THE ORIGIN OF THE MAMILLO-THALAMIC TRACT IN THE RAT

By T. P. S. POWELL and W. M. COWAN
Department of Human Anatomy, University of Oxford

INTRODUCTION

The gross projection of the mamillary nuclei to the anterior nuclei of the thalamus has been established for many years, and it has been shown with the Marchi technique that the fibres of the mamillo-thalamic tract end in all three elements of the anterior nuclear group (Glorieux, 1929; Le Gros Clark, 1932). The exact origin of the different components of this tract, however, is still uncertain; Kölliker (1896) and Ramón y Cajal (1911) considered that they arise as collaterals of the phylogenetically older mamillo-tegmental tract, whereas van Valkenburg (1912) and Fortuyn (1912) claimed that the two tracts were quite independent. The importance of the mamillo-thalamic tract as one of the two pathways connecting the hypothalamus with the thalamus and cortex has been stressed by Le Gros Clark (1938; Le Gros Clark & Meyer, 1950). In an experimental study of the fornix system (Daitz & Powell, 1954) the anterior thalamic nuclei were on occasion incidentally damaged. By correlating the extent of this damage with the resulting degeneration in the mamillary nuclei information concerning the origin of the mamillo-thalamic tract has been obtained.

MATERIAL AND METHODS

The brains of twenty albino rats in which unilateral lesions had been placed in the fimbria and preoptic areas were used. The animals varied in age from newborn infants to mature adults, and they were allowed to survive for 1–10 months after operation. The brains were fixed in 70 % alcohol and 2 % acetic acid and embedded in paraffin wax. Serial sections were mounted and stained with Borrel's methylene blue.

OBSERVATIONS

The extent of the damage to the anterior nuclei of the thalamus was very similar in many experiments; for the purpose of description they may be classified into those in which: (*a*) the fimbria was completely divided without any thalamic involvement; (*b*) all the anterior nuclei were completely destroyed; (*c*) the antero-medial nucleus suffered the major damage; (*d*) the antero-dorsal and antero-ventral were chiefly involved; and (*e*) the antero-ventral nucleus was principally involved. Representative examples of each of these groups will be described (Table 1).

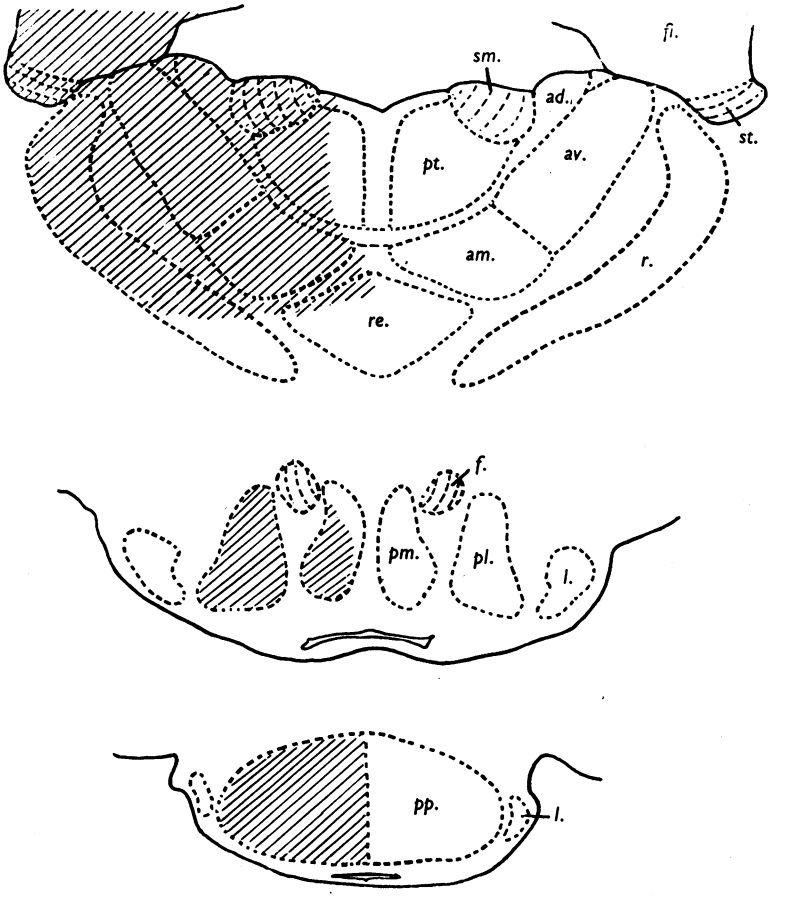
Gurdjian's terminology (1927) for the mamillary nuclei of the rat will be followed here; he described a distinct large-celled lateral nucleus and a medial nucleus which is divided into a pars medianus, a pars medialis, a pars lateralis and a pars posterior.

