ANATOMICAL STUDY OF FIBER CONNECTIONS OF THE TEMPORAL POLE

IN THE CAT AND MONKEY

by

Choh-luh Li, B.S., M.D.

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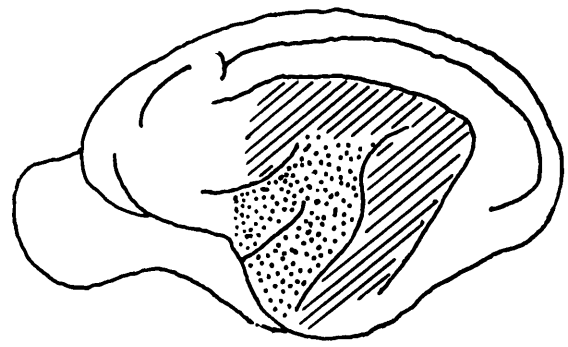
I. INTRODUCTION

The understanding of the functions of a certain portion of the cortex ultimately is dependent on a knowledge of the connections or interrelationships of that particular cortex. Consequently, the visual cortex and the auditory area are better understood because of the works of Poliak (1932), Talbot (1942) , Talbot, Woolsey and Thompson (1946), and of Walker (1937a,1937b), of Ades and Felder (1942, 1945), Ades (1943), Woolsey and Walzl (1942), Walzl and Woolsey (1943), Tunturi (1944, 1945), Rose (1949), and Rose and Woolsey (1949). For the same reason, the temporal cortex is, perhaps, the least understood. Having analyzed a large group of patients with an epileptic focus in the temporal lobe, Penfield (1949, 1950a, 1950b) advances the theory that the temporal cortex exclusive of the auditory area projects directly to the "highest level" (Penfield and Jasper, 1947), from which it also receives afferent fibers. It is the purpose of this research to find out whether or not such pathways exist. The area investigated has been confined to the polar region of the temporal lobe, the reasons being that it is readily recognized, at least in the primates, and that it is without known connections with the subcortical structures.

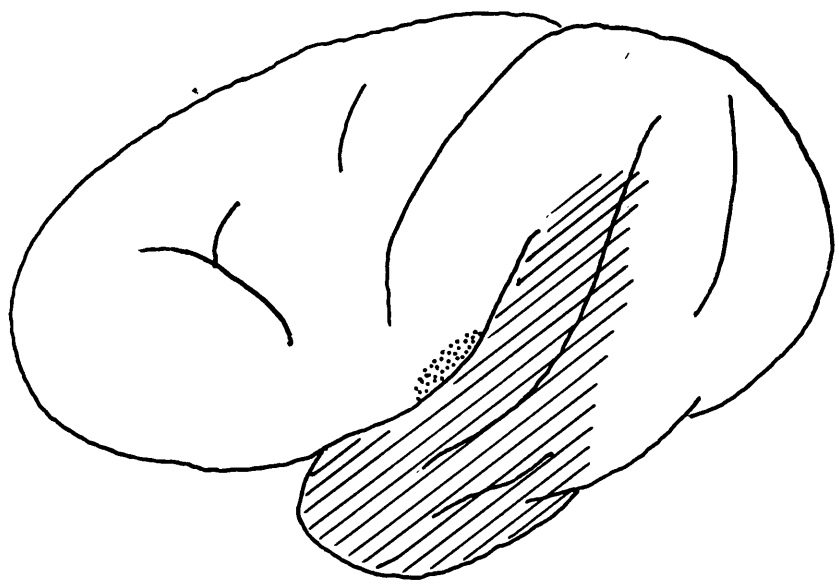
II. GENERAL CONSIDERATIONS AND REVIEW OF LITERATURE

While the temporal lobe in the primates and in man is a distinct mass below the sylvian fissure, in the lower mammals it is ill defined. In the cat, the temporal area is around the peak of the pseudosylvian sulcus, and resembles a horseshoe, in the hollow of which is the insula. The recognition of the cortical areas in lower mammals results from the histological studies of Campbell (1903, 1904 and 1905), whose map has been adopted in this laboratory (Fig. 1).

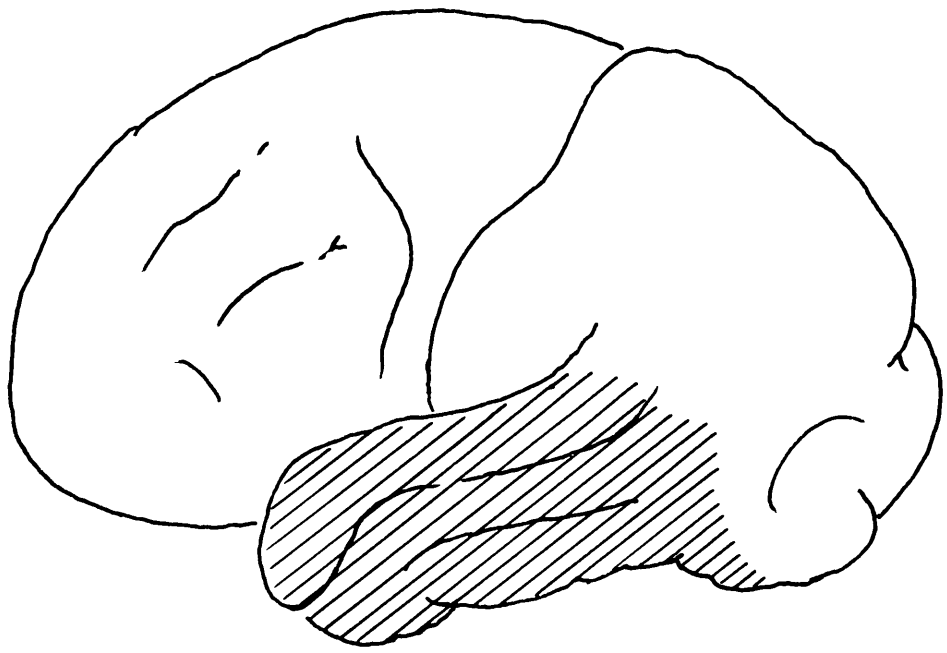
As the phylogenetic scale advances, the expansion of the neocortex gradually enfolds the insula into the sylvian fossa. This takes place more rapidly in the region of the insula anterior than in the region posterior to the pseudosylvian sulcus. Thus the anterior sylvian gyrus (or gyrus arcuatus primus or gyrus sylvius anterior of the cat) is absent from the surface of the hemisphere in the bear. In the primates the anterior ectosylvian gyrus (or gyrus arcuatus secundus) sinks into the island, while the anterior suprasylvian sulcus approaches the pseudosylvian sulcus. In the case of man, the anterior suprasylvian sulcus further migrates to the island and becomes the superior limiting sulcus of the insula (sulcus limitans superior insulae); and the upper part of the anterior ectosylvian gyrus forms the transverse convolution



Cat



Monkey



Man

Fig. 1

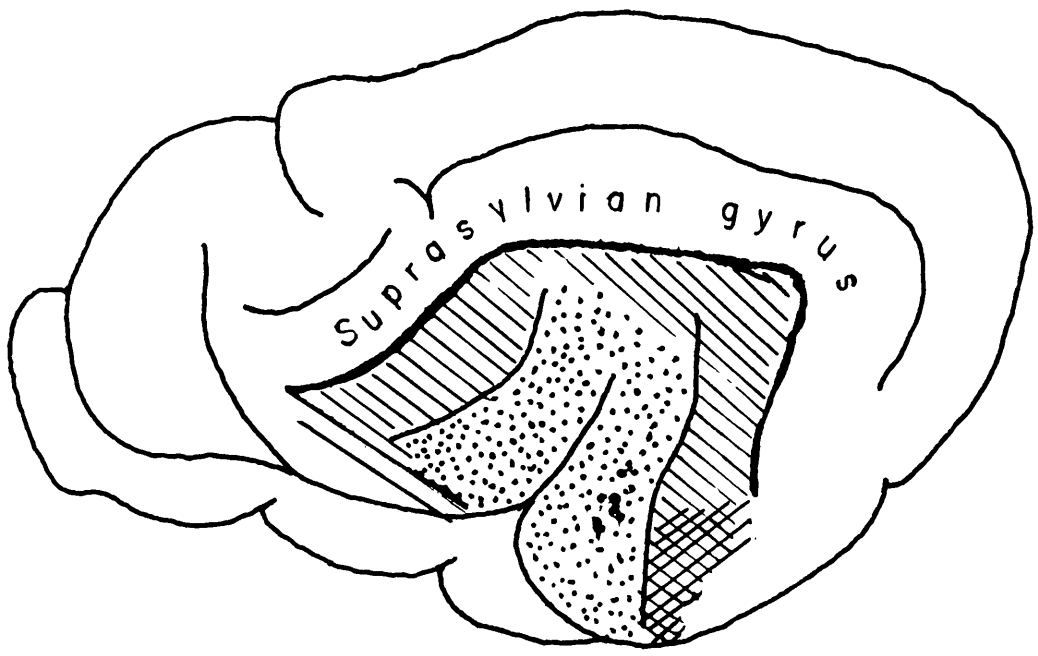
The temporal cortex and the insula of the cat, monkey and man (redrawn from Campbell, 1905, after Kappers, Huber and Crosby, 1936).

of Heschl. On the other hand, the change in the region posterior to the pseudosylvian sulcus is not as great. In primates and in man, the posterior suprasylvian sulcus of the cat remains on the lateral surface as the superior temporal sulcus.

The concept of evolution is based upon the works of Turner (1891), Elliot Smith (1903, 1907), Winkler and Potter (1914) and many others, and is summed up by Kappers, Huber and Crosby (1936). Should this concept be accepted it appears reasonable to place the temporal polar region in the cat in the lower extremity of the posterior ectosylvian gyrus (or the posterior limb of the secondary arcuate gyrus) (Fig. 2). However, we are aware that there is no support for this homology aside from the embryological data and the comparative morphological studies. Von Bonin and Bailey (1947) pointed out that evolution proceeds along divergent lines, and that "the attempt to homologize the fissures of the primates with those of other mammals is bound to appear as ill-founded".

A. Temporal Polar Cortex

The temporal polar region in man is designated by Brodmann (1909) as area 38 and by Economo (1929) as area TG. While Brodmann did not recognize a cytoarchitectonically



The insula, stippled, the temporal, shaded, and the proposed temporal polar region, crossed. (redrawn from K.H.G.).

Fig. 2

The proposed temporal polar region in a cat (modified from Kappers, Huber and Crosby, 1936).

similar area in the monkey, von Bonin and Bailey (1947) observed structural changes where the temporal cortex approaches the pole, in which region the cortex as a whole becomes thicker and the distinction between various layers (excepting 1) is vague. This is the area TG of von Bonin and Bailey (Fig. 3).

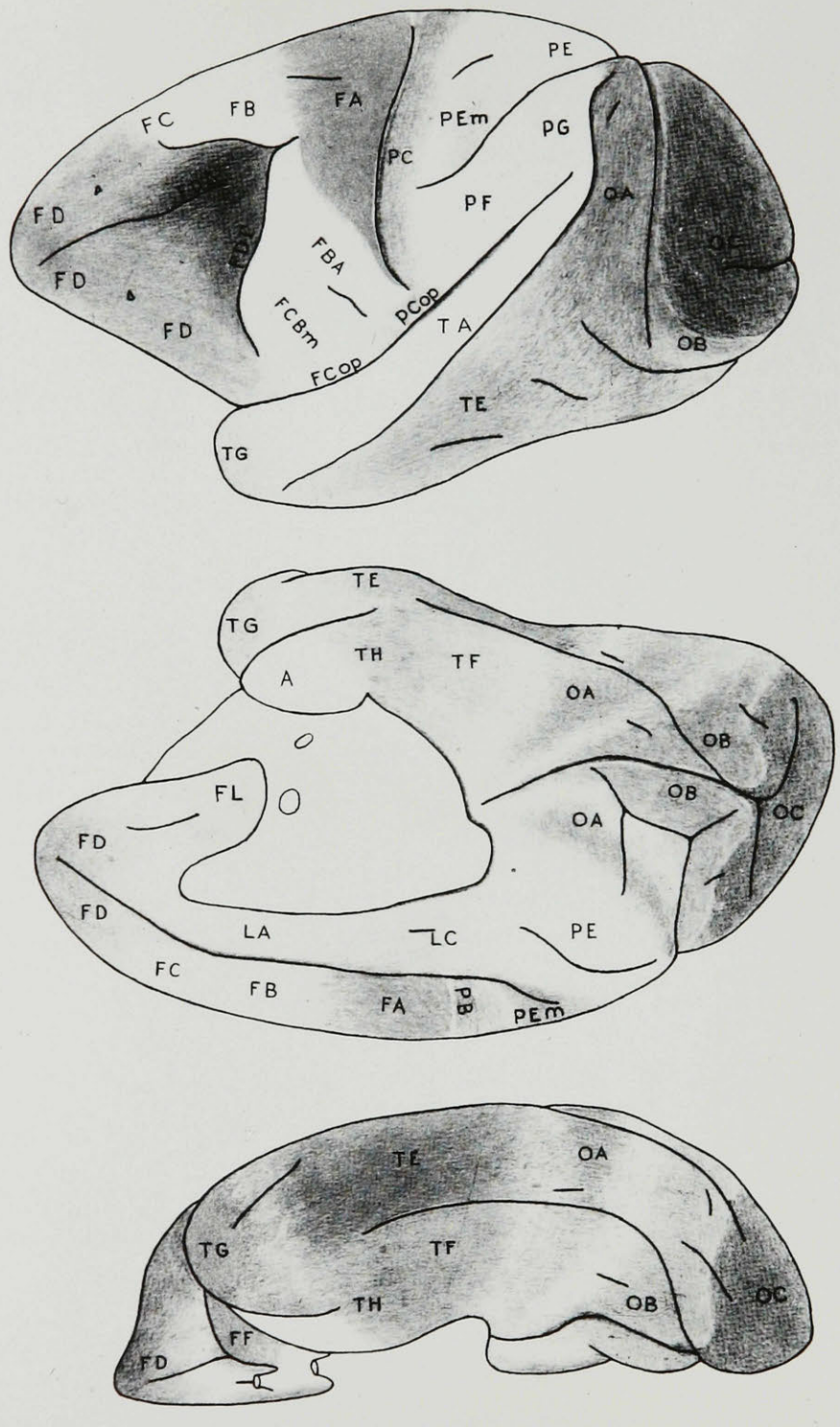
In the cat the cortex in the lower region of the posterior ectosylvian gyrus is distinguishable from its upper region. According to Winkler and Potter (1914) this is area 36 or area ectorhinica*, characterized by an increase of thickness in layers I and IV and the widening of the clear zone between layers III and V, as a result of which the relatively large cells of V are placed between two clear zones.

B. Temporal Projection Fibers

1. Temporo-thalamic pathway.

According to Dejerine (1901) certain fibers in the medullary centers of the temporal convolutions (probably all three convolutions) assemble towards the lateral border of the lateral geniculate body and the postero-inferior part of the pulvinar forming a compact bundle. The same had been previously described by Arnold (1851) as fasciculus temporo-thalamicus and by Brissand as sub-optic band. This fasciculus

* This must not be confused with the entorhinal area which is separated from the ectorhinal area by a perirhinal area.



CORTICAL AREAS OF MACACA
(See page 57)

Fig. 3

The cortical areas of the Macaca mulatta (von Bonin and Bailey, 1947).

passes under the temporo-pontine bundle and the retrolenticular segment of the internal capsule. This is illustrated by Dejerine's Figure 27 (Fig. 4). However, recent workers (Minkowski, 1923; Poliak, 1932; Clark and Boggon, 1935; Clark, 1936; Clark and Northfield, 1937; Walker, 1936, 1937a, 1937b, 1938; Rundles and Papez, 1937-38) deny the existence of direct temporo-thalamic pathways. Mettler (1935) stated that in monkey the dorsal anterior portion of the temporal cortex sends fibers to the lateral nucleus of the thalamus, and the dorsal posterior portion of the temporal cortex, to the pulvinar. Later (1942) he declared that the so-called temporo-thalamic bundle is probably from the posterior parietal cortex to the pulvinar (PL).

2. Temporo-pontine tract.

In the last half century, from Dejerine (1901) to Ranson (1947), almost all anatomists have designated the temporo-pontine tract as Türck's bundle. It was, nevertheless, Flechsig (1876, 1896) who first observed and described this tract. With myelin stain, Flechsig was able to trace the fibers from the temporal lobe to the lateral segment of the base of the cerebral peduncle, and finally to the pons. He called this fiber bundle "temporale grosshirnrinde Brüchenbahn". Many later workers misplaced the credit, possibly due to the fact that Türck's contribution towards

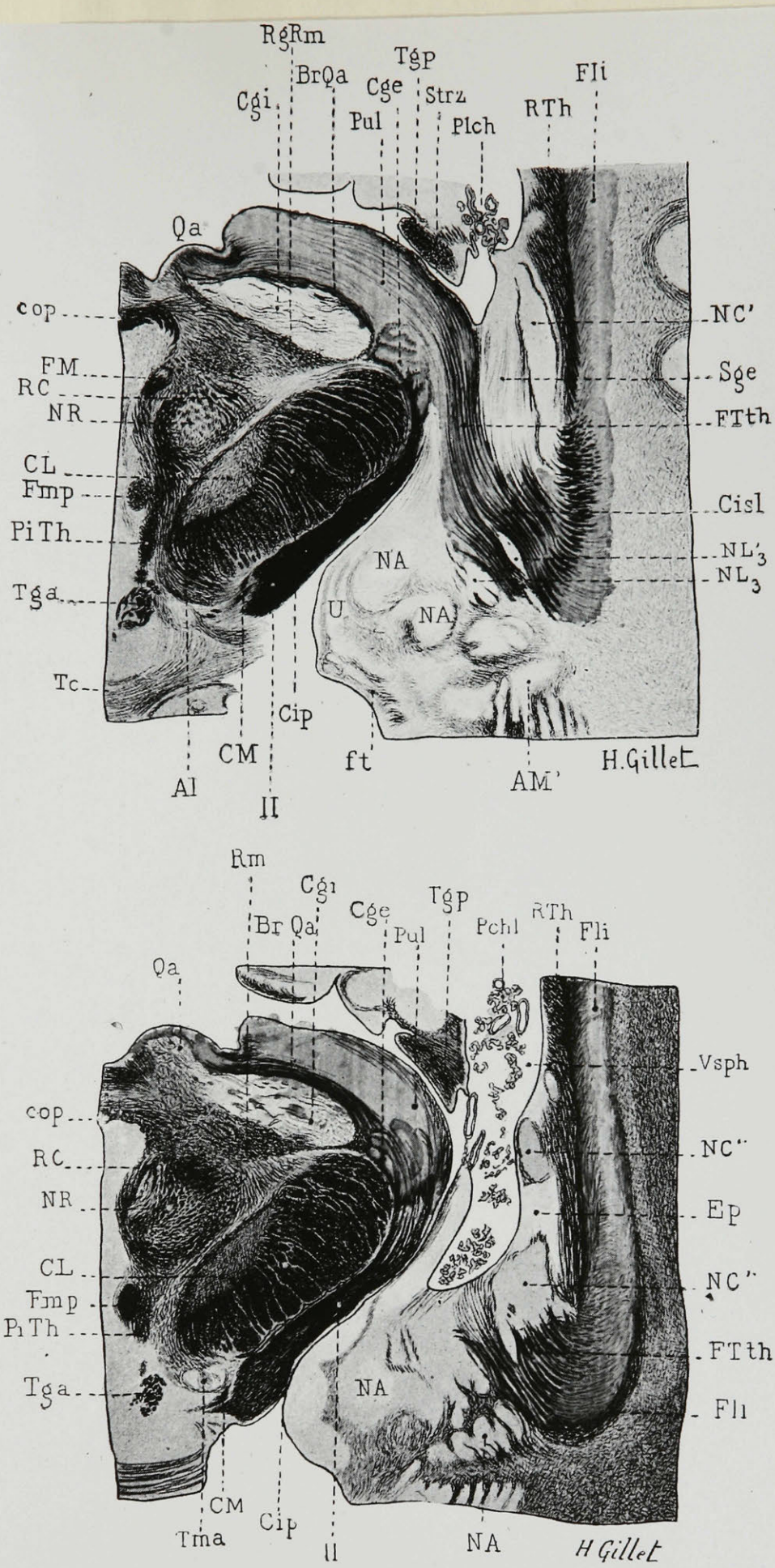


FIG. 31 et 32. — Dégénérescence partielle du segment sous-lenticulaire de la capsule interne (en particulier du faisceau temporo-thalamique d'Arnold) à la suite d'une

Fig. 4

The temporo-thalamic pathway FTth (Arnold bundle) as described by Dejerine (1901).

the knowledge of secondary degeneration was frequently associated with the discovery of a new fiber tract during his lifetime, and the fact that early in 1852 he reported secondary degeneration of the middle segment of the cerebral peduncle in a patient who died of a long-standing hemiplegia. Barker (1899) pointed out that the temporo-pontine tract is separated by a wide area from the region found diseased in Türck's case. Furthermore, Türck's bundle is sometimes applied to the anterior uncrossed pyramidal fibers (Türck's Hülsen-Vorderstrangbahn). It is, therefore, somewhat confusing to use this term for the temporo-pontine tract (Obersteiner, 1896).

