than is indicated in the diagrams. Gerebtzoff (1941–2), however, described a component of the fornix terminating in a distinct nucleus of the bulbar reticular formation.

A hippocampo-habenular component of the descending column of the fornix has been described on the basis of the examination of normal material (Young, Humphrey and others), and has recently been described also in Marchi experiments by Gerebtzoff. Edinger & Wallenberg, and also Probst, do not agree with this conception and were unable to show the existence of such a component in their Marchi material. Moreover, Cajal, in his normal preparations, concluded that there is no connexion between fibres of the fornix and the stria medullaris. Only in one of our cases (R. 2) in which the fornix was cut successfully did the stria medullaris itself escape involvement by the lesion, and in this case no terminal degeneration was found in the habenular nuclei. The lesions in the other experiments injured the medial superficial fibres of the stria medullaris, and degeneration was traced from the primary lesion

* After interrupting the mammillo-tegmental tract in the rabbit, van Valkenburg observed retrograde degeneration in the dorsal part of the medial mammillary nucleus. The ventro-medial part remained intact, together with the mammillo-thalamic tract. If this evidence is valid, then, at least in the rabbit, impulses received from the fornix would be conveyed directly to the anterior thalamic nucleus and Cajal's concept that fibres of the mammillo-thalamic tract are collaterals of the older mammillo-tegmental tract would not be acceptable.

mainly into the medial habenular nucleus (Text-fig. 2). Thus, although the possibility that in case 2 not all fibres of the fornix were severed cannot be entirely excluded, it seems justifiable to conclude that the existence of a cortico-habenular component of the fornix is at least very doubtful.

It is of interest to note that fibres of the stria medullaris terminate in the medial habenular nucleus by way of boutons terminaux, which, after axonal interruption, swell and become argentophil (Pl. 2, fig. 3). It appears, however, that the synaptic connexions established by the fibres of the fornix system as a whole are made by means of free endings, which by contrast show a drop-like disintegration after axonal interruption (Pl. 1, fig. 1). In cases 1 and 5 the difference in the mode of termination of the two tracts was observed in the corresponding parts of the same section.

Gerebtzoff recently described Marchi degeneration in the pineal body, after sectioning the fornix. In two of our experimental cases in which the stria medullaris was severely injured, fibre degeneration in the pineal stalk was found. In other cases with no significant injury of the stria medullaris the pineal stalk was consistently normal. Thus, our results do not provide evidence for a direct connexion between the hippocampus and the pineal body.

Fibres of the *precommissural fornix* terminate in the lateral and medial septal nuclei and in the nucleus accumbens. That the degeneration seen in these nuclei is the result of interruption of the fornix system proper and is not due to the involvement of the septum by the lesion is demonstrated in case 2, for in this experiment the fornix was cut on the left side and degenerating fibres could be traced into the septum. On the right side, on the other hand, although the lesion passes deeply into the lateral septal nucleus itself, leaving the fornix almost intact, the septal nuclei and also the fibres of the fornix column are almost free of degeneration. Moreover, in case 4 (Text-fig. 6), the lesion is deep and sufficiently far forward to sever those collaterals or direct fibres of the fornix—beautifully illustrated by Cajal (1911, figs. 505 and 511)—which pass out at right angles into the septum. The resulting degeneration in the septal nuclei and the nucleus accumbens was found to be the same as that observed when the fimbria alone has been cut. Apart from terminating fibres, fascicles of fibres from the fornix traverse the septal nuclei to converge into a subcallosal bundle of fine degenerating fibres. In our opinion most of these terminate in the nucleus accumbens, while others appear to join the medial forebrain bundle and pass caudally to an undetermined destination. This may represent the olfactory part of Zuckerkandl's (1888) 'Riechbündel des Ammonshorns', which, according to him, terminates in the olfactory lobe (prepiriform cortex). The preoptic region, the olfactory tubercle and the nucleus of the diagonal band of Broca were normal in all cases.

Descriptions of normal material had suggested a crossing of fornix fibres over the midline anterior to the anterior commissure. Examination of R. 2 (right side) and R. 5 now make it clear that such a crossing does not exist and that the projection of the precommissural fornix is unilateral.

