

THALAMIC GLIOSIS IN DEMENTIA PRÆCOX.

By MARY ELIZABETH MORSE, M.D.

(*From the Laboratory of the Worcester State Hospital, Worcester State Hospital Series No. 25, 1915-2.*)

Theoretically the thalamus offers a good field for investigation in dementia præcox. All sensory impulses except those of smell and possibly also of taste pass through it on their way to the cortex, and in addition it receives a contingent of impulses from the cerebellum. From it, on the other hand, fibers radiate to all parts of the cortex. A grave or extensive lesion of the thalamus would therefore in all probability alter or diminish the sensory data received by the cortex. In addition a central mechanism for the sympathetic is probably located in the vicinity of the third ventricle. It was the possibility of finding in the thalamus of dementia præcox cases a lesion demonstrable by ordinary histological methods, and one perhaps selective in its site, that prompted the present study.

There is considerable uncertainty as to the number of nuclei in the thalamus of the higher mammals, and as to the relations of these nuclei to various cortical areas. The differentiation of nuclei here is difficult, because they are not sharply separated from one another, and the cell type and arrangement in each are not strikingly distinctive. Subdivision, however, has been carried to a high point by Cécile Vogt¹ from the myelo-architectural, and by Friedmann² from the cyto-architectural standpoint. The former author distinguishes 41 fields in the monkey thalamus, and the results of Friedmann agree essentially with hers.

The chief nuclei, which are recognized almost universally, are the anterior; the median, with its posterior expansion, the pulvinar; the lateral group, which is composed of an upper part, the lateral nucleus proper, and a lower part, the ventral nucleus (sensory nucleus of Cajal); the ganglion habenulæ, and lastly the central gray matter surrounding the third ventricle. The cells of these

¹ Jour. f. Psych. u. Neur., Bd. XII, 285, 1908.

² Jour. f. Psych. u. Neur., Bd. XVIII, 309, 1911.

nuclei are sufficiently characteristic in form and grouping for the identification of these areas in a broad way. The lateral and median geniculate bodies are continuous with the thalamus and should be considered as a part of it.

From a phylogenetic standpoint³ the chief part of the ventral nucleus, together with the ganglion habenulæ, are the oldest parts of the thalamus. They are present in fishes and are well developed in reptiles and birds. The anterior and median nuclei are also of pale-encephalic origin, and in the lower vertebrates are connected almost exclusively with the corpus striatum. The high development of the pulvinar, on the other hand, is characteristic of the primates. With the evolution of the neopallium, the paleo-thalamic nuclei have acquired connections with the forebrain, with a corresponding increase in complexity and the resulting development of the neothalamus.

All sensory paths entering the thalamus (excluding for the moment the geniculate bodies) end in the ventral nucleus. The chief of these tracts are the main fillet, most of the fibers of which arise in the nuclei of the columns of Goll and Burdach; the spino-thalamic tract, the central tract of the cranial nerves, derived from the sensory nuclei of the afferent cranial nerves, and lastly the central tract of the trigeminus. These tracts without doubt carry the kinesthetic, thermal, tactile and pain impulses from the extremities, trunk, head and viscera. In addition, the ventral nucleus receives fibers from the dentate nucleus of the cerebellum, via the superior peduncle, and with these are combined also fibers from red nucleus. The geniculate bodies are continuous with the posterior part of the thalamus. The lateral receives fibers from the optic tract; the median is the end station of many of the fibers of the secondary acoustic path.

The connections of the thalamic nuclei with various cortical regions have recently been studied by Sachs⁴ in the cat and monkey by the production of electrolytic lesions, and by Mingazzini⁵ from the standpoint of human pathology. Sachs' conclusions are that functionally the thalamus is made up of two relatively independent divisions. The inner, which consists of the

³ See Edinger. *Bau der Nervösen Zentralorgane*, 1911.

⁴ *Brain*, XXXII, p. 95, 1909.

⁵ *Folia neurobiolog.*, VII, Nos. 1 and 2, Jan. and Feb., 1913.

anterior and median nuclei, is in association with the caudate nucleus and rhinencephalon, and, in the cat and monkey, sends no fibers to the cortex. The outer division, which is represented by the ventral and lateral nuclei, is closely connected with the pre- and postcentral cortices, the fibers to the precentral being more numerous than those to the postcentral, and differing from them also morphologically.

Mingazzini,⁶ from a study of the atrophy of the thalamus following atrophy of the occipital, parietal and the posterior half of the temporal lobes, concludes as follows: The median nucleus is connected with the prefrontal gyri; the anterior part of the ventral nucleus with the operculum and the anterior part of the precentral convolution; the lateral nucleus with the second parietal, the precentral and the supramarginal and angular gyri; the proximal half of the anterior nucleus with the prefrontal region, the distal half with the paracentral lobule.

The groups of cells on the sides and floor of the third ventricle appear to be the site of a central apparatus for the sympathetic. Karplus and Kreidl⁷ conclude from their recent experiments on monkeys and carnivora that there is a central mechanism for the cervical sympathetic situated chiefly in the hypothalamus. This center is interposed in the path from the frontal region to the cervical sympathetic and mediates the pupillary reflex in response to painful stimuli.

In a case of focal lesion in the region of the ventral part of the thalamus Schrottenbach⁸ has demonstrated by the plethysmographic method loss of the vasomotor reactions accompanying psychic reactions. He believes that this center forms a link between the central processes and the peripheral sympathetic innervation, and that it mediates the vasomotor reactions accompanying psychic states.

Selection of Material.—From the autopsy material of the Worcester State Hospital was collected a series of ten cases of dementia præcox who had died sufficiently young to exclude ordinary senile and arteriosclerotic changes in the brain, and

⁶ *Folia neurobiolog.*, VII, Nos. 1 and 2, Jan. and Feb., 1913.

⁷ *Pflüger's Arch. f. Physiol.*, Bd. 135, 401, 1910.

