EXPERIMENTAL STUDIES ON THE SUBTHALAMIC REGION IN THE CAT

by

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(Chairman, Graduate Council)

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I would like to express my most sincere appreciation to Dr. William A. Stotler, professor in charge of this research and thesis, for the friendship, kindness and instruction he has given to me during the last few years.

Descriptions of the anatomy and connections of the subthalamic nucleus or corpus Luysii are scattered in text books and the periodical literature of the basal ganglia and diencephalon. The multitude and diversity of the connections of this nucleus appearing in the literature illustrates the complexity of fiber systems involved in this region. For the most part, the classical works of Sano (36), Cajal (32), Wilson (44), Foix and Nicolesco (6), Kodama (16) and Dejerine (5) have been the basis for most of these studies.

Much of the anatomical interest in this region stems from the pathologic changes associated with the classical clinical entity of hemiballismus. Hemichorea or hemiballismus, as it appeared first in the German literature, became associated with pathologic changes in the subthalamic nucleus during the early part of the twentieth century (42). Prior to this time, confusion in nomenclature from various parts of the world prevented a clear understanding of this clinical entity. Anatomical interest at that time was stimulated by the concept of the extrapyramidal motor system and its probable implication of this system in various unexplained clinical syndromes.

The terms hemichorea and hemiballismus have been used interchangeably. It is believed that a German named Kussmaul coined the term "hemiballism", although many

authors have been unable to verify this reference. Others associated with this term have been such persons as von Economo, Fischer and Jakob. Bonhoeffer was one of the first to designate chorea definitely to the subthalamic lesion in 1897 (25). "Ballism" comes from the Latin ballista and from the Greek meaning "to throw".

One of the most important contributions to the subject of hemichorea was made by Martin (19) in 1927. On the basis of his studies he postulated a clearly defined syndrome associated with the corpus Luysi. Martin also believed that symptoms occurred when the interruption was at or below the main nucleus of the subthalamic system and accepted this as evidence that the system was physiologically a descending one. He had no evidence that focal injury of the upper part of the system caused chorea. He supported the view that a chorea resulted either from destruction of the body of Luys itself or from interruption of the fibers which descend from it. He also believed that the anatomical connections suggested that there was a higher control, possibly cerebral in origin, though widespread, in the striatum and pallidum.

The subthalamic nucleus is usually named by most neuroanatomists Corpus Luysi or subthalamic nucleus of Luys; historically Forel used this term. According to Dejerine (5), the corpus of Luysi was described incorrectly by Luys in 1865. Luys first described the nucleus of his

name, the accessory tract of the superior olive. In 1879 Henle named the corpus Luysi the corpus subthalamicum. Dr. Jules Bernard Luys (1828-1897) was a French physician who did neuroanatomical studies on the hypothalamus and was noted for his work in connection with the observation of degeneration of the anterior horn cells in progressive muscular dystrophy. Later in life he did research work in hypnotism; his contribution to the nucleus bearing his name remains obscure (2, 14).

In the literature there is very little mention about afferent connections to the subthalamic nucleus other than those from the striatum. Winkler (46) in 1928 gave a description of an abnormal or aberant bundle in a human brain. He believed that the bundle originated rostral to the subthalamic area and coursed caudally through its central part exchanging fibers and becoming smaller. He thought that this bundle of fibers continued on into the substantia nigra. Mettler (2) described a cortico-pontine tract but made no mention of an afferent subthalamic connection from the cortex. Dejerine (5) also noted subthalamic fibers but they proceeded from the internal capsule. He considered them unimportant in comparison to the large strio-subthalamic contribution. Levin (18) found that no degeneration could be traced to the subthalamic nucleus of Luys after frontal lobe lesions in the monkey.

Ramon y Cajal (32) described collateral fibers from the internal capsule ending in the subthalamic nucleus

and he thought these fibers were most probably cortical in origin. Papez (29) makes no mention of cortico-subthalamic fibers in his review of the fiber connections of the basal ganglia but he does describe a subthalamo-peduncular tract. Meyer, Beck, and McLardy (24) in 1947 reported a neuroanatomical investigation in human brains following prefrontal leucotomy. They noted gliosis in the subthalamic nucleus following leucotomy of the frontal lobe thereby confirming a pre-fronto-pontine tract (Arnold's Bundle) in the human brain. They claimed it passed down the medial aspect of the anterior limb of the internal capsule and terminated in dorso-medially situated cells of the anterior pons.