It is not possible to determine from our material whether different parts of the hippocampus project to different terminal areas. Fox's experiments (1943) have provided some evidence for a rough topographical localization in the hippocampus. He found that in the cat precommissural fornix fibres degenerate after lesions of the anterior end of the inferior portion of the hippocampus, and that they could be traced to the lateral septal nucleus and also to the dorsal surface of the nucleus accumbens.

The dorsal fornix, as most observers agree, consists of afferent and efferent systems, and the experimental method which we have employed has enabled us to trace many of these fibres to their destination. In the rabbit, the dorsal fornix is composed of two fibre types—a fine fibre component and a group of thicker fibres.

In case 3, the dorsal fornix was selectively cut without injuring any other part of the fornix projection system. It is apparent from the sections of this case that the fine degenerating fibres of the descending dorsal fornix turn into the descending column of the fornix as it curves through the septum (Text-fig. 5) and pass with the column through the hypothalamus and mammillary body to contribute directly to that component of the fornix which projects into the tegmentum. The lateral septal nucleus receives only a few fibres, and the medial septal nucleus and the nucleus accumbens none. In case 2 (right side, Text-fig. 4), this pathway was confirmed. The evidence presented permits the inference that the descending fibres of the dorsal fornix project largely into the tegmentum.

The origin of the descending fibres of the dorsal fornix has been a matter for conjecture. Of the considerable literature written on the subject, Kölliker's (1894) description of the dorsal fornix still appears to be substantially correct. He describes the dorsal fornix as a 'tract of longitudinal fibres which penetrate the corpus callosum from the deepest layer of the cingulate gyrus and also from the superior part of the hippocampus and terminate in the septum pellucidum and in the descending column of the fornix'. He goes on to say that some fibres pass into the septum at the point where fibres of the dorsal fornix join the descending column. Others penetrate the more rostral part of the corpus callosum and enter the septum directly. The latter observation accounts for the small amount of degeneration observed in the septal nuclei in cases 2 (right side) and 5. In normal material fibres have been described passing between the supracallosal striae (Kölliker's deepest layer of the cingulate gyrus) and the dorsal fornix, perforating the corpus callosum, and it has been suggested that they are mainly related to the septal areas. The supracallosal striae arise largely in the indusium griseum, that is, the supracallosal remnant of the hippocampus where Humphrey (1936) found (in the bat) all elements of the hippocampus represented. It would be possible, therefore, to regard the penetrating fibres of the striae Lancisii, and with them the descending fibres of the dorsal fornix, as a remnant of the supracallosal hippocampus-fornix system which rejoins the main column of the fornix in its course through the hypothalamus and, together with some fibres of the descending fornix, passes into the tegmental region.

In all the experiments some of the thick ascending fibres of the dorsal fornix were found to be degenerated posterior to the lesion. These fibres penetrate the corpus callosum, join the deep layers of the cingulum, and apparently curve around the splenium of the corpus callosum to terminate in the hippocampus. However, it cannot be said from our material whether the fibres curving around the splenium are those of the dorsal fornix or are derived from the cingulum, whether the changes observed in the hippocampus are the result of lesions in the ventral or dorsal hippocampal commissures or the dorsal fornix, or whether they are, as in case 5, due to the immediate injury to the hippocampal formation. At the same time, it must be noted that in this material the medially placed thick fibres associated with the columns of the fornix, which curve up through the septum and enter the dorsal fornix, have always been found to be normal, even when the entire descending column is degenerated. The experimental work of Gerebtzoff (1939) elucidates this matter. By a series of well-placed lesions in the medial telencephalon and the medial frontal and cingulate cortex,* he found that the cingulum could be excluded as a direct afferent pathway to the hippocampal formation, but concluded that the dorsal fornix (colonne horizontale), which arises (according to Gerebtzoff) ventro-medial to the septal nuclei (nucleus of diagonal band of Broca) provides one of the afferent projections to the hippocampus itself.