In Exp. D84 a 17-day-old rat was operated upon and allowed to survive for 2 months. The fimbria had been completely divided without any concomitant damage to the thalamus. Careful comparison of all the elements of the mamillary

Table 1. *Extent of damage and the distribution of the resulting degeneration*

Group	No.	Extent of damage			Distribution of degeneration		
		Antero-medial n.	Antero-ventral n.	Antero-dorsal n.	Pars medialis	Pars posterior	Pars lateralis
b	49 54 168 205	All anterior nuclei completely destroyed			Ventro-lateral two-thirds shows cell loss; and shrinkage and pallor of remaining cells	Severe cell loss; few shrunken pale cells persisting	
c	P3	Completely destroyed	Medial third involved	Unaffected	Ventro-lateral two-thirds shows cell loss; shrinkage and pallor of remaining cells	In ventro-medial third the cells are shrunken and pyknotic	Unaffected
d	48	Lateral margin involved	Completely destroyed	Dorso-lateral two-thirds destroyed	Slight cell loss in lower lateral part	Whole nucleus shows severe cell loss and shrinkage and pallor of remaining cells	Almost the whole nucleus shows degeneration but many shrunken cells persist
	50	Not affected	Lateral margin of both involved		Not affected	Lateral part of each shows slight cell loss	
	57	Lateral margin involved	Both are severely damaged but some cells persist		Not affected	Both show severe degeneration, but some shrunken cells remain, particularly in dorso-medial parts of each	
	80	Not affected	Both are completely destroyed		Not affected	Both show marked cell loss and only a few shrunken cells remain	
	82	Not affected	Completely destroyed	Severely damaged but caudally about a third of the nucleus remains	Not affected	Severely degenerate but some normal cells remain	More or less normal at rostral end; the rest is very degenerate
e	83	Not affected	Lateral two-thirds severely damaged	Slight involvement of lateral margin	Not affected	Middle half is severely degenerate	No significant change
	150	Not affected	Dorsal one-third and lateral half of the ventral two-thirds destroyed	Dorsal part slightly involved	Not affected	Moderate cell loss and shrinkage and pallor of cells in the lateral two-thirds	Little cell loss but pallor and shrinkage of many cells
	170	Not affected	Lateral part involved	Intact	Not affected	Dorso-lateral quadrant shows slight cell loss and shrinkage of cells	Not affected
	197	Not affected	Dorso-lateral two-thirds damaged—more marked anteriorly	Lateral third involved	Not affected	Ventro-lateral two-thirds shows cell loss and shrinkage and pallor of cells—more marked caudally	Lower lateral third shows cell loss and shrinkage and pallor of remaining cells
	207	Not affected	The dorso-lateral half is damaged	Lateral margin involved	Not affected	Cell loss and shrinkage in the lateral half	Not affected
	209	Not affected	Dorso-lateral two-thirds damaged	Not affected	Not affected	Cell loss and shrinkage of cells in the lateral half	Not affected
	213	Not affected	Ventro-lateral half damaged	Lateral margin involved	Not affected	Cell loss and shrinkage in the lateral third of each	

nuclei showed no difference between the normal and operated sides. This, and the other experiments in this group, have been included to obviate the possible criticism that the degenerative changes to be described below may be transneuronal following interruption of one of the principal afferent pathways to the mamillary nuclei rather than to involvement of the anterior thalamic nuclei.



Text-fig. 1. All anterior thalamic nuclei destroyed. In this and the following text-figures, the extent of the damage to the thalamic nuclei and the resulting retrograde degeneration in mamillary nuclei are indicated by hatching. The outlines have been traced from transverse sections.