Dejerine (1901) believed that a small portion of the temporo-pontine tract originates from the first convolution and the rest from the second and third temporal convolutions. These fibers converge to form the "faisceau de Türck" visible in the posterior part of the sublenticular segment of the internal capsule, where the fibers course downwards and medially to occupy the lateral portion of the base of the cerebral peduncle, and finally terminate at the pontine nuclei. This concept of the origin, distribution and termination of the temporo-pontine tract is generally accepted, although questions as to which temporal convolution contributes more fibers to the tract are occasionally raised (Marie and Guillain, 1903). Rundles and Papez (1937-38), nevertheless, denied the existence of this tract. One to two years after an extensive

removal of the temporal cortex in a baboon and a mangabey monkey, these two authors found no change in the lateral segment of the cerebral peduncle. Their result was supported by the findings of some of the previous workers (Minkowski, 1923, 1924; Biemond, 1930; Clark and Boggon, 1935; Mettler, 1935). From studies based upon human specimens with temporal lobe softening, Rundles and Papez (1937-38) further concluded that the so-called temporo-pontine tract (if there is one) does not descend to the pontine level. In 1940, Bucy and Klüver reported on the anatomic changes secondary to temporal lobectomy in monkeys (see also Klüver and Bucy, 1937, 1938, 1939), ". . . no evidence of any degeneration in a temporo-pontine bundle could be found." Later Grinker and Bucy (1949) consistently stated that there is no temporo-pontine bundle but a parieto-pontine bundle.

Besides the descriptions of Flechsig, Dejerine, Marie and Guillain, of Winkler (1927), and of many others, there have been experimental evidences of the existence of this fiber bundle. Descending degeneration of fibers from the temporal lobe to the pons in the dog was observed by Gerwer (1899). Marchi preparation after temporal cortical ablation in the monkeys showed degeneration of fibers from the first convolution (Ferrier and Turner, 1898; Sunderland, 1940), and from the second and third convolutions (Mettler, 1935), to the pons.

3. Temporo-striatal fascicles.

References to the temporo-striatal connections in the literature are scant. In fact, no connections between the temporal polar cortex and the subcortical structures have been found. In a monkey with cortical removal from the temporal convolution, Mettler (1935, experiment 14) found that Marchi degenerated fibers terminated in the oculomotor nucleus, interstitial and red nuclei, substantia nigra and inferior colliculus. These findings have been open to question (Rundles and Papez, 1937-38) and have never been confirmed either by other anatomical evidences or by physiological studies.

C. Temporo-Commissural Fibers

Fibers from one hemisphere to the other take a route through the hippocampal commissure, the corpus callosum or the anterior commissure.

1. Hippocampal commissure.

From Ammon's pyramids arises the fornix which forms the main efferemt fiber system of the hippocampus. As the fornix courses toward the diencephalic centers some of its fibers swerve, cross the midline and rejoin its fellow fornix. These decussating fibers form the psalterium or the hippocampal commissure. In the guinea pig, Morin (1950) observed

that fibers of apparently septal origin also contribute to the hippocampal commissure. From the literature (Kappers, Huber and Crosby, 1936; Brodal, 1948), and from the observation of the present investigation, no evidence of fiber connections between the temporal cortex and the hippocampal system is established.

2. Corpus callosum.

Prior to the development of the corpus callosum on the phylogenetical scale, the interconnection fibers of the neopallial cortex of the two hemispheres pass solely through the anterior commissure, such as in certain monotremes and marsupials (Kappers, Huber and Crosby, 1936). With the emergence of the corpus callosum the interneopallial fibers pass through both the anterior commissure and the corpus callosum (Kappers, 1921; Winkler and Potter, 1911). In the highest mammals in which the corpus callosum is fully developed almost all the interneopallial fibers take their course through the corpus callosum and the neopallial component of the anterior commissure is reduced to a minimum. Lengthy discourses on the development of the corpus callosum were delivered by Kappers (1921) and subsequently by Kappers, Huber and Crosby (1936). It is interesting to recall the work of Streeter (1912) who examined the human fetus at various stages and found that the new fibers are distributed diffusely between the old ones in the corpus callosum. This observation

is not in conformity with Mingazinni's description (1922) in which the commissural fibers are systematically attributed to the four lobes of the hemisphere from the genu to the splenium of the corpus callosum. The presence of Marchi granules in the corpus callosum as a result of precise cortical lesions in monkeys led Sunderland (1940) to arrive at a general conclusion: "The frontal fibers are spread over chiefly the genu and anterior third of the body, with some occupying the middle third, the occipital over the splenium and posterior third of the body, and the parietal and temporal over the posterior two-thirds of the body with those from the temporal occupying a position anterior to those coming from the parietal." Bucy and Klüver (1940) likewise observed degeneration of the fibers in the posterior part of the corpus callosum following complete temporal lobe removal.

The distribution of the fibers after crossing the corpus callosum was studied by Mettler (1935, 1935-36). According to Mettler, almost all parts of one hemisphere send fibers to their corresponding but larger and related portion of the other hemisphere through the corpus callosum. At the same time, there are certain parts which send fibers to many portions of the opposite hemisphere. McCulloch and Garol (1941), Bailey, Garol and McCulloch (1941), Garol (1942), Bailey, von Bonin, Davis, Garol and McCulloch (1944), and

McCulloch (1944) investigated the cortical origins of the commissural connection and found that strychninization of the lateral surface of one hemisphere (excepting areas 12, 4, 1, 17, 22, probably also area 38) caused firing to a symmetrical point in the opposite cortex. After severance of the corpus callosum cessation of interfiring was observed over the cortical areas examined except area 21 over which the evoked potential, though diminished, still persisted.

In addition to the commissural fibers above mentioned, the corpus callosum, some authors maintain, also consists of decussating collaterals of projection fibers from certain areas of the cortex. As a result of a lesion in the motor area, contralateral and homolateral degeneration in the pyramidal tract was reported by Sherrington (1890). Ugolotti (1900) noted that 18 out of 20 cases of unilateral brain lesion showed bilateral degeneration of the tract. That tumors of the corpus callosum often cause bilateral pyramidal disturbance is commonly acknowledged. Nevertheless, no record exists to prove that the temporal cortex is one of the sources of the decussating collaterals of projection fibers. In the cat and in the monkey Poliak (1927, 1932) found no projection fibers in the corpus callosum at all.

3. Anterior commissure.

The anterior commissure is phylogenetically ancient, and is commonly assumed to be composed of fibers connecting the olfactory structures on the two sides. Yet in the majority of mammals, there is a group of fibers which interconnects the neopallial cortices of the two hemispheres in addition to the olfactory component. These interneopallial fibers constitute the neopallial component of the anterior commissure.

The olfactory component of the anterior commissure consists, in a general sense, of fibers interconnecting the two olfactory bulbs (Probst, 1901; Cajal, 1911), or the two anterior olfactory nuclei (Young, 1941; Brodal, 1948), and fibers interconnecting the amygdaloid complex. The latter account is credited to Brodal (1948), who with his own modification of Gudden's method (Gudden, 1870; Brodal, 1940) produced retrograde degeneration in the "medial and cortical and to some extent the small celled part of the basal amygdaloid nuclei", as well as the anterior amygdaloid area and the cortico-amygdaloid area, after the transection of the anterior commissure in the rat. In connection with this fact it should be stated that there are intrinsic connections between the nuclei of the amygdaloid complex (Krieg, 1947), and that the amygdalo-thalamic connections are likely to be present (Fox,

1949). Aside from the fibers mentioned above there are yet others found in the olfactory component of the anterior commissure. They are those arising from the pyriform cortex (Gurdjian, 1925; Young, 1936; Brodal, 1948), the lateral olfactory tract, olfactory tubercle, the entorhinal area, and the red nucleus of the stria terminalis (Brodal, 1948). Excluding the entorhinal area which, as Brodal suggested, probably owes most of its association connections to areas of the temporal lobe, there is no proof of fiber connections from the temporal lobe to any of the other structures here listed.

The neopallial component of the anterior commissure is commonly called the transverse limb of the anterior commissure.* The fibers of this component can be readily traced from the anterior commissure to the external capsule from which they are eventually linked to the neopallial cortex. When the corpus callosum is either lacking or poorly developed in certain animals, as has been stated, this neopallial component is exceedingly prominent. Thus in the opossum (Loo, 1931), in the bat (Humphrey, 1936) and in the rabbit (Young, 1936) this component is the largest in the anterior commissure. Since the corpus callosum transmits the

* The author does not adopt the usual classification of fibers in the anterior commissure as given by Kappers, Huber and Crosby (1936) who group them under the names of interbulbar, intertemporal, and stria terminalis fibers; nor does he employ anterior and posterior limbs to designate the two major fiber bundles in the anterior commissure.

vast majority of the commissural fibers from the neocortex in the highest animals, the neopallial component of the anterior commissure decreases to a minimum. Dejerine (1895) described in the anterior commissure of man a temporal pole component which, in his opinion, is a remnant of this phylogenetically oldest connection.

Experimental data in regard to the distribution of the neopallial commissural fibers are few. After an ablation of the anterior half of the superior temporal gyrus in a monkey Mettler (1935) observed a great number of Marchi granules in the anterior commissure passing through the globus pallidus. Through the Pal-Weigert method, Rundles and Papez (1937-38) discovered that the anterior commissure is almost totally degenerated following extensive removal of the temporal pallium of a mangabey and a baboon. The monkeys of Bucy and Klüver (1940) displayed similar changes in the anterior commissure. Sunderland (1940) made a circumscribed lesion identified as area 22 of Brodmann in a monkey by devascularization (1938) and found large Marchi granules scattered diffusely over the rostral half of the commissure. Following the transection of the anterior commissure in the midline, Marchi degeneration took place in the region between the putamen and the claustrum of the cat (Fox, 1943), and in the medullary center of the middle temporal convolution of the monkey (Fox, Fisher and Desalva, 1948). With the modified

Gudden method (Brodal, 1940), Brodal (1948) demonstrated retrograde degeneration in the posterior and ventral parts of the neopallial cortex of the rat. The physiological evidence of interconnection by way of the anterior commissure between area 21 of the two temporal lobes in the monkey was obtained by McCulloch and Garol (1941). Bailey, Garol and McCulloch (1941) arrived at the same conclusion in the chimpanzee. In the anterior commissure of the cat, Garol (1942) also found a pathway interconnecting the posterior ectosylvian gyri of the two hemispheres.

D. Temporal Association Fibers

Among the major association bundles of the hemisphere three are particularly responsible for the connections of the temporal lobe: the cingulum, the inferior longitudinal fasciculus, and the uncinate fasciculus. Using Meynert's (1867) method of gross dissection of the long association fibers of the brain Dejerine (1901) demonstrated the course of the cingulum. Tilney and Riley (1938) described the cingulum arising in the anterior perforated space in relation to the olfactory tract and coursing upwards and backwards along the dorsal surface of the corpus callosum, thus connecting the first limbic convolution with the convolutions of the orbital surface. Posteriorly the cingulum sweeps downwards and forwards

toward the tip of the temporal lobe (Fig. 5). The posterior portion of the cingulum originates from the hippocampus which it joins with the lobulus lingualis and the convolutions of the temporal lobe. Redlich (1903) declared that the antero-posterior fibers above the callosum are long whereas the dorsoventral fibers are short and interconnect the adjoining convolutions. Gardner and Fox (1948) cut the cingulum in the region of area 24 and traced the Marchi granules to the hippocampus.

Burdach (1822) was the first person to believe that the function of the inferior longitudinal fasciculus was associational. Putnam (1926a, 1926b), however, insisted that this bundle carries optic projection fibers. Tilney and Riley (1938) stated that the origins of the fibers of this fasciculus are many and that one of them is the lateral geniculate body. In the temporal lobe this bundle gives off many fibers which terminate in the hippocampal gyrus, the fusiform lobe and the three temporal convolutions. "The majority of them pass to the first temporal gyrus and extend to the temporal pole" (Tilney and Riley, 1938).

The uncinate fasciculus extends from the temporal pole to the under-surface of the frontal lobe. Its fibers, said Tilney and Riley (1938), also come into relation with the amygdaloid nucleus.

Aside from the long association bundles the temporal lobe also possesses short association fibers which

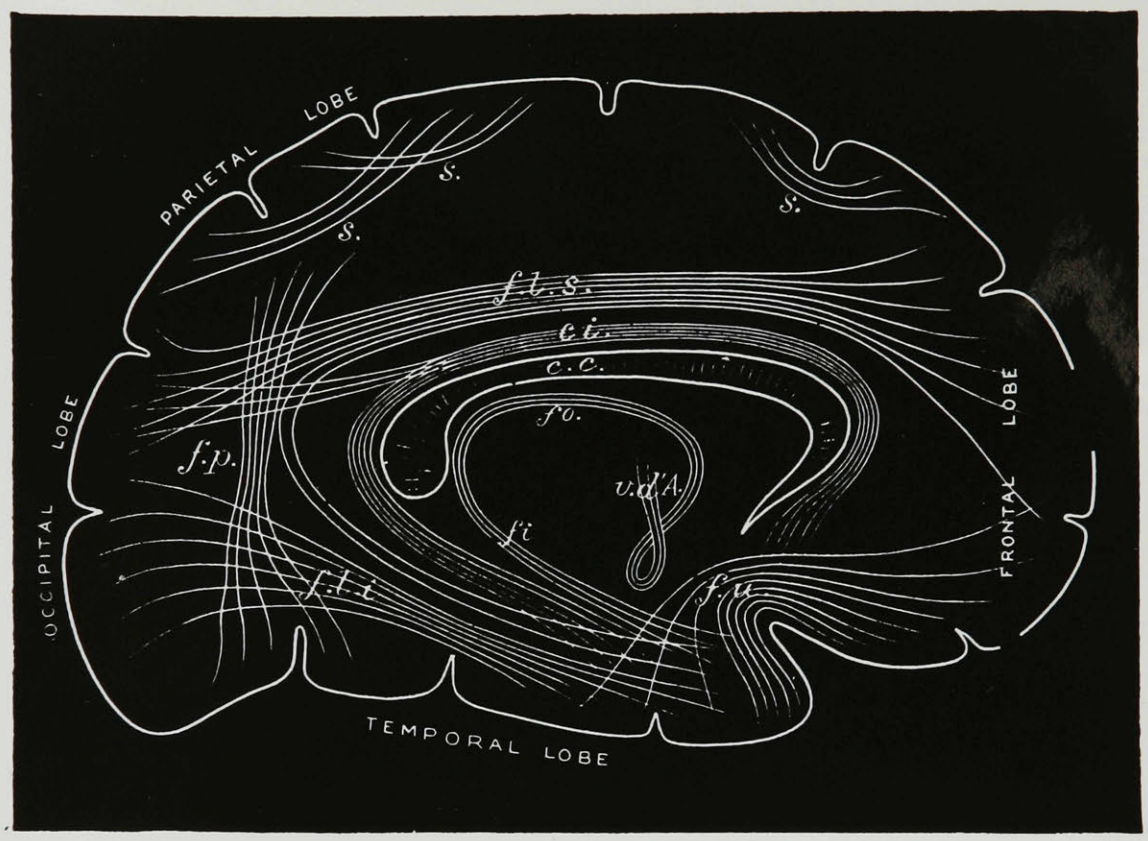


FIG. 548. Diagram to show the general course of the association fibers of the cerebral hemisphere. (*Meynert.*)

s. Short association fibers, connecting adjacent gyri. *f.l.s.* Fasciculus longitudinalis superior. *ci.* Cingulum. *f.p.* Fasciculus perpendicularis. *f.l.i.* Fasciculus longitudinalis inferior. *f.u.* Fasciculus uncinatus.

Fig. 5

The association fiber bundles of the cerebral hemisphere (Tilney and Riley, 1938).

interconnect the various areas within the same lobe. It is interesting to note that in certain convolutions of the hemisphere, the short association fibers occasionally constitute almost the entire amount of the white matter. For instance, in the gyri breves of the insula (Tilney and Riley, 1938).

Description of the association fibers after an operation on the temporal lobe in the monkey was supplied by Mettler (1935). This author traced the association fibers from the superior temporal gyrus to the middle temporal gyrus, the region of Brodmann's cortex types 1, 2,3 , 4, 5, 6, the inferior temporal gyrus, the striate cortex of the occipital operculum and the parietal and prefrontal cortices. Rundles and Papez (1937-38) observed in the monkey demyelinization of the short association fibers surrounding the lesion, and of the long association fibers extending from the lesion through the corona radiata to the cortex on the medial side including the cingulate gyrus. Bucy and Klüver (1940) noted some fibers from the uncinate fasciculus crossing the rostrum of the corpus callosum to the olfactory trigone of the opposite hemisphere. These authors also observed fibers from the temporal lobe to the posterior frontal, parietal and the occipital regions, as well as to the posterior part of the cingulum.

By applying strychnine to the cerebral cortex of the monkey and chimpanzee, and recording the electrical activities,

Bailey, von Bonin, Garol and McCulloch (1943) discovered that from area 18 arises a tract leading to area 20, and that another leads from area 47 to area 38; and that these pathways conduct in one direction only. Further data obtained by this group of workers (Bailey, von Bonin, Davis, Garol and McCulloch, 1944) indicated a third pathway from area 38 to area 10. Studies of the corticocortical connections in monkey (Sugar, French, and Chusid, 1948 a and b) suggested that the temporal pole does not receive association fibers from the auditory cortex on the same side but probably has direct interconnections with its corresponding pole on the opposite side. Recently Peter, Holden and Jirout (1949) presented evidence of connections between the uncus and the temporal pole in the monkey.

III. EXPERIMENTAL STUDIES

A. Material and Methods

Fourteen cats and four monkeys were used. All the cats were adult cats from 1.5 to 5.8 kilograms in weight.

The monkeys belonged to Macaca Mulatta species. Three of the monkeys in this series had been previously operated on for other purposes. One female monkey (P6-20) was first operated upon February 23, 1946, by Drs. Penfield and Jasper who put aluminum gel on its left precentral cortex. As a result the animal developed repeated attacks of right Jacksonian seizures. On August 23, 1946, the cortex of the monkey was re-explored and after the electrocorticographic studies the epileptic focus was removed. In addition a piece of the cortex in the right motor area and another in the left parieto-occipital region were excised for histological studies. The right-sided seizures disappeared after the second operation, but right-sided hemiparesis developed, persisting throughout the rest of its life. In November, 1948, the operative site was re-opened and electric stimulation of the excised area was carried out. The condition of this animal did not change after the third operation. The second monkey (P7-26) had undergone an operation on

March 18, 1947, by Dr. Gerber who placed an aluminum gel disc on the mesial surface of the left hemisphere. Nothing happened after this operation and the disc was removed on August 2, 1947. The third monkey (P9-241) was used for an experiment on May 11, 1949, at which time Dr. Hunter implanted an electrode into the intralaminar system of the thalamus. Ten days later the same experimenter inserted another electrode into its brain and burnt the left nucleus medialis dorsalis of the thalamus.

All the animals were operated on under either intravenous or intraperitoneal nembutal anesthesia (0.5 cc. of 5% for each kilogram of body weight for cat; much less for monkey). In the cats, all the lesions were made through a subtemporal trephine opening. After the cortical lesion was made the dura was not closed, but the bone button was placed back so as to prevent adhesions of the cortex to the muscle. In the monkeys, the temporal pole was exposed through either a right frontal craniotomy or a subtemporal approach. In the latter case the jaws of the animal were held widely open in order to make more room for access to the under-surface of the temporal fossa. The removal of the temporal pole was, with constant endeavor, confined to von Bonin's and Bailey's area TG lateral to the collateral sulcus. The dura was sutured after the cortical excision.

The cortical lesions were made by several different

methods. For the cat it was found that subpial removal by a small dissector served better than the suction, as the latter might produce a deeper lesion than had been intended. The best way was to use a diathermy* (Sunderland, 1938). By applying the loop of the diathermy on the surface of the cortex a proper-sized and well-circumscribed lesion could be made. For the monkey, removal of the temporal pole was always carried out by suction.

The span of the survival periods of the animals after operation depended upon the histological method employed. With silver staining technique the animals were preserved from two to twelve days. With Marchi method, it varied from 7 to 20 days. The two cats used for retrograde degeneration studies both lived for 73 days; under similar circumstances, a monkey survived for 42 days after operation. During the survival period frequent observations were made.

All the animals were sacrificed with an overdose of nembutal either applied intraperitoneally or intravenously; the latter route was adhered to for the monkeys. For Marchi studies the brains were removed without perfusion, whereas for other studies they were perfused through the carotid arteries.

The gross appearance of the cortical lesion was examined and sketches were made, most of which were in turn photographed.

* This was suggested by Dr. Francis McNaughton

Retrograde Degeneration Method.