Hippocampal commissures

The interpretation of the changes in the hippocampal formation itself, which were observed in our experiments, can only be of a very preliminary nature. It is obvious that the greater the lesion in the ventral hippocampal commissure, the more severe are the degenerative changes in the hippocampus (compare cases 1 and 2). The changes are present in the inferior and superior parts of the hippocampus, and all layers, as well as the dentate gyrus, are affected (Pl. 2, fig. 5).† The question whether one area of the hippocampus projects to the same or to different areas of the hippocampus of the opposite side, and the question whether there exists a temporo-ammonic tract which crosses in the dorsal hippocampal commissure (as Cajal propounded) must be left to further study.

It has been established by our experiments that the ventral hippocampal commissure is not a pathway for decussating projection fibres, but is entirely interhippocampal in its connexions. Thus, any influence which the hippocampus of one side may exert on the projection fields of the contralateral fornix must be mediated through the contralateral hippocampus.

SUMMARY

1. Lesions have been placed in various parts of the fornix projection system in the rabbit, and the resulting degeneration of the different components of this system has been followed to their termination by a silver method.

2. It was found that the descending column of the fornix terminates in the basal and intermediate parts of the medial mammillary nucleus. There is no evidence that hypothalamic nuclei which lie in front of the mammillary body, with the exception of the perifornical nucleus, receive any contribution from the fornix. The capsule which surrounds the mammillary body consists partly of fibres from the fornix.

* According to Gerebtzoff, after lesions ventral to and in front of the septum in the rabbit, Marchi degeneration occupying the most medial part of the diagonal band of Broca can be traced through the corpus callosum into the deepest layer of the cingulum and extends into the hippocampus, while fibres of the cingulum remain intact. After lesions resulting in degeneration of the cingulum, the hippocampus was found always to be normal.

† It is interesting to note that the fine fibre and terminal degeneration found in the hippocampal formation in our experiments has never been detected by us either after excision of the olfactory bulb (Le Gros Clark & Meyer, 1947) or after ablation of the prepiriform cortex.

3. The descending column of the fornix and the dorsal fornix contribute to a tract which passes beyond the mammillary body into the mesencephalon.
4. No definite evidence for a hippocampo-habenular or hippocampo-pineal component of the descending column of the fornix could be obtained.
5. Fibres of the precommissural fornix, which are either direct fibres or collaterals of the fimbria, terminate in the lateral and medial septal nuclei and in the nucleus accumbens.
6. Most of the fibres of the descending part of the dorsal fornix pass into the fornix column and continue into the mesencephalon. These fibres may have their origin in the supracallosal remnant of the hippocampus, the indusium griseum. There is evidence that fibres of the ascending component of the dorsal fornix terminate in the hippocampus.
7. Lesions in the ventral hippocampal commissure resulted in fibre and terminal degeneration in all layers of the hippocampus.
8. The entire fornix system is unilateral in its projection, with the exception of some fibres of the descending column of the fornix which cross the midline in the posterior part of the mammillary body.

We wish to express our gratitude to Prof. W. E. Le Gros Clark for his advice and for the facilities offered to one of us (J.M.S.) who was a visitor to his laboratory. We are also indebted to Mr A. C. Allison for help in many ways. Our thanks are due to Mrs Purves for the preparation of the drawings and to Messrs T. Thompson and L. Cooper for technical assistance. The investigation was undertaken while one of us (M.M.) was receiving a grant from the Medical Research Council.

REFERENCES

Allen, W. F. (1944). Degeneration in the dog's mammillary body and Ammonshorn following transection of the fornix. *J. comp. Neurol.* **80**, 283–291.

Cajal, S. Ramon y (1911). *Histologie du système nerveux de l'homme et des vertébrés*, **2**. Paris: A. Maloine.

Clark, W. E. Le Gros (1938). The Hypothalamus. Edinburgh: Oliver and Boyd.

Clark, W. E. Le Gros, & Meyer, M. (1947). The terminal connexions of the olfactory tract in the rabbit. *Brain*, **70**, 304–328.

Edinger, L. & Wallenberg, A. (1902). Untersuchungen ueber den Fornix und das Corpus Mammillare. *Arch. Psychiat. Nervenkr.* **35**, 1–21.

Elliot Smith, G. (1896). The fornix superior. *J. Anat. Physiol.* **31**, 80–94.

