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THE
JOURNAL OF MENTAL SCIENCE

[*Published by Authority of the Royal Medico-Psychological Association.*]

No. 337 [NEW SERIES No. 301.] MARCH, 1936. VOL. LXXXII

Part I.—Original Articles.

FUNCTIONAL LOCALIZATION IN THE THALAMUS AND HYPOTHALAMUS.*

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THE sensory material which provides the essential data for conscious activity is conveyed to the higher functional levels of the brain by impulses which stream up the olfactory tracts, the optic tracts, and the tracts of the brain-stem and spinal cord. With the exception only of the olfactory impulses, all these sensory impulses are filtered through the thalamic region of the brain, or diencephalon, before they can be relayed to the cerebral cortex which forms the anatomical substratum of the more elaborate mental processes. It is an interesting fact that, while the functional localization in the cerebral cortex and the functional localization in regard to the numerous fibre tracts in the brain-stem and spinal cord have been established in quite considerable detail by anatomical, physiological and clinical studies extending over many years, the localization and the connections of the various relay mechanisms in the diencephalon still remain obscure. Since the nature of the sensory material which is delivered to the cerebral cortex depends ultimately on the influences and modifications which may be imposed on the afferent impulses during their passage through the diencephalon, it becomes a matter of extreme importance, from the point of view of the study of the physiology of sensation and of psychological interpretation of sensory experience, that attention should be concentrated on this diencephalic mechanism. The minute anatomy of the diencephalon has recently been worked out in great detail, and it is now the task of the anatomist, physiologist and clinician to discover the functional significance of the numerous cell groups and fibre tracts which have been defined.

* A lecture delivered before the Midland Mental Pathological Society, October 24, 1935.

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The general disposition and subdivisions of the diencephalon can readily be appreciated if a median section through the brain of a three-months human embryo is examined (Fig. 1). The diencephalon is hollowed out by the median third ventricle. Close to the roof is a rounded ridge, the epithalamus, which includes the pineal body and certain cell groups (such as the habenular ganglion) in close topographical relation with it. The floor of the ventricle is formed by the hypothalamus, which includes the pituitary body and a number of cell groups in close relation with the optic chiasma and the pituitary stalk,

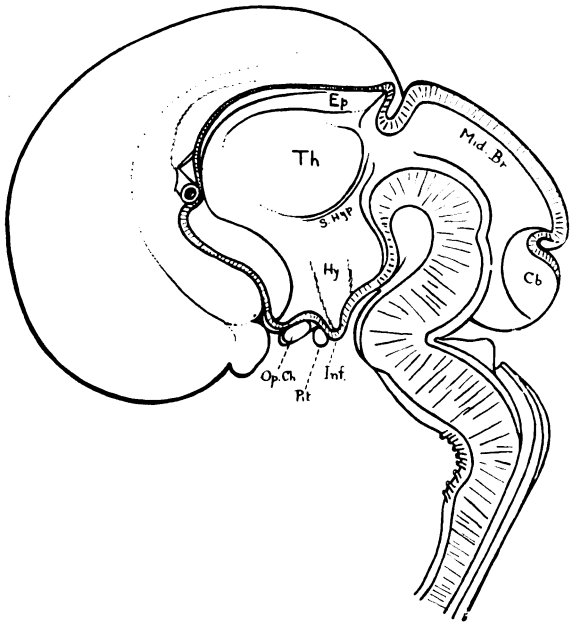


FIG. 1.—Median section of the brain of a three months' human embryo to show the main parts of the diencephalon. *Cb.* Cerebellum. *Ep.* Epithalamus. *Hy.* Hypothalamus. *Inf.* Infundibulum. *Mid. Br.* Mid-brain. *Op. Ch.* Optic chiasma. *Pit.* Pituitary gland. *S. Hyp.* Hypothalamic sulcus. *Th.* Thalamus.

and, behind, the mammillary bodies and their immediate relations. In the lateral wall of the third ventricle is a large rounded swelling which is the thalamus proper. The thalamic swelling laterally, and the eminence formed by the developing hypothalamus below, are separated by a conspicuous furrow, the *sulcus hypothalamicus*. We are here concerned with the thalamus and the hypothalamus. Comparative anatomy (6) indicates that the thalamus is primarily a relay station through which impulses which have their origin in stimuli arising in the external environment or in such somatic structures as muscles, tendons and joints are projected on to the cerebral cortex. In other words, it is concerned with the reception of stimuli on the basis of which the

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organism can adapt its behaviour objectively in accordance with environmental changes. The hypothalamus, on the other hand, comprises (with the pituitary gland) a neuro-glandular mechanism which is intimately concerned with the visceral activities of the body. In lower vertebrates it has been possible to trace visceral tracts into the hypothalamus (25), and clinical and physiological studies have shown that disturbances of the hypothalamic mechanism are commonly associated with disturbances of vegetative functions such as carbohydrate and water metabolism, gastric, intestinal and bladder movements, vasomotor reactions, sleep and sexual activities. Since functional disturbances of this kind form an essential element in all emotional reactions, it will be realized how important it is to acquire a knowledge of functional localization in the hypothalamus as a necessary preliminary to a clinical or experimental study of emotional experience.

The Thalamus.

In Fig. 2 are shown diagrammatically three transverse sections through the human thalamus in which a number of the cell groups or nuclei which have been described anatomically are outlined. We may deal with these nuclei separately and consider their functional significance.