Recent reviews of the literature on the subthalamic region and basal ganglia by Whittier and Mettler (43), Ranson, Ranson and Ranson (34), and Woodburne (47) deal mostly with pathologic human and monkey specimens. These investigators and most of the earlier information on these fiber systems was obtained by studying normal material stained by the Weigert or Weil technique. The Marchi method was also used and these techniques resulted in conflicting reports in the literature due to the limitation of the technique. Papez (29), Johnson and Clemente (13) and Morgan (27) presented studies in the cat and dog brain regarding the connection of the basal ganglia using silver impregnation methods which are more suitable for this type of study.

The purpose of this investigation was to attempt to resolve some of the conflicts in the afferent and efferent connections of the subthalamic region by the experimental method.

MATERIALS AND METHODS

The series of experimental animals used for this study was composed of forty-five healthy young adult cats weighing between 1.5 and 3.5 kilograms. Electrocoagulative lesions were made with the Johnson Krieg modification of the Horsley-Clarke stereotaxic instrument. Coordinates for the stereotaxic instrument were taken from Winkler and Potter's Atlas (45); also Snider and Neimer's Atlas (38).

The lesions were made by a unipolar electrode, consisting of a tungsten wire insulated and enclosed in a twenty-five gauge needle tubing. After careful craniotomy and appropriate exposure, the electrode was inserted into the subthalamic nucleus, entopeduncular nucleus, lateral globus pallidus, field H of Forel and then a current of 4 ma. for forty to sixty seconds was used for electrocoagulation.

Several different approaches were made in an attempt to preserve fiber connections which would otherwise be destroyed by the electrode tract. The conventional posterior and vertical approaches proved valuable but also posterior angulation from the vertical was utilized. A curette was used for cortical extirpations which were made by manual removal of the cerebral cortex and underlying projection fibers anterior to the middle ectosylvian sulcus. Light intraperitoneal Nembutal was employed for anesthesia. The animals were allowed to survive for seven to fourteen

days, the optimum time lapse for recognition of primary neuronal and terminal degeneration. Three chronic cats were maintained for thirty days. The animals were then sacrificed by means of a lethal dose of intraperitoneal Nembutal followed by immediate thoracotomy and intracardiac perfusion with a 15% solution of formalin to insure adequate fixation necessary for the preservation of intact synaptic terminals. The brain was removed and fixed further in 15% formalin for a period of four weeks to six months. Following dehydration and parafin imbedding every fifth or tenth section was mounted and stained by a modification of the intensified protargol method as described by Stotler (40). The blocks were cut in transverse, horizontal and sagital planes. The sagital plane was particularly favorable for this study. Normal cats were prepared in the same manner for comparison with the experimental material using the silver and Weigert technique. A pathological human brain specimen using the Marchi stain technique was presented to illustrate certain fiber connections.

Investigators previously relied on the accepted Weigert, Marchi and Weil methods of staining for analysis of their material. Ramon y Cajal (32) in his investigation of the normal nervous system used the silver staining technique. Glees (9), Brodal (3), Stotler (39,41) and Nauta (28) and others in experimental studies of major fiber systems have also used various silver methods as a more reliable and

precise means of studying fiber degeneration in the central nervous system. The superiority of silver methods in the demonstration of degenerated axons, fine fibers and terminal ending degeneration prompted their use in this study.

In the histologic study of these silver preparations, degenerated fibers appear swollen, grossly argyrophilic and fragmented. Cellular detail is lost and the nuclei become eccentric and sometimes deformed in cells undergoing retrograde degeneration.

Forty-five animals were used during the course of the experiments but the histological analysis of only fifteen lesions will be presented to demonstrate the results of this investigation.

As a result of the many investigators' work on the subthalamic region, the connections most strongly advocated by one group have been denied or ignored by other groups, thereby leading to confusion and controversy. For this reason, a description of the subthalamic region of the cat with the nomenclature to be used in this paper seems necessary before describing the results. A diagramatic summary of the results of this study is shown in Figure 10.