⁸ *Zeitsch. f. d. ges. Neurologie. u. Psychiatrie*, Orig. XXIII, H. 4/5, 431, 1914.

from causes which would not produce confusing nervous lesions. A control series of seven cases of approximately the same ages was prepared, this consisting of two cases of depressions of the involutional period, two of epilepsy, and one each of manic depressive, imbecility, and chronic alcoholism with delirium tremens. Two cases of cerebral arteriosclerosis and one each of senile dementia and senile deterioration in manic-depressive insanity were added, merely to estimate the degree of gliosis to be expected in these conditions.

Technical Methods.—The brains had been preserved in formalin for periods varying from one month to three years. The hemispheres had been separated, and the pons and cerebellum removed by cutting the cerebral peduncles. A rectangular block of tissue was cut from each hemisphere, passing anteriorly through the anterior commissure, posteriorly just behind the pulvinar, and above along the under surface of the corpus callosum. Below, the block included the hypothalamus, corpora quadrigemina and the cerebral peduncles. Each large block was then cut in the frontal plane into four segments, which were hardened in alcohol and embedded in paraffin. Two sections were cut from the anterior surface of each block; one was stained with thionin to bring out the cells, while the other was put for 24 hours in Zenker's fluid and stained by Mallory's phosphotungstic-acid-hematoxylin method for neuroglia. A series of four sections was thus obtained from each side of the thalamus, passing through approximately the same plane on both sides, and comparable planes in the different thalami. The first section passed anterior to the thalamus through the lenticular and the head of the caudate nuclei. The second passed through the anterior nucleus, and the most anterior parts of the median, lateral and ventral nuclei; the third through the centers of the median, lateral and ventral nuclei; the fourth through the pulvinar and the anterior corpora quadrigemina.

There were available for study in connection with the thalami routine sections from six cortical areas, the cerebellum, medulla, and three levels of the cord, stained by the Nissl and Weigert methods and by Mallory's neuroglia stain.

Cases.—Brief abstracts of the clinical histories and of the microscopic examination of the thalamus and other parts of the central nervous system are as follows:

CASE I (autopsy No. XV-68).—A case of the paranoid form of dementia præcox of 19 years' duration in a woman æt. 57. Father alcoholic. Two nieces insane. One of patient's children is dull. Psychosis began gradually at 36 years and was evidenced by unreasonable miserliness and erratic conduct in business relations.

Hospital residence 9 years.

On admission patient was quiet, oriented, and docile. Grasp on surroundings and memory for recent and remote events poor. She apparently reacted to hallucinations; had vague ideas of influence through mesmerism and was suspicious. Talked in an incoherent, senseless way. No insight. Physical examination negative.

During her hospital stay patient showed a slowly advancing deterioration, with auditory and visual hallucinations and ideas of reference and persecution. Died of dysentery.

The brain showed a mild cortical atrophy with slight increase of density to palpation in the frontal and superior precentral zones. Microscopically, slight focal losses of pyramidal cells, moderate zonal gliosis of hippocampal cortex, and focal gliosis of the frontal cortex.

Thalamus.—No abnormalities noted in the gross. The cells stain well; are heavily pigmented. No satellitosis. Very small amounts of green perivascular pigment. The vessel walls are not remarkable. Sections stained for neuroglia show a moderately heavy superficial layer, with penetration inward in a few places, but without active cells. Considerable perivascular gliosis throughout the thalamus. No foci of gliosis.

Lateral and Median Geniculate Bodies.—The cells are normal and there is no gliosis.

Hypothalamus.—Gliosis of the same degree and distribution as in thalamus.

Lenticular and Caudate Nuclei.—Slight perivascular gliosis; otherwise negative.

CASE II (autopsy XV-74).—A case of catatonic hirntod after an illness of eight days in a woman 22 years old. This case has been reported by Orton.* The brain showed chromatolysis of the pyramidal cells in the various cortices, particularly marked in the Betz cells; amœboid glia cells, and large accumulations of lipoid substances in the subcortical white matter, ganglion cells, glia cells, and the phagocytes of the perivascular spaces. No fibrillar gliosis.

Thalamus.—Not remarkable macroscopically. The nerve cells throughout the thalamus are blurred, stain faintly, show chromatolysis, and contain small amounts of green pigment. Many are surrounded by five or six satellites, some of which suggest neurophages. A small amount of green perivascular pigment is present (less than in cortex). There is apparently an increase of glia nuclei about the vessels. As the technical method was not adapted to bringing out the amœboid character of the glia cells or the

* AM. JOUR. OF INSAN., LXIX, No. 4, April, 1913.

lipoid deposits in the white matter, no definite statement can be made about them, but they are probably present. No fibrillar gliosis.

Lateral and Median Geniculate Bodies.—The cells stain better than in the thalamus and there is no undue satellitosis.

Hypothalamus.—Conditions as in thalamus.

Caudate and Lenticular Nuclei.—The cells stain as in the thalamus, but there is no satellitosis.

CASE III (autopsy No. XV-79).—A case of catatonic dementia præcox of at least four years' duration in a man 41 years old. Mother was feeble-minded in latter part of her life. An uncle and a sister of patient are in insane hospitals. Patient was always peculiar. At 37 years he had an outbreak of impulsive violence, for which he was committed to an insane hospital. Made a partial recovery, but was committed to Worcester State Hospital a year later. On admission patient was quiet and orderly; oriented with a fair grasp on surroundings. Memory for recent events impaired, for remote events good. Talked in rambling, disconnected sentences. Poor judgment. No insight. Physical examination—left pupil larger than right, both react to light and accommodation. Right knee kick greater than left.

For the first two years of his stay patient was quiet and industrious. He then had a period of excitement characterized by destructiveness, restlessness and exhilaration. Said he "felt ossified and suspended from the earth." Died of septicemia. Autopsy showed, in addition, old infarcts of the kidneys and chronic otitis media; in the brain slight leptomeningitis, subpial edema, and granulations on the floor of the fourth ventricle. Microscopically, satellitosis, possible cell losses in postcentral and temporal cortices, a focus of atrophy with gliosis in the frontal region, hyaline in the vessel walls of the occipital cortex and atrophy of a cerebellar lamella. Practically no subpial gliosis.