The *ventral nucleus* occupies a ventral position and extends throughout the length of the thalamus. Actually it can be subdivided into several elements (19) (12), but for the sake of simplicity most of these can be ignored here. The ventral nucleus is the main sensory nucleus, and at least its posterior half (or more accurately, the posterior half of the pars externa of the ventral nucleus) is the terminal station of a large proportion of the fibres of the great sensory tracts which form the spinal fillet (from the posterior horn-cells of the spinal cord), the medial fillet (from the cuneate and gracile nuclei in the medulla), and the trigeminal fillet (from the sensory nucleus of the trigeminal nerve). From the ventral nucleus, the impulses conveyed by these sensory tracts are relayed on to the post-central gyrus of the cerebral cortex. The question now arises whether there is any topographical localization in the ventral nucleus in regard to the different parts of the body from which these impulses come, or in regard to the different types of sensory impulses which the fibres of the fillet system convey. The first part of the question can now be answered quite definitely. It has been established that impulses arising in the lower or caudal end of the body terminate in the lateral part of the ventral nucleus, while those arising in the head region end in the most medial part (12) (45). In other words, there is the same type of functional localization in the ventral nucleus as obtains in the post-central convolution. Whereas in the latter, the body is represented vertically in an approximately upside-down position, in the ventral nucleus the length of the body is represented rather transversely, with the head-end most medially. The question

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whether fibres conveying different types of sensory impulse end in correspondingly different nuclear elements in the thalamus is still uncertain. That there is a functional localization of this order might be inferred from the conclusion, based on clinical observations, that on their approach to the thalamus, sensory tracts become progressively segregated in accordance with the nature of the sensory impulses which they carry. Experiments are now being carried out in my laboratory in order to study this anatomical problem. So far as they have gone, they indicate that the spino-thalamic tracts, the medial fillet, and all parts of the trigeminal fillet terminate in the same region of the thalamus, i.e., in the pars externa of the ventral nucleus. If these tracts are concerned with the conduction of sensory impulses of diverse types

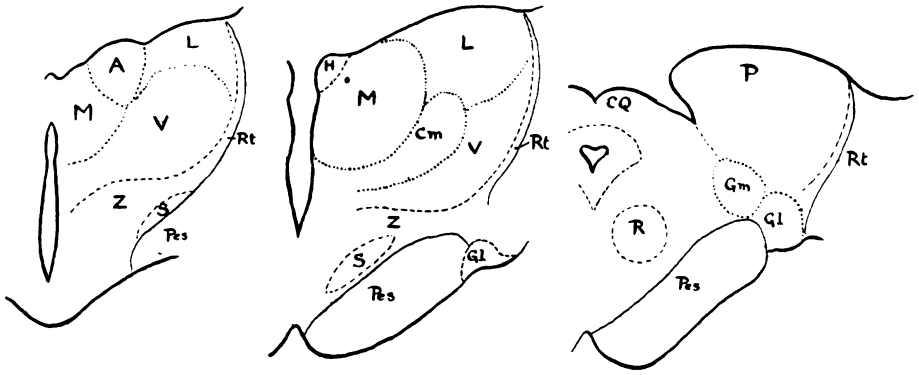


FIG. 2.—Diagrams of transverse sections through the human diencephalon from before backwards. *A*. Anterior nucleus. *Cm*. Centre median nucleus. *Gl*. Lateral geniculate body. *CQ*. Superior corpus quadrigeminum. *Gm*. Medial geniculate body. *H*. Habenular ganglion. *L*. Lateral nucleus. *M*. Medial nucleus. *P*. Pulvinar. *Pes*. Pes pedunculi. *R*. Red nucleus. *Rt*. Reticular nucleus. *S*. Subthalamic nucleus. *V*. Ventral nucleus. *Z*. Zona incerta of the subthalamus.

(as clinical studies indicate to be the case), this termination in a common sensory station in the thalamus is very remarkable. From time to time it has been suggested that the trigeminal fillet ends in other elements such as the medial nucleus of the thalamus or the centre median nucleus, but this has not been confirmed satisfactorily, and there is evidence against it.

This question of the termination of different sensory neurones in the thalamus is of fundamental importance in the problem of the central representation of different aspects of sensation, and especially of those types which come under the categories of protopathic and epicritic. It has been suggested again, on the basis of clinical studies, that, in the thalamus, sensory impulses are grouped in such a way that some are projected on to the cortex (providing the basis for the discriminative types of sensation), and others are redistributed to the thalamus itself. The latter are believed to be relayed to the central grey matter of the thalamus, perhaps the medial nucleus. This central grey matter

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has been termed the central organ of the thalamus, and it has been deemed responsible for endowing sensation with feeling tone which is either painful or pleasurable. Now if all the sensory tracts from the brain-stem and spinal cord which reach the thalamus terminate in the pars externa of the ventral nucleus (as seems to be the case), it must be supposed on current hypotheses that there are two categories of cells in this nucleus, one of which is concerned with relaying the afferent impulses to the cortex, and the other to the "central organ" of the thalamus. But it has been shown that ablation of the sensory area of the cortex (the post-central cortex) leads to complete atrophy of *all* the cells of the pars externa of the ventral nucleus. Thus it seems that the terminal nucleus of the fillet system is concerned entirely with projecting afferent impulses on to the cortex. It is, of course, possible that impulses underlying protopathic sensation are carried up the spinal cord and brain-stem by several relays of neurones, so that the whole course to the thalamus taken by these impulses cannot be displayed by the Marchi technique following lesions at relatively low levels. Consequently, our present information may afford no positive data regarding the terminal nucleus for these impulses in the thalamus. This question may perhaps be settled by making a series of hemisections at high levels in the mid-brain and hind-brain and studying the ensuing Marchi degeneration.

There is another element of the ventral nucleus which deserves attention here, and that is the *pars arcuata*, or the arcuate nucleus. This nucleus lies between the pars externa of the ventral nucleus and the centre median nucleus, and it has been shown to be the end-station of the brachium conjunctivum fibres which come from the cerebellum (38). It is interesting to note, therefore, that this nucleus sends relays to the precentral or motor cortex (12). It has been known for some time that the ventral nucleus of the thalamus projects on to both the pre- and post-central gyri, and it has been supposed on these grounds that both these convolutions have an equivalent value as sensory cortical mechanisms. It seems, however, that the motor cortex receives by way of the thalamus only afferent impulses emanating from the cerebellum, and is not concerned with the reception of sensory impulses which are brought up by the fillet system.