The determination of fiber connections of the subthalamic area is made especially difficult because of the intricacy with which sheets and tracts of nerve fibers are woven in its immediate vicinity. In the early anatomic literature there was some controversy concerning the presence or absence of a well-defined or circumscribed subthalamic nucleus in carnivores. Kollicker, according to Sano (36), in 1893 was first to describe a subthalamic nucleus in cats, mice and rats. Ramon y Cajal (32) illustrated the nucleus in the cat as a string of cells several layers in thickness also describing an accessory subthalamic nucleus. He described the accessory nucleus as well developed only in cats and dogs. He reasoned that this cell group was split from the other part of the nucleus by a fascicle of fibers. Kodama (16) also recognized these two areas. Winkler and Potter (45) in Plate XXII in their atlas shows the subthalamic nucleus as part of the zona

incerta while the subthalamic nucleus is labeled the nucleus proprius pedunculi cerebri.

For purposes of this paper, the subthalamus in the cat can be divided into two main divisions; ventral and dorsal. The ventral nucleus is the nucleus which is usually thought of as the main subthalamic nucleus of Luys and can be seen in the cat, dog, monkey and human, while the dorsal division is that accessory nuclear area described by Cajal. The subthalamus develops from the lateral-ventral edge of the diencephalon. In three dimensions the ventral division has the shape of a biconvex lens or ellipsoid. It has its greatest transverse diameter at the level of the mamillary nuclei. In the sagital plane, it is found partially embedded in the internal capsule just before it forms the corpus peduncularis. The optic chaism is just ventral to this area. In horizontal section, the structure is ovoid and oriented at an angle of forty-five degrees to the mid-sagital plane; again its ventral most part imbedded in the internal capsule. Orientation of the rostral pole is dorsal-lateral and the caudal pole is ventral-medial. The dorsal division of this nuclear complex is located dorso-lateral to the aforementioned ventral division. It is also slightly rostral but in continuity with the ventral division. In the mid-sagital plane, the dorsal division is prominent, while in the more sagital plane the ventral division is more prominent. These two divisions of the subthalamus are bounded medially by the

mamillary nuclei of the hypothalamus and supramamillary decussation, laterally by the internal capsule and lateral globus pallidus, ventrally by the internal capsule or peduncle and dorsally by the fasciculus lenticularis and prerubral field of Forel. The blood supply to the subthalamic area comes from the posterior and inferior direction.

In the histologic study of the silver impregnated preparations, primary degeneration of efferents appeared as swollen, tortuous, darkly appearing, grossly fragmented fibers. With increasing length of survival period, the degeneration appeared as faint linear accumulations of argyrophilic debris lying along the course of the persisting axonal membrane.. Evaluation of cytological changes resulting from various lesions followed the usual criteria of: deformed and eccentric nucleus, shrinkage of cell mass, disruption and fragmentation of cytoplasmic and nuclear material, degeneration of neuropil with clearing of neuropil and loss of normal cell distribution and population. The striatum and pallidum in the cat are similar to the human, the striatum consisting of the caudate and putamen and the pallidum, the lateral globus pallidus and medial globus pallidus. In the cat, the medial globus pallidus is called the entopeduncular nucleus.

Cat 357. Manual cortical extirpation; Sagital section; five day degeneration.

The lesion and resulting degeneration in this case are

summarized in Figure 1. This lesion destroyed the left cerebral cortex anterior to the mid ectosylvian sulcus unilaterally. The gyri were undercut to destroy the fibers afferent to the internal capsule. Gyrus proreus was included in this extirpation.

The entire internal capsular fibers on homolateral side of the brain were destroyed; a slight vascular infarction is noted macroscopically and microscopically extending into the dorsal thalamus.

There was moderate degeneration noted in the dorsal aspect of the internal capsule beneath the subthalamus. The fascicles of fibers coursing through the dorsal and ventral subthalamic nuclei are diminished with subsequent loss of cellularity noted in dorsal lateral part of dorsal nucleus especially.

Thorough search of the lateral globus pallidus and entopeduncular nucleus revealed no degeneration.