Thalamus.—Not notable macroscopically. The nerve cells stain normally, and there is no satellitosis. The superficial glia is much thickened and in places radiates inward, accompanied by rather numerous glia cells. In these areas there is some perivascular gliosis. In the outer part of the right ventral nucleus in about its central portion antero-posteriorly, is a focus 2.5 mm. in diameter in the stained specimen, in which there is a loss of nerve cells. This area surrounds a group of vessels, the walls of which, however, show no evident change. There is a suggestion of alteration of the myelin sheaths. The focus is filled in with loose-meshed glia, containing rather numerous nuclei and some phagocytes. The anilin blue stain shows no increase of collagen fibers in this area.

Lateral and Median Geniculate Bodies.—Negative.

Hypothalamus.—Superficial gliosis as over thalamus.

Lenticular Nuclei.—Nerve cells not remarkable. No gliosis. A perivascular lymphocytic infiltration in a few places.

CASE IV (autopsy No. XVII-39).—A case of late catatonia of five years' duration in a 52-year-old woman. Psychosis began with a period of

confusion, destructiveness and depression. Patient expressed the idea that she was "dead and buried."

Hospital Residence.—Four and a half years. On admission patient was resistive, apprehensive, disoriented, and without insight. Answers were irrelevant and trifling. Physical examination not significant. She had a period of excitement and destructiveness six months after admission, but the rest of the time she was apathetic. Was resistive and at times mute. Hallucinations of sight and hearing. Increasing dementia. Death from pernicious anemia.

The central nervous system showed encephalitic foci in precentral cortex and in cervical and lumbar cords; satellitosis; moderate subpial and subcortical gliosis and gliosis in Goll's columns.

Thalamus.—Normal macroscopically. The nerve cells stain well and there is no undue satellitosis. Small amount of green perivascular pigment. The subependymal glia forms a very broad fibrillar layer in which are numerous fibril-forming cells. The median nucleus contains numerous large vesicular glia nuclei and some strands of fibrils. Perivascular gliosis is prominent near the surface. No gliosis in other nuclei. Comparison of the thalamus with neopallial cortices, ventricular surface of the hippocampus, and the medulla shows that the superficial glia is far heavier in the former than in any of the other situations and that active glia cells are not present in notable numbers elsewhere.

Lateral and Median Geniculate Bodies.—Not remarkable.

Hypothalamus.—The superficial glia is equally as heavy as over thalamus, and fibril-forming cells are numerous in the underlying tissue.

Lenticular and Caudate Nuclei.—No gliosis.

CASE V (autopsy No. XVII-43).—A Finn woman, æt. 34. Psychosis began gradually 10 months before admission with auditory hallucinations and ideas of persecution. On admission patient was quiet, imperfectly oriented and without insight. During her stay she was resistive, and noisy by crying and talking. Death three and a half months after admission from tubercular enteritis.

The brain showed a satellite reaction and small amounts of perivascular pigment. Practically no gliosis.

Thalamus.—No gross abnormality. Microscopically there is a decided suggestion of a scarcity of nerve cells in the ventral and lateral nuclei. The cells are heavily pigmented. No satellitosis. The glial surface mat is in general delicate, but in a few places it dips into the stratum zonale, and is then accompanied by perivascular gliosis. No deep foci of gliosis.

Lateral and Median Geniculate Bodies.—Not remarkable.

Hypothalamus.—The superficial glia is rather thicker than over the thalamus and a few fibril-forming cells are present on the ventricular floor.

Caudate and Lenticular Nuclei.—Not remarkable.

CASE VI (autopsy No. XIII-3).—A case of three years' duration, probably belonging to the paraphrenic group, in a woman of 44. Father peculiar and two paternal cousins were cases of dementia præcox. Patient was

always eccentric; was seclusive and parsimonious. At 41 years she began to act strangely; was found on a relative's doorstep in a snowstorm at midnight, etc. Gave no explanation. Was irritable, and had outbreaks of impulsive violence. Increasing dementia. On admission patient was quiet and indifferent. Comprehended questions with difficulty and answered slowly and evasively with monotonous reiteration. Orientation and memory good; grasp on surroundings poor. No evidence of hallucinations. Physical examination showed facial tic and internal strabismus. Coarse tremor of tongue. Death four months after admission from lobar pneumonia.

The brain presented a slight chronic leptomeningitis, slight subpial edema, and a rather marked increase in density to palpation of the convolutions bordering on the central fissures, and of the upper portions of the frontal fields, including chiefly pre- and postcentral and intermediate precentral fields. Microscopically, mild degenerative changes in the cortical nerve cells, satellitosis, perivascular pigment; very slight subpial gliosis, but considerable subcortical gliosis in postcentral, frontal and hippocampal areas.

Thalamus.—Both thalami give a rather marked suggestion of induration. In both there is a suggestion of nodular induration behind and on a level with the gray commissure. On the right this nodule forms a definite mass; on the left it is considerably less prominent. The whole of the posterior surface of both thalami has a wrinkled appearance suggesting atrophy.

The left thalamus was unfortunately spoiled during the technical routine. Sections of the right show a large focus of gliosis, the central part of which corresponds in position to the lamina medullaris interna. This area extends mesially to the midline; laterally it radiates into the ventral nucleus, and posteriorly sends a network of broad bands into the pulvinar. Microscopical examination shows that it is chiefly the median and ventral nuclei and the pulvinar which are encroached upon by the focus. The anterior nucleus is relatively free from gliosis, as is also the anterior part of the median. The lateral nucleus is narrowed by an ingrowth of glia from the internal capsule. The entire posterior part of the thalamus presents a dense fibrillar gliosis. The large gliotic focus is composed of a close network of fibrils containing numerous nuclei, which in the denser portions are small and pyknotic; in the looser areas, large and vesicular. Hyaloid droplets are present. The vessels show a marked perivascular gliosis and moderate numbers of lymphocytes in the perivascular spaces. The vessel walls are not thickened. A thick layer of fibrillar glia covers the ventricular surface and sends prolongations inward, some of which join the large focus. There is a remarkably good representation of nerve cells in the various nuclei, considering the degree of gliosis. The cells are fairly well preserved; contain considerable lipochrome, and are usually surrounded by small numbers of satellites.