The *lateral nucleus* also consists of several elements, some of which are well circumscribed, while some are only indistinctly demarcated from the subjacent ventral nucleus. But the lateral nucleus is distinguished by the fact that no fillet fibres have been traced into it. Yet the lateral nucleus has been regarded as functionally equivalent to the ventral nucleus, and it has been assumed to receive fillet fibres conveying impulses from the caudal end of the body and to project on to the leg region of the post-central gyrus. However, ablation of the upper end of this gyrus only leads to cell atrophy in the pars externa of the ventral nucleus. On the other hand, cell atrophy in the lateral nucleus (at least in its caudal half) follows cortical lesions in the

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parietal lobe behind the post-central gyrus—that is to say, in the so-called " association " areas of the parietal cortex. The significance of the lateral nucleus therefore remains obscure, although when the afferent connections of this nucleus are established by anatomical studies we may get some light thrown on this problem.

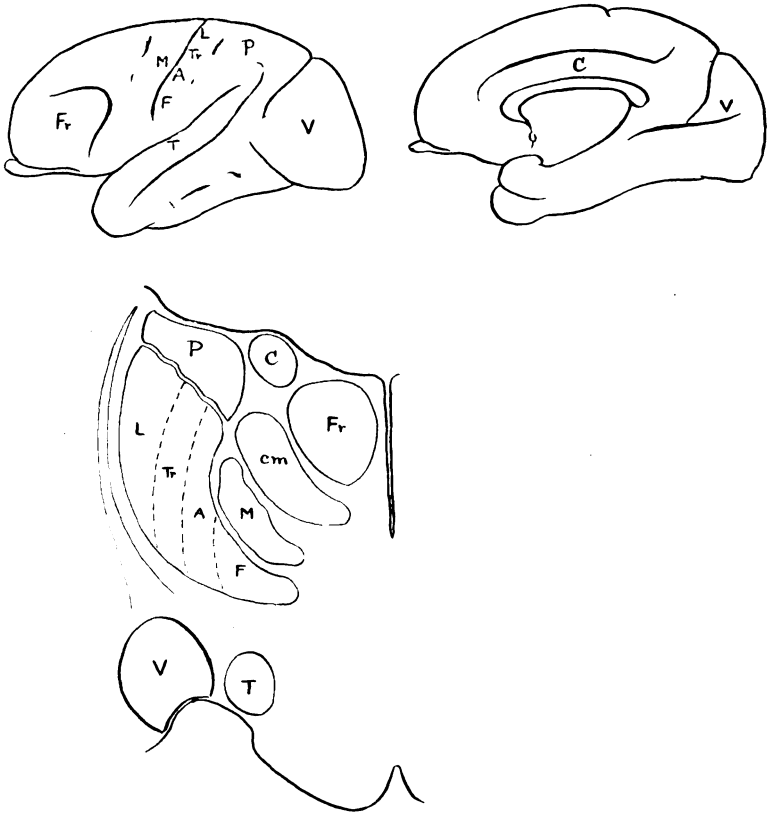


FIG. 3.—Diagram showing the projection of the thalamic nuclei on the cortex. Above are shown the lateral and medial aspects of the cerebral hemisphere of a monkey, and below a schematic transverse section through the thalamus. The anterior nucleus is projected on to the gyrus cinguli (*C*), the medial nucleus on to the frontal cortex (*Fr.*), the lateral nucleus on to the parietal association areas (*P*), the ventral nucleus (pars externa) on to the post-central gyrus (in which the areas for the legs, trunk, arms and face are represented diagrammatically), the pars arcuata of the ventral nucleus on to the motor cortex (*M*), the lateral geniculate body on to the visual cortex (*V*), and the medial geniculate body on to the superior temporal gyrus (*T*). The centre median nucleus (*cm.*) has no afferent cortical connection.

The *pulvinar* is a descriptive term of gross anatomy applied to the posterior projecting pole of the thalamus, and it includes several " nuclei ". Most of it, however, is made up of a caudal extension of the lateral nucleus of the thalamus. It was rather unexpected to find that in a series of experiments in which (in

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the monkey) various discrete portions of the parietal cortex were removed (12), the cells of the main element of the pulvinar apparently remained normal and unaffected, for it is generally held that the pulvinar projects on to the parietal cortex. In a recent study of the thalamus in a monkey following complete hemi-decortication it has been shown that the cell groups of the pulvinar undergo complete degeneration (46). Either the main element of the pulvinar projects diffusely over the whole area of the parietal cortex (so that limited cortical ablations lead to atrophy which is not easily detectable), or the pulvinar projects on to some other cortical region. This question needs further investigation. It may be noted that the old description that the pulvinar is one of the terminal stations of the optic tract (which still finds a place in some text-books) is incorrect. Optic fibres pass *through* the pulvinar on their way to the anterior colliculus, but do not end in the pulvinar.

The *lateral and medial geniculate bodies*, developed from the same mass of cells in the thalamus that gives rise to the ventral nucleus, are on the same functional level as the latter. The lateral geniculate body is the main terminal station of the optic tract, and, as is well known, relays retinal impulses on to the visual cortex in the occipital pole of the cerebral hemisphere. The functional localization in this nucleus is extremely precise. In man and other Primates it is laminated, being subdivided into six layers. It has been shown that three of these layers of cells receive fibres from the homolateral eye, and three from the heterolateral eye (13). Moreover, each lateral geniculate nucleus shows practically a point-for-point representation in regard to various sections of the retina from which it receives optic fibres. This has been demonstrated by the study of Marchi material and, more accurately, by the study of transneuronal degeneration following localized lesions in the retina. It has also been established that each limited part of the lateral geniculate nucleus is projected on to a corresponding limited area of the visual cortex (35), so that the point-for-point representation of the retina is thus carried on to the cortical level. It seems that the lateral geniculate nucleus is entirely concerned with the relay of retinal impulses to the cortex. Probably none of its cells serve the purpose of transmitting these impulses to other parts of the brain, for on ablation of the visual cortex the whole of the lateral geniculate nucleus undergoes complete cell atrophy.

The medial geniculate body is the terminal station of a part of the lateral fillet which conveys auditory impulses from auditory nuclei in the hind-brain, and these impulses are further projected on to a limited part of the superior temporal gyrus. The details of these connections and the question of a functional localization within the medial geniculate body have still to be worked out. The medial geniculate body has often been regarded as a mesencephalic element because of its topographical position alongside the mid-brain. Developmental and comparative anatomical studies have now

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shown that, like the lateral geniculate body, it is really a part of the thalamus which has become secondarily displaced backwards (8).