There are finely myelinated fibers ascending or descending as the case may be from the peduncle into the posterior aspect of the ventral subthalamus. These fibers appear grossly intact but a few show degenerating qualities. More laterally there is loss of fascicles going into the rostral subthalamic area. Again, a few posterior inferior fibers are degenerated with the larger percentage remaining intact.

Good detail can be seen in the degenerating fibers arising from the peduncle and coursing singly or in small

Figure 1. A series of three drawings to illustrate representative sections of cat 357. (1) The extant of the lesion is shown in the hatched area. (2) Note degeneration in dorsal internal capsule with loss of fascicles from internal capsule into the subthalamic nucleus. Slight degeneration in fibers in the posterior inferior ventral subthalamic nucleus. Note degeneration in ascending cortico-reticular tract. (3) Note degeneration in the lateral part of the dorsal subthalamic nucleus also loss of fascicles from the internal capsule.

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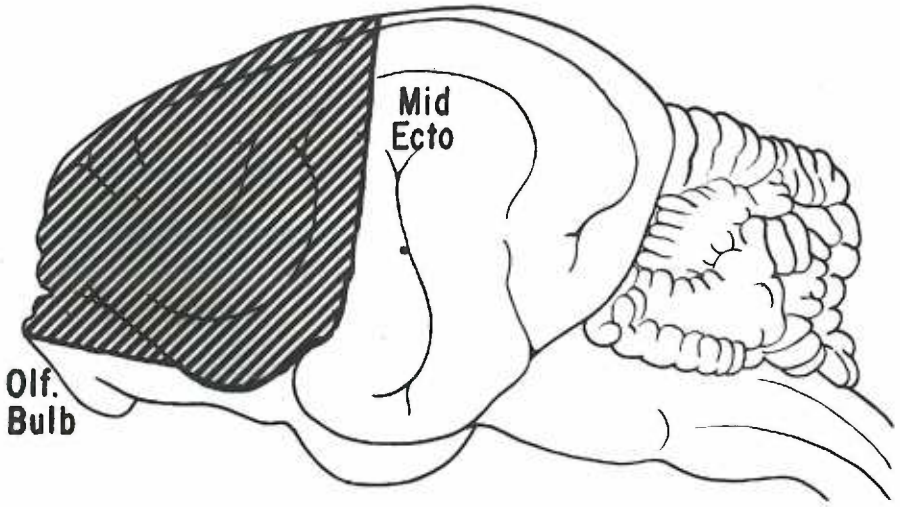

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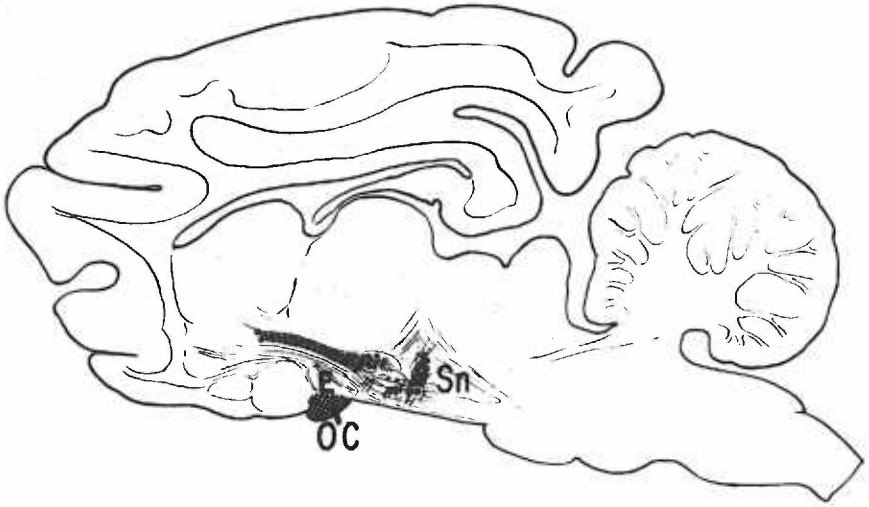