Lateral Geniculate Body.—Not remarkable except for heavy superficial glia. Median geniculate body negative.

Hypothalamus.—The superficial glia is thick and numerous active cells are present beneath the surface. Radiations from the gliotic area in the pulvinar extend to a slight extent into the hypothalamus.

Lenticular Nucleus.—Quite a pronounced fibrillar gliosis accompanying the strands of nerve fibers, but not elsewhere.

Caudate Nucleus.—The superficial glia is dense and shows slight focal thickenings. One large radiating perivascular focus of fibrillar glia, with active cells at its periphery, is present. No other gliosis in section.

CASE VII (autopsy No. XIII-10).—A case of paranoid dementia præcox of six years' duration in a 45-year-old man. Family history and patient's early history not remarkable. At 39 years he had a fever resembling typhoid, and was never mentally well afterward. Became irritable, lost affection for family, and developed an elaborate system of delusions of persecution by hypnotism.

Hospital residence four years.

On admission patient was intelligent in appearance, but was suspicious, irritable and reticent. Orientation and memory were good, but grasp on surroundings was superficial and insight absent. Patient stated that he was followed by a man, whom he had seen and heard, who was able by hypnotism to throw parts of his body into patient. All patient's movements, thoughts and words were a duplicate of his persecutor's. Itching, tickling, and painful sensations, of which the patient complained continuously, were the methods of torture, the object of which was to drive him insane. Physical examination on admission negative. No Wassermann reaction done. During his residence patient was controlled by his delusions, and showed a slowly progressing deterioration. Sudden death due to aneurysmal dilatation of the left ventricle.

The brain presented slight atrophy at the frontal poles and an increase of density of the pre- and postcentral gyri. Microscopic examination showed a mild satellitosis and small perivascular deposits of pigment; practically no increase of glia over the neopallial cortices or the ventricular surface of the hippocampus; a slight increase of glia in the white matter of the cerebellum, a moderate thickening on the floor of the fourth ventricle; a marked fibrillar gliosis in the posterior columns of the cord and a lesser gliosis in the lateral columns.

Thalamus.—No gross atrophy. Microscopically, the nerve cells are in good condition and there is no undue satellitosis. Small amounts of pigment in the perivascular spaces. The ventricular surface is covered with a heavy layer of fibrillar glia, and the median nuclei contain very numerous large glia cells, the fibrils of which form a prominent network throughout the nuclei. The glia cells are scattered diffusely, but there are also foci in the centers of the nuclei, in which they are more closely set. These areas are visible macroscopically. Perivascular gliosis is also marked throughout the median nuclei. A similar active gliosis is present in the pulvinar. The ventral and lateral nuclei show no gliosis.

Hypothalamus.—There is a marked fibrillar gliosis about the floor of the third ventricle, radiating for some distance inward, and containing numerous active cells.

Lateral and Median Geniculate Bodies.—Not remarkable.

Caudate and Lenticular Nuclei.—The cells are not remarkable, and there is no gliosis.

CASE VIII (autopsy No. XIII-46).—A case of catatonic dementia præcox of six months' duration in a girl of 17. One maternal cousin was epileptic and another insane. Patient went half way through high school and was a bright scholar. Was always very nervous, stubborn and "hysterical." She became wayward, acquired syphilis, and was sent to an industrial school. The psychosis began acutely six months before admission with a period of confusion and destructiveness, accompanied by auditory and olfactory hallucinations. During the first part of her hospital stay she was confused, often mute, and at times showed a tendency to cerea flexibilitas. Later she was quiet, inactive, and silly in manner. She showed secondary syphilitic lesions. The serum gave a positive Wassermann reaction, the cerebrospinal fluid a suggestion of a positive reaction, but no pleocytosis or increase of globulin. Patient tolerated mercury and iodide badly, and grew progressively weaker. Autopsy showed an enteritis and gastritis, acute nephritis, and atrophy of the ovaries. Microscopically, fatty infiltration of the myocardium and liver, and necrosis of the splenic follicles.

Brain.—The paracentral and marginal gyri on the left were very broad, were simple in arrangement, and not well approximated. The nerve cells in the various cortical areas showed mild degenerative changes. There were lipid accumulations in the nerve cells and perivascular spaces, and a slight satellite reaction. No gliosis.

Thalamus.—Is of normal contour. The nerve cells stain well as a rule, although there are a few shadows. The cells contain considerable lipochrome. A marked satellite reaction is present, some of the cells having the appearance of neurophages. A suggestion of a cell body is seen about some of the glia nuclei surrounding the vessels. No gliosis.

Lateral and Median Geniculate Bodies.—Show a slight satellitosis.

Hypothalamus.—Conditions as in thalamus.

Lenticular and Caudate Nuclei.—Some of the cells show a satellite reaction, but this is not as general or as marked as in the thalamus.

CASE IX (autopsy No. XIV-7).—A case of paranoid dementia præcox of one year's duration in a man 29 years of age. Father was intemperate. Patient always showed some eccentricities of conduct. Psychosis began gradually with visual hallucinations and ideas of reference and persecution.

On admission patient was tractable and responded promptly and relevantly. Was oriented, but without insight. Marked cyanosis of the hands and dermatographia. During his stay patient showed steady mental failure; was defiant and violent in response to somatic sensations ("shivering all over" and "can't breathe"), suspicious of poisoning, and finally refused food altogether on account of religious delusions. Tube-feeding was necessary for three months before death, which was due to abscesses of the lung.