The *anterior nucleus* is a very conspicuous element in the thalamus of the human brain. The nucleus to which I refer is really one element of a composite anterior nucleus, the antero-ventral element. In man this element forms the main part of the whole nucleus. As is well known, it is the terminal station of a remarkably well circumscribed tract of fibres—the bundle of Vicq d'Azyr or mammillo-thalamic tract—which arises in the mammillary body (from the medial mammillary nucleus) of the same side. This fibre tract serves therefore to connect the hypothalamus with the thalamus proper. It may perhaps be regarded as a local specialization of a diffuse periventricular system of fibres, which dorsally is related to the more medially situated nuclei of the thalamus proper and below has numerous connections with the hypothalamic nuclei (12). The nature of the impulses which the mammillo-thalamic tract conveys to the anterior nucleus is obscure. The mammillary body itself receives impulses which are brought to it from the hippocampus of the cerebral hemisphere, but beyond the fact that these impulses are presumed to be olfactory in nature, nothing is known of them. We may refer to the experimental evidence (cited below) that the mammillary body is functionally related to the phenomenon of sleep. If this is so, its direct connection with the anterior nucleus suggests that the latter also may be a part of a central neural mechanism which regulates sleep processes. Formerly it was held that the anterior nucleus had no connections with the cerebral cortex. It has now been established that it is related by direct thalamo-cortical radiations with the whole length of the gyrus cinguli—the strip of neopallial cortex which extends along the dorsal aspect of the corpus callosum (7) (10). The functional significance of this convolution is quite unknown, and it would be of great interest to study the functional results of its bilateral ablation in experimental animals. It may be pointed out that in an ascending series of mammals the anterior nucleus, the mammillo-thalamic tract and the medial nucleus of the mammillary body from which it arises, all become progressively more differentiated structurally. This suggests that the functional implications of this system become progressively more important in the evolutionary scale, culminating in man himself.

The *medial nucleus* (or the nucleus dorso-medialis of comparative anatomy) is a relatively large element in the human thalamus. For many years this nucleus has been commonly regarded as a phylogenetically ancient part of the thalamus, and supposed therefore to be concerned with quite primitive thalamic functions. This conception, however, is hardly in accord with the observation that the medial nucleus becomes relatively larger and better defined in higher mammals, reaching its maximum differentiation in the higher Primates (6). Moreover, it has recently been shown that it projects on to the cortex of the frontal pole—the granular cortex of the area frontalis of the

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neopallium—for on removal of this area almost the whole of the medial nucleus undergoes complete cellular atrophy (11) (12) (9). This cortical area is one of the latest areas to acquire its full development and, indeed, in Man reaches its greatest elaboration. The functional importance of this frontal cortex as a neural mechanism underlying the more elaborate mental processes is evidenced by clinical studies. According to Elliot Smith (17), "this area, in far greater measure than any other part of the brain, deserves to be regarded as the seat of the higher mental faculties and the crowning glory and distinction of the human fabric". What, then, is the nature of the sensory material which is conveyed to it by the medial nucleus? Unfortunately nothing is known of this, for the afferent connections of the medial nucleus itself are still very uncertain. It has already been remarked that the common statement that the medial nucleus receives impulses from the trigeminal nucleus rests on quite inconclusive evidence and is almost certainly not correct. On the other hand, it has been shown that fibres run up alongside the third ventricle (forming a part of the periventricular system of fibres), and terminate in the medial aspect of the nucleus (11) (42). It seems probable, on anatomical grounds, that these fibres relay impulses which have their origin in the hypothalamus. If the hypothalamus is regarded as a region for the central representation of visceral activities and as an essential element in the integration of emotional reactions, then the medial nucleus may be regarded as a relay station through which the neural processes associated with these activities are ultimately projected on to a cortical level. In other words, the medial nucleus provides a mechanism whereby the highest functional levels of the brain are enabled to control the more primitive elements of mental activity, such as are represented in emotional reactions, instinctive impulses, etc. On the basis of anatomical considerations, I have suggested elsewhere (6) (and I hold it to be legitimate to give expression to such suggestions, even though they are speculative and entirely tentative), that the frontal area of the cortex "may thus be regarded as a final product of cerebral development, where the activities of the purely cortical mechanisms underlying the intellectual components of personality are equated with the activities of the hypothalamic region which are associated with the more fundamental and primitive components", and, "in this way a means is provided for harnessing the impulses which are indissolubly linked up with elementary forms of emotional experience to the intentions and resolves which have their origin in ideational processes taking place at the highest intellectual levels". It is interesting to note that just as the somatic sensory cortex of the post-central convolution is immediately adjacent to the motor cortex from which somatic reactions are initiated, so the frontal area of the cortex is immediately bounded behind by the pre-motor cortex, from which certain visceral reactions have been elicited by electrical stimulation (22).

The centre median nucleus.—The principal nuclei of the thalamus are

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separated by fibre laminæ which are more or less distinct, and in among the fibres of these laminæ are strewn groups of cells which form what are termed the intra-laminar nuclei. In lesions involving the cerebral cortex, these intra-laminar nuclei remain mainly unaffected, showing that they have few or no cortical connections (46). In higher mammals, one of these intra-laminar nuclei enlarges and becomes differentiated to form the centre median nucleus which lies just below the caudal part of the medial nucleus. Comparative anatomical studies suggest that the centre median nucleus is entirely an intra-thalamic mechanism unconnected with the cortex (6), but this conception has been contradicted by certain authorities. As a result of an experimental study on the monkey's brain (12), it was stated that " until and unless more convincing evidence of a positive nature is forthcoming, the conception of a direct cortical connection of the nucleus should be abandoned ". It has recently been conclusively shown by Walker (46), that following complete hemi-decortication in the monkey, the cells of the centre median nucleus remain entirely normal, although almost every other nucleus undergoes complete atrophy. The significance of the centre median nucleus remains unknown. Like the medial nucleus, it has been presumed to be a primitive element of the thalamus. This is certainly not the case, for it is hardly definable at all as a separate nucleus in lower mammals, and in higher mammals it becomes progressively larger and better differentiated. In man it is relatively very large and, moreover, it becomes differentiated quite early in embryonic development. The suggestion made in some quarters that it receives fibres of the trigeminal fillet is not based on good evidence.