This method was applied to two cats and one monkey. The brain was perfused with saline followed by 5 per cent solution of formalin in saline. The entire brain was fixed in 10 per cent formalin for two days (cat) or five days (monkey), after which period it was cut in the coronal plane into three blocks at a point slightly anterior to the optic chiasm, and through the posterior limb of the suprasylvian sulcus (cat) or the upper extremity of the lunate sulcus (monkey). Afterwards the blocks were fixed in formalin for three days (cat) or seven days (monkey). They were then dehydrated, embedded in paraffin and cut in 30 μ thickness. Every tenth section was taken for cresyl violet stain and its adjacent section for Weil stain.

Drawings of the serial sections of the operative lesion were made by tracing the projected slides on paper. These drawings were then enlarged ten times and finally photographed. In a similar manner, a retrograde degenerated nucleus was illustrated by a series of diagrams.

Marchi Method.

Six cats and three monkeys were used for this purpose. After the brain was removed without perfusion, it was placed

in a large amount of 10 per cent neutral formaldehyde solution. Whenever possible no further handling of the specimen took place. Sketches of the specimens were made by examining them through the glass container. In most cases photography was eliminated. After being fixed in formalin for seven days the brain was taken out and sliced coronally with a thin, sharp blade on an "encephalotome"; each slice of brain was about 4 mm. thick. The slices were threaded and suspended in 10 per cent neutral formaldehyde solution for two days. They were transferred into freshly prepared 1 per cent potassium chlorate solution for five to fifteen minutes, and finally immersed in a large quantity of freshly prepared solution according to Swank and Davenport (1935). About 400 cc. of this Swank-Davenport mixture* (containing 0.8 gram of osmic acid) for one monkey's brain or two cats' brains were required. The glass container was sealed air-tight and wrapped with black paper. It was placed on a Mag-mix** so that a constant current was created in the staining mixture. The mixture was changed on the fifth day, and on the twelfth day the threaded slices were transferred to another container and washed with running tap water for 24 hours. They were dehydrated, embedded in paraffin and

* Roy Swank of this Institute suggested that lower percentage of formaldehyde solution in the mixture is to be used if weaker penetration is desired. He also advised perfusion of the brain before its removal with 5% anhydrous magnesium sulfate solution; but the author found that the brownish background of the sections made from this preparation is not suitable for microphotography.

**Made by Precision Scientific Co., Chicago, U.S.A.

cut 30 μ thick. Every tenth section was taken, except certain portions in which structures of interest were present, such as the anterior commissure; every fifth or sometimes third section was mounted, cleared and covered. The Marchi granules appeared black on a faintly yellow background. Counter staining of the adjacent section with hematoxylin van Gieson was carried out only when desirable.

A series of diagrams to illustrate the cortical lesion was made as has been described above. The representative slides were photographed and enlarged ten times. The Marchi granules and fibers on the prints were checked with those on the slides under the microscope. They were stained with India ink, the same being also used to trace the outlines of the sections. The photographs were then bleached, and the final drawings, showing only the outlines of the sections and the degenerated granules and fibers, were rephotographed. In this manner a series of diagrams illustrating the Marchi degeneration was obtained.

Silver Staining Method.

Frozen sections of two cats' brains were stained according to Glees' technique (1946). All the sections from the first cat turned out to be either too dark or too light, and, therefore, were of no use. The failure to obtain a consistent result led to numerous trials with

various modifications. The following procedures proved to be satisfactory. The brain was removed without perfusion and was fixed in 10 per cent neutralized formaldehyde solution in saline for four days. It was then sliced in coronal sections one-half centimeter thick. The slices were replaced in the same solution for another six days. Selected areas were cut, and the block taken from the sliced piece was restricted to one centimeter square. Frozen sections 10 μ thick were made and washed thoroughly in distilled water. They were transferred to ammoniacal alcohol for 24 to 48 hours after which they were run down to distilled water. A fresh solution of 10 per cent silver nitrate was prepared and the sections were transferred into this solution. They were kept in the dark at room temperature* for 5 to 7 days. After being washed briefly in distilled water the sections were one by one reduced in 10 per cent neutralized formalin in saline. Each section was soaked for approximately 30 seconds in each of the three small dishes containing the reducing agent and passed through all three in set order. In general no precipitation formed as a section was transferred from the second to the third bath. The section was then placed in a freshly prepared ammoniacal silver solution until it became brownish in hue. It was again subjected to three baths of formalin in saline, each lasting for a few seconds.

* It was found that sections in the silver nitrate solution kept in an oven at 37° C did not give a satisfactory result for small (or fine) unmyelinated fibers.

It was washed in three changes of distilled water and finally fixed in 5 per cent sodium thiosulphate solution for five minutes.* Afterwards it was washed in two changes of distilled water and mounted on a slide. The section was then blotted, dried, cleared in toluol and covered with Canadian balsam.

With this procedure the frozen sections of the other cat's brain were studied. The result was still not entirely consistent. Furthermore it was not possible to avoid precipitations which might be so close to a fiber** as to be mistaken for fragmented fibers or globules. Finally, as the impregnation was uneven most of the time, comparison of the sections of one area of the hemisphere with the sections of the corresponding area of the other hemisphere was nearly impossible. Other points with regard to the use of this method for tracing fibers to their unknown destination will be discussed separately from this report.

Due to the difficulties in the interpretation of the findings obtained by this method of Glees, the results from these two experiments have been omitted from this report.

* Sometimes it required longer.

**Most of the precipitations could be recognized under oil immersion since they usually gathered on the surface of the section.

Other silver staining methods including Cajal's original descriptions and modified versions (Gibson, 1937a, 1937b) have been tried, but they seemed either inconsistent (such as Bielschowsky's, 1931) or inadequate for demonstrating degenerated fibers and their terminals in the brain (such as those of Gibson, 1937a, 1937b; Bodian, 1936; Romanes*, 1946). This failure prompted us to develop a modification** of Cajal's method. The procedure was as follows: The brain was removed without perfusion and fixed in 10 per cent neutralized formaldehyde solution for five days. It was sliced 4 mm. thick and again fixed for two days. The slices were washed briefly in distilled water and transferred to a freshly prepared 20 per cent chloral hydrate solution (Lhotka and Vaz Ferreira, 1949). The chloral hydrate solution was changed twice in 24 hours. The slices were transferred to 50 per cent pyridine aqueous solution and kept there for 24 hours. They were washed thoroughly until the smell of pyridine disappeared; and were placed in ammoniacal alcohol for 24 hours. The slices were transferred onto a filter paper, while a fresh solution of 1.5 per cent silver nitrate was being prepared. In the bottom of the container of the silver nitrate solution a

*Romanes, in 1949, during a visit to this laboratory suggested utilizing his recent modification in which a mixture of silver nitrate and sodium chloride is used. The author found this method very satisfactory for the study of normal nerve fibers yet inadequate for that of degenerated fibers.

**This method was worked out with the collaboration of Dr. Kenneth Earle in this laboratory.

layer of filter paper was placed. The slices of the brain were then transferred to the silver nitrate solution. The container was wrapped with black paper and kept in an oven of 37° C for four days, after which period the slices were washed briefly with distilled water and transferred to pyroformol* reducer. The reduction was also carried out in the dark for six hours. Thereafter the material was washed, dehydrated, embedded in paraffin and cut 10 μ thick.

By this process two cats' brains** were studied after a lesion had been made in the inferior extremity of the posterior ectosylvian gyrus. The brain slices were cut 10 μ thick, and every tenth section was taken.

* Hydroquinone as a reducer in this case is unsatisfactory.

**The remaining two cats in this series were saved for trying out various silver staining methods.

B. Results

The results of this investigation are based upon the findings from brain specimens, 1) of six cats and three monkeys, prepared by Marchi method, 2) of two cats and one monkey, prepared by Nissl method, and 3) of two cats, prepared by the silver staining method. Since there has been only one monkey available for retrograde degeneration studies,the findings of that experiment will be reported in detail. The positive findings as obtained by the Marchi method will be illustrated by a detailed description of one cat experiment and one monkey experiment. The findings from the silver stained material from two cats are similar and will be described together.

1. Retrograde Degeneration

a) Cat 50-06. Inferior posterior ectosylvian lesion. Postoperative survival period 73 days. Retrograde degeneration absent.

The cortical lesion occupied the inferior and ventral portion of the posterior ectosylvian gyrus. It was more or less circular shaped, measuring 3 mm. in diameter, but with its peripheral transitional damaged cortex measuring 5 mm. in diameter. Anteriorly the damaged cortex extended slightly beyond the lower end of the posterior ectosylvian sulcus but

did not involve its posterior bank. Posteriorly the lesion reached the vertical level of the inferior limit of the posterior limb of the suprasylvian sulcus. Ventrally it approached the posterior rhinal sulcus and encroached upon its dorsal bank (Fig. 6).

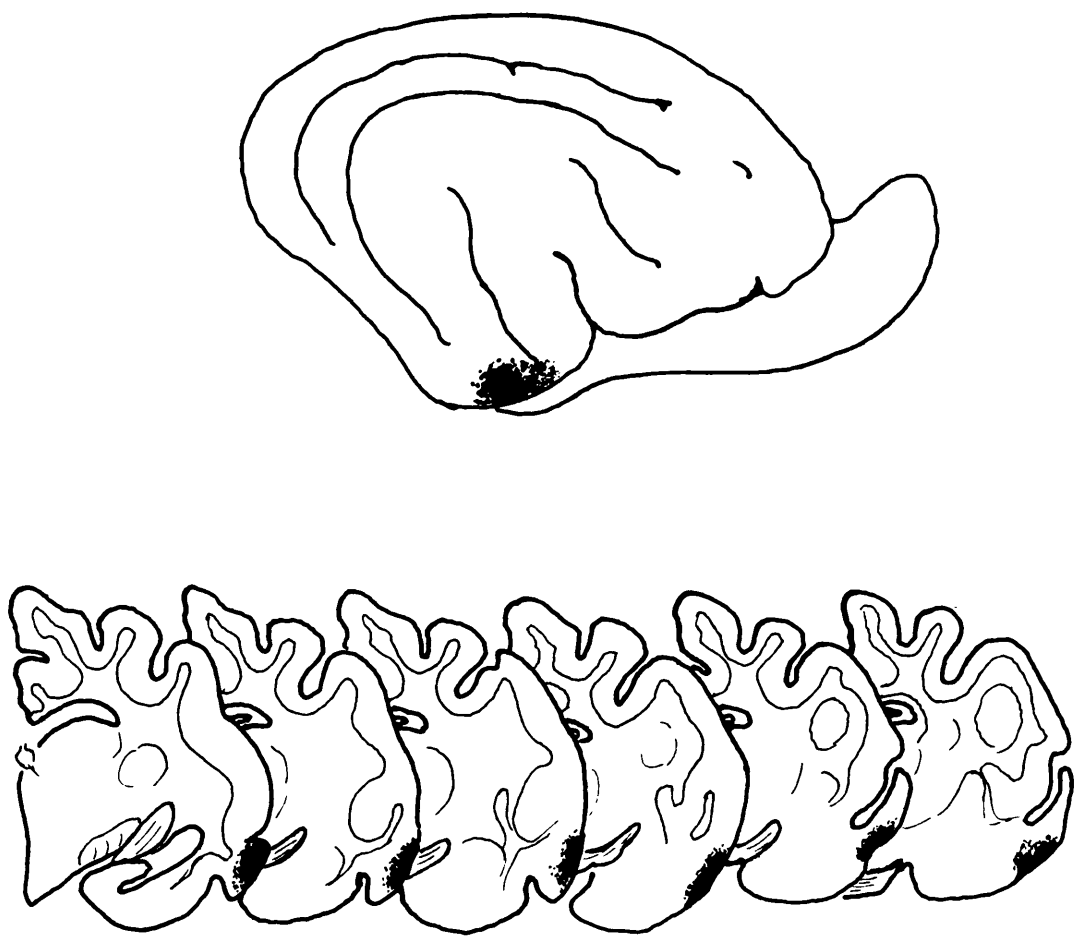
The coronal sections revealed that the lesion involved chiefly the gray matter. Section 42 showed involvement of the inferior posterior sylvian cortex and the banks of the posterior rhinal sulcus, thus the whole perirhinal area at that level and a small portion of the entorhinal area were damaged. The posterior sections revealed complete loss of the ectorhinal cortex which Winkler and Potter (1914) referred to a as area 36.

The cresyl violet stained sections indicated no retrograde degenerations in any of the subcortical structures.

The Weil series showed demyelination of the distal arm of the anterior commissure ventral to the amygdaloid nucleus.

b) Cat 50-07. Inferior posterior ectosylvian lesion. Postoperative survival period 73 days. No retrograde degeneration.

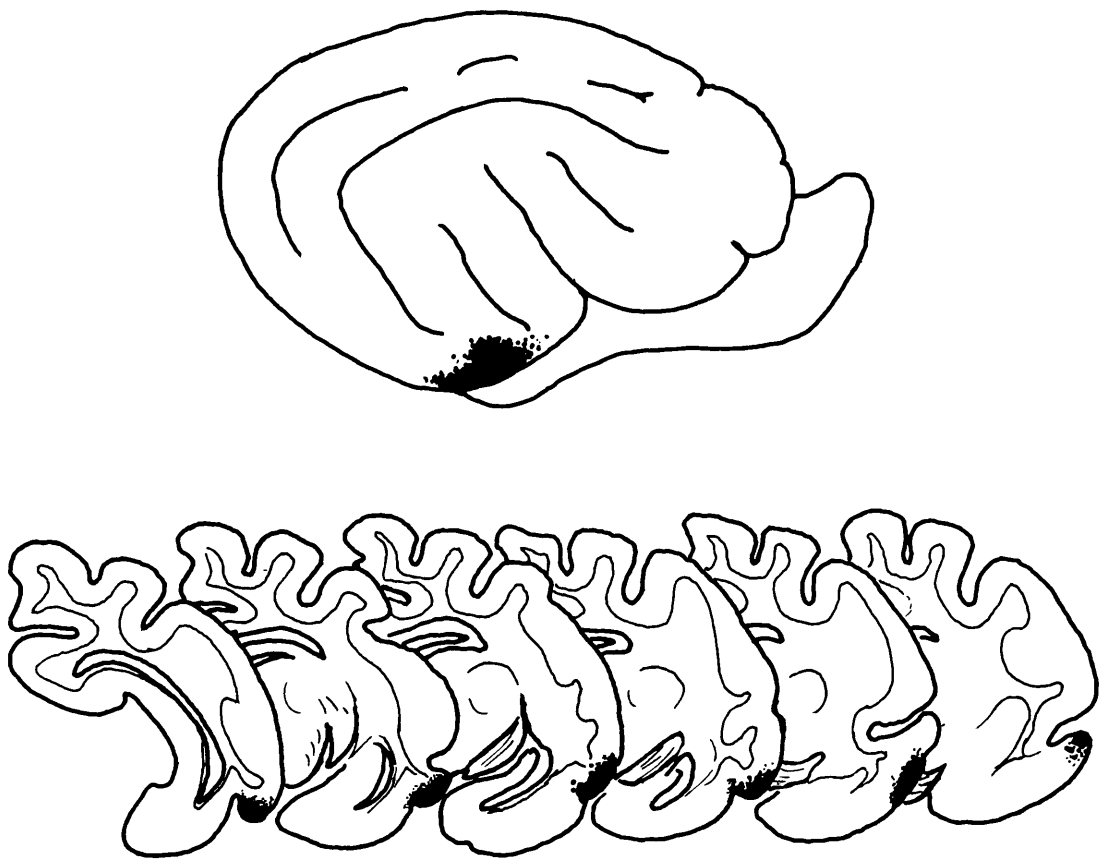
This experiment was almost identical to experiment number 50-06 except for the fact that the lesion involved posteriorly the inferior prolongation of the posterior limb of the suprasylvian gyrus and did not extend across the posterior rhinal sulcus. (Fig. 7)



50 - 06

Fig. 6

Cat 50-06. Cortical lesion and the extent of damage as illustrated by diagrams.



50-07

Fig. 7

Cat 50-07. Cortical lesion and the extent of damage as illustrated by reconstructed diagrams.

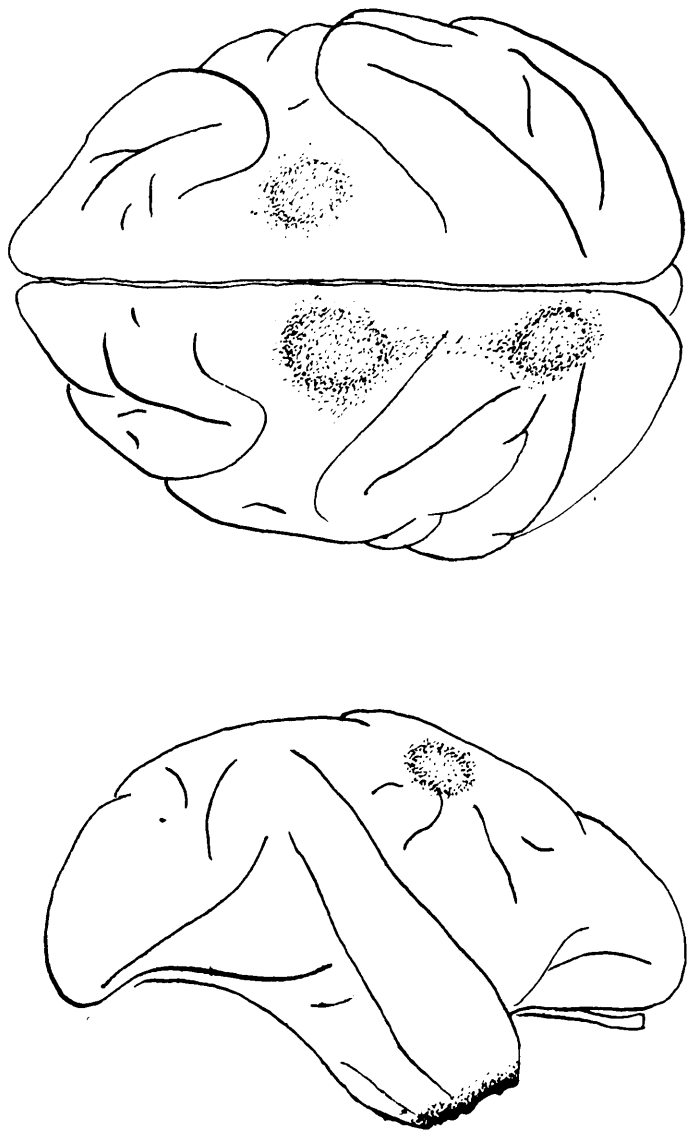
No area of retrograde degeneration was found.

c) Monkey P6-20. Operations: 1) Electrocorticographic exploration of left cerebral cortex and application of aluminum gel on left motor cortex (February 23, 1946). 2) Electrocorticographic exploration of left cerebral cortex, and local excision of the left precentral and parieto-occipital and the right precentral cortices (August 23, 1946). 3) Re-exploration and electrical stimulation of left cerebral cortex (November 8, 1948). 4) Right frontal craniotomy and excision of right temporal pole (January 26, 1950). Post-operative survival period after last operation - 42 days. Cortical lesions: right temporal polar, right precentral, left precentral and left parieto-occipital. Retrograde degenerations: right caudate nucleus and putamen, nuclei ventralis lateralis and ventralis posterolateralis on both sides of the thalamus, red nuclei and left lateral geniculate body. After the last operation no change of physical condition and behavior occurred.

As the brain was removed serious difficulties arose as a consequence of the presence of extensive adhesions. The lesions over the lateral surfaces of the brain sank into the brain substance, and were pale, yellow, and firmer in

consistency. The intervening cortex of the two lesions on the left side had apparently undergone cicatricial change; the effect gave the impression of a dumbbell with the anterior ball lying in the precentral area and being joined to the other ball in the parieto-occipital area. The anterior lesion occupied the usual position of the precentral dimple. It measured 15 mm. by 8 mm. with its longest diameter antero-posteriorly placed. Its posterior border lay 5 mm. anterior to the central sulcus and its medial border 4 mm. from the midline. The parieto-occipital lesion, situated near the confluence of the superior temporal and lunate sulci, was slightly oval in shape with a diameter of 6 to 7 mm.; and its medial border was 2 mm. from the midline. The right lesion was almost identical and symmetrical to the left precentral lesion except for being smaller (Fig. 8, dorsal view). The right temporal polar lesion involved the anterior extremities of the three temporal gyri. The lesion extended posteriorly to a line about 4 mm. from the tip of the temporal lobe. Ventrally it encroached on the rhinal sulcus involving its lateral bank (Fig. 8, lateral and basal view).

The extensiveness of the cortical lesions on the lateral surfaces was illustrated by a series of diagrams (Figs. 9a and 9b).