Macroscopically the brain showed a slight general atrophy, and subpial edema; microscopically, a moderate satellite reaction and a mild fibrillar

gliosis on the ventricular surface of the hippocampus, the floor of the fourth ventricle, and in the white matter of the cerebellum.

Thalamus.—No gross abnormality. Microscopically, the cells are well preserved. A mild satellite reaction is present, which is more prominent in the pulvinar than in the other nuclei. The superficial glia is very slightly thickened and in a few places dips into the underlying tissue, accompanied by a few active cells, and slight perivascular gliosis.

Hypothalamus.—A slight thickening of the superficial glia as over the thalamus.

Lateral and Median Geniculate Bodies.—The former is negative; the latter shows a mild satellitosis.

Caudate and Lenticular Nuclei.—Not remarkable.

CASE X (autopsy No. XIV-27).—Dementia præcox of three years' duration in a 40-year-old Irish woman. Waitress. Father was alcoholic. At 37 years patient gave up work on account of somatic delusions. She was arrested for vagrancy, but after examination was sent to an insane hospital. During her stay at the Worcester State Hospital patient was apathetic, contented and neat, volunteered no conversation, but answered relevantly and coherently. Orientation, memory and grasp on education were good. No delusions were elicited, but hallucinations of sight and hearing were probably present. No insight. Physical examination was not remarkable, and the Wassermann reaction on serum and cerebrospinal fluid was negative. Patient died following an operation for carcinoma of the sigmoid.

The cerebral convolutions were well filled out. The entire region anterior to the pericentral gyri gave a suggestion of increased firmness. Microscopically, the nerve cells in the various cortices showed mild degenerative changes. Satellitosis in the deeper layers. The perivascular spaces were dilated and contained scattered lymphocytes and pigmented phagocytes. The subpial glia was not increased, but there was a moderate fibrous gliosis in the central core of the cerebellum.

Thalamus.—Was not large in the gross, and appeared somewhat firm. Nerve cells are present in good numbers and stain well. The majority of them are surrounded by satellites, some of which have the appearance of neurophages. There is a considerable lymphocytosis, accompanied by the deposition of pigment, about one of the vessels in the pulvinar. The subependymal glia over the anterior part of the thalamus is not especially increased, but over the pulvinar it is thick. Beneath the surface of the median nuclei are small numbers of active glia cells and also a perivascular gliosis. No active gliosis about the gray commissure. There is a heavy perivascular gliosis throughout the pulvinar and in most places an increase of glia nuclei with a network of fibrils. In the lower part of the right ventral nucleus is an area containing considerable numbers of active glia cells and a prominent fibrillar network. Nerve cells are present in this area, however, in apparently normal numbers and distribution.

Hypothalamus.—Satellitosis is more marked than in the thalamus, and a few shrunken, opaque, darkly staining nerve cells with excentric nuclei

are present. The superficial glia is increased, and there are a few active glia cells beneath the ventricular floor.

Lateral Geniculate Bodies.—Show nothing notable.

Median Geniculate Bodies.—Satellitosis of the same degree as in thalamus.

Caudate and Lenticular Nuclei.—Show a satellite reaction resembling that in the thalamus. The subependymal glia is heavy and there is some perivascular gliosis near the surface.

The findings in the control cases may be summarized in a few words:

1 (autopsy No. XVII-49). A case of manic-depressive insanity in a woman of 41 years; a single attack of the depressed phase lasting five years. Death from acute colitis.

The brain showed a slight satellitosis, a slight perivascular pigmentation, and an absence of gliosis.

Thalamus.—Not notable macroscopically. The nerve cells stain normally and there is no undue satellitosis. No perivascular pigment. The superficial glia over the anterior part of the thalamus is delicate; over the pulvinar it is somewhat heavier, and there are a few fiber-forming cells beneath the surface.

Lateral and Median Geniculate Bodies.—Not remarkable.

Hypothalamus.—The superficial glia is slightly thicker than over the thalamus and a few fibril-forming cells are present.

Caudate and Lenticular Nuclei.—Not remarkable.

2 (autopsy No. XVI-40). A depression of the involutional period, of 18 months' duration, in a woman 54 years old. Symptoms of central neuritis for two weeks before death.

Autopsy showed chronic endocarditis, chronic nephritis, cortical atrophy and increase of density in frontal and central gyri. Microscopically the axonal reaction in the giant pyramids of the precentral cortex, prominent satellitosis in the various cortices, great numbers of hyaloid droplets; no gliosis in the cerebrum, but a peripheral gliosis in medulla and cord.

Thalamus.—Not remarkable macroscopically. The nerve cells contain large amounts of lipochrome, but are otherwise not remarkable except in the pulvinar where there are a few cell shadows and a slight satellitosis. The glia over the anterior and median parts of the thalamus is not increased, but over the pulvinar it shows focal thickening with slight extension inward, but with very few cells. Considerable perivascular pigment.

Geniculate Bodies.—Not remarkable.

Hypothalamus.—The cells resemble the thalamus. The glial mat bordering the lower part of the third ventricle is thicker than over the thalamus, but does not radiate inward.

Lenticular and Caudate Nuclei.—Pigmented satellites are fairly numerous. No gliosis.

3 (autopsy No. XVII-68). An unclassified psychosis of the involutional period in a woman of 50 years. Onset at 47 years with worry, agitation,

and ideas of reference and persecution. Patient cleared up somewhat after a few months, but later lapsed into a mute, confused and agitated condition. Death from acute colitis.

Microscopically the brain showed normal cortical architecture, small amounts of green perivascular pigment, slight zonal gliosis, and an absence of arteriosclerosis.

Thalamus.—Normal macroscopically. The nerve cells contain considerable lipochrome, but otherwise appear normal. A number of vessels in both thalamus and hypothalamus are surrounded by lymphocytes. Green perivascular pigment is present in moderate amount. The subependymal glia over both the thalamus and hypothalamus is slightly thickened, but does not extend inward, and there are no deep foci. Slight perivascular gliosis particularly near the ventricular surface.