In this brief survey we have dealt with the more important nuclei of the thalamus proper. Mention may perhaps be made of the reticular nucleus which forms a thin plate of cells bounding the whole thalamus laterally, and lying among the thalamo-cortical radiations as they emerge from the thalamus. The cells of this nucleus undergo degeneration following cortical lesions, from which it may be assumed that their axones extend to the cortex. It remains possible, however, that the degeneration may be secondary to the mechanical effect of the degeneration of the fibres of the thalamo-cortical radiations among which they are so intimately interspersed. Anatomically, the reticular nucleus appears to be an upward extension of the subthalamus, and there is no evidence that the cells of the subthalamus project on to the cortex.

The Hypothalamus.

It has been pointed out that the hypothalamus is separated from the thalamus proper on the ventricular surface by the hypothalamic sulcus. It was supposed that this sulcus represents the upward continuation of the *sulcus limitans*, which separates the sensory from the motor lamina of the embryonic neural tube. Inferences were drawn regarding the functional

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significance of the hypothalamus on the basis of this topographical relation. Embryologists are now generally agreed that the hypothalamic sulcus is developed independently of the sulcus limitans, and is merely a secondary groove formed between the swellings of the developing thalamus and hypothalamus.

The hypothalamus is intimately connected with the olfactory regions of the cerebral hemisphere, and since there is good evidence in certain lower vertebrates that ascending tracts from gustatory and other visceral centres of lower levels terminate there (25), it has come to be regarded as primarily an olfacto-visceral correlation mechanism. It is probable, however, that the most valuable clue to the ultimate significance of the hypothalamus is to be found in its close association with the pituitary gland. The neural portion of this gland is developed embryologically as a downgrowth from the floor of the third ventricle, and conspicuous masses of nerve-cells are differentiated to form a number of hypothalamic nuclei in close topographical relation to its stalk. The hypothalamus, from this point of view, appears to be a complex ganglion directly associated with the pituitary, and forms with it a common neuro-glandular mechanism. Certain hypothalamic nuclei are directly connected with the pituitary gland by tracts of nerve-fibres (34, 14, 15). There is also a very intimate vascular connection between the pituitary and the hypothalamus—the so-called hypophyso-portal system (36, 37, 1). Minute vessels run up from the gland to be distributed among the cells of some of the hypothalamic nuclei, and colloid of pituitary origin has been traced histologically up these vessels either in their lumen or in perivascular spaces. It is supposed that by this means the colloid is brought into functional relation with the cells of the nuclei.

In man the hypothalamus can be divided into four fairly distinct areas from before backwards—the *pars supra-optica*, which lies just above the optic chiasma, the *pars infundibularis*, which corresponds to the eminence of the tuber cinereum, the *pars retro-infundibularis*, and the *pars mammillaris*. These main subdivisions are particularly well defined in the human fœtus.

Pars supra-optica.—This region contains two of the best defined and most constant nuclei of the mammalian hypothalamus, the paraventricular nucleus and the supra-optic nucleus. The *paraventricular nucleus* forms a flat plate of cells lying close against the ependymal lining of the third ventricle. Its relative extent can be seen in Fig. 4. It consists of closely packed and rather large cells which show certain characteristic features. They appear vacuolated, the Nissl granules are peripherally placed and the nucleus is often eccentric. Cell inclusions of colloid material in both the paraventricular and supra-optic nuclei have been described by Scharrer and Gaupp, who believe that this colloid provides evidence of an independent secretory activity of the cells themselves (23). They include the two nuclei under the term "Zwischenhirndrüse". That the colloid is not derived from the pituitary gland via

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the hypophysio-portal system is indicated by the fact that it can still be demonstrated some time after hypophysectomy. Another characteristic shared by the paraventricular and supra-optic nuclei is their great vascularity, which may be indicative of some special functional relation between the cells and the blood vascular system. The relation of the paraventricular nucleus to visceral functions is suggested by the statements that its cells undergo atrophy after puncture of the dorsal vagus nucleus (44), and after extirpation of the superior cervical ganglion (24). It is said also to show degenerative

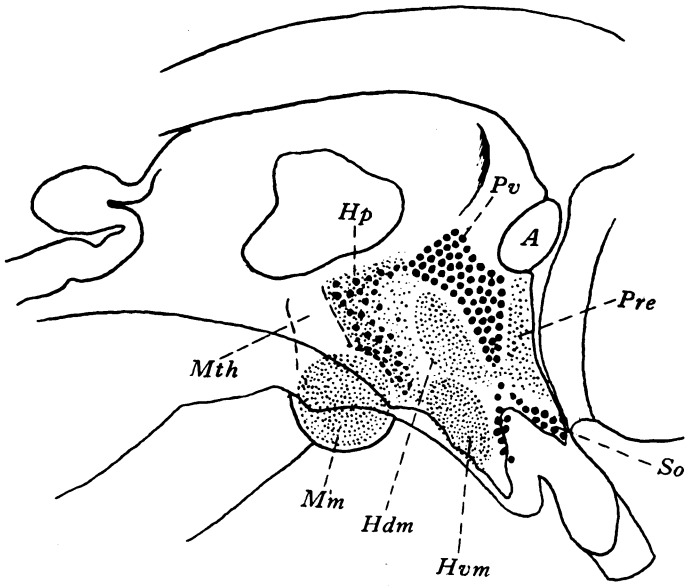


FIG. 4.—The ventricular surface of the hypothalamus is shown in this diagram, with the relative position and extent of a number of the hypothalamic nuclei. *A*. Anterior commissure. *Hdm*. Dorso-medial hypothalamic nucleus. *Hvm*. Ventro-medial hypothalamic nucleus. *Hp*. Posterior hypothalamic nucleus. *Mm*. Medial mammillary nucleus. *Mth*. Mammillo-thalamic tract. *Pre*. Pre-optic nucleus. *Pv*. Paraventricular nucleus. *So*. Supra-optic nucleus.

changes in hyperglycæmia and in diabetic coma, and following experimental pancreatectomy (44). It must be emphasized, however, that the unusual cytological features of the cells of this nucleus may be mistaken by the unwary for chromatolytic changes.