In D168, a 7-day-old rat was operated upon and allowed to survive for 8 months. In addition to division of the fimbria all the anterior thalamic nuclei of the left side have been completely destroyed. Severe cellular degeneration was found in almost the entire extent of the medial mamillary nucleus of the operated side (Text-fig. 1). In the ventrolateral two-thirds of the cross-sectional area of the pars

medialis a marked cell-loss has occurred and the remaining cells are all shrunken and stain less intensely than normal. In the dorso-medial third there is no cell loss but a few of the cells appear shrunken. The pars lateralis and the pars posterior have both undergone almost total atrophy, only an occasional pale shrunken cell remaining. The changes are accompanied by a moderate gliosis. The pars medianus and the lateral mamillary nucleus showed no change.

In another experiment, D49, with a similar lesion but with a survival period of 5 weeks the distribution of the degeneration is the same but many more shrunken neurons persist. Further, in this experiment and in others with longer survival periods in which the premamillary nuclei were available for histological examination both the dorsal and ventral premamillary nuclei showed slight degeneration; only a few cells have disappeared but many of the cells were shrunken and less deeply staining.

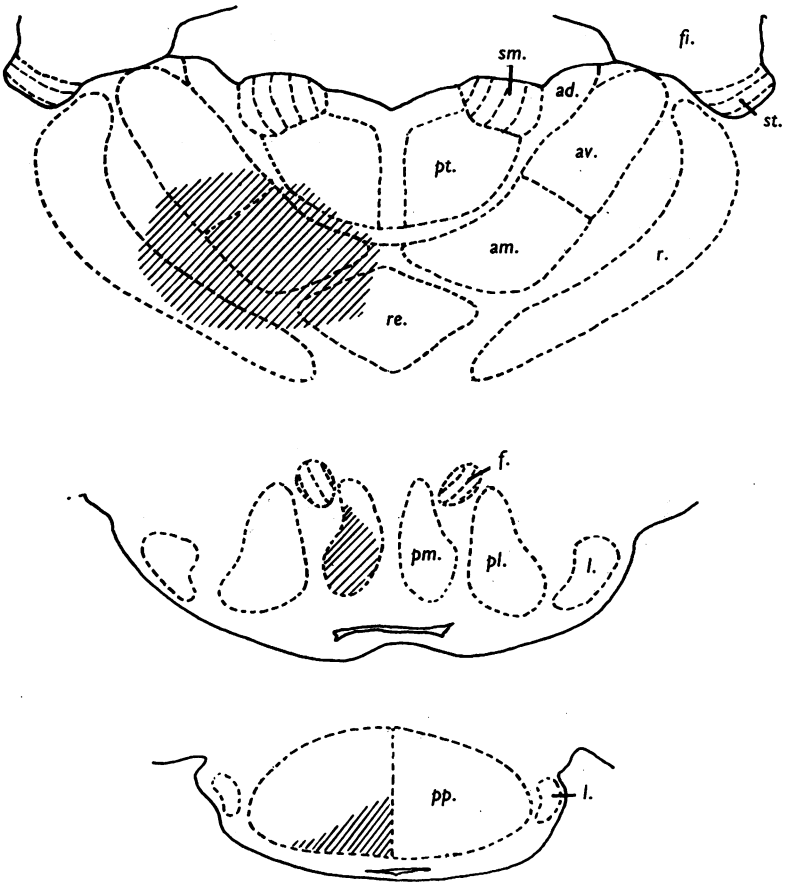
In Exp. P3 a lesion had been placed primarily in the preoptic areas. This extended back however into the thalamus destroying the ventral anterior nucleus, the whole of the antero-medial nucleus and the medial third of the antero-ventral nucleus; the antero-dorsal nucleus was not involved by the lesion. The animal used was a young adult and was allowed to survive for 7 months after operation. In the mamillary nuclei of the operated side the pars medialis shows the most striking changes. Except for the dorso-medial third, the nucleus showed cell loss and shrinkage and pallor of the remaining cells (Pl. 1, fig. 2). In the pars lateralis and pars medianus there was no change, but in the ventro-medial third of the pars posterior the majority of the cells are shrunken and pyknotic (Text-fig. 2). In the premamillary nuclei a proportion of the cells appeared shrunken and pyknotic. It is apparent from this experiment that the pars medialis projects to the antero-medial nucleus.