Lenticular and Caudate Nuclei.—Not remarkable except for lipochrome content of nerve cells.

4 (autopsy No. XVI-1). A low-grade imbecile, dying at 40 years from chronic nephritis. The brain showed lack of approximation of the frontal convolutions, thickening of the pia, and small foci of disintegration in frontal cortex, medulla and cerebellum, increase of subependymal glia over the hippocampus and a perivascular focus of gliosis in the medulla.

Thalamus.—Negative macroscopically. The nerve cells are heavily pigmented, but are otherwise not notable. No satellitosis. No increase of glia, either superficial or deep.

Geniculate bodies, hypothalamus, and caudate and lenticular nuclei are not remarkable.

5 (autopsy No. XVII-33). A case of delirium tremens in a chronic alcoholic 42 years old. The gross autopsy findings were cardiac hypertrophy and dilatation, infarct of the lung, and subpial edema. The brain showed degenerative changes in the cortical nerve cells, marked satellitosis, and practically no gliosis.

Thalamus.—Macroscopically not notable. Most of the nerve cells appear normal; a few are shrunken and angular and stain deeply. Clusters of four to five satellites are found about some of the nerve cells, but on the whole satellitosis is not prominent. There is a rather dense glial network on the ventricular surface, but no deep foci or active cells.

6 (autopsy No. XVI-46). A much demented epileptic woman, aet. 42, dying of acute colitis. Brain weighed 1210 gms., and showed no gross atrophy and no increase of consistence in any particular region. Microscopically the cortex in many places gave the impression of being thin, but there was no obvious scarcity of nerve cells. A mild satellitosis was present, and a slight peripheral gliosis in medulla and cord.

Thalamus.—The nerve cells contain much lipochrome, but otherwise stain well. The subependymal glia is moderately thickened, and is prolonged inward for a short distance along the vessels, but there are no active cells, and no deep gliosis.

Geniculate bodies.—Not remarkable.

Hypothalamus.—Peripheral gliosis as over thalamus.

Caudate and Lenticular Nuclei.—A superficial gliosis over the head of the caudate, but no deep foci.

7 (autopsy No. XIII-50). A case of epilepsy of three years' duration in a man 34 years old. Death in status epilepticus. The brain showed degenerative changes in the nerve cells, intense satellite reaction with the presence of neurophages, amœboid glia cells about the vessels, collections of lipoid materials around the vessels and in nerve cells, and a marked fibro-cellular gliosis in the cornu ammonis.

Thalamus.—Not notable macroscopically. Changes in nerve cells and satellitosis resemble those in cortex, but are rather less intense. Amœboid glia cells are present. Lipoid deposits are less prominent than in cortex. The glia over the thalamus is in general not thickened, but in a few places accompanies the vessels inward.

Geniculate Bodies.—The cells of the median resemble those of the thalamus; those of the lateral are free from satellites and stain normally.

Hypothalamus.—The superficial glia is very heavy, and numerous active cells are present beneath the surface.

Caudate and Lenticular Nuclei.—The cells stain well, but a marked satellitosis is present. The glia over the head of the caudate nucleus is much thickened, but does not radiate inward to any extent. No gliosis in the lenticular nucleus.

Arteriosclerotic and senile cases:

8 (autopsy No. XIII-6). A man, 61 years old. Symptoms dating back nine years. Major anatomical diagnoses were bilateral acute otitis media and coronary sclerosis. The cortex showed thickening of the small arteries, moderate perivascular cell losses, heavy lipochrome content of nerve cells, zonal gliosis, and foci of softening in the right postcentral convolution.

Thalamus.—Not remarkable macroscopically. The nerve cells contain much lipochrome. The arteries are markedly sclerotic. There is an extremely heavy layer of fibrillar glia over the ventricular surface, including the head of the caudate nucleus, the thalamus, and hypothalamus. Moderate numbers of glia cells with coarse fibrils are situated at short distances below the surface, and there is considerable perivascular gliosis throughout the structures. No focal gliosis.

Geniculate Bodies.—Not notable.

9 (autopsy No. XIII-28). A case of cerebral arteriosclerosis of three years' duration in a woman 60 years old. Cysts of softening in both temporal regions. Microscopically the brain showed thickening of the small arteries, with perivascular devastations, heavy lipochrome deposits in nerve and neuroglia cells, and very moderate zonal and perivascular gliosis.

Thalamus.—At the upper pole of the left anterior nucleus is a focus of softening surrounding several almost obliterated vessels. The area is filled with granule cells, but shows no surrounding glia reaction. The subependymal glia is very heavy and extends deeply inward. There is a marked perivascular gliosis and some increase of small glia nuclei throughout the thalamus. The gliosis, however, is not active and there are no deep foci. Miliary hemorrhages on floor of third ventricle.

Caudate and Lenticular Nuclei and Hypothalamus.—Gliosis as in thalamus.

Geniculate Bodies.—Negative.

10 (autopsy No. XIV-33). Senile deterioration in a case of manic-depressive insanity—a woman, 78 years old, dying of chronic nephritis. Brain showed very marked atrophy in the frontal, central and parietal regions. The most prominent microscopic changes were satellitosis, perivascular accumulations of lipoid pigment and heavy subpial gliosis. Arteriosclerosis was slight and no senile plaques were found.

Thalamus.—The nerve cells stain well. Mild satellitosis. Very little arteriosclerosis. There is in places considerable perivascular infiltration of lymphocytes, polymorphonuclear leukocytes and pigmented phagocytes. There is marked thickening of glia about the sides and floor of the third ventricle and moderate perivascular gliosis throughout the thalamus.

Caudate and Lenticular Nuclei.—Satellitosis and perivascular infiltration as above. Gliosis about some of the large arteries in the lenticular nuclei. Small numbers of active glia cells near the ventricular surface, but no thickening of the peripheral glia layer.

Hypothalamus.—Shows thickening of the superficial glia, but no deep foci.