The *supra-optic nucleus* consists of a closely packed group of cells which straddles across the optic chiasma and the anterior end of the optic tract, with a tendency to extend down on the anterior aspect of the tuber cinereum. The existence of a supra-optico-hypophyseal tract has been shown by a number of investigators, and the intimate functional relation of the nucleus to the pituitary gland is well established. Degenerative changes ensue in its cells after injury to the posterior lobe of the pituitary (29), while lesions

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of the nucleus have been stated to be followed by atrophy of the posterior lobe (4). The relation of the supra-optic nucleus and its connections to diabetes insipidus also seems certain now. Richter (41) produced permanent glycosuria in rats by a puncture of the hypothalamus in front of the tuber cinereum and in the region of the optic chiasma, and it is probable that his injuries involved the nucleus or the supra-optico-hypophyseal tract. Biggart has recently described a clinical case of diabetes insipidus in which the lesion in the hypothalamus is represented as being quite small and confined to the site of this tract. Fisher, Ingram and Ranson have also shown that experimental diabetes insipidus can be produced by bilateral injury limited to the supra-optico-hypophyseal system in cats. These authors emphasize the superficial position of the tract—a position where it is particularly liable to be involved by pathological processes affecting the meninges in the neighbourhood.

Pars infundibularis.—The medial part of the tuber cinereum—that part lying between the ependymal lining of the ventricle and the fornix column—is filled with a dense collection of small rounded cells which are rather embryonic in character. This mass of cells can be subdivided into dorsal and ventral condensations which are termed the dorso-medial and the ventro-medial hypothalamic nuclei. The *ventro-medial hypothalamic nucleus* is of special interest, because of all the hypothalamic nuclei it bears the closest topographical relation to the pituitary gland. In the fœtus it is particularly well defined, but in the adult it loses its clear-cut outline (9). Like most of the hypothalamus, it receives fibres from the stria terminalis and the medial forebrain bundle (both primitive tracts which have their origin largely in olfactory regions of the forebrain), and it is also connected with the subthalamus by a small tract called the fasciculus tuberis descendens. The *dorso-medial hypothalamic nucleus* is less well defined than the ventro-medial nucleus and its connections are not clear. The lateral part of the tuber cinereum is somewhat complex cyto-architecturally, and is therefore not easy to analyse anatomically. It may be termed the *lateral hypothalamic area*. By many recent authors it is included under such cumbrous names as the "tubero-mammillary nucleus", "mammillo-infundibular nucleus" or "tubero-mammillo-trigonal nucleus". In essence, the lateral hypothalamic area is characterized by conspicuous but scattered groups of large cells which pervade it. Another distinctive feature is the presence in its superficial part of spherical and sharply circumscribed groups of small cells which are termed the *nuclei tuberis*. These nuclei frequently raise up small tubercles on the lateral aspect of the tuber cinereum which are easily seen with the naked eye. It is of interest to note that the lateral hypothalamic area is more differentiated structurally in man and the higher Primates than it is in lower mammals (9). Indeed, the characteristic groups of large cells and the presence of well-defined nuclei tuberis are distinctive features of man and the anthropoid apes.

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The lateral hypothalamic area is of particular importance for the reason that viscero-motor effects following experimental stimulation of the hypothalamus have in many cases been produced in this region (27, 28, 40, 26, 2, 20). It is well known that there is a pupillary dilator mechanism in the hypothalamus, and it has been shown that the most marked reactions are to be obtained by stimulation of the lateral hypothalamic area. Stimulation of the same region may cause cessation of peristalsis, and loss of tone in the stomach and small intestine.

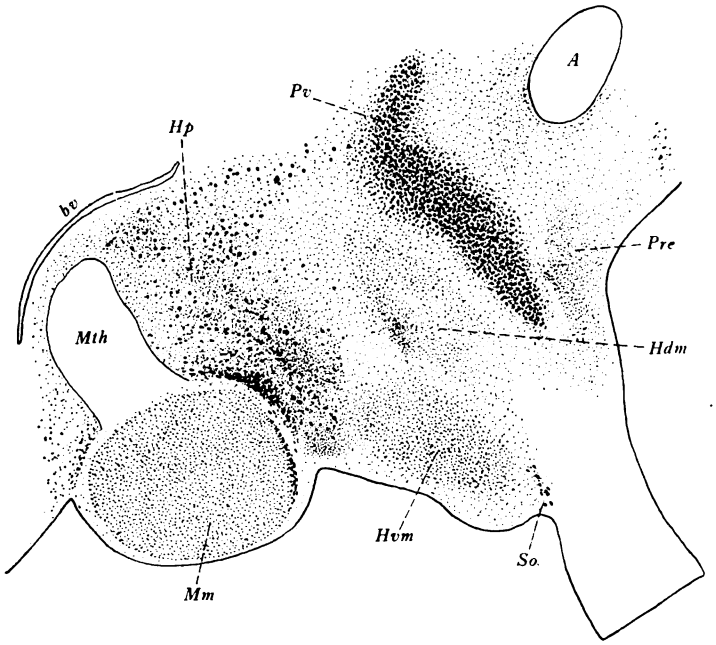


FIG. 5.—Sagittal section of the hypothalamus near the mid-line. *A*. Anterior commissure. *bv*. Blood-vessel. *Hdm*. Dorso-medial hypothalamic nucleus. *Hvm*. Ventro-medial hypothalamic nucleus. *Hp*. Posterior hypothalamic nucleus. *Mm*. Medial mammillary nucleus. *Mth*. Mammillo-thalamic tract. *Pre*. Pre-optic nucleus. *Pv*. Paraventricular nucleus. *So*. Supra-optic nucleus.