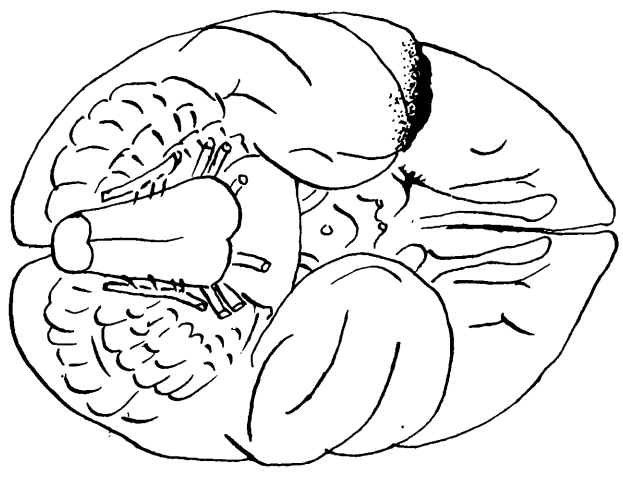


Fig. 8

Monkey P6-20. Dorsal, Lateral and basal views showing the position and extent of the cortical lesions.

P6-20-112

P6-20-152

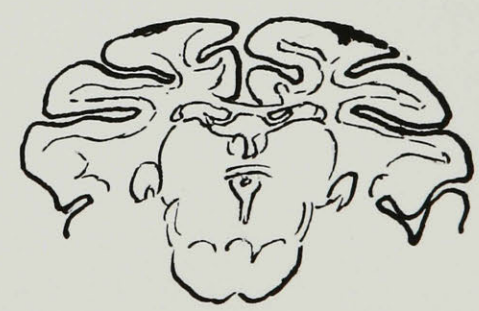
P6-20-182

P6-20-222

P6-20-262

P6-20-312

P6-20-362

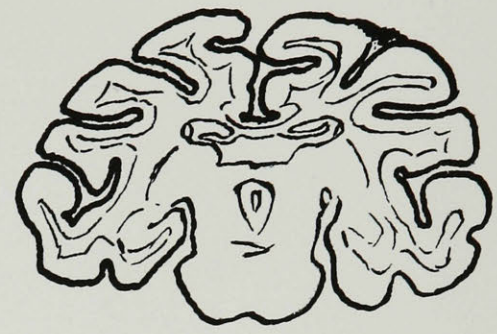


P6-20-402

Fig. 9a

(P6-20) Diagrams showing the extent of the cortical lesions on the lateral surface of the hemisphere.

P6-20-432



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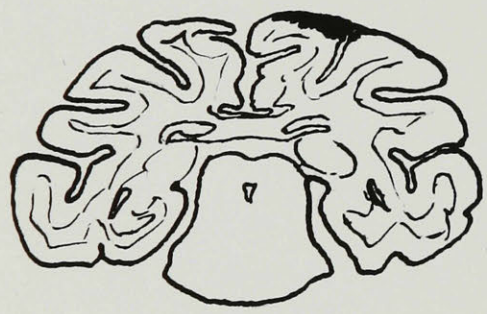

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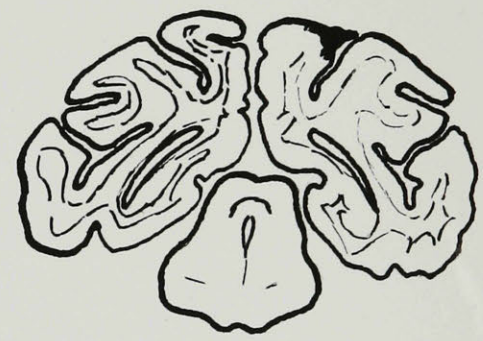

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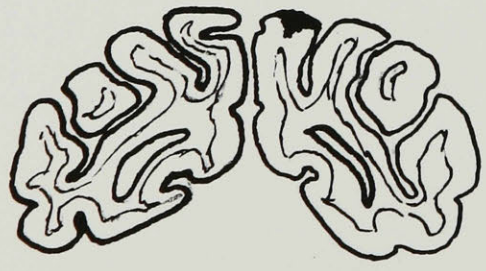

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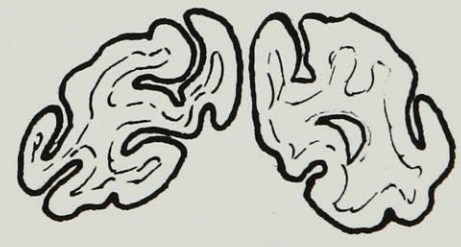


P6-20-772

Fig. 9b.

(P6-20) Diagrams showing the extent of the cortical lesions on the lateral surface on the hemisphere.

Since it is beyond the scope of this study to describe these lesions in great length a brief mention must suffice. The bilateral precentral lesions were found in a cortical area corresponding to the confluent zone of Vogt's areas 4a, 4b and 6a (Vogt, 1919), or to areas FA and FB of von Bonin and Bailey (1947). The left parieto-occipital lesion situated in an area comparable to the superior portions of areas 17, 18 and 19, and probably also comparable to 5b and 7a of Vogt (1919), to areas in the upper part of OA, OC, PG, and to area PE of von Bonin and Bailey (1947).

The temporal removal as shown by the diagrams (Fig. 10) deserves a longer description here. As has been said before, the damaged cortex extended posteriorly from the primary lesion to a considerable distance on the latero-ventral surface of the temporal lobe. At a level (section P6-20-52) where the rhinal sulcus began to appear, the cortices of the first, second and third convolutions were all involved, but the inferior bank of the sylvian fissure was intact. In section P6-20-82 the damage was only confined to the ventral surface of the third convolution and did not invade the rhinal sulcus. This corresponded, therefore, to area TG of von Bonin and Bailey (1947).

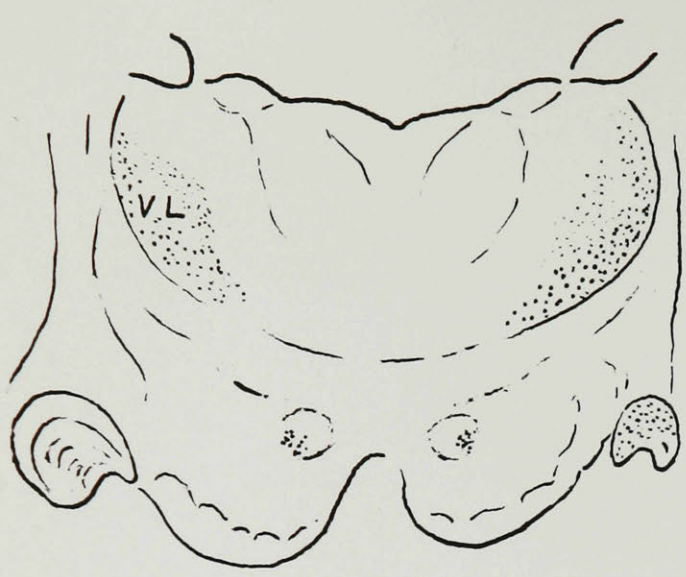
Retrograde degeneration as a result of the above lesions included the head of the caudate and putamen, the nuclei ventralis lateralis and ventralis postero-lateralis of the

Fig. 10

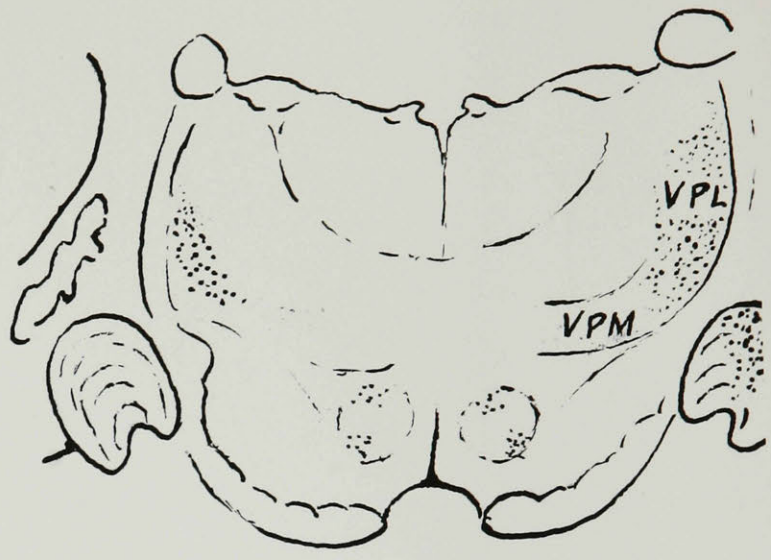
(P6-20) Diagrams showing the extent of the temporal polar removal.

thalamus of both sides, the left lateral geniculate body and the red nuclei. As the thalamic (the lateral geniculate included) reaction toward lesions in the precentral and parieto-occipital areas is well known, no details of this degeneration will be given. Suffice it to say that there was complete loss of cells in the left nucleus ventralis lateralis, whereas well-preserved cells were occasionally found scattered in the right nucleus ventralis lateralis, especially over its anterior and superior portions. This was accompanied by marked gliosis. Similar change was observed in the nuclei ventralis postero-lateralis. In the left lateral geniculate body retrograde degeneration extended from the anterior part of the medial horn to the posterior part of the lateral pole, thus sweeping across the middle cone and sparing the anterior portion of the lateral pole and the posterior portion of the medial horn (Fig. 11).

The oral small-celled portion of the red nuclei began to appear in section P6-20-311, and the caudal large-celled portion in section P6-20-371 of the Nissl sections of this series. There was marked infiltration of glial cells to the small-celled portion and a moderate amount to the large-celled portion. This phenomenon was less apparent in the right red nucleus. No chromatolytic change of either the small cells or the big cells was observed (Fig. 12).



P6-20-331



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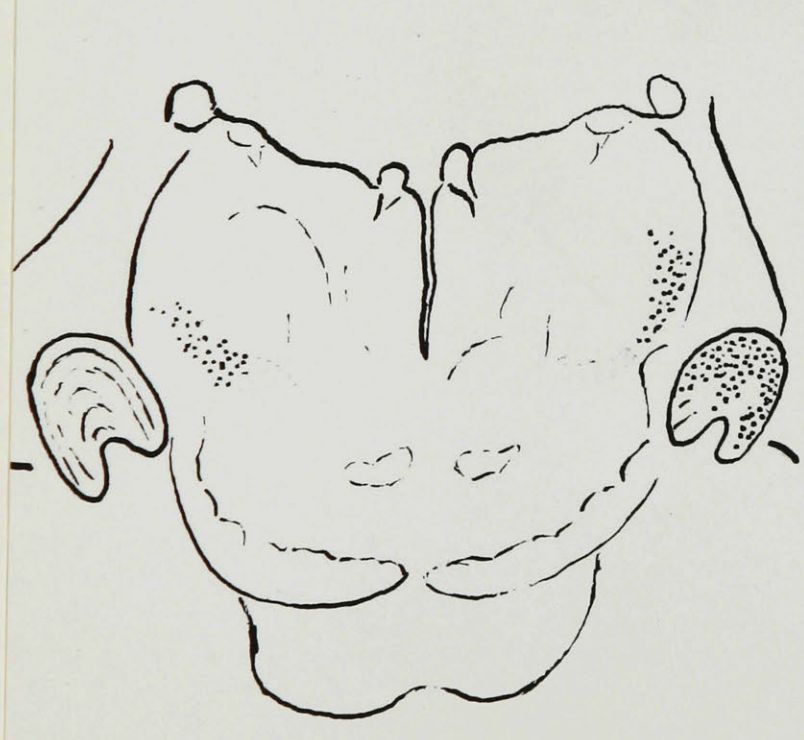

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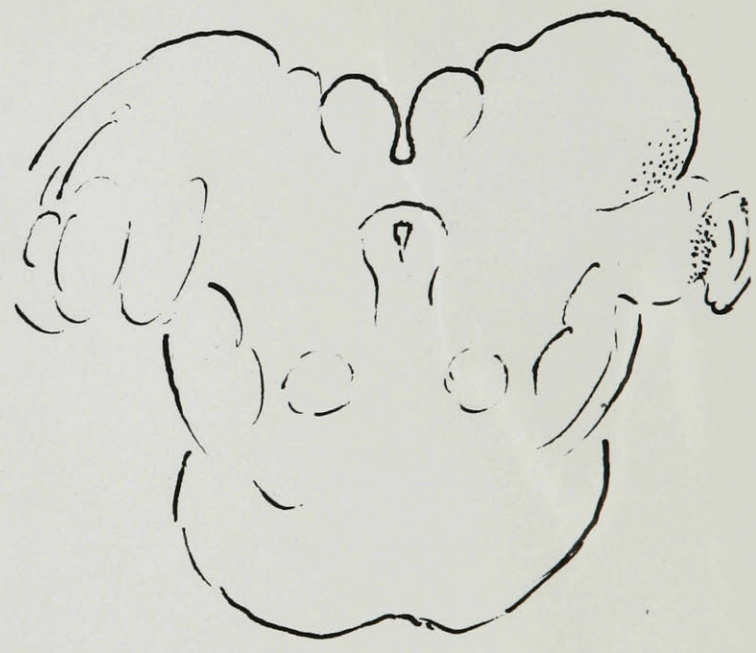


P6-20-411

Fig. 11

(P6-20) Retrograde degeneration of the nuclei ventralis lateralis, ventralis postero-lateralis, left lateral geniculate and red nuclei.

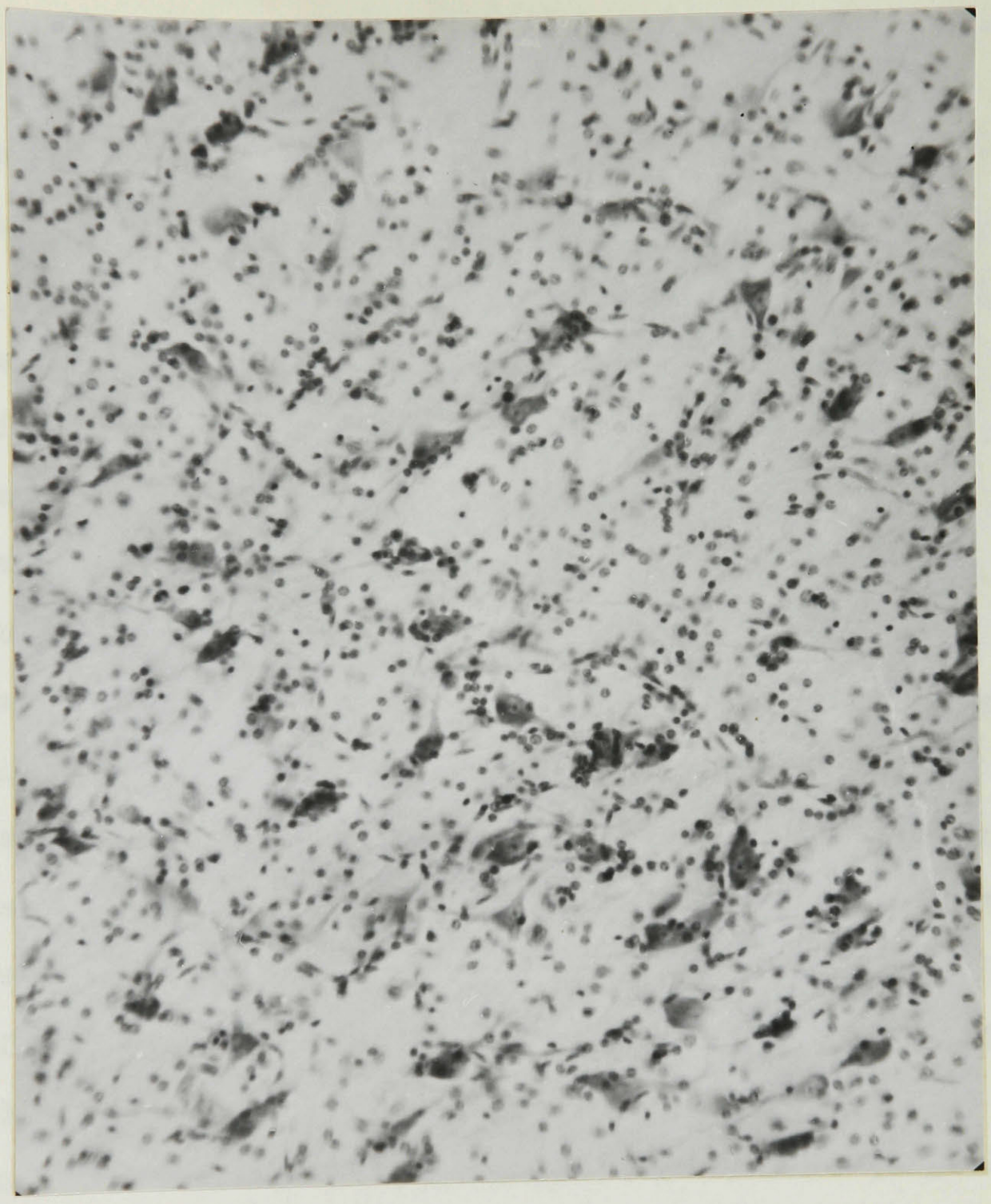


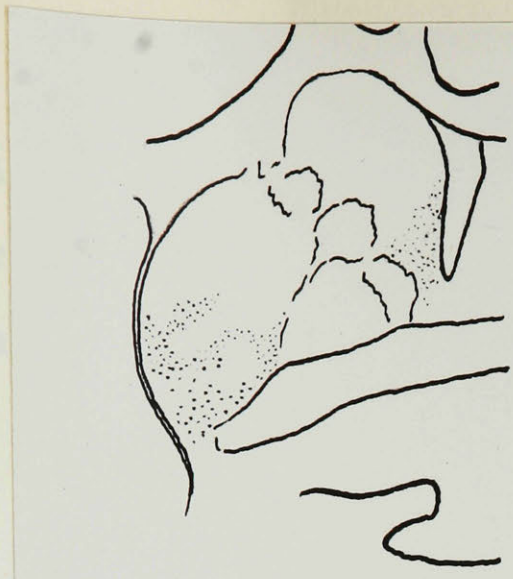
Fig. 12

(P6-20) Microphotograph of the left red nucleus showing marked gliosis. Similar change is found in the right red nucleus.

The caudate nucleus and the putamen (the striatum) on the side of the temporal polar removal underwent similar changes. Extending from the anterior end of the caudate nucleus (section P6-20-21) cellular change occurred in the medio-inferior portion which gradually expanded over the entire inferior half of the nucleus. In section P6-20-141 (Fig. 13), the demarkation between the intact superior and the changed inferior portions was clearly recognizable. From this level backwards, the cellularly-changed area receded, thus leaving scattered patches of degeneration here and there in the inferior part of the nucleus. At the level where the tail began, degeneration was seen in the middle portion of its medial half (Fig. 13, section P6-20-341). This rapidly disappeared so that the rest of the tail remained intact. The change in the putamen began anteriorly in its latero-inferior portion and gradually migrated toward its upper and medial part. This cellular change could be observed in the putamen in its entire antero-posterior extent (Fig. 13).

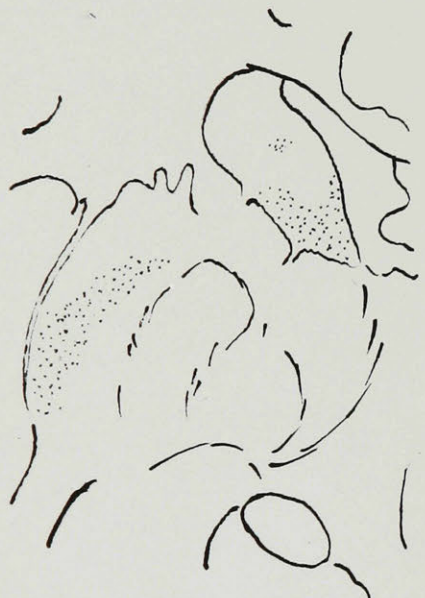
In the striatum, the cellular change was limited to the small cells, and here, the cells were correspondingly much smaller (two-thirds smaller), and, as there was no increase in the number of cells*, the right caudate nucleus as a whole became smaller in comparison to the left caudate

* A preliminary data of cellular count of the caudate nucleus would indicate the ratio of the large cells and small cells of the caudate to be between 1:100 and 1:150. This was not in accord with the result of others. Papez (1942), by quoting Foix (1925), stated that the ratio is 1:20.

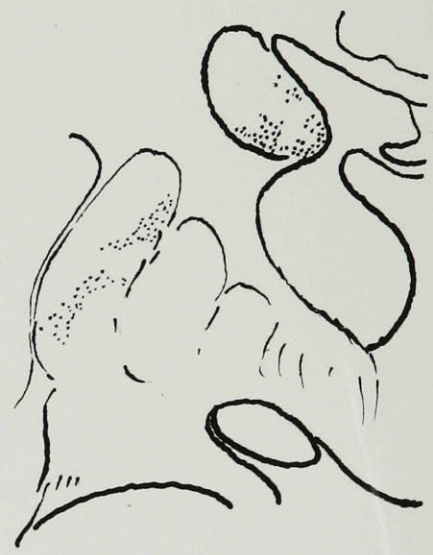


P6-20-111

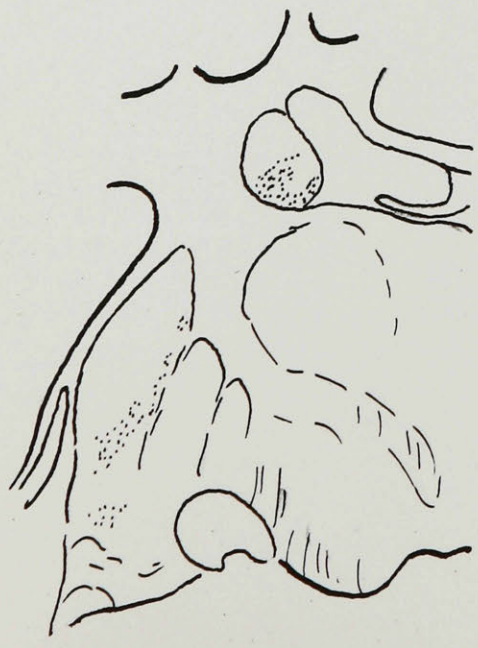
P6-20-141



P6-20-181



P6-20-221



P6-20-281

P6-20-341

Fig. 13

(P6-20) Area of atrophic change of the small cells in the right caudate nucleus and the putamen.

nucleus. The cells appeared pale, and many had lost their short processes. The cytoplasm may disintegrate or vanish totally in some cells. On the other hand, the nuclei of the cells were well preserved (Fig. 14, Fig. 15 a and b).