11 (autopsy No. XIV-35). A case of senile dementia of six years' duration in a woman 76 years old. Death from lobar pneumonia. The brain showed cell losses in the cortex, senile plaques, zonal and cortical gliosis, and moderate arteriosclerosis.

Thalamus.—The nerve cells are heavily pigmented, but are otherwise not remarkable. Mild satellite reaction in the pulvinar. Over the anterior and middle parts of the thalamus the glia is moderately heavy. There are fairly numerous large, active glia cells in the various nuclei, and much perivascular gliosis. The pulvinar shows a marked gliosis, consisting of a very heavy superficial layer, and numerous active cells throughout the tissue.

Caudate and Lenticular Nuclei.—Heavy superficial glia and considerable perivascular gliosis.

Hypothalamus.—More subependymal gliosis than over thalamus. Very numerous active glia cells about the floor of the third ventricle.

Geniculate Bodies.—Negative.

Summarizing the findings in the two series:

Dementia Præcox Cases.—In case I, gliosis is present in the thalamus, but is not limited to it, being found also in the subpial layer over the cerebrum.

In cases II and VIII the changes in the nerve cells of the thalamus are similar to those in the various cortices, and there is no gliosis in the thalamus or other parts of the central nervous system examined.

In case III the thalamic focal lesion is not an isolated one, as similar, though smaller, areas are present in the frontal region and cerebellum. This fact, however, would not necessarily detract from the importance of the thalamic lesion. The degree of superficial gliosis found in the thalamus is not duplicated in the other regions examined.

Case IV shows a superficial gliosis in the thalamus which is more advanced and more active than in other parts of the nervous system examined.

In case V no lesions were noted in the thalamus.

The thalamus of case VI is the site of an extensive and advanced gliosis which is sufficient to cause a macroscopic atrophy. The lesion is old and inactive. A gliosis is present to a lesser degree in adjacent structures, *i. e.*, the hypothalamus, internal capsule and basal ganglia. A subcortical gliosis is found in the postcentral, frontal and hippocampal areas, but does not at all approximate the degree found in the thalamus.

Case VII shows a thickening of the superficial glia and an active gliosis beneath the surface. A fibrillar gliosis is present in the posterior columns of the cord and a moderate gliosis on the floor of the fourth ventricle, but in neither of these locations has the gliosis the active character found in the thalamus.

Case IX showed slight thickening of the glia over the thalamus, and mild gliosis in the hippocampus, the central white matter of the cerebellum, and on the floor of the fourth ventricle.

In case X the thalamus, hypothalamus and basal ganglia showed a satellite reaction. The pulvinar was the site of a mild gliosis. The lower part of the right ventral nucleus also showed an increase of glia nuclei and fibrils, not sufficient, however, to distort the normal architecture. The gliosis in the thalamus is comparable in degree to that present in the central white matter of the cerebellum, the only other place in which gliosis was present.

Control Cases.—Cases 1 and 2 showed a slight gliosis over the pulvinar, but not elsewhere in the thalamus; an absence of gliosis in the cerebrum in both cases, but a peripheral gliosis in the medulla and cord of case 2.

In case 3 there was in places a perivascular lymphocytic infiltration, which was not found in the cortex. There was also a

slight increase of peripheral and perivascular glia in the thalamus. Slight zonal gliosis in the cortex.

In case 4 the thalamus presented no noteworthy changes. Subependymal gliosis over the hippocampus and a focus of gliosis in the medulla.

In cases 5 and 7 the acute changes in the thalamus resemble those in the cortex; in case 5 there is some thickening of the glia over the thalamus, but none in case 7. No cortical gliosis in either case, but a gliosis of the cornu ammonis in case 7.

In case 6 there was a slight peripheral gliosis of the thalamus; none in the cortex.

The cases of cerebral arteriosclerosis and senile dementia (8, 9 and 11) showed advanced peripheral and perivascular gliosis in the thalamus with the presence of large fibril-forming cells in cases 8 and 11. In all these cases there was also a zonal gliosis over the cerebrum, and in addition in case 9 a perivascular, and in case 11 a sub-cortical gliosis. In the case of senile deterioration in manic-depressive (10) there was a mild perivascular lymphocytic infiltration in the thalamus; also a moderate perivascular and marked peripheral gliosis. The cerebrum showed a heavy zonal gliosis.

It is evident on review of these findings:

First. That the distinctive change in the thalamus is a gliosis. Degenerative changes in the nerve cells, satellitosis and perivascular accumulations, when present in the thalamus, were found also in the cortex, except in control cases 3 and 10, in which perivascular infiltration was confined to the thalamus. Some of the dementia præcox cases gave an impression of scarcity of cells as compared with the manic-depressive cases, but as this point could not be proved without accurate methods of enumeration to which the present sections were unsuited, it has not been emphasized. Changes in the hypothalamus were as a rule similar to those of the thalamus. The superficial glia was often rather heavier than over the thalamus, and active glia cells were frequently present beneath the floor of the ventricle, but no gliosis was found at any distance from the ventricular wall. No essential changes were found in the lateral or median geniculate bodies. In the lenticular and caudate nuclei the cellular findings were similar to those of the thalamus, but satellitosis was less marked.

The glia over the head of the caudate nucleus was thickened in the arteriosclerotic and senile cases, also in dementia præcox cases VI and X. Case VI, which showed extensive gliosis in the thalamus, had also a focus in the lenticular nucleus.

Second. That this thalamic gliosis occurs more frequently in dementia præcox patients than in those with other psychoses who die at about the same ages.

Third. That a marked gliosis may occur in the thalamus in dementia præcox cases at a period when there is little gliosis in other parts of the nervous system. In none of the cases was the gliosis strictly limited to thalamus, but in four of the six cases in which it was present there, it exceeded that found elsewhere.

The distinctive points about the thalamic gliosis in dementia præcox are the early age at which it appears and its occurrence in the absence of arteriosclerosis. The senile and arteriosclerotic cases showed marked peripheral and perivascular gliosis in the thalamus, as well as in other parts of the nervous system, but in them the thalamic gliosis was less active than in the dementia præcox cases, and had a more uniform distribution, lacking the focal character seen in several of the dementia præcox cases.