In the majority of the experiments both the antero-ventral and antero-dorsal thalamic nuclei were involved to a greater or lesser extent. A good example of this group is D80 in which the antero-ventral and antero-dorsal nuclei were completely destroyed without involvement of the antero-medial nucleus. The rat was 4 weeks old when operated upon and was allowed to survive for 1 month. In the medial mamillary nucleus of the operated side the pars lateralis and pars posterior are severely degenerated; a marked cell loss has occurred and all the remaining cells are shrunken. The pars medialis and pars medianus are unaffected (Text-fig. 3). This experiment indicates that the pars lateralis and pars posterior are related to the antero-dorsal and antero-ventral nuclei of the thalamus. Further, by correlating the extent of the damage to the antero-dorsal and antero-ventral nuclei in other experiments with the distribution of the degeneration in the mamillary nuclei it is inferred that the pars lateralis projects to the antero-dorsal nucleus and that the pars posterior projects to the antero-ventral nucleus. This is confirmed by the final group of experiments of which D197 is an example.

In this experiment fimbrial section was performed on an adult rat and the survival period was 8 months. The incidental damage to the thalamus involved the dorsal and lateral parts of the antero-ventral nucleus and the lateral third of the antero-dorsal nucleus. In the medial mamillary nucleus the resulting degeneration was found in the lower lateral third of the pars lateralis and in the ventro-lateral two-

thirds of the pars posterior; in these areas marked cell loss had occurred and the persisting cells were shrunken and stained less deeply than normal (Text-fig. 4).

In all the experiments in which the antero-ventral and antero-dorsal nuclei were only partially involved degeneration was localized to discrete portions of the pars posterior and pars lateralis, and from this it appears that there is a medio-lateral

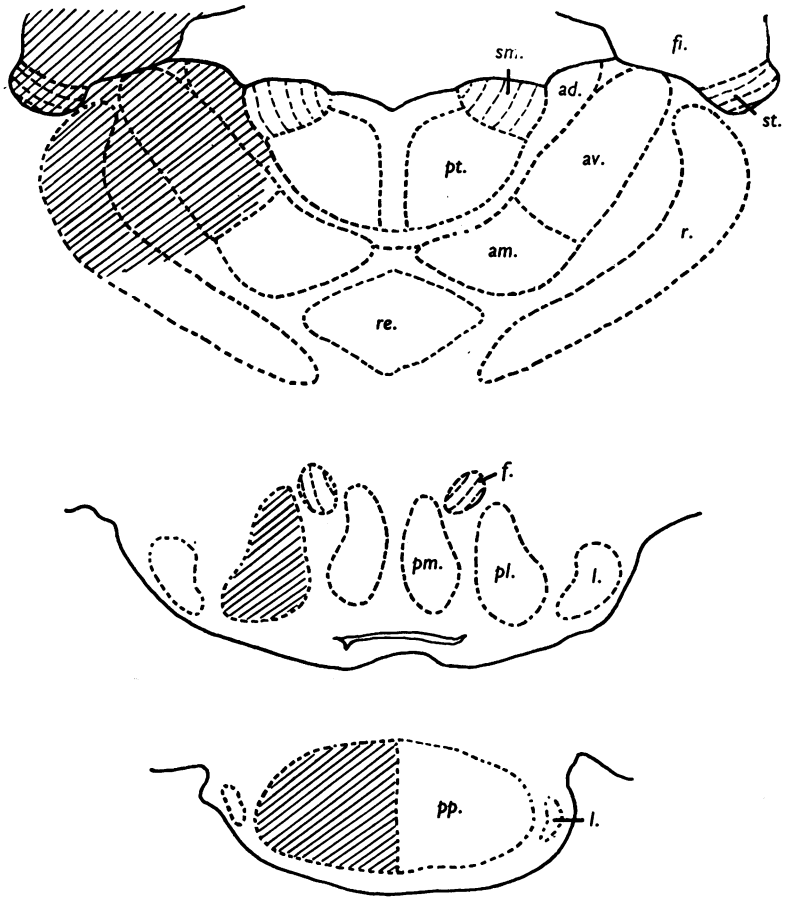


Text-fig. 2. The antero-medial nucleus has been completely destroyed with partial involvement of the antero-ventral nucleus.

organization in the projection of these elements in the sense that medial parts of the mamillary nuclei project to the medial parts of the corresponding anterior nuclei and vice versa. Further, in some experiments there is evidence to suggest that the rostral parts of these two subdivisions of the medial mamillary nucleus project to the caudal parts of the corresponding anterior nuclei and vice versa. It should be pointed out that this is only a tentative conclusion, and more material is necessary to establish this point.