2) Marchi Preparations.

That the Marchi method for the study of degenerated fibers has many shortcomings is well known. In spite of the utmost caution and a variety of modifications (Mettler, 1932; Swank and Davenport, 1934, 1935; Glees, 1943), the appearance of pseudo-Marchi granules is sometimes unavoidable. As the brain was fixed without perfusion, the osmic stained blood corpuscles in a small capillary on a faintly yellow-tinged background might resemble a chain of degenerated globules. Fortunately these stained corpuscles and the pseudo-Marchi granules could be distinguished under high magnification. The worst intrusion was the "Marchi artifact" occasionally seen in the corona radiata and the corpus callosum, counterfeiting the "genuine Marchi fibers". This was observed oftener in large sections, therefore harming the monkey specimens most. There have been many criteria proposed for the recognition of true Marchi fibers or granules (Vogt, 1902; Mettler, 1932). In this study only one criterion was pursued: an osmic acid stained

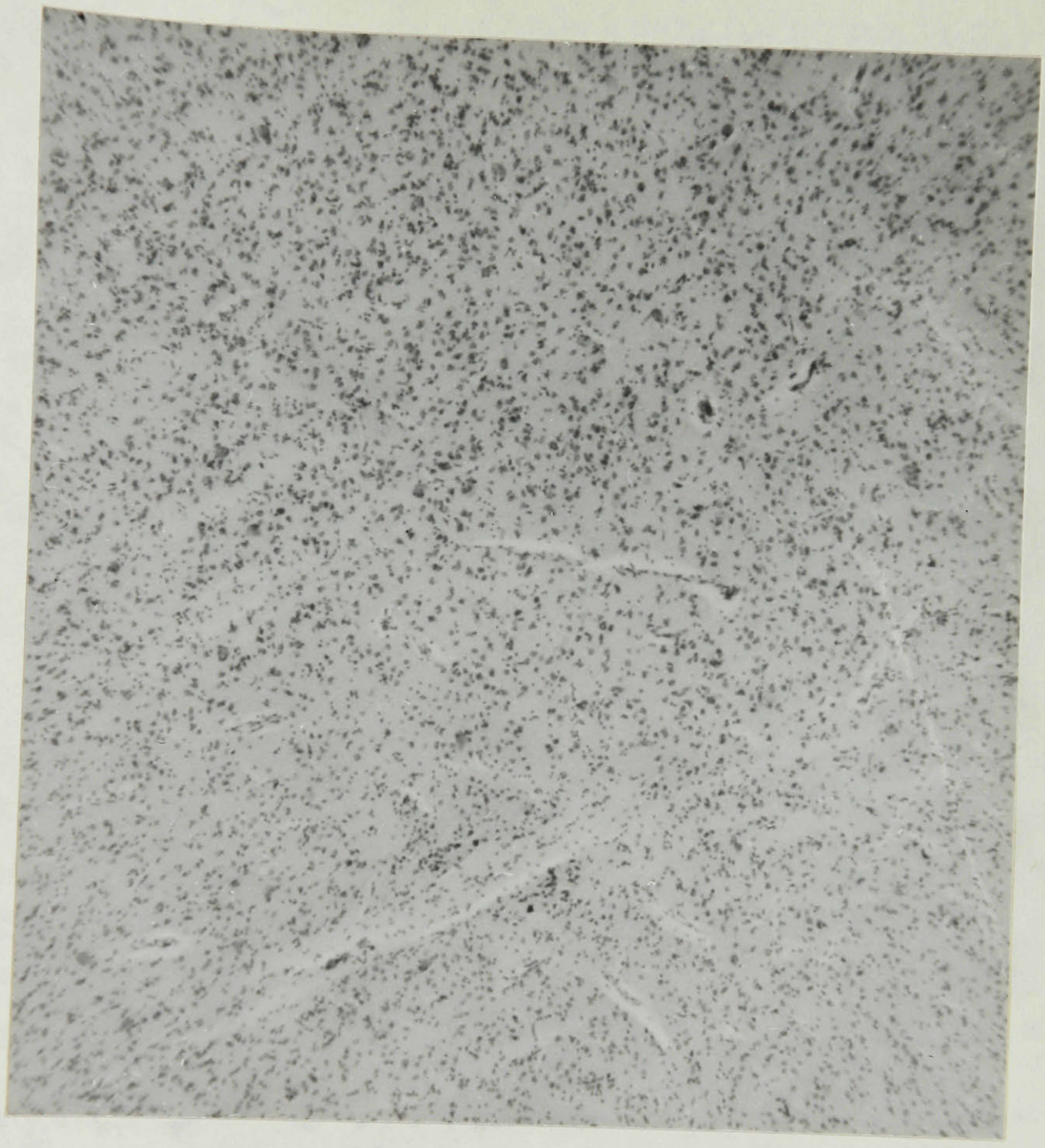


Fig. 14

(P6-20-181) Microphotograph (X 40) of the right caudate nucleus. Cellular changes of the inferior portion are characterized by light staining and reduction in size of the small cells. Note the difference between the upper and lower portions.

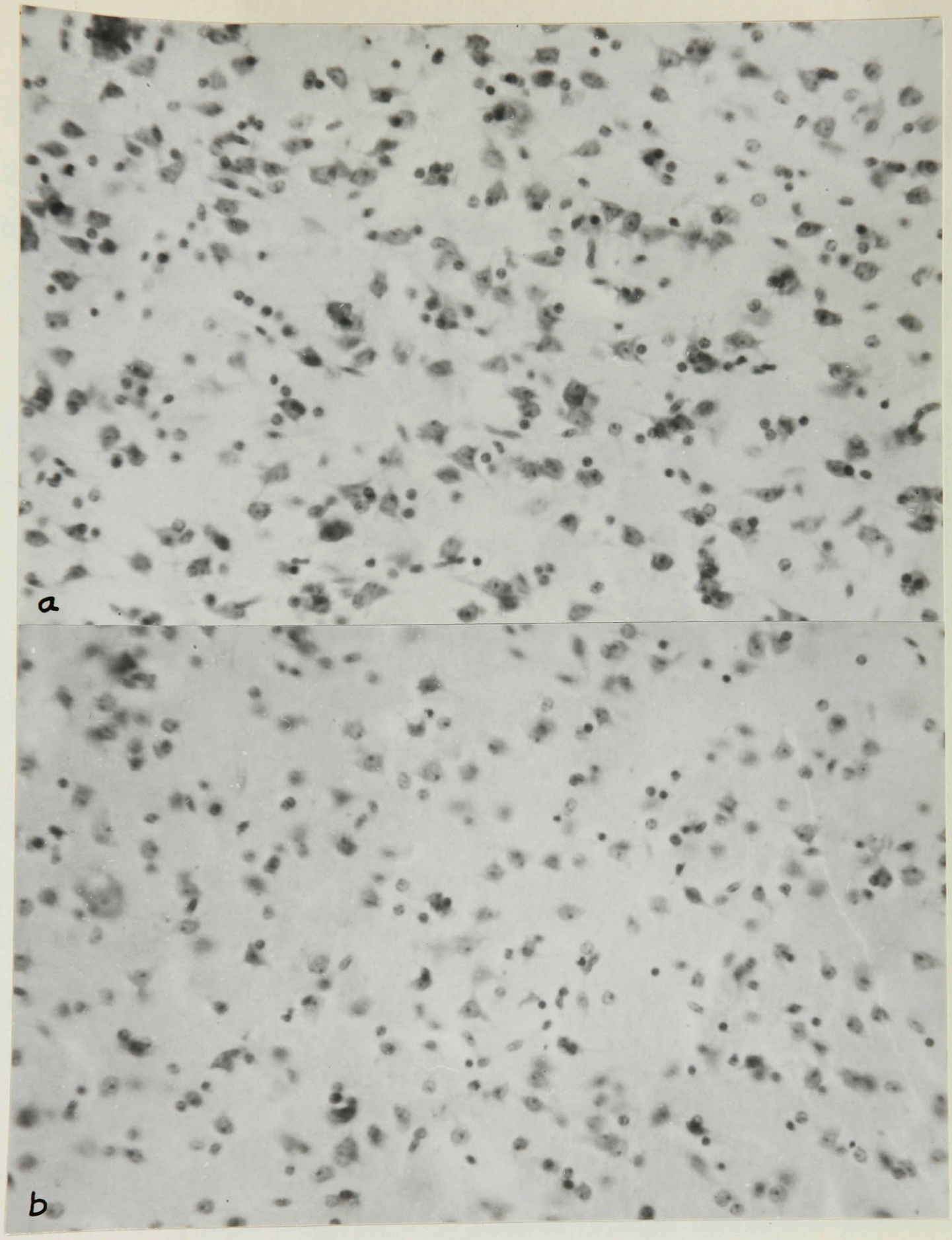


Fig. 15

(P6-20-181) Higher magnification (X180) of Figure 14.

a. Upper portion.

b. Inferior portion.

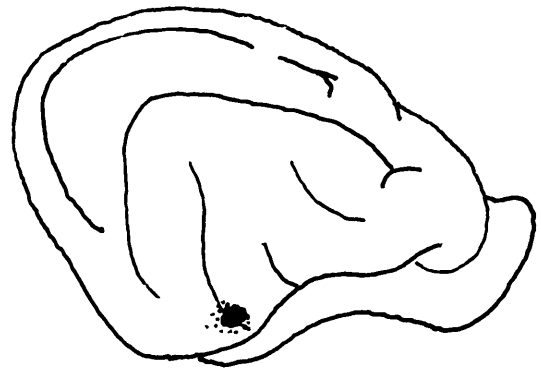
fiber, which may be broken into globules or fragmented, and the origin of which can be traced to the operative site. With this criterion in mind the following experiments were chosen for this report.

a) Cat P50-164. Right inferior ectosylvian and sylvian lesion. Postoperative survival period 7 days. Marchi degenerated fibers were traced to the medullary centers of the anterior sylvian and medial ectosylvian gyri, the external sagittal stratum, to the posterior part of the pulvinar, to the posterolateral portion of the nucleus lateralis posterior, the parageniculate body, and to the pons on the same side.

The cortical lesion occupied the inferior end of the posterior ectosylvian sulcus and its adjacent cortices in the postsylvian gyrus in front and the postectosylvian gyrus behind. It measured 3 mm. in diameter, with the periphery showing reactive changes especially towards the posterior direction (Fig. 16).

The coronal sections P50-164-5-34 indicated superficial damage of the inferior postsylvian gyrus, whereas coronal sections P50-164-6-30 to 7-55, that of the inferior posterior ectosylvian gyrus. The lesion was shallow and nowhere involved the white matter.

The Marchi degenerated fibers and granules were traced anteriorly through the capsula extrema to the white matter of the anterior sylvian gyrus. Fibers were also followed to the



P50-164

7-55 7-5 6-30 6-15 5-50 5-34

Fig. 16

(P50-164) Cortical lesion and diagrams illustrating the extent of the lesion.

medial ectosylvian gyrus, and found more marked in its middle portion. Through the external capsule (capsula externa) and partly through the capsula extrema degenerated fibers coursed to the corona radiata. From the corona radiata one group could be traced to the thalamus. This was plainly seen at the level where the optic tract entered the lateral geniculate body (Fig. 17, section P50-164-5-25). Some of these fibers followed the course of the optic fibers, though most of them mixed with the reticular formation. They may run medially to the superior portion of the posterior part of the pulvinar (Fig. 18) or cap around the lateral geniculate and disperse in the lateral portion of the posterior part of the nucleus lateralis posterior (Fig. 19), involving both portions a and b of the nucleus lateralis according to Winkler and Potter (1914). Posteriorly degenerated fragmented fibers extend to the parageniculate body (Hornet, 1933) or the magnocellular division of the mediate geniculate (Rioch, 1929; Rose and Woolsey, 1949) (Fig. 20).

From the corona radiata a few degenerated fibers crossed the corpus callosum through its posterior third. These fibers were scant and could not be followed with certainty beyond the corona radiata of the opposite hemisphere.

The size of the degenerated fibers in the external capsule was thinner. At the level of the posterior ectosylvian

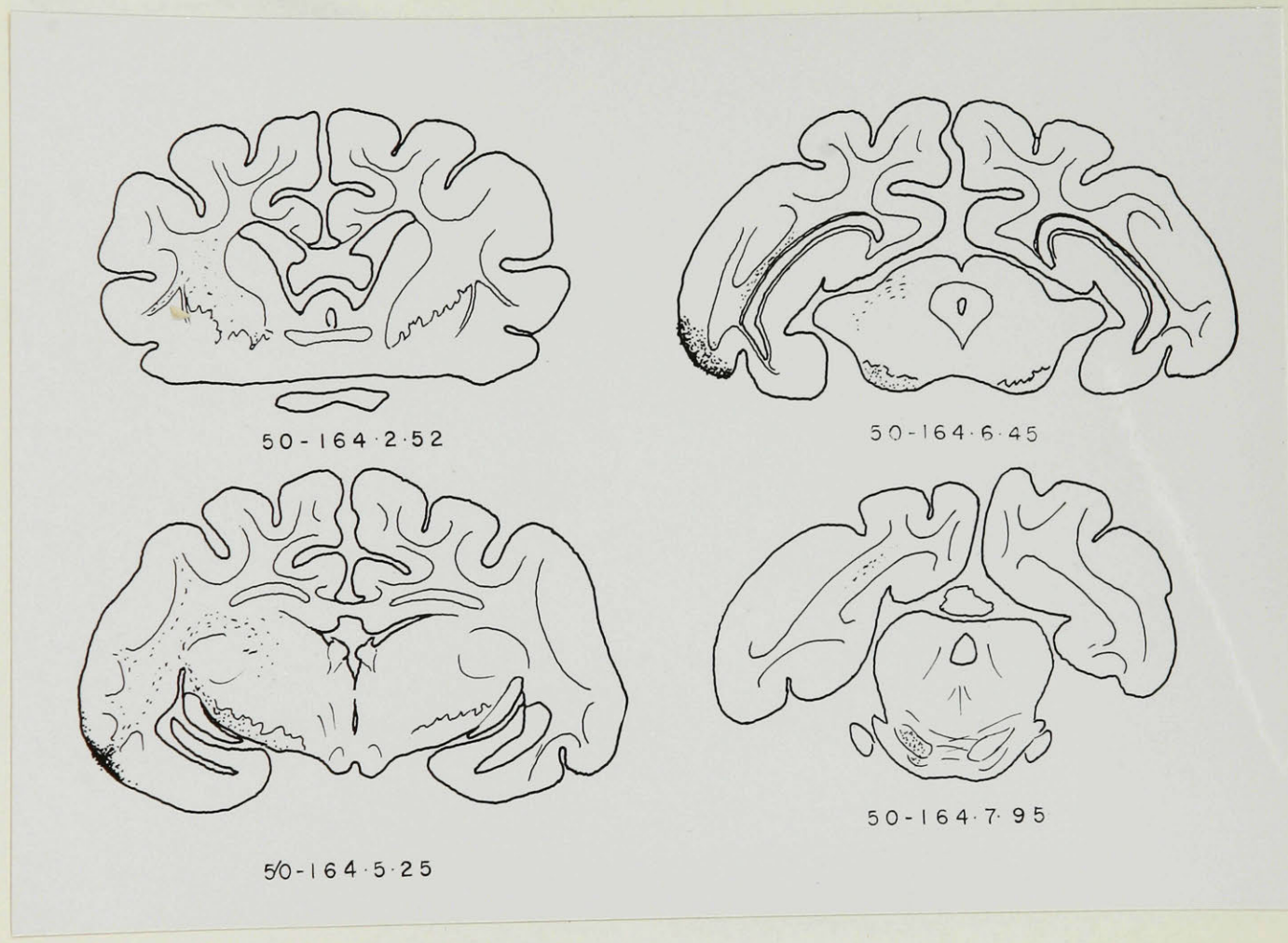


Fig. 17

(P50-164) Photographic tracings showing Marchi degeneration.

Fig. 18

(P50-164) Microphotograph (X 40) of a Marchi preparation at level of pulvinar. The upper group of osmic stained fibers cross medially (from left to right of the picture) to reach the superior part of the pulvinar. The lower group of degenerated fibers can be traced to the nucleus lateralis posterior (see Fig. 20).

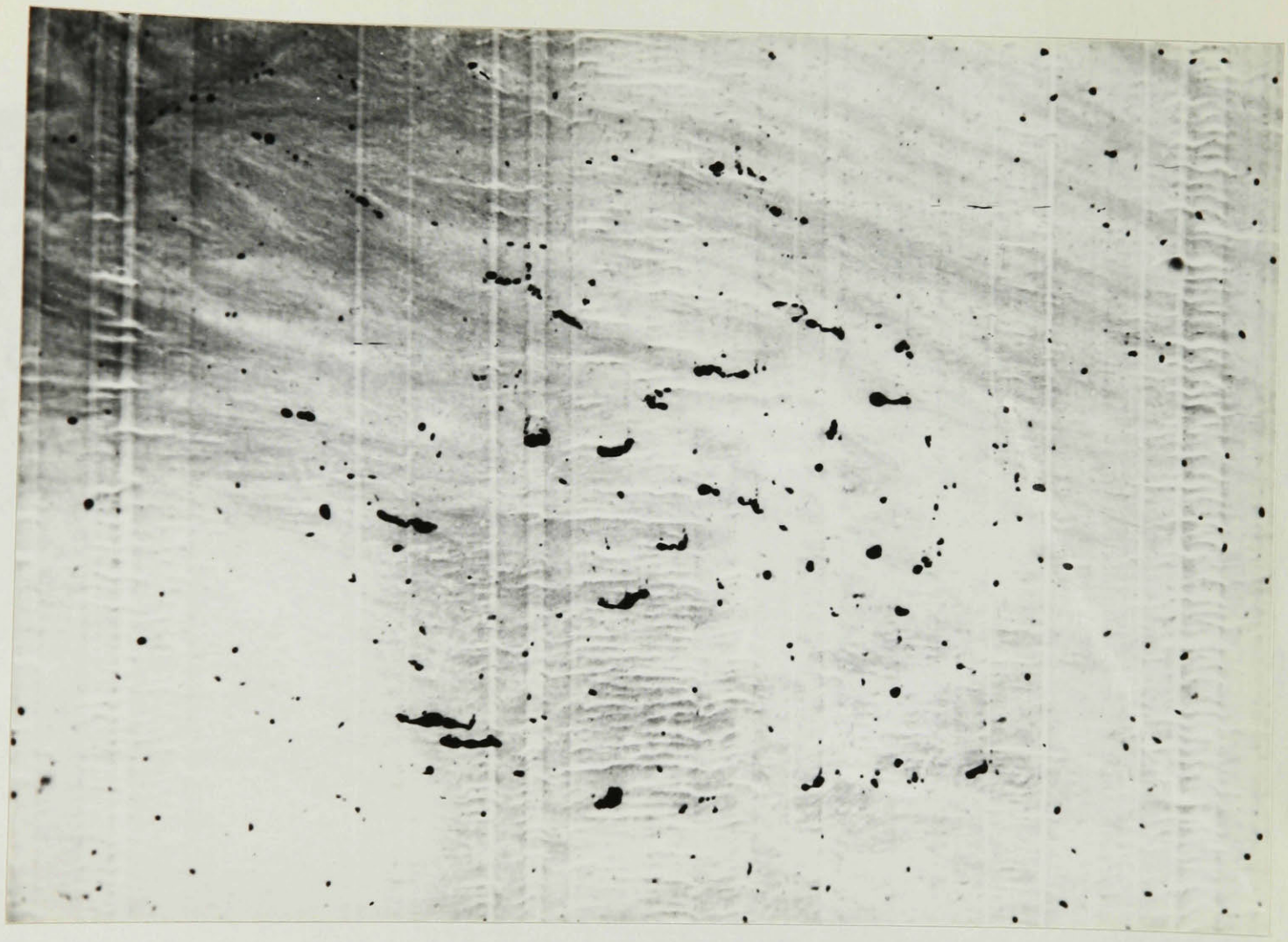


Fig. 19

(P50-164) Microphotograph (X 40) of a Marchi preparation at the level of the lateral geniculate which is seen at the left lower corner. The osmic stained fragmented fibers disperse in the lateral portion of the posterior part of the nucleus lateralis posterior.