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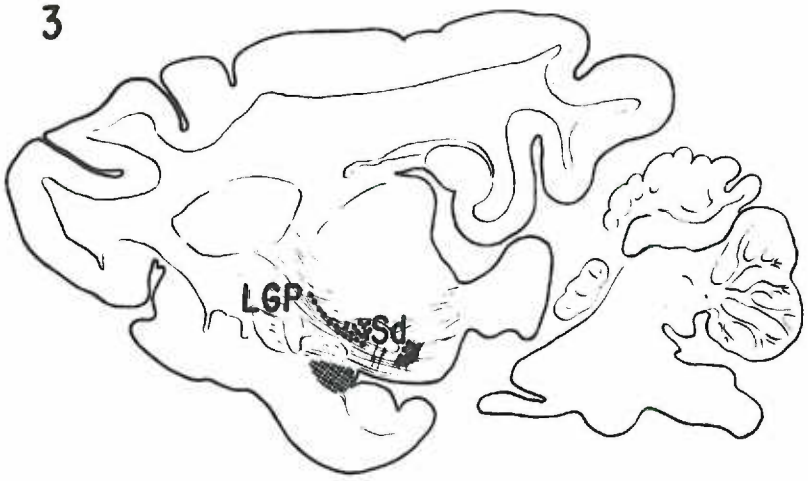

groups in an ascending direction caudal to the ventral subthalamic nucleus and rostral to the substantia nigra. Fibers ascending are moderately swollen with occasional fragmentation and small amounts of axonal debris are present. These fibers are seen ascending from the mid peduncle until they disappear higher in the midbrain tegmentum. It was not possible to follow these fibers to their termination.

Cat 358. Manual cortical extirpation; Sagital section; fourteen day degeneration.

This lesion destroyed the same unilateral left cortical area as that of 357 but a longer degeneration period was allowed post-operatively. Again, loss of dorsal internal capsule fibers just ventral to the subthalamic nucleus is present with loss of fascicles from the internal capsule to the subthalamic nucleus. Swollen fibers and loss of cellular detail in the dorsal division of the subthalamic area where the internal capsule or cortical fibers come into the subthalamus was noted; also a decrease in cellularity, swollen and distorted fibers are evident.

Thorough examination revealed no degeneration of lateral globus pallidus or entopeduncular nucleus. A very minimal extension by vascular infarction was noted in the lateral tip of the putamen.

Fibers from the peduncle to the caudal ventral subthalamic nucleus appeared grossly intact with only minimal degeneration changes noted. Again, the ascending

fibers caudal to the subthalamic complex and rostral to the substantia nigra showed degeneration as described in Cat 357.

Cat J13. Electrocoagulation lesion; Transverse section; seventeen day degeneration.

The lesion and degeneration are summarized in Figure 2. This lesion was made by the posterior approach through the midbrain on the left side. The needle tract is very small with only minimal surrounding infarction and cellular reaction. The more rostral area shows the electrocoagulation to be in the corpus peduncularis immediately ventral and lateral to the ventral division of the subthalamic nucleus. Degeneration is noted in the lateral part of the ventral subthalamic nucleus with loss of cellular detail and decreased cellularity. Inspection of lateral globus pallidus and entopeduncular nuclei shows no degeneration.

Cat J33. Electrocoagulation lesion; Sagital section; nine day degeneration.

The lesion and resulting degeneration are summarized in Figure 3. This was a vertical electrocoagulation from a slight anterior angulation. The electrode needle in its course into the left lateral globus pallidus passed through the genu of the internal capsule thereby destroying the fibers in this area. It was therefore a combination of lateral globus pallidus and partial internal capsular lesion.

As in the cortical lesions of Cat 357 and 358, there is loss and degeneration of fascicles through the subthalamic nucleus but not as marked in this case. The dorsal peduncle

Figure 2. A series of three drawings to illustrate representative sections of cat J-13. (1) This shows the well localized electrode tract with no extension into the surrounding tissue. (2) Rostral extension of needle tract, no vascular infarction of nearby tissue, slight secondary infarction around needle tract (stipple). (3) Well localized lesion in peduncle beneath the subthalamic nucleus with minimal infarction. Degeneration in homolateral subthalamic nucleus (fine stipple).