DISCUSSION

So far as is known, the precise origin of the mamillo-thalamic tract in respect of the different components of the mamillary complex has not been demonstrated experimentally. The results described here show conclusively that in the rat this tract has no origin from the large-celled lateral mamillary nucleus (nucleus



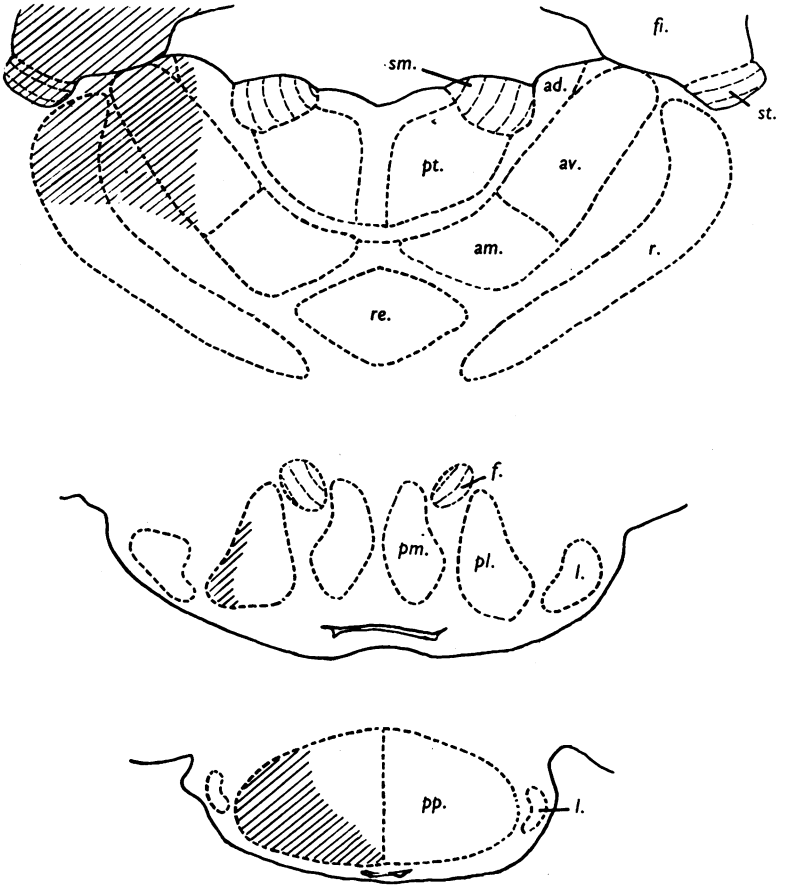
D 80

Text-fig. 3. The antero-dorsal and antero-ventral nuclei have been destroyed without involvement of the antero-medial.

intercalatus in the human brain described by Le Gros Clark, 1938), nor from the pars medianus of the medial mamillary nucleus. Our findings indicate that it arises from the pars lateralis, pars posterior and the ventro-lateral two-thirds of the pars medialis and possibly in part from the dorsal and ventral premamillary nuclei.

It should be noted that even after survival periods of 10 months a small proportion of shrunken cells persist in the affected elements and more particularly in the pars medialis. The persistence of these cells may be due to the presence of intact collaterals, and this is of interest in view of the opinion of Kölliker (1896) and

Ramón y Cajal (1911) that the fibres of the mamillo-thalamic tract arise as collaterals of the mamillo-tegmental tract. However, van Valkenburg (1912) found retrograde cell degeneration localized to the dorsal part of the medial mamillary