The tuber region forms a part of what Beattie (2) has called the anterior mechanism of the hypothalamus, and which he suggests is to be regarded as a parasympathetic centre. Stimulation of the tuber nuclei is stated to lead to increased motility of the stomach and bladder, and to an increase in gastric secretion and a slowing of the heart-rate. The effects on the stomach and heart are, moreover, abolished by section of the vagus. These reactions are the opposite to those which have been obtained from stimulation of the posterior hypothalamic region immediately behind. It has been suggested from time to time that the tuber region of the hypothalamus has some relation

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to temperature regulation, though the evidence for this is perhaps not yet convincing. Reference may be made here to a recent paper by Morgan and Gregory (33), who found marked pathological changes in the nuclei of the tuber cinereum in cases of idiopathic epilepsy and in certain psychoses.

Area retro-infundibularis.—This region of the hypothalamus is made up of the *nucleus hypothalamicus posterior*. In man this nucleus is a fairly well-defined element as seen in sagittal sections. It lies just in front of the mammillary bodies and the lower end of the mammillo-thalamic tract, and

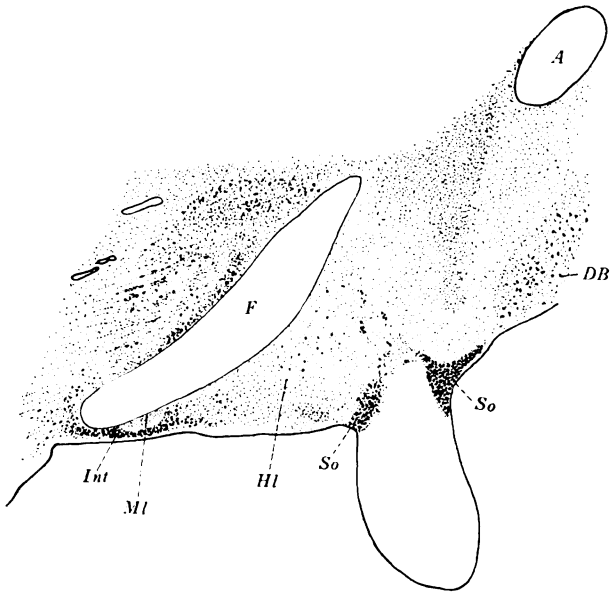


FIG. 6.—Sagittal section of the hypothalamus to one side of the median plane. *A*. Anterior commissure. *DB*. Nucleus of the diagonal band. *F*. Fornix. *Hl*. Lateral hypothalamic area. *Int*. Nucleus intercalatus. *Ml*. Lateral mammillary nucleus. *So*. Supra-optic nucleus.

consists of scattered large cells in a matrix of small cells. This nucleus appears to give rise to a great proportion (perhaps the majority) of the periventricular system of fibres (30, 2), and it may thus be regarded as an important efferent mechanism through which impulses from the hypothalamus as a whole are transmitted to the brain-stem and spinal cord. The periventricular system of fibres also takes origin in part from other hypothalamic elements—they have been traced in silver preparations from the supra-optic nucleus, para-ventricular nucleus, ventro-medial and dorso-medial hypothalamic nuclei, as well as from the posterior hypothalamic nucleus. Most of the fibres curve upwards and backwards close to the mid-line towards the dorsal aspect of the brain-stem, and collect to form a longitudinal bundle immediately below

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the posterior commissure. From this point they are continued back immediately ventral to the cerebral aqueduct, forming the fasciculus longitudinalis dorsalis of Schütz. The termination of this tract is somewhat obscure, but the prevailing opinion is that it connects with the motor nuclei of the brain-stem and particularly with the viscero-motor nuclei, and perhaps reaches the spinal cord. It seems probable, however, that at least the greater part of this tract is made up of short relays of neurones. The only experimental studies of an anatomical nature on the course of the tract are those of Beattie, Brow

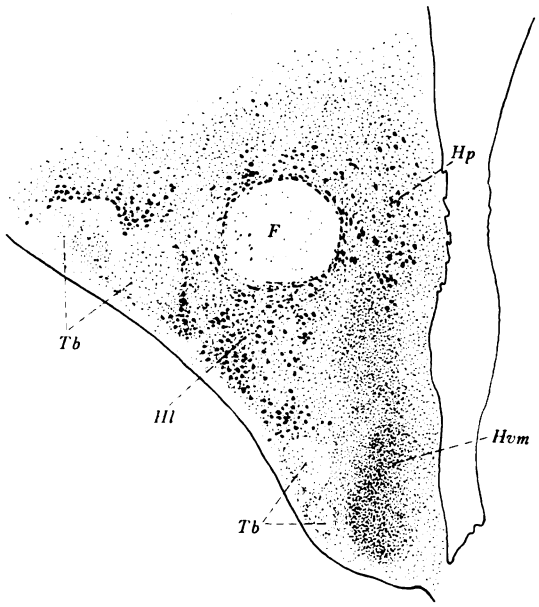


FIG. 7.—Transverse section through the hypothalamus in the region of the tuber cinereum. *F*. Fornix. *Hl*. Lateral hypothalamic area. *Hp*. Posterior hypothalamic nucleus. *Hvm*. Ventro-medial hypothalamic nucleus. *Tb*. Nuclei tuberis.

and Long (3), who traced the Marchi degeneration which followed lesions involving the posterior hypothalamic nucleus. They claimed to have demonstrated by this method fibres passing down in the grey matter of the floor of the fourth ventricle after partial decussation above the mammillary bodies, and finally terminating in the grey matter of the lateral horn in the thoracic region of the spinal cord. Their physiological evidence indicates that efferent impulses certainly pass from the hypothalamus along this route. Krieg has recently found that injuries to the periventricular tract in rats are associated with alterations of feeding reactions. It should be noted that while the main part of the periventricular system is undoubtedly an efferent tract from the hypothalamus to the brain-stem, there is anatomical evidence that some of

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the more anterior fibres run up alongside the third ventricle to the mid-line nuclei and the medially situated nuclei of the thalamus proper (42, 43). Thus, the medial nucleus of the thalamus is apparently linked up in this way to the posterior hypothalamic nucleus, though experimental evidence suggests that this connection is made by short relays of neurones. The posterior hypothalamic nucleus forms a part of what Beattie (2) has called the posterior mechanism of the hypothalamus, and experimental studies suggest that this mechanism is a controlling centre for the sympathetic system, and for the secretion of adrenaline. Stimulation in this part of the hypothalamus leads to acceleration of the heart, vaso-constriction, dilation of the pupil and pilomotor effects, etc.