Fox, C. A. (1943). The stria terminalis, longitudinal association bundle and precommissural fornix in the cat. *J. comp. Neurol.* **79**, 277–295.

Gerebtzoff, M. A. (1939). Sur quelques voies d'association de l'écorce cérébrale. *J. belg. Neurol. Psychiat.* **39**, 205–221.

Gerebtzoff, M. A. (1941–2). Notes anatomo-expérimentales sur le fornix, la corne d'ammon et leur relation avec diverses structures encéphaliques, notamment epiphysiques. *J. belg. Neurol. Psychiat.* **41/42**, 199–206.

Glees, P. (1946). Terminal degeneration within the central nervous system as studied by a new silver method. *J. Neuropath. exp. Neurol.* **5**, 54–59.

Gudden, B. von (1881). Beitrag zur Kenntnis des Corpus Mammillare und der sogenannten Schenkel des Fornix. *Arch. Psychiat. Nervenkr.* **11**, 428–452.

Humphrey, T. (1936). The telencephalon of the bat. *J. comp. Neurol.* **65**, 603–711.

Johnston, J. B. (1913). The morphology of the septum, hippocampus and pallial commissures in reptiles and in mammals. *J. comp. Neurol.* **23**, 371–478.

KAPPERS, C. U. A., HUBER, G. C. & CROSBY, E. C. (1936). *The comparative Anatomy of the Nervous System of Vertebrates*, **2**. New York: The Macmillan Company.

KÖLLIKER, A. v. (1894). Ueber den Fornix longus von Forel und die Riechstrahlungen im Gehirn des Kaninchens. *Verh. anat. Ges. Jena*, **8**, 45–52.

KÖLLIKER, A. v. (1896). *Handbuch der Gewebelehre des Menschen*, **2**. Leipzig: W. Engelmann.

PROBST, M. (1901). Zur Kenntnis des Faserverlaufes des Temporallappens, des Bulbus Olfactorius, der vorderen Kommissur, und des Fornix nach entsprechenden Extirpations und Durchschneidungsversuchen. *Arch. Anat. Physiol., Lpz*, pp. 338–356.

ROSE, J. (1939–40). The cell structure of the mammillary body in mammals and in man. *J. Anat., Lond.*, **74**, 91–115.

ROSE, M. (1935). Das Zwischenhirn des Kaninchens. *Extr. Mém. Acad. Polon.* Ser. B, pp. 1–108.

VALKENBURG, C. T. VAN (1912). Caudal connexions of the corpus mammillare. *Proc. Acad. Sci. Amst.* **14**, 1118–1121.

YOUNG, M. W. (1936). The telencephalon of the rabbit. *J. comp. Neurol.* **65**, 295–401.

ZUCKERKANDL, E. (1888). Das Riechbündel des Ammonshorns. *Anat. Anz.* **3**, 425–434.

LIST OF ABBREVIATIONS

ant.com.	anterior commissure.
b.	basal part of the medial mammillary nucleus.
caps.	mammillary capsule.
c.c.	corpus callosum.
dors.(asc.)f.	dorsal ascending fornix.
dors.(desc.)f.	dorsal descending fornix.
d.hip.com.	dorsal hippocampal commissure.
f.	descending column of the fornix.
hab.-ped.tr.	habenula-peduncular tract.
hip.	hippocampus.
hyp.	hypothalamus.
i.	intermediate part of the medial mammillary nucleus.
l.	nucleus mammillaris lateralis.
m.	medial part of the medial mammillary nucleus.
mam.b.	mammillary body.
m.ped.	mammillo-peduncular tract.
m.teg.	mammillo-tegmental tract.
m.th.	mammillo-thalamic tract.
n.acc.	nucleus accumbens.
n.caud.	nucleus caudatus.
n.d.b.b.	nucleus of the diagonal band of Broca.
n.hab.	nucleus habenulae.
n.hab.l.	nucleus habenulae lateralis.
n.hab.m.	nucleus habenulae medialis.
n.olf.ant.	nucleus olfactorius anterior.
n.perif.	nucleus perifornicalis.
ocul.n.	oculomotor nerve.
olf.ped.	olfactory peduncle.
olf.tub.	olfactory tubercle.
op.tr.	optic tract.
pre.m.	nucleus premammillaris.
preop.a.	preoptic area.
sept.	septum.
str.med.	stria medullaris.
sub.	subiculum.
v.	ventricle.
v.hip.com.	ventral hippocampal commissure.