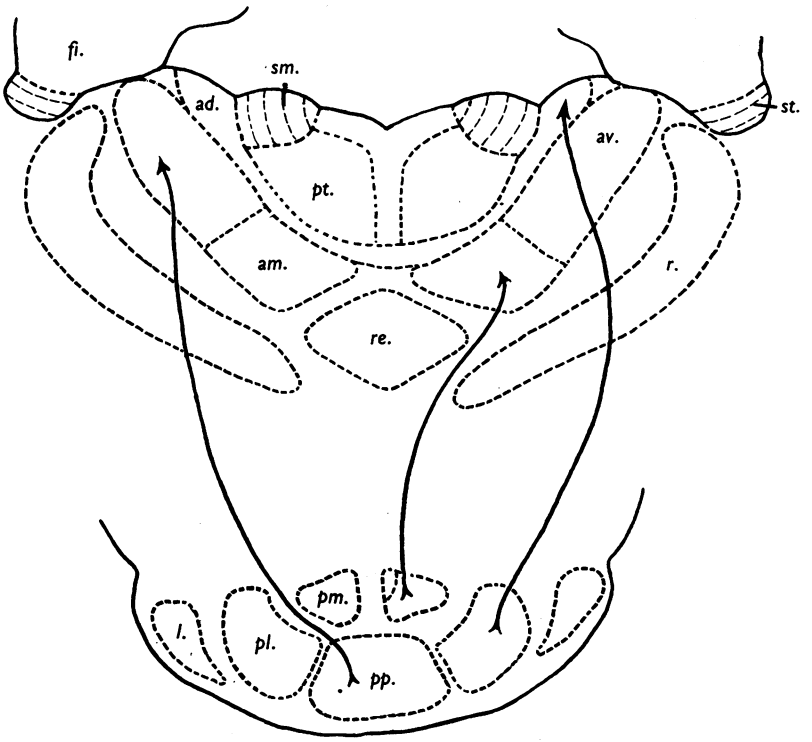
D 197

Text-fig. 4. The antero-ventral nucleus has suffered the principal damage.

nucleus after section of the mamillo-tegmental tract. Our findings are in close agreement with this as the dorso-medial part of the pars medialis of the medial mamillary nucleus always remained virtually unaffected even when all the anterior thalamic nuclei had been completely destroyed.

Not only has the origin of the mamillo-thalamic tract in the rat been established, but a precise projection from each subdivision of the medial mamillary nucleus to each element of the anterior thalamic nuclei has been shown to exist. The ventro-medial two-thirds of the pars medialis (and possibly the dorsal and ventral pre-mamillary nuclei) are connected with the antero-medial nucleus, the pars lateralis with the antero-dorsal nucleus and the pars posterior with the antero-ventral nucleus (Text-fig. 5). Within this nuclear projection there is some evidence which indicates a medio-lateral and rostro-caudal organization.

It has been known for some time that the anterior nuclei project to the cortex of the cingular gyrus (Le Gros Clark, 1932), and Rose & Woolsey (1948) have shown that in the rabbit and cat each of the anterior nuclei projects to a distinct architectonic field. Taken in conjunction with the present observations, it is apparent that not only are the different anterior nuclei related to distinct cortical fields but



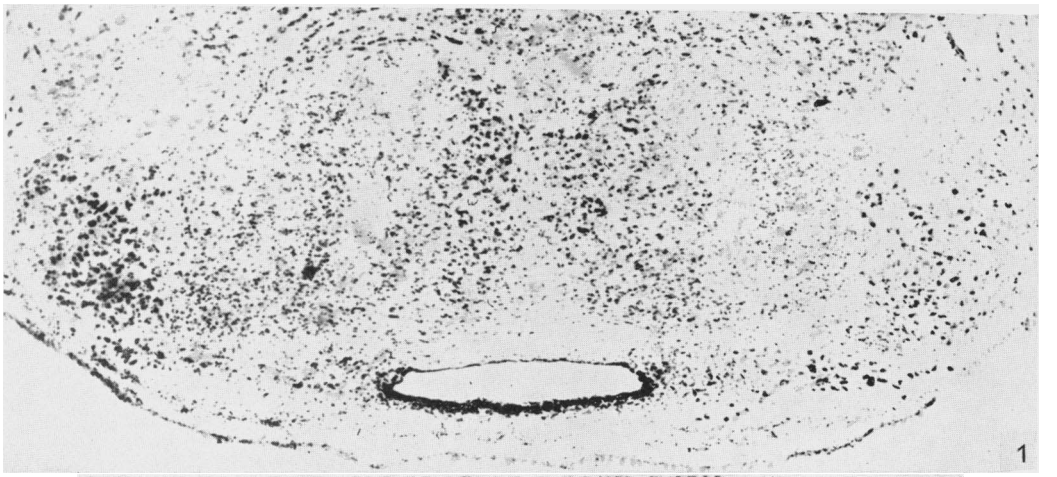
Text-fig. 5. The projection of the individual elements of the medial mamillary nucleus (traced from a horizontal section) to the three anterior nuclei.