The areas most frequently involved are the median nuclei and the pulvinar.

Arranging the dementia præcox cases with reference to thalamic gliosis, age at death and duration of the psychosis (see Table I), it is found that the four cases showing no gliosis were all under 40 years, and that the psychosis was of short duration (not over one year). Of the four cases having a gliosis more marked and more active in the thalamus than elsewhere, three fall in the fifth decade, the third early in the sixth, and their psychoses were of three to five years' duration. Of two cases presenting a gliosis of roughly comparable degree both in the thalamus and in other parts of the nervous system, one was in the second half of the sixth decade and the disease was of long standing (19 years); the second was in the middle of the fifth decade and the disease was of six years' duration. The group presenting a gliosis either almost limited to the thalamus or more advanced there is therefore intermediate in duration, and, with the exception of case IV, intermediate also in age.

The interpretation of the lesion and its relation, if any, to the symptoms, are problematical. Correlations with the age of the patient and the duration of the disease suggest that it is dependent to some extent on these factors. The findings may mean simply that the gliotic process in general begins early in the thalamus as compared with other parts of the nervous system, and that it begins here earlier in dementia præcox than in other psychoses. The controls were not numerous enough (see Table II) to prove the first hypothesis, but the second is probable from the study of the present series.

As to the gravity of the lesion, not much weight can be attached to a mere thickening of the superficial glia mat, but its extension inward, accompanied by perivascular gliosis and fibril-forming cells, would appear to have some importance. The changes in III, IV, VI, VII and X are of the latter character. In addition, focal glioses are present in III, VI and X; those in III and X are situated in an area of the first importance, the ventral nucleus; that in VI occupies the larger part of the thalamus.

Study of the patients' histories adds nothing that, in the present state of our knowledge, can be pointed to as suggesting a correlation between the thalamic lesion and the clinical symptoms. Cases III, IV and X expressed somatic ideas, but, according to the histories, they were not prominent or persistent. In case VI, which showed the most marked and extensive lesion, no information on this point was elicited. In case VII cutaneous and visceral sensations form a conspicuous part of the clinical picture, but, in addition to the thalamic lesion, this patient presented posterior and lateral column gliosis.

CONCLUSIONS.

Some cases of dementia præcox in the fifth and sixth decades show a gliosis in the thalamus, which is more advanced and active than in other parts of the nervous system. This gliosis may be both peripheral and focal. Patients with other psychoses who died at about the same ages did not in the cases examined present a similar thalamic gliosis.

TABLE I.—DEMENTIA PRÆCOX CASES.

Group A.	No.	Age.	Form of dementia præcox.	Duration.	Thalamic gliosis.	Gliosis on other parts of nervous system.
No gliosis in thalamus	II	22	Catatonic hirtod.	8 days.	None.	None.
	V	34	Probably paranoid.	1 yr.	None.	None.
	VIII	17	Catatonic.	6 mos.	None.	None.
	IX	29	Paranoid.	1 yr.	Very slight thickening of peripheral glia.	Slight subependymal gliosis in hippocampus and on floor of fourth ventricle. Slight gliosis in central white matter of cerebellum.
Group B. Gliosis more marked in thalamus than in other parts of nervous system.	III	41	Catatonic.	4 yrs.	Peripheral; focal atrophy with gliosis.	Small focus of gliosis in frontal cortex and cerebellum.
	IV	54	Catonia (late).	5 yrs.	Peripheral; active gliosis in median nucleus.	Moderate subpial and subcortical of cerebrum.
	VI	44	Paranoid (paraphrenia).	3 yrs.	Peripheral; extensive focal.	Subcortical in post-central, frontal and hippocampal areas.
	X	40	Paranoid?	3 yrs. +	Fibrillar gliosis throughout pulvinar with perivascular and subependymal gliosis. Active glia cells and perivascular gliosis in median nuclei. Mild focal gliosis in ventral nucleus.	Moderate in central core of cerebellum.
Group C. Gliosis not limited to thalamus.	I	57	Paranoid.	19 yrs.	Peripheral and perivascular.	Moderate subpial gliosis of cerebrum.
	VII	45	Paranoid.	6 yrs.	Peripheral and perivascular; active gliosis, diffuse and focal, in median nucleus and pulvinar.	Posterior and lateral column gliosis.

TABLE II.

Group D.	No.	Age.	Psychosis.	Duration.	Thalamic gliosis.	Gliosis in other parts of nervous system.
Control cases.	1	41	Manic depressive.	5 yrs.	Slight peripheral over pulvinar.	None.
	2	54	Depression of involutional period.	1½ yrs.	Very slight peripheral over pulvinar.	Peripheral of medulla and cord.
	3	50	Depression of involutional period.	3 yrs.	Very slight peripheral and perivascular.	Slight zonal of cortex.
	4	40	Imbecile.	—	None.	Subependymal of hippocampus. Small perivascular focus in medulla.
	5	42	Chronic alcoholism, delirium tremens.	Alcoholism many years.	Very slight peripheral.	None.
	6	42	Epileptic dementia.	Many years.	Slight peripheral.	Slight peripheral of medulla and cord.
	7	34	Epilepsy. Status epilepticus.	Epilepsy 3 yrs.	None.	Marked in cornu ammonis.
Group E. Arteriosclerotic and senile.	8	61	Cerebral arteriosclerosis.	9 yrs.	Very heavy peripheral. Considerable perivascular.	Zonal throughout cortex
	9	60	Cerebral arteriosclerosis. Cysts of softening.	3 yrs.	Very heavy peripheral and perivascular.	Moderate zonal and perivascular throughout cortex.
	10	78	Senile deterioration in manic depressive.	6 yrs. +	Marked peripheral. Moderate perivascular.	Heavy zonal throughout cortex.
	11	76	Senile dementia.	6 yrs.	Heavy peripheral and perivascular, most marked in pulvinar.	Zonal and cortical.