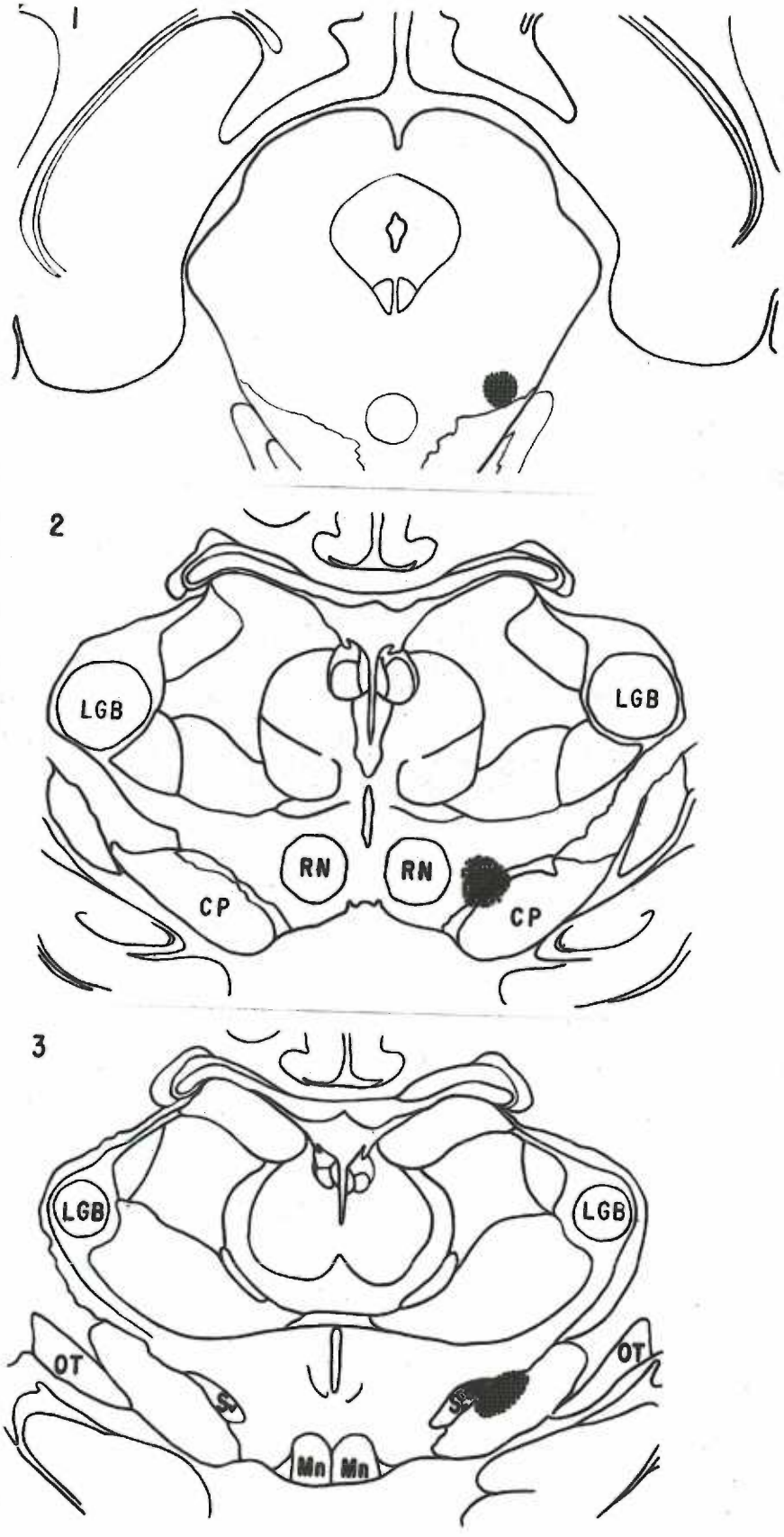
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Figure 3. A series of three drawings illustrating representative section of Cat J33. (1) Schematic of lesion with electrode angled toward the lateral globus pallidus (grid). (2) Very minimal degeneration in fascicles passing through the ventral and dorsal subthalamic nucleus. Also minimal loss in cortical reticular fibers (fine stipple). (3) Lesion shows destruction of lateral globus pallidus and partial interruption of the internal capsule. No destruction of the entopeduncular nucleus is noted.