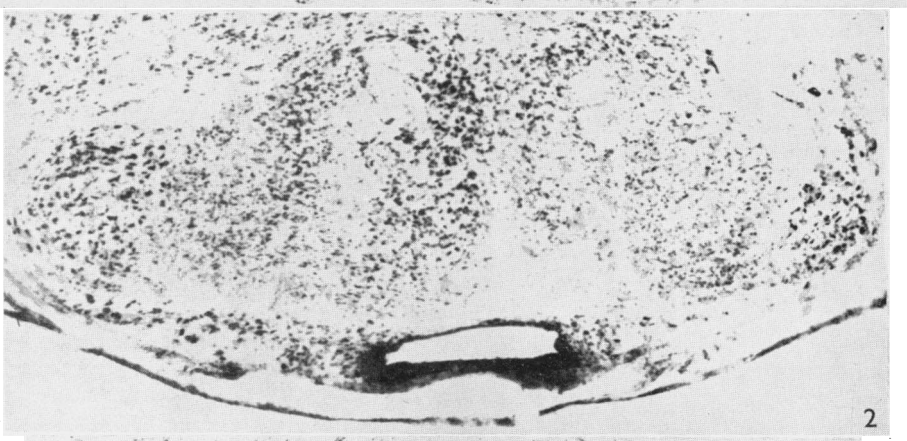
that each element of the medial mamillary nucleus is likewise connected with a different subdivision of the cingular gyrus: i.e. pars medialis with the anterior cingular cortex (area 24 of Brodmann), the pars posterior with the posterior cingular cortex (area 23) and the pars lateralis with the retrosplenial area (area 29). This relationship may be of significance in view of the recent physiological and clinical work on the cingular gyrus (see Kaada, 1951, 1953; Fulton, 1951).

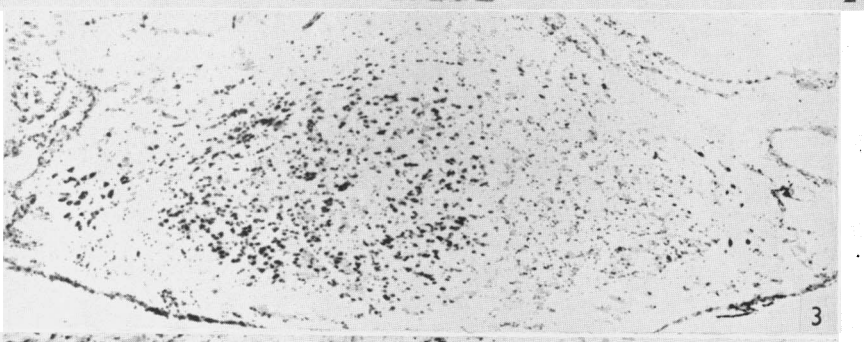
SUMMARY

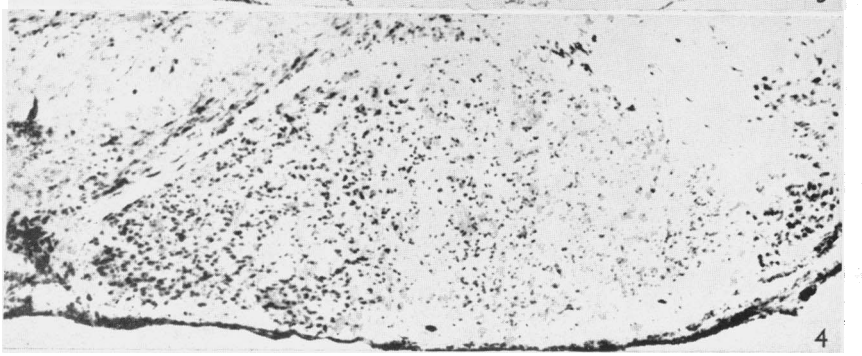
1. The origin of the mamillo-thalamic tract in the rat has been studied by the method of retrograde cell degeneration following damage to the anterior nuclei of the thalamus.