EXPLANATION OF PLATES

PLATE 1

Fig. 1. Degeneration of the fine pericellular plexus in the basal part of the medial nucleus of the mammillary body 5 days after section of the fornix. ×1150.

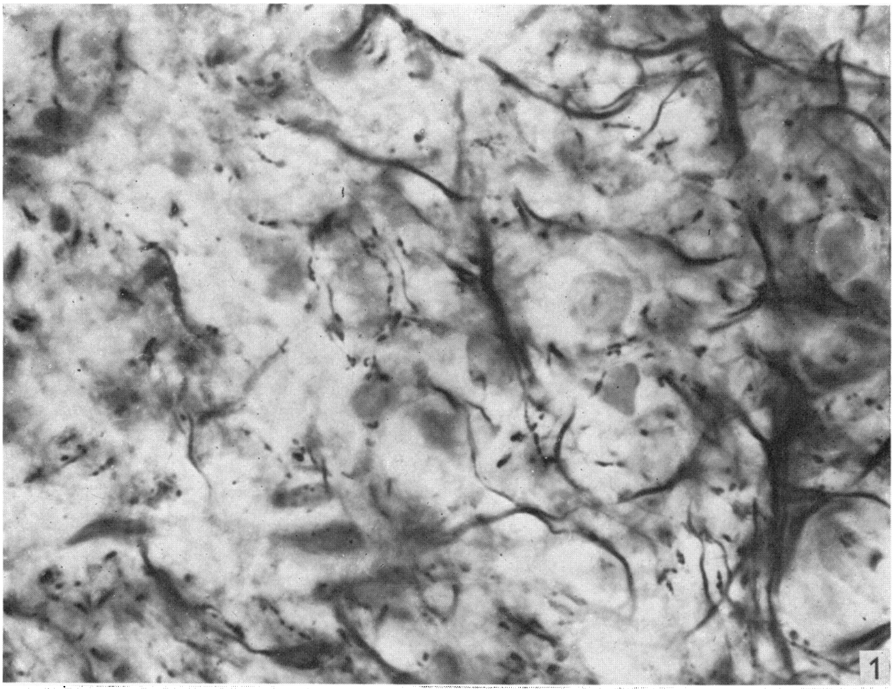
Fig. 2. Degenerating fibres passing into the basal part of the medial nucleus of the mammillary body from the surrounding capsule. ×1150.

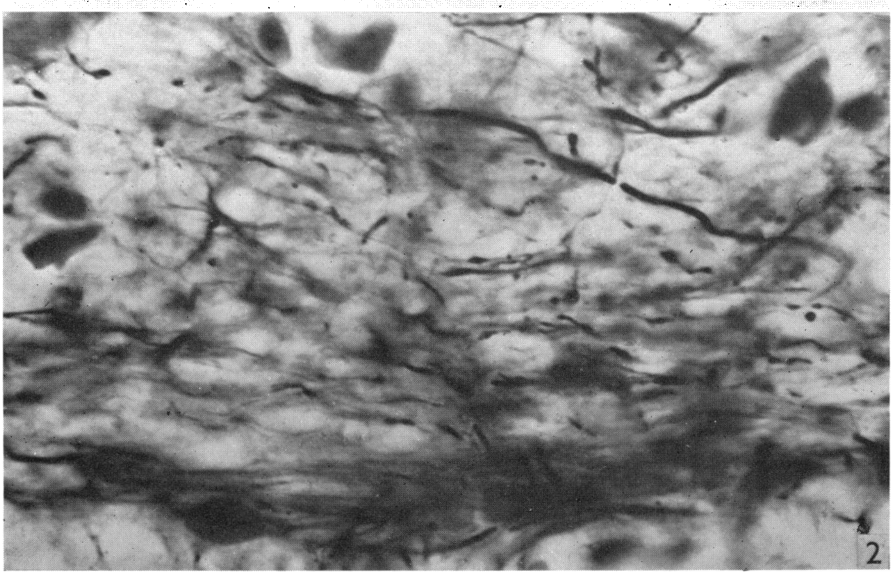
PLATE 2

Fig. 3. Degenerating boutons terminaux in the medial habenular nucleus 3 days after incidental injury of the stria medullaris. ×1600.