Fig. 20

(P50-164) Microphotograph (X 40) of a Marchi preparation showing degenerated fragmented fibers in the paragenículate body.

lesion they passed medially underneath the putamen, some passing through the substance of the inferior portion of the putamen, and joined the sublenticular part of the internal capsule. However, in this segment of the internal capsule there was a great proportion of degenerated fibers coming from the corona radiata. From the latter region some of the degenerated fibers migrated into the internal capsule, occupying first, the upper part of its posterior limb, then the lateral part, and finally the sublenticular segment. From the sublenticular segment of the internal capsule the degenerated fibers descended on the lateral part of the base of the cerebral peduncle (Fig. 21). In the more posterior sections the degenerated fibers gradually spread out until they were distributed throughout the entire ventral portion of the peduncle (Fig. 22). In the pons, they were present here and there, densest among the dorso-lateral bundles (Fig. 23).

The degenerated fibers in the caudal part of the corona radiata were directed backwards reaching the lateral aspect of the posterior horn of the lateral ventricle. There they were distributed throughout the middle part of the external sagittal stratum (Fig. 17).

Extremely few Marchi granules were located in the distal limb of the external capsule underneath the amygdaloid

Fig. 21

(P50-164) Microphotograph (X 40) of a Marchi preparation. Note Marchi granules in lateral part of base of cerebral peduncle.

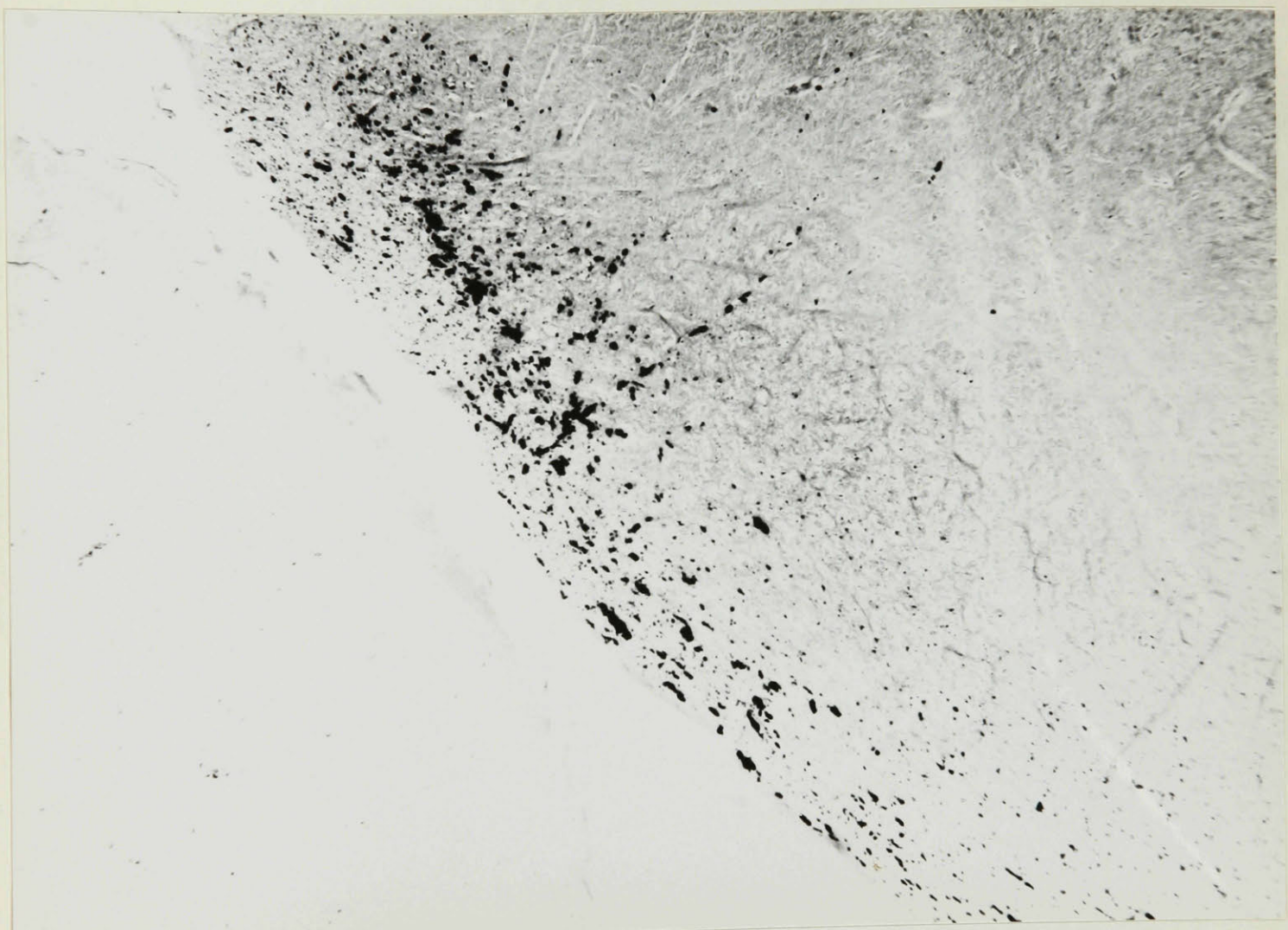


Fig. 22

(P50-164) Photomicrograph (X 40) showing Marchi fibers spreading throughout the entire ventral portion of the peduncle.

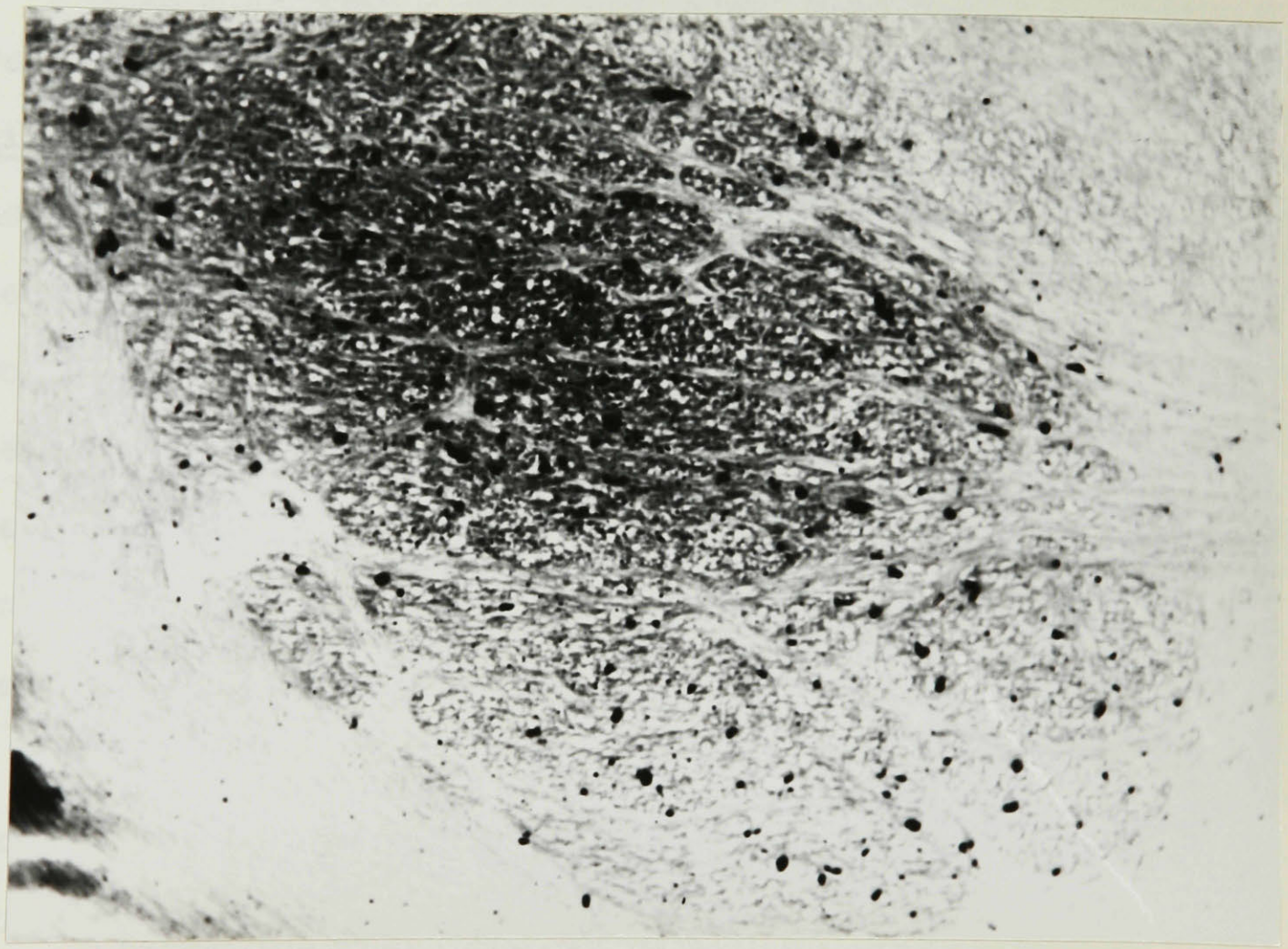


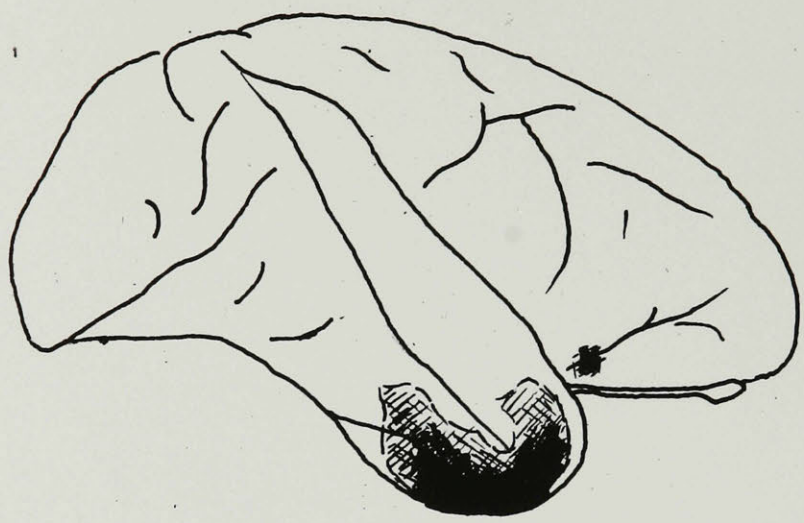
Fig. 23

(P50-164) Microphotograph (X 40). In the pons Marchi granules are found here and there, but densest among the dorso-lateral bundles.

nucleus, and none at all in the anterior commissure (Fig. 17). Many of the Marchi globules in the medullary centers of the opposite hemisphere could not be traced back to the site of the lesion and were, consequently, not regarded as evidence of connections.

b) Monkey P9-241. Temporal polar lesion and orbito-frontal damage. Postoperative survival period ten days. Marchi degeneration: Through the anterior commissure to the medullary centers of the second and third convolutions of the opposite anterior temporal lobe; through the external capsule and partly through the capsula extrema to the corona radiata and to the opposite hemisphere through the posterior portion of the corpus callosum; through the sublenticular segment of the internal capsule (also the lateral zone of Wernicke) to the general area of Forel's field and to the cerebral peduncle, and from the latter to the pons; through the uncinate fasciculus to the under-surface of the frontal lobe.

The cortical lesion (Fig. 24) viewed on the lateral surface resembled a "U" encroaching on the lower end of the superior temporal sulcus. The anterior portion of the middle temporal sulcus was involved. From the tip of the temporal lobe to the posterior border of the lesion in the superior temporal convolution measured 12 mm., in the middle convolution 20 mm. Ventrally most of the lesion involved



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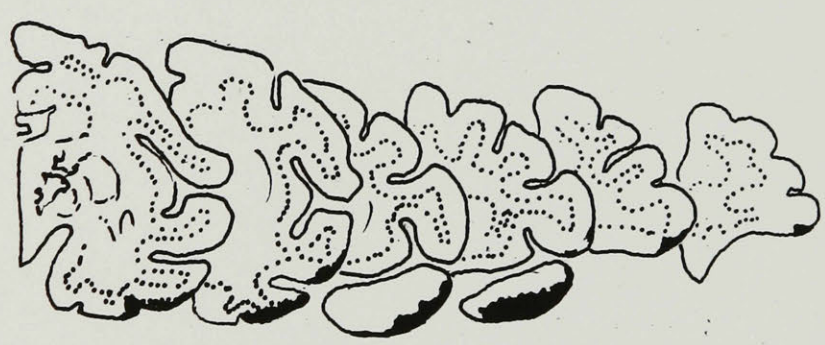

315 240 170 125 85 35

Fig. 24

(P9-241) Cortical lesion and diagrams showing the extent of the lesion.

the cortex anterior and lateral to the rhinal sulcus, while a small caudal portion extended beyond the rhinal sulcus and involved a small portion of the hippocampal gyrus.

In the frontal lobe at the posterior end of the orbito-frontal sulcus a small superficial lesion of 2 to 3 mm. in diameter was produced by retraction of the frontal lobe during the operation.

Diagrams made from the coronal sections revealed cortical damage of the latero-ventral surface of the inferior frontal gyrus. In this area there was no loss of the cortex, but accumulation of Marchi stained macrophages (or microglia) (Fig. 25). This lesion did not invade the white matter, nor extend posteriorly to involve the cortex of the frontal operculum. In the temporal lobe a large part of the medial portion of the temporal pole was spared. Sections #395 and #450 showed densely packed Marchi granules over the lateral third of the hippocampal cortex, although the general configuration of the hippocampal gyrus was preserved.

The degenerated fibers were traceable from the lesion along the usual position of the uncinate fasciculus to the orbito-frontal cortex (Fig. 25). They were present below the white matter of the inferior frontal gyrus and were much smaller than the fibers of the orbito-frontal cortex (Fig. 25). One could not tell in which layer of the orbito-frontal cortex these fibers terminated, since the degenerated granules became finer and finer, finally disappearing as they approached the cortex.

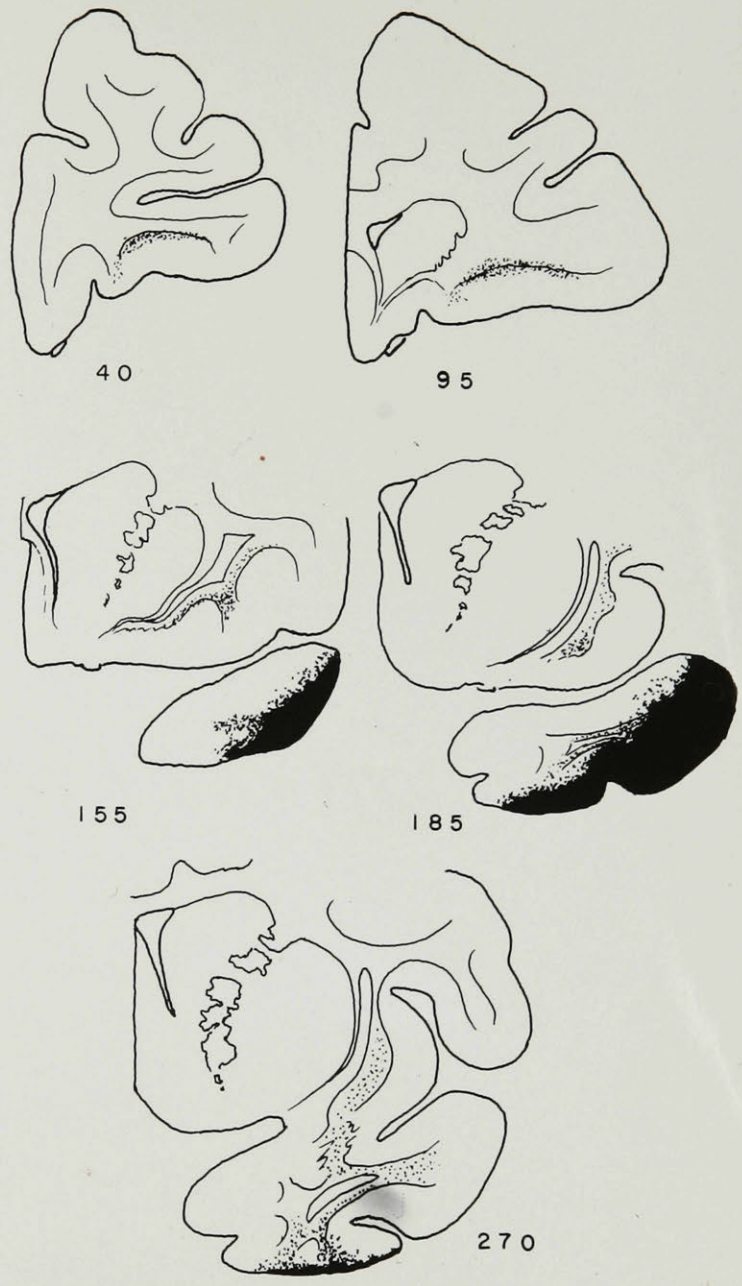

Fig. 25

(P9-241) Marchi degenerated fibers and granules as seen at different levels. Note the uncinate fasciculus the fibers of which are small and spread out below the white matter of the inferior frontal gyrus. Degenerated fibers in the capsula extrema do not penetrate the claustrum.

The degenerated fibers could be traced to the anterior commissure where the degenerated globular fibers were small and scattered throughout its entire dorsoventral and antero-posterior extent although they tended to concentrate on its dorsoposterior portion. From the commissure degenerated fibers could be followed to the white matter of the second and third, and a few to that of the first, temporal convolutions of the opposite hemisphere.

The degenerated granules in the capsula extrema were a continuation of those in the operated cortex. These granules were exceedingly fine and did not extend to the dorsal part of the capsula extrema, but occupied its inferior part as far as the posterior limit of the claustrum. Nevertheless, there was no evidence of penetration of these fine granules into the claustrum.

Posterior to the anterior commissure some of the degenerated fibers from the temporal medullary centers swerved medially and dorsally to cap the amygdaloid nucleus (Fig. 26 and Fig. 27). In the more posterior sections these fibers were found between the tail of the caudate nucleus and the putamen. They reached the lateral wall of the capsule of the lateral geniculate body and ascended along the dorsal surface of the lateral geniculate to join the posterior limb of the internal capsule (Fig. 28). Some of these fibers

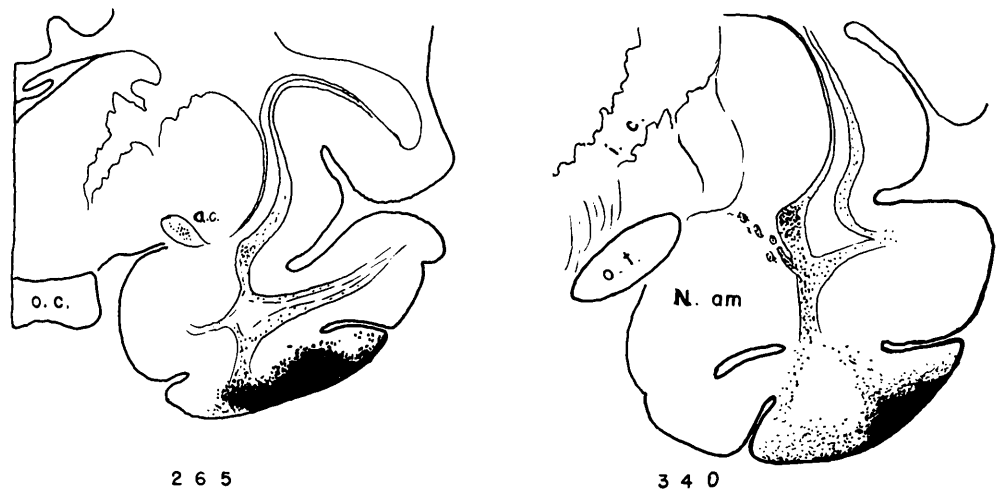

Fig. 26

(P9-241) Marchi preparations at different levels. Note degenerated fibers capping the amygdaloid nucleus, the tail of the caudate and the lateral geniculate body.