Pars mammillaris.—The mammillary bodies form conspicuous structures in the interpeduncular space on the base of the brain. Each body consists mainly of the spherical *medial mammillary nucleus*—a nucleus which becomes relatively large and exceedingly well defined in Man and the higher Primates. There is also described a *lateral mammillary nucleus* and the *nucleus intercalatus*, which are both quite small. As has been already mentioned, the mammillary body is the main terminal station of the fornix column, and gives rise to the mammillo-thalamic tract which links it with the anterior nucleus of the thalamus and, through this nucleus, with the gyrus cinguli of the neopallium. The functional significance of the mammillary bodies is still in doubt. Recently experimental evidence has been brought forward suggesting that they are intimately related with sleep processes. It has been known for some time, mainly on the clinical evidence offered by cases of encephalitis lethargica (16), that a neural mechanism regulating sleep exists somewhere in the posterior part of the hypothalamus, and not very far from the nucleus of the third cranial nerve, which lies in the floor of the cerebral aqueduct. Ranson (38) has now reported that it is easy to produce catalepsy and somnolence in cats by lesions confined to the mammillary bodies and the immediately adjacent territory. He states that large bilateral lesions situated a short distance behind the mammillary bodies, lesions in the grey matter adjacent to the caudal part of the third ventricle and the neighbouring part of the cerebral aqueduct which do not extend ventrally into the region of the mammillary body, or lesions in the tuber cinereum in front of the mammillary body, do not cause any disturbance of sleep. Ranson's control series seems, therefore, to be particularly good. It would be clearly a matter of some interest to study the mammillary body histologically in those pathological conditions which are associated with catalepsy or hypersomnolence.

Cortical connections of the hypothalamus.—The possibility of a cortical control of the vegetative neural apparatus in the hypothalamus is obviously of great significance to the psychologist. It is important, therefore, to consider the fibre paths by which the hypothalamus is related to the neopallial cortex. It has already been shown that by way of the mammillo-thalamic tract and the thalamo-cortical fibres from the anterior nucleus of the thalamus, it is

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possible for impulses to be conveyed from the hypothalamus to the gyrus cinguli. There is evidence that impulses may also be conducted in the reverse direction. Thus, descending fibres in the mammillo-thalamic tract have been demonstrated by the Marchi method in the cat (10), while cortico-thalamic fibres from the gyrus cinguli to the anterior nucleus of the thalamus have been recorded by the same method in the rat (7). Clearly, therefore, an anatomical path is here provided by which it is possible for impulses from the gyrus cinguli to influence the activities of the hypothalamus through the medial mammillary nucleus.

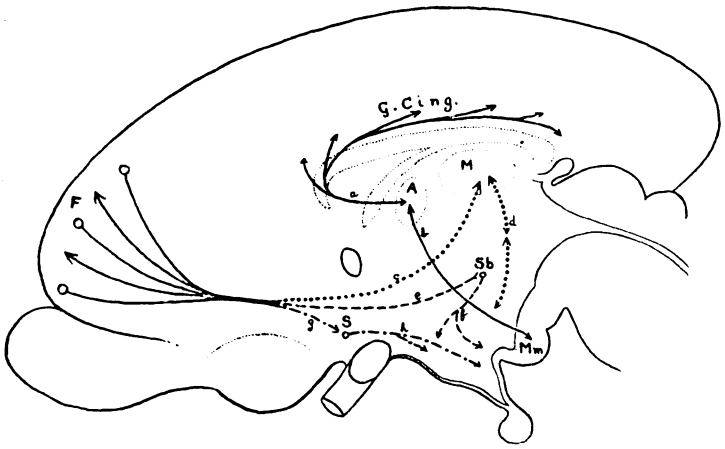


FIG. 8.—Diagram showing the connections of the neopallial cortex with the hypothalamus. *A*. Anterior nucleus of the thalamus, connected to the gyrus cinguli (*G. Cing.*) by fibres (*a*). The anterior nucleus is connected to the medial mammillary nucleus by the bundle of Vicq d'Azyr (*b*). *F*. Frontal cortex connected with the medial nucleus of the thalamus (*M*), with the subthalamus (*Sb*), and with the septal area (*S*) by fibre paths (*c*, *e* and *g*). The medial nucleus is related to the posterior part of the hypothalamus by periventricular fibres (*d*). The subthalamus is connected to the hypothalamus by descending fibres (*f*), and the septal area is connected to the hypothalamus by a septo-hypothalamic tract (*h*).

Another and perhaps more important connection is to be found with the frontal pole of the cerebral hemisphere. By the Marchi method it has been demonstrated that corticifugal fibres run from the area frontalis of the cortex to the medial nucleus of the thalamus (7), and it has already been noted that the medial nucleus in its turn is related to the posterior hypothalamic nucleus by way of the periventricular fibres (42, 43). Other possible routes for such impulses from the frontal cortex are offered by the septal region and the subthalamus. A *tractus neocortico-septalis* has been described by Wallenberg in the guinea-pig from the frontal pole to the dorsal part of the septum pellucidum, and Mettler (32) has recently traced similar connections in the monkey. It is also known that the septal nuclei contribute a bundle of

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fibres, the septo-hypothalamic tract, which connects with a number of hypothalamic nuclei. Lastly, corticifugal fibres have been demonstrated to run from the frontal pole of the hemisphere into the zona incerta of the subthalamus (7), and it is known that some of the hypothalamic nuclei receive fine fibres which run medially from the zona incerta. Here, then, are the alternative anatomical routes through which the cortex of the frontal pole can exert a controlling influence over hypothalamic activities. In this connection reference may be made to the experiments of Fulton and Ingraham (21), who, by making an incision in the prechiasmatic region of the medial surface of the hemisphere in cats, were able to alter profoundly the emotional behaviour of these animals. It is probable that this lesion involved the course of the fibres from the frontal cortex which are eventually relayed on to the hypothalamus, whether by the medial nucleus of the thalamus, the septal region or the subthalamus.

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