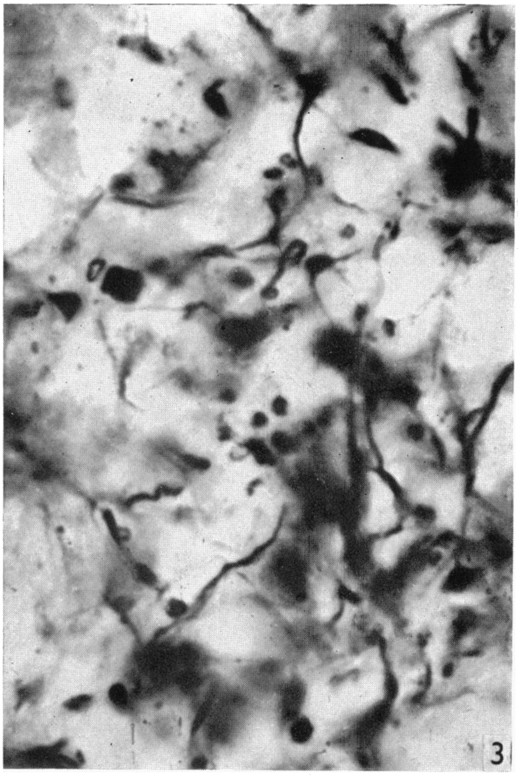
Fig. 4. The normal fibre pattern of the medial habenular nucleus. ×1600.

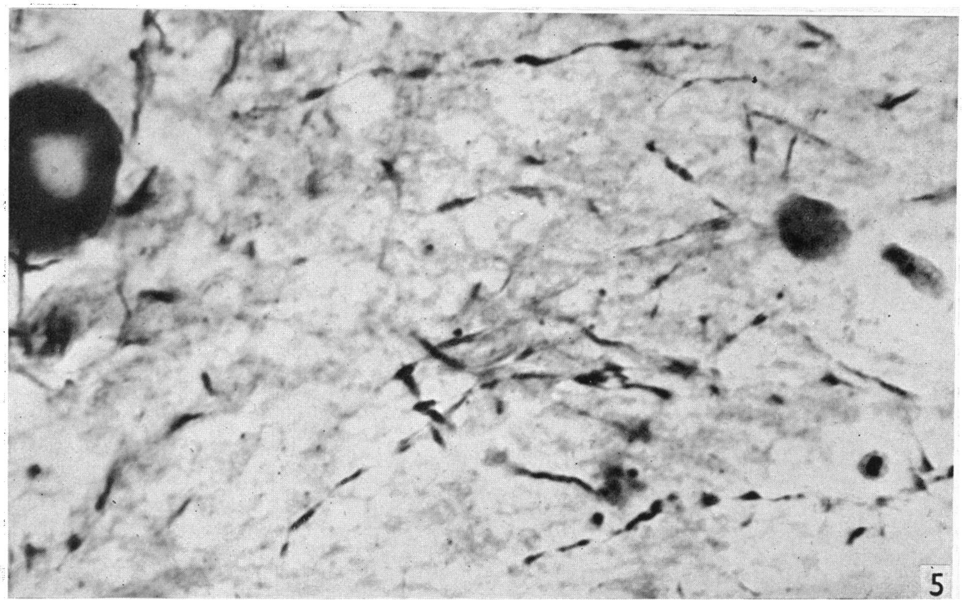
Fig. 5. Degenerating fibres passing through the molecular layer of the hippocampus towards the dentate gyrus 5 days after an extensive lesion in the hippocampal commissure. ×950.





SPRAGUE AND MEYER—AN EXPERIMENTAL STUDY OF THE FORNIX IN THE RABBIT





SPRAGUE AND MEYER—AN EXPERIMENTAL STUDY OF THE FORNIX IN THE RABBIT