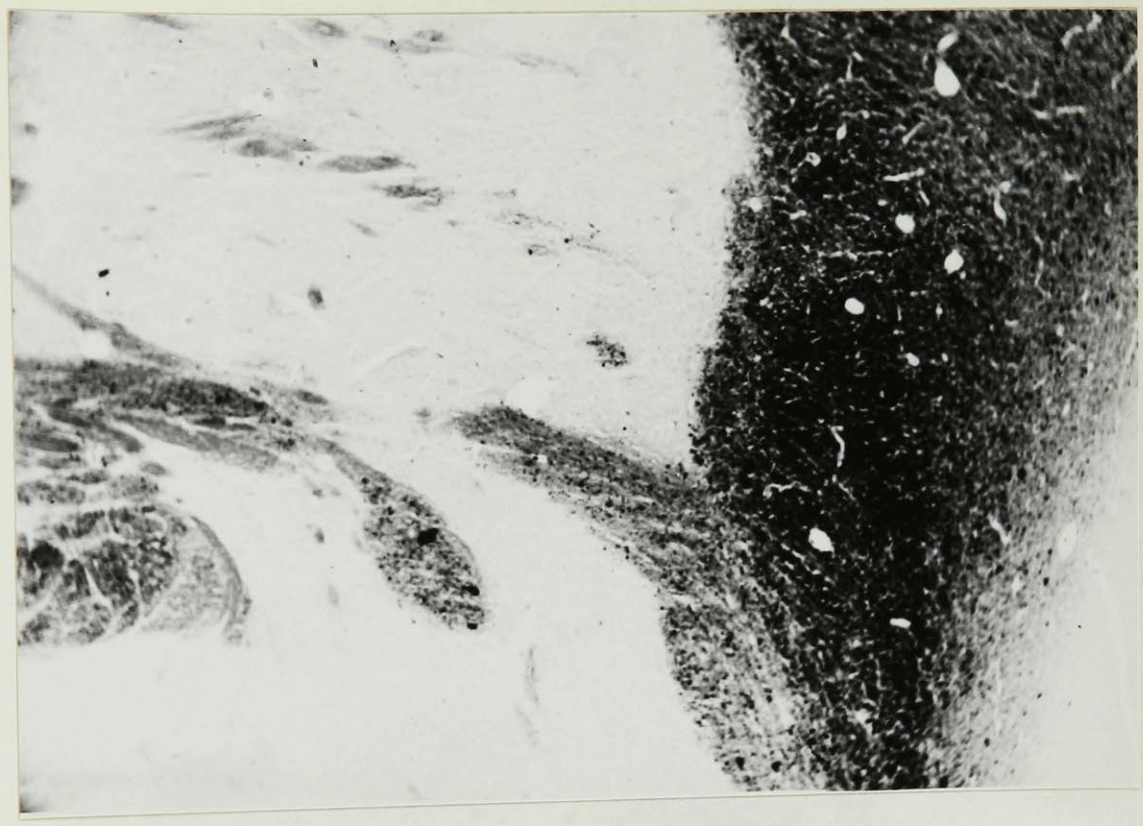

Fig. 27

(P9-241) Microphotograph (X 40) of a Marchi preparation showing swerving of osmic stained fibers over the amygdaloid nucleus. Compare Figure 26 #340.

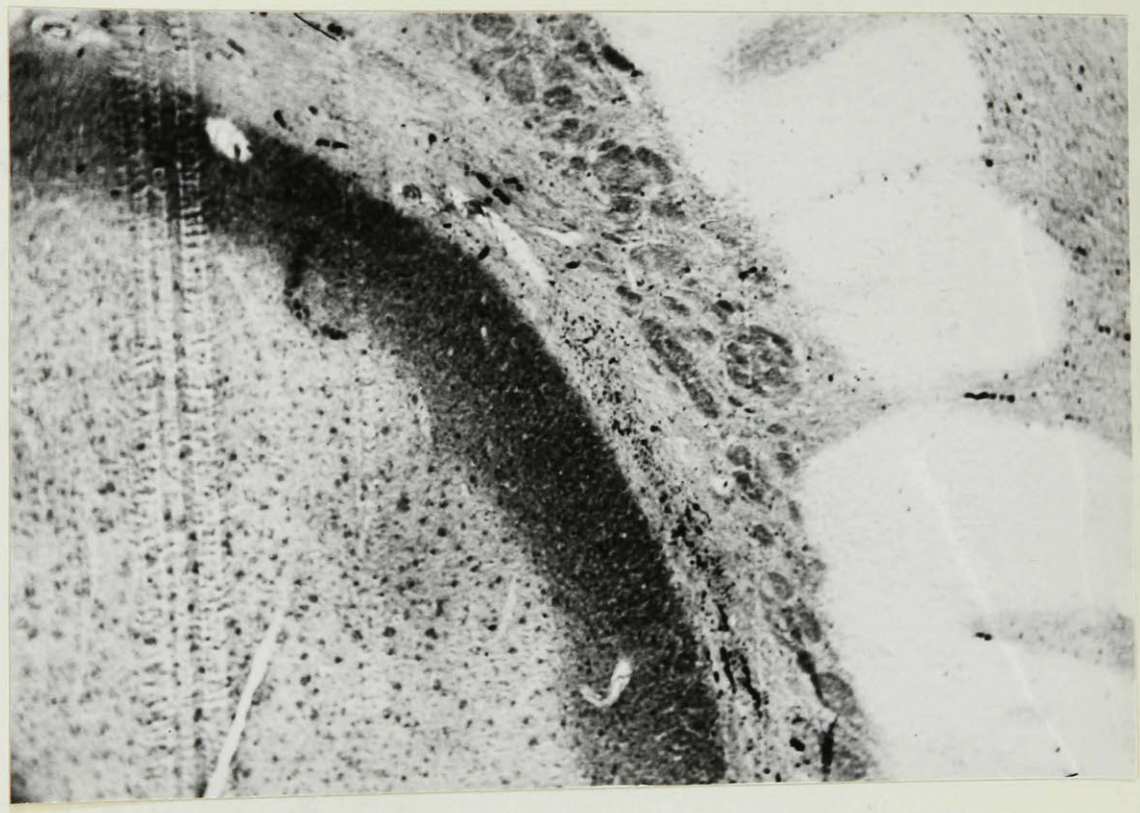

Fig. 28

(P9-241) Microphotograph (X 40) of a Marchi preparation. Fragmented fibers are found along the capsule of the lateral geniculate body. Compare Figure 26 #395 and #450.

travelled medially along the course of the ansa lenticularis and were distributed on the "general area" of Forel's field (Fig. 29). But the majority of the fibers turned ventrally to occupy the lateral portion of the base of the cerebral peduncle. In the peduncle they rapidly spread to its ventral part and finally migrated to the dorso-lateral bundles in the pons.

Many of the Marchi fibers in the corona radiata crossed through the "posterior portion"* of the corpus callosum. In the corona radiata, all three of the Marchi specimens showed "Marchi artifact". This interference with the course of the degenerated fibers rendered the interpretation difficult, and for this reason, the dubious Marchi fibers, as observed in the white matter of the gyri in the other parts of the brain, were not reported.

3) Silver Staining Method.

Two cat brains were treated by this method in the manner already described under Section A of this chapter. Cat P50-165 was kept alive for 5 days after the operation. The lesion was found to be 3 mm. in diameter near the inferior end of the right posterior ectosylvian sulcus occupying both the posterior sylvian and posterior ectosylvian gyri. Ventrally it encroached

* It was impossible to determine the coronal level of the corpus callosum from which the fibers began to cross since many of the sections were lost due to technical difficulties.

Fig. 29

(P9-241) Microphotograph (X 40) showing degenerated fibers along the course of the ansa lenticularis. Compare Figure 26 #450.

on the lateral bank of the posterior rhinal sulcus and extended, without damaging the medial bank, across the posterior rhinal sulcus to involve superficially a small portion of the entorhinal area. The other cat (50-194) had a large lesion of 6 mm. in diameter situated in the lower portion of the posterior ectosylvian gyrus, from which it extended forwards to involve the posterior sylvian gyrus and backwards to involve the posterior limb of the suprasylvian gyrus. This cat was sacrificed 7 days after the operation.

The results of these two experiments were similar. The fine network of fibers in the cortex surrounding the lesion had lost its regular pattern with the formation of vacuoles. Many of the fine fibers were fragmented and swollen and were very heavily stained. A few rings with fine tails and end bulbs identical to those which have been described as degenerated boutons terminaux were present. These might not be found on the surface of a cell but in the midst of the degenerated fibers (Fig. 30). In the white matter the fibers were very black and thick (Fig. 31). This change in the fibers continued for some distance, and then they seemed to resume their normal appearance; thus in the corona radiata no degenerated fibers stained by this method could be recognized. A general survey of the corpus callosum and the anterior commissure failed to

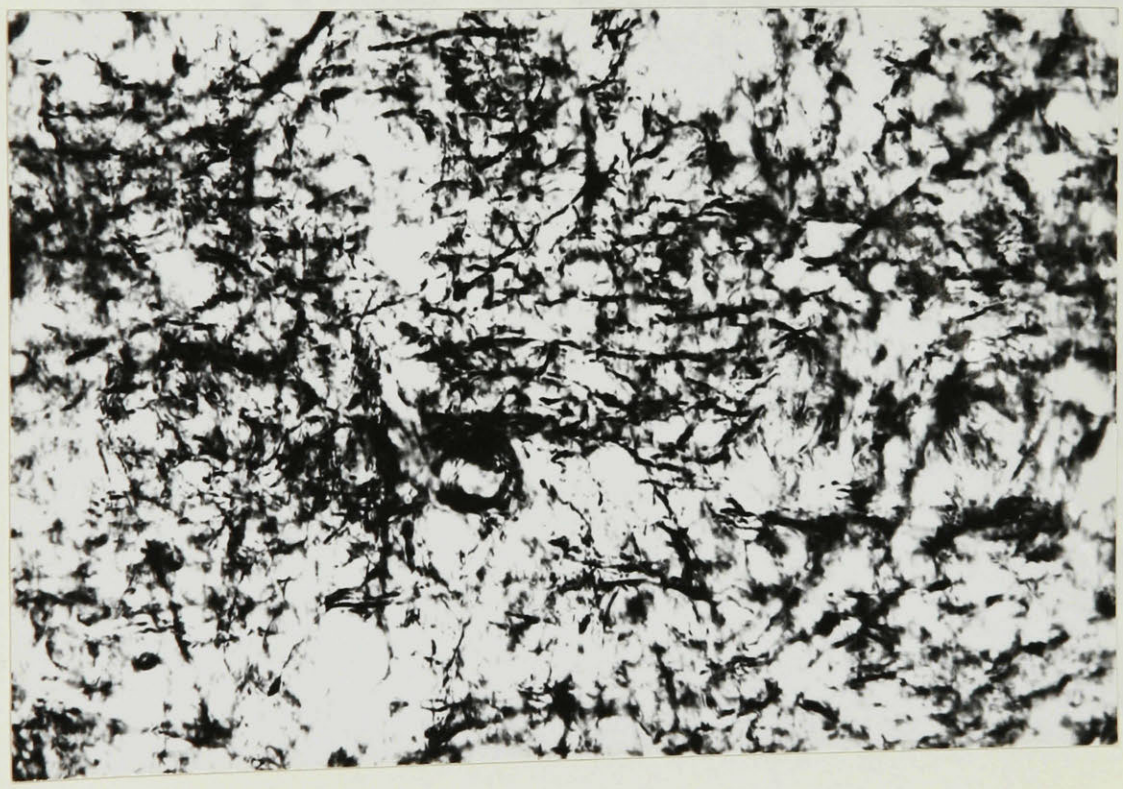

Fig. 30

(P50-165) Microphotograph (X 940) of a modified Cajal's silver stained preparation of the cortex near the operative site. The fine fibers are fragmented and swollen and have lost their regular pattern. There is vacuole formation. Degenerated boutons terminaux are seen here and there.

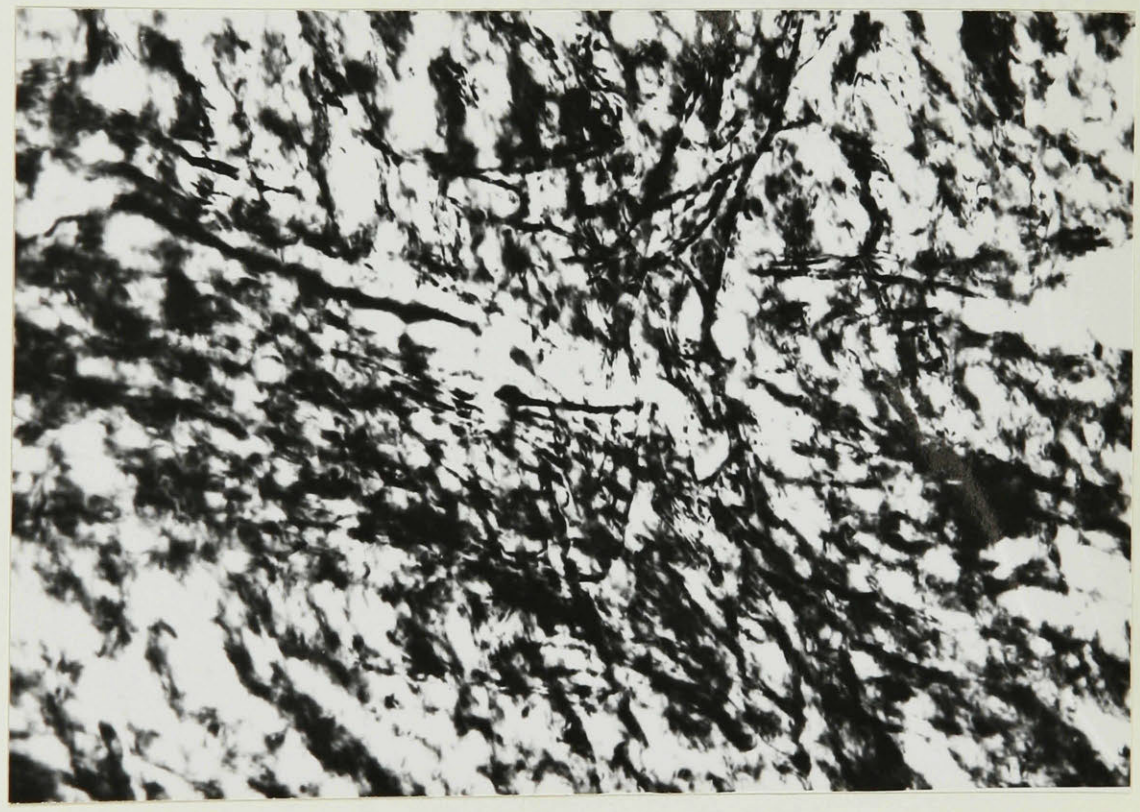

Fig. 31

(P50-165) Microphotograph (X 940) of a modified Cajal's silver stained preparation showing swollen and thick fibers in the white matter.

disclose any degenerated fibers. The septal nuclei and their axons appeared normal. There was no change in the hippocampal system including the fornices. There was no sign of degeneration in the thalamus. Occasionally boutons terminaux were observed in the lateral geniculate bodies, medial geniculate bodies and the nucleus lateralis posterior.* When the nuclei lateralis posterior of the two sides were compared, there was no difference in their fibers and boutons.

* Boutons terminaux are numerous in the motor nuclei of the brain stem, such as the motor cells of the reticular formation, oculomotor, trochlear nuclei, etc. They are also demonstrated in the vestibular nucleus and red nucleus by this method.

IV. DISCUSSION

The discrepancies in the findings obtained by the methods employed in these experiments require an explanation. Since Gudden (1870) demonstrated that atrophic change was present in the subcortical structures of a rabbit eight to twelve months following an operation on the cortex, retrograde degeneration has been the most widely used, and is considered to be the most reliable method for the study of fiber connection. Almost all the corticothalamic pathways were worked out by this method. Basing his conclusions on a wide experience, Walker (1938) pointed out that a small lesion in the cortex gives only suggestive evidence of degeneration in the thalamus. Thus the experiments carried out in monkeys in the literature have been invariably accomplished by extensive cortical removals (except a few such as Walker's experiments 20 and 22, etc.). In the cat the excision of the cortex for a similar purpose has been also large as compared to the total area of the cortex. When small lesions are used, entirely different results may be obtained from two identical experiments. Waller (1940) reported partial degeneration of the central portion of the medial geniculate following a lesion in the posterior sylvian gyrus (Waller's experiment 121).* Rose

* It is interesting to note that when, due to unknown cause, atrophy of the cortex occurred over the same area, this same worker did not find any change in the medial geniculate (Waller's experiment 127).

and Woolsey (1949) repeated the same experiment (experiment 12a) and noted that "there is a possible cell rarefaction in the medial portion of the dorso-anterior segment of the principal division" of the medial geniculate. But in their conclusion, Rose and Woolsey did not consider the finding significant. When these experiments were performed the authors concentrated their study on the auditory pathway and made no mention of the possible reactive change elsewhere than in the medial geniculate body. It is probable, however, that in the second auditory area it had not been possible to demonstrate the thalamo-cortical projections by the retrograde degeneration method. The repeated failure to show cellular change in the thalamus of the monkey following temporal removal, exclusive of the first auditory area, affords a reason to believe that similar results would be obtained in the cat after the temporal region below the auditory cortex is excised.

Another explanation may be offered. In Rose and Woolsey's experiment (1949), while no retrograde degeneration was obtained as a result of second auditory area removal, neurono-graphy indicated the presence of a pathway between this area and the thalamus. These workers postulated that the second auditory area might receive axon collaterals from a wide area of the thalamus. If this is true, the temporal cortex, which has been known to be highly associational, would have afferent fibers from wider sources.

Retrograde degeneration in the caudate nucleus in the monkey should be discussed. The character of the change in the small cells suggests a simple atrophy, thus a trans-neuronal degeneration. Whether this was due to the lesion in the temporal polar cortex or to that in the precentral area needs further investigation. Cajal (1911) and Dejerine (1901) suggested that there are connections of the cortex with the caudate nucleus through the collaterals from the internal capsule. Bianchi and d' Abunda (1886) had shown neuroglial proliferation in the caudate nucleus and the putamen following cortical lesions. Marinesco (1895) demonstrated a pathway from the frontal lobe to the caudate nucleus in the dog. In the cat destruction of an area corresponding to area 4s in primates was claimed by Glees* to result in degeneration of the fine unmyelinated nerve network in the caudate nucleus. On the other hand, Wilson (1913-14) and Vogt (1920) were not able to find cortico-caudate connections. With Marchi method, Verhaart and Kennard (1940) could not find definite evidence of the existence of the cortico-caudate fibers. Similarly, previous workers have never succeeded in showing a connection between the caudate and the temporal pole. Even so, the evidence produced by Glees furnishes a possi-bility that the caudate receives its afferent fibers from

* Cited by Bucy (1944).

several sources. If so, and if the temporal polar cortex also contributes fibers, by collaterates or transneuronal pathways, to the caudate, these fibers must be related to the inferior portion and to the small cells of the nucleus only. Similar reasons may be given for the cellular change in the putamen.

The retrograde changes in the other structures of this animal (P6-20) deserve little discussion since they have been frequently described as a result of precentral and visual cortical removals. It is to be remembered that although Marchi fibers have been traced from the precentral motor cortex to the anterior (microcellular) portion of the red nucleus (Levin, 1944), there has been no report of reactive gliosis to this effect. The criteria for the interpretation of the Marchi preparations and the silver-stained materials as well as their disadvantages have been presented. So far established evidence has been obtained through the Marchi method only. With the limitations of Marchi technique, these findings must be considered fragmentary. Discrepancies between the results of this investigation, and those of other workers (Mettler, for instance) call attention to the need of a great deal more work in the field.

V. SUMMARY

1. The literature of the connections of the temporal lobe is discussed.

2. That an area in the posterior ectosylvian gyrus of the cat may be comparable to the temporal pole in the primates is suggested.

3. Fiber connections of the polar cortex of the cat and the monkey are studied by retrograde degeneration method, Marchi method and silver staining method after cortical ablation.

4. In the cat, efferent fibers from the temporal polar cortex project to the posterior portion of the pulvinar, posterior nucleus, posterolateral portion of the nucleus lateralis posterior, and the paragenículate body. It is associated with the anterior sylvian gyrus, the medial ectosylvian gyrus and the external saggital stratum on the same side. Commissural fibers are not found in the anterior commissure, but in the posterior portion of the corpus callosum. The existence of a temporo-pontine bundle is evident.

5. In the monkey, the temporal polar cortex does not show a direct connection with the thalamus. It is associated with the fronto-orbital cortex through the uncinate fasciculus. Some commissural fibers pass through the anterior commissure to the white matter of the second and third temporal convolution; the rest pass through the posterior portion of the corpus callosum. The evidence of the presence of a temporo-pontine tract is, likewise, established. A possible connection with the "general area" of Forel's field is suggested. Finally, the caudate nucleus, as suggested, may have many sources of afferent connections, the temporal polar cortex being one of the sources.

BIBLIOGRAPHY

Ades, H.W.	1943	A secondary acoustic area in the cerebral cortex of the cat. J. Neurophysiol., 6: 59-63.
Ades, H.W., and Felder, R.	1942	The acoustic area of the monkey (Macaca mulatta). J. Neurophysiol., 5: 49-54.
Ades, H.W., and Felder, R.	1945	The acoustic projection system. J. Neurophysiol., 8: 463-470.
Arnold	1851	Handbuch der Anatomie der Menschen. Vol.2, p.762. Cited by Dejerine (1901)
Bailey, P., Garol, H.W., and McCulloch,W.S.	1941	Cortical origin and distribution of corpus callosum and anterior commissure in the chimpanzee (pan satyrus). J. Neurophysiol. 4: 564-571.
Bailey, P., von Bonin, G., Garol, H.W., and McCulloch, W.S.	1943	Long association fibers in cerebral hemispheres of monkey and chimpanzee. J. Neurophysiol., 6: 129-134.
Bailey, P., von Bonin, G., Davis, E.W., Garol, H.W., and McCulloch, W.S.	1944	Further observations on associational pathways in the brain of Macaca mulatta. J. Neuropath. & Exper. Neurol., 3: 413-415.
Barker, L.F.	1899	The Nervous System. New York, D. Appleton & Co., 1122 pp.