2. The tract arises from all elements of the medial mamillary nucleus (except the pars medianus) and possibly from the premamillary nuclei. No contribution is made by the lateral mamillary nucleus.


1


2


3


4

3. There is a precise projection from each element of the medial mamillary nucleus to each of the anterior thalamic nuclei: the pars medialis projects to the antero-medial nucleus, the pars lateralis to the antero-dorsal nucleus and the pars posterior to the antero-ventral nucleus.

This work was done while one of us (T.P.S.P.) held a Medical Research Council Fellowship in Clinical Research.

REFERENCES

CLARK, W. E. LE GROS (1932). An experimental study of thalamic connexions in the rat. *Phil. Trans.* B, **222**, 1–28.

CLARK, W. E. LE GROS (1938). *The Hypothalamus.* Edinburgh: Oliver and Boyd.

CLARK, W. E. LE GROS & MEYER, M. (1950). Anatomical relationships between the cerebral cortex and the hypothalamus. *Brit. Med. Bull.* **6**, 341–345.

DAITZ, H. M. & POWELL, T. P. S. (1954). Studies of the connexions of the fornix system: retrograde cell degeneration following lesions of the fornix. *J. Neurol. Neurosurg. Psychiat.* (In the Press.)

FORTUYN, A. B. D. (1912). Die Ontogenie der Kerne des Zwischenhirns beim Kaninchen. *Arch. Anat. Physiol., Lpz.*, Anat. Abt., pp. 303–352.

FULTON, J. F. (1951). *Frontal Lobotomy and Affective Behaviour.* London: Chapman and Hall.

GLORIEUX, P. (1929). Anatomie et connexions thalamiques chez le chien. *J. Neurol., Brux.*, **29**, 525–554.

GURDJIAN, E. S. (1927). The diencephalon of the albino rat. Studies on the brain of the rat, no. 2. *J. comp. Neurol.* **43**, 1–114.

KAADA, B. R. (1951). Somato-motor, autonomic and electrocorticographic responses to electrical stimulation of 'rhinencephalic' and other structures in primates, cat and dog. *Acta physiol. scand.* **24**, Suppl. 83.

KAADA, B. R. (1953). Electrical activity of the brain. *Ann. Rev. Physiol.* **15**, 39–62.

KÖLLIKER, A. V. (1896). *Handbuch der Gewebelehre des Menschen*, vol. II. Leipzig: W. Engelmann.

RAMÓN Y CAJAL, S. (1911). *Histologie du système nerveux de l'homme et des vertébrés*, vol. II. Paris: A. Maloine.

ROSE, J. E. & WOOLSEY, C. N. (1948). Structure and relations of limbic cortex and anterior thalamic nuclei in rabbit and cat. *J. comp. Neurol.* **89**, 279–348.

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

EXPLANATION OF PLATE

All the sections were stained with methylene blue and the magnification throughout is × 58.

Fig. 1. Transverse section of mamillary nuclei in H57 to show retrograde degeneration in the pars lateralis only.

Fig. 2. Transverse section of mamillary nuclei of P3 to show degeneration confined to the ventro-lateral two-thirds of the pars medialis.

Fig. 3. Transverse section of pars posterior of the medial mamillary nucleus of D49 to show complete cellular atrophy on the operated side.

Fig. 4. Transverse section of pars posterior of the medial mamillary nucleus of D150 to show degeneration mainly in the lateral half of this element in the operated side.

In some of these sections there is apparent cell loss in the lateral mamillary nucleus, which is due to slight obliquity of the sections.

LIST OF ABBREVIATIONS

ad.	antero-dorsal nucleus	*pm.*	pars medialis
am.	antero-medial nucleus	*pp.*	pars posterior
av.	antero-ventral nucleus	*pt.*	parataenial nucleus
fi.	fimbria	*r.*	reticular nucleus
f.	fornix	*re.*	nucleus reuniens
l.	lateral mamillary nucleus	*sm.*	stria medullaris
	medial mamillary nucleus:	*st.*	stria terminalis
pl.	pars lateralis		