Bianchi, L., and D'Abundo, G.	1886	Die ins Gehirn und Rückenmark herabstreigenden experimentalen Degenerationen als Beitrag zur Lehre von den cerebralen Lokalisierungen. Neurol. Centralbl. vol.17, p.385.
Bielschowsky, M.	1931	Nerve silberimpregnationsversuche zur darstellung der neuroglia und denen ergebnisse. Ztschr. f.d. ges. Neurol. u. Psychiat. 135: 253-278.
Biemond, A.	1930	Experimentell-anatomische Untersuchungen über die corticofugalen optischen Verbindungen bei Kaninchen und Affen. Zeitzchr. f.d. ges. Neurol. u Psychiat., 129: 65-127.
Bodian, D.,	1936	A new method for staining nerve fibers and nerve endings in mounted paraffin sections. Anat. Rec., 65: 89-97.
Bodian, D.	1937	The staining of paraffin sections of nerve tissues with activated protargol. The role of fixatives. Anat. Rec., 69: 153-162.
Bodian, D.	1937-38	The structure of the vertebrate synapse. A study of the axon endings on Mauthner's cell and neighbouring centers in the goldfish. J. Comp. Neurol. 68: 117-159.
Brissand	[n.d.]	Cited by Dejerine (1901).
Brodal, A.	1940	Modification of Gudden method for study of cerebral localization. Arch. Neurol. & Psychiat. 43:46-58.
Brodal, A.	1947	The hippocampus and the sense of smell. Brain, 70: 179-224.

Brodal, A.	1948	The origin of the fibers of the anterior commissure in the rat. Experimental studies. J. Comp. Neurol., 88: 157-206.
Brodmann, K.	1909	Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipen dargestellt auf Grund des Zellenbaues. Leipzig, Barth, 324 pp.
Bucy, P.C.	1944	The Precentral Motor Cortex. Illinois, University of Illinois Press, 605 pp. See p. 137.
Bucy, P.C., and Klüver, H.	1940	Anatomic changes secondary to temporal lobectomy. Arch. Neurol. & Psychiat., 44: 1142-1146.
Burdach, K.F.	1822	Vom Bane und Leben des Gehirns. Leipzig. Cited by Barker, 1899.
Cajal, Ramon y	1911	Histologie du système nerveux de l'homme et des vertébres. Paris, A. Maloine.
Cajal, Ramon y	1928	Degeneration and regeneration of the nervous system. Translated by R.M. May. London, Oxford University Press. 2 vols.
Campbell, A.W.	1903	Histological studies on cerebral localization. Proc. Roy. Soc. 72: 488-492.
Campbell, A.W.	1904	Histological studies on the localization of cerebral function. J. Ment. Sci., 50: 651.
Campbell, A.W.	1905	Histological studies on the localization of cerebral function. Cambridge University Press, 360 ppp.

Clark, W.E.L. 1936 The thalamic projection of the temporal lobe of the brain in the monkey. J. Anat., 70: 447-464.

Clark, W.E.L. 1939 Structural changes in the isolated visual cortex. J. Anat., 73: 563-574.

Clark, W.E.L., and Boggon, R.H. 1935 The thalamic connections of the parietal and frontal lobes of the brain in the monkey. Phil. Trans. Roy. Soc. London, series B, 224: 313-359.

Clark, W.E.L., and Meyer, M. 1947 The terminal connections of the olfactory tract in the rabbit. Brain, 70: 304-328.

Clark, W.E.L., and Northfield, D.W.C. 1937 The cortical projections of the pulvinar in the Macaque monkey. Brain, 60: 126-142.

Clark, W.E.L., and Penman, G.G. 1934 The projection of the retina in the lateral geniculate body. Proc. Roy. Soc., London, 114: 291-313.

Davenport, H.A. 1930 Staining nerve fibers in mounted sections with alcoholic silver nitrate solution. Arch. Neurol. & Psychiat., 24: 690-695.

Dejerine, J. 1895 Anatomie des Centres Nerveux. Paris, J. Rueff.

Dejerine, J. 1901 Anatomie Des Centres Nerveux (Tome Deuxieme). Paris, J. Rueff, 720 pp.

Duncan, D. 1931 The Marchi method. A discussion of some sources of error and the value of this method for studying changes in the myelin sheath. Arch. Neurol. & Psychiat., 25: 327-355.

Economo, C.von	1929	The Cytoarchitectonics of the Human Cerebral Cortex. Oxford University Press, 186 pp.
Economo, C.von, and Koskinas, N.	1925	Die Cytoarchitektonik der Hirnrinde des erwachsenen Menschen. Vienna and Berlin, Julius Springer.
Edinger, L., and Wallenberg, A.	1913	Untersuchungen über den Fornix und das Corpus mamillare. Arch. f. Psychiat., 35:1.
Elliot Smith, G.	1896	Morphology of the true "limbic lobe", corpus callosum, septum pellucidum and fornix. J. Anat. & Physiol., 30: 157-167.
Elliot Smith, G.	1903	On the morphology of the brain in the mammalia. Trans. Linnean Soc., 8: 317-431.
Elliot Smith, G.	1907	A new topographical survey of the human cerebral cortex, being an account of the distribution of the anatomically distinct cortical areas and their relationship to the cerebral sulci. J. Anat. & Physiol., 41: 237-254.
Ferrier, D., and Turner, W.A.	1898	Philos. Trans., 190:1. Cited by Sunderland (1940).
Flechsig, P.	1876	Plan des menschlichen Gehirns. Leipzig.
Flechsig, P.	1896	Gehirn und Seele. Leipzig.

Foix, C.H., and Nicolesco,J.	1925	Les noyaux gris centraux et la région mésencéphalo-sous-optique. Paris, Masson et Cie., 581 pp.
Fox, C.A.	1940	Certain basal telencephalic centers in the rat. J. Comp. Neurol. 72: 1-62.
Fox, C.A.	1943	The stria terminalis, longitudinal association bundle and precommissural fornix fibers in the cat. J. Comp. Neurol., 79: 277-295.
Fox, C.A.	1949	Amygdo-thalamic connections in Macaca mulatta. Anat. Rec., 103: 537-538.
Fox, C.A., Fisher, R.R., and Desalva, S.J.	1948	The distribution of the anterior commissure in the monkey (Macaca Mulatta). J. Comp. Neurol., 89: 245-278.
Fox, C.A., and Schmitz, J.T.	1943	A Marchi study of the distribution of the anterior commissure in the cat. J. Comp. Neurol., 79:297-314.
Gardner, W.D., and Fox, C.A.	1948	Degeneration of the cingulum in the monkey. Anat. Rec., 100:663-664.
Garol, H.W.	1942	Cortical origin and distribution of the corpus callosum and anterior commissure in the cat. J. Neuropath. & Exper. Neurol., 1: 422-429.
Gerwer	1899	Neurol. Centralbl., v.18. Cited by Bechterew, W., Les voies de conduction du cerveau et de la moelle. Paris, 1900.

Gibson, W.C.	1937a	Silver methods for boutons terminaux and neurofibrils. In McClung, C.E., Handbook of Microscopic Technic, New York, Paul B. Hoeber, Inc.,
Gibson, W.C.	1937b	Degeneration of the boutons terminaux in the spinal cord. Arch. Neurol. & Psychiat., 38: 1145-1157.
Glees	(n.d.)	Cited by Bucy (1944).
Glees,P.	1943	The Marchi reaction: Its use on frozen sections and its time limit. Brain, 66: 229-232.
Glees, P.	1946	Terminal degeneration within the central nervous system as stained by a new silver method. J. Neuropath. exper. Neurol., 5: 54-59.
Grinker, R.R., and Bucy, P.C.	1949	Neurology. 4th ed. Springfield, Charles C. Thomas, 1138 pp.
Gudden, B.	1870	Experimentaluntersuchungen über das peripherische und centrale Nervensystem. Arch. f. Psychiat., 2: 693-723.
Gurdjian, E.S.	1925	Olfactory connections of the albino rat, with special reference to stria medullaris and anterior commissure. J. Comp. Neurol., 38: 127-163.
Humphrey, T.	1935	Certain relations and connections of the amygdaloid complex and of the commissures of the hemispheres in the bat. Anat. Rec., 61: 26.

Humphrey, T.	1936	The telencephalon of the bat. The noncortical nuclear masses and certain pertinent fiber connections. J. Comp. Neurol. 65: 603-711.
Hornet, T.	1933	Vergleichend anatomische untersuchungen über das corpus geniculatum mediale. Arb. a.d. Neur. Inst. a.d. Wiener Univ., 35: 76-92.
Kappers, Ariëns C.U.	1921	Vergleichende Anatomie des Nervensystems. Haarlem, E.F. Bohn.
Kappers, Ariëns C.U.	(n.d.)	Tabulae Anatomo-comparative Cerebri. A series of nine colored maps with description. Descriptive text. Amsterdam, The Kosmos Publishing Co., 30 pp.
Kappers, Ariëns C.U. Huber, G.C., and Crosby, E.C.	1936	The Comparative Anatomy of the Nervous System of Vertebrates, Including Man. 2 vols. New York, MacMillan, 1845 pp.
Klüver, H., and Bucy, P.C.	1937	"Psychic blindness" and other symptoms following bilateral temporal lobectomy in rhesus monkeys. Am. J. Physiol., 119: 352-353.
Klüver, H., and Bucy, P.C.	1938	An analysis of certain effects of bilateral temporal lobectomy in the rhesus monkey, with special reference to "psychic blindness". J. Physiol., 5: 33-54.
Klüver, H., and Bucy, P.C.	1939	Preliminary analysis of functions of the temporal lobes in monkeys. Arch. Neurol. & Psychiat., 42: 979-1000.
Krieg, W.J.S.	1947	Connections of the cerebral cortex. I. The Albino rat. C. Extrinsic connections. J. Comp. Neurol., 86: 267-394.

Kubie, L.S., and Davidson, D. 1928 The ammoniacal silver solution used in neuropathology. Their staining properties, chemistry and methods of preparation. Arch. Neurol. & Psychiat., 19: 888-903.

Lhotka, J.F., and Vaz Ferreira,A. 1949 Removal of formalin from formalin-fixed tissue. Anat. Rec., 103: 161.

Loo, Y.T. 1931 The forebrain of the oppossum, Didelphis virginiana. J. Comp. Neurol., 52: 1-148.

Marie, P., and Guillain,G. 1903 Le faisceau de Türck (faisceau externe du pied du pédoncule) Sém. Med., 23: 229-233.

Marinesco, G. 1895 Les connexions du corps strié avec le lobe frontal. Compt. rend. Soc. Biol., 2: 77.

McCulloch, W.S. 1944 Functional organization of cerebral cortex. Physiol. Rev., 24: 390-407.

McCulloch, W.S., and Garol, H.W. 1941 Cortical origin and distribution of corpus callosum and anterior commissure in the monkey (Macaca mulatta). J. Neurophysiol., 4: 555-563.

Mettler, F.A. 1932 The Marchi method for demonstrating degenerated fiber connections within the central nervous system. Stain Technol., 7: 95-106.

Mettler, F.A. 1935 Corticofugal fiber connections of the cortex of Macaca mulatta. The parietal region. J. Comp. Neurol. 62: 263-291.

Mettler, F.A. 1935-36 Corticofugal fiber connections of the cortex of Macaca mulatta. The temporal region. J. Comp. Neurol., 63: 25-47.

Mettler, F.A. 1942 Neuroanatomy. St. Louis, C.V. Mosby, 476 pp.

Mingazinni 1922 Der Balken: Eine anatomische, Physiopathologische und klinische Studie. Berlin, Julius Springer, 212 pp.

Minkowski, M. 1923 Etude sur les connections anatomiques des circonvolutions rolandiques, pariétales et frontales. Schweiz. Arch. f. Neur. u. Psychiat., 12: 227-268. (Cited by Rundles and Papez,1937-38).

Minkowski, M. 1924 Etude sur des connections anatomiques des circonvolutions rolandiques pariétales et frontales. Schweiz. Arch. f. Neur. u. Psychiat. (Cited by Rundles and Papez, 1937-38).

Morin, F. 1950 An experimental study of hypothalamic connections in the guinea pig. J. Comp. Neurol., 92: 193-213.

Meynert, T. 1867 Der Bau der Grosshirnrinde und seine artlichen Verschildenheiten, nebst einem pathologischanatomischen corollarium. Vierteljahrschr. f. Psychiat., 1:77. (Cited by Kappers, Huber and Crosby, 1936)

Obersteiner, H.	1896	Anleitung beim studium des Baues der Nervösen Centralorgane ein gesundun und kranken Fustande. Leipzig und Wien.
Papez, J.W.	1942	A summary of fiber connections of the basal ganglia with each other and with other portions of the brain. A. Research Nerv. & Ment. Dis., Proc. (1940) 21: 21-68.
Penfield, W.	1949	The anatomy of memory. Read at a combined meeting of the Montreal Neurological Society and the Montreal Medico-Chirurgical Society, on November 4, 1949.
Penfield, W.	1950a	Functional localization in the cerebral cortex of man. Address to the Séminar in Neuroanatomy and Neurophysiology. April 24, 1950.
Penfield, W.	1950b	Functional levels in the nervous system. Address to the Seminar in Neuroanatomy and Neurophysiology. May 14, 1950.
Penfield, W., and Jasper, H.	1947	Highest level seizures. A. Research Nerv. & Ment. Dis. Proc.(1946) 26: 252-271.
Peter, R., Holden, L.B., and Jirout, J.	1949	The efferent intercortical connections of the superficial cortex of the temporal lobe (Macaca mulatta). J. Neuropath. & Exper. Neurol., 8: 100-103.
Poliak, S.	1927	An experimental study of the association, callosal, and projectional fibers of the cerebral cortex of the cat. J. Comp. Neurol. 44: 197-258.

Poliak, S.	1932	The Main Afferent Fiber Systems of the Cerebral Cortex in Primates. Berkeley, Calif., University of California Press, 370 pp.
Poliak, S., and Rei Hayashi	1936	The cerebral representation of the retina in the chimpanzee. Brain, 59: 51-60.
Probst	1901	Cited by Kappers, Huber and Crosby (1936).
Putnam, T.J.	1926a	Studies on the central visual system. A comparative study of the form of the geniculostriate visual system of mammals. Arch. Neurol. & Psychiat. 16: 285-300.
Putnam, T.J.	1926b	Studies on the central visual system. The details of the organization of the geniculo-striate system in man. Arch. Neurol. & Psychiat. 16:683-707.
Ranson, S.W.	1947	The Anatomy of the Nervous System, Its Development and Function. 8th ed. Revised by S.L. Clark. Philadelphia, W.B. Saunders, 532 pp.
Redlich, E.	1903	Zur vergleichenden Anatomie die Associations-systeme des Gehirns der Säugetiere. Das Cingulum. Arb.a.d. Inst. a.d. Wien. Univ. (Obersteiner's), 10: 104.
Rioch, D. McK.	1929	Studies on the diencephalon of carnivora. The nuclear configuration of the thalamus, epithalamus and hypothalamus of the dog and cat. J. Comp. Neurol., 49: 1-119.

Romanes, G.J. 1946 A new silver method for staining paraffin sections of the nervous system. J. Anat., 80: 205-206.

Rose, J.E. 1949 The cellular structure of the auditory region of the cat. J. Comp. Neurol.,91: 409-440.

Rose, J.E., and Woolsey,C.N. 1949 The relations of thalamic connections, cellular structure and evocable electrical activity in the auditory region of the cat. J. Comp. Neurol., 91: 441-466.

Rundles, R.W., and Papez, J.W. 1937-38 Fiber and cellular degeneration following temporal lobectomy in monkey. J. Comp. Neurol., 68: 267-296.

Sherrington, C.S. 1890 Note on bilateral degeneration in the pyramidal tracts resulting from unilateral cortical lesion. Brit.Med.J., Jan. 4th, p.14.

Streeter, G.L. 1912 The Development of the Nervous System. Philadelphia, J.B. Lippincott & Co., vol. 2.

Sugar, O., French, J.D., and Chusid, J.G. 1948a Corticocortical connections of the superior surface of the temporal operculum in the monkey (Macaca mulatta). J. Neurophysiol., 11: 175-184.

Sugar, O., French, J.D., and Chusid, J.G. 1948b Corticocortical connections of the superior bank of the Sylvian fissure of the monkey (Macaca mulatta). J. Neurophysiol., 11: 185-192.

Sunderland, S. 1938 The production of cortical lesions by devascularization of cortical areas. J. Anat., 73:120-129.

Sunderland, S. 1940 The distribution of commissural fibers in the corpus callosum in the macaque monkey. J. Neurol., Psychiat., 3: 9-18.

Swank, R.L., and Davenport,H.A. 1934 Marchi's staining method. II. Fixation. Stain Technol., 9: 129-135.

Swank, R.L., and Davenport,H.A. 1935 Chlorate-osmic formalin method for staining degenerating myelin. Stain Technol., 10: 87-90.

Talbot, S.A. 1942 A lateral localization in cat's visual cortex. Federation Proc. 1: 84.

Talbot, S.A., Woolsey, C.N., and Thompson,J.M. 1946 Visual areas I and II of cerebral cortex of rabbit. Federation Proc. 5: 103.

Tilney, F., and Riley,H.A. 1938 The Form and Functions of the Central Nervous System. 3rd ed., New York, Paul B. Hoeber, Inc.

Tunturi, A.R. 1944 Audio frequency localization in the acoustic cortex of the dog. Am. J. Physiol., 141: 397-403.

Tunturi, A.R. 1945 Further afferent connections to the acoustic cortex of the dog. Am. J. Physiol., 144: 389-394.

Türck, L. 1852 Uber secundare Erkrankung einzelner Rückenmarksstrange und ihren Fortsetzungen zum Gehirne. Ztschr. d.k.k. Gesellsch. d. Aerzte zu Wien ii, 511.

Turner, W. 1891 The convolutions of the brain. J. Anat. Physiol. 25: 105-153.

Ugolotti, F. 1900 Contribuzione allostudio delle vie peramidali nell' uomo. Anat. Anz. Ergänzungshefte, 18: 154. Cited by Kappers, Huber and Crosby (1936).

Verhaart, W.J.C., and Kennard,M.A.	1940	Corticofugal degeneration following thermocoagulation of areas 4, 6 and 4s in Macaca mulatta. J. Anat., 74: 239-254.
Vogt, C. and O.	1902	Zur Erforschung der Hirnfaserung. Neurobiolog. Arbeit., 1: 1-145.
Vogt, C. and O.	1919	Allgemeinere Ergebnisse unserer Hirnforschung. J. f. Psychol. u. Neurol., 25: 277-462 (Heft 1).
Vogt, C. and O.	1920	Zur Lehre der Erkrankungen des Striären Systems. J. f. Psychol. u. Neurol., 25: 208-253 (Heft 3).
von Bonin, G., and Bailey, P.	1947	The Neocortex of Macaca Mulatta. Urbana, Ill., University of Illinois Press, 163 pp.
Walker, A.E.	1936	An experimental study of the thalamo-cortical projection of the macaque monkey. J. Comp. Neurol., 64: 1-40.
Walker, A.E.	1937a	The thalamus in relation to the cerebral cortex. J. Nerv. & Ment. Dis., 85: 249-261.
Walker, A.E.	1937b	The projection of the medial geniculate body to the cerebral cortex in the macaque monkey. J. Anat. 71: 319-331.
Walker, A.E.	1938	The Primate Thalamus. The University of Chicago Press, 321 pp.
Waller, W.H.	1940	Thalamic degeneration induced by temporal lesions in the cat. J. Anat. 74: 528-536.

Walzl , E.M., and Woolsey,C.N.	1943	Cortical auditory areas of the monkey as determined by electrical excitation of nerve fibers in the osseous spiral lamina and by click stimulation. Federation Proc. 2: 52.
Wilson, S.A.K.	1913-14	Experimental research into the anatomy and physiology of the corpus striatum. Brain, 36: 426-492.
Winkler, C.	1927	Manuel de Neurologie. Haarlem, E.F. Bohn.
Winkler, C., and Potter, A.	1911	An anatomical guide to experimental researches on the rabbit's brain. Amsterdam, W. Versluys.
Winkler, C., and Potter, A.	1914	An anatomical guide to experimental researches on the cat's brain. Amsterdam, W. Versluys.
Woolsey, C.N., and Walzl, E.M.	1942	Topical projection of nerve fibers from local regions of the cochlea to the cerebral cortex of the cat. Johns Hopkins Hosp. Bull., 71: 315-344.
Young, M.W.	1936	The nuclear pattern and fiber connections of the non-cortical centers of the telencephalon in the rabbit. Johns Hopkins Hosp. Bull., 65: 295-401.
Young, M.W.	1941	Degeneration of the fiber tracts following experimental transection of the olfactory bulb. Anat. Rec., 79: 65-66.