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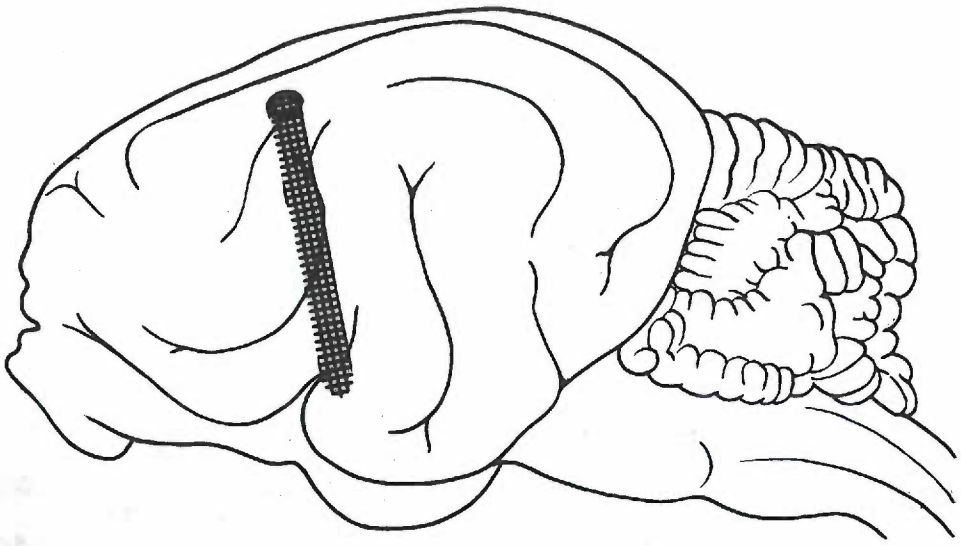

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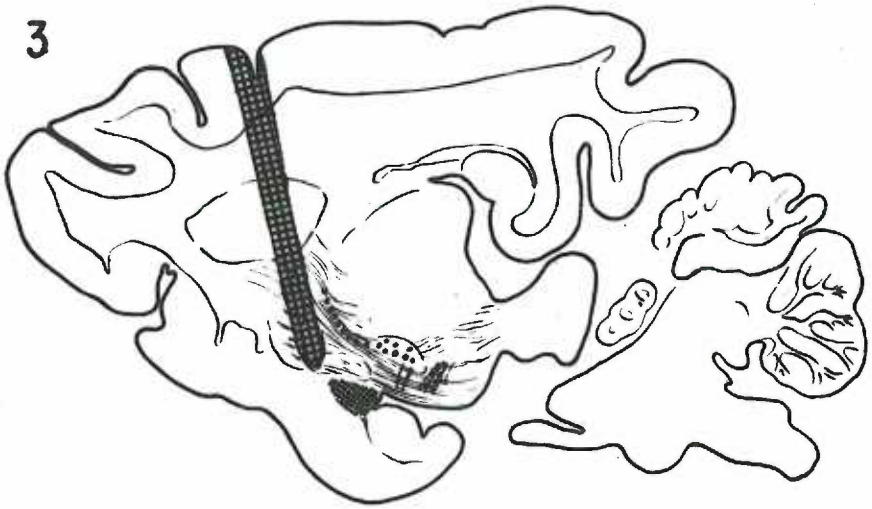

beneath the subthalamus is also mildly degenerated. There is moderate degeneration in the lateral part of the dorsal division of the subthalamus, with only very minimal loss in the ventral division. No degeneration is noted in the lightly myelinated fibers ascending from the peduncle into the caudal-inferior portion of the ventral subthalamus.

There is mild degeneration of ascending fibers caudal to subthalamus and rostral to substantia nigra, but not as marked as seen in the pure cortical lesion of Cats 357 and 358. The entopeduncular nucleus is intact with no primary or secondary degeneration.

Cat J21. Electrocoagulation lesion; Sagital section: seven day degeneration.

This lesion was made by posterior approach, the electrode tip extended to the caudal tip of the left ventral subthalamic nucleus. It is also extended ventrally into a portion of the dorsal peduncle beneath the subthalamus. In selected sagital sections some fibers can be seen ascending from the peduncle both normal and some with very minimal degenerating qualities. This ascending pathway is caudal to the subthalamus and rostral to the substantia nigra.

Cat J8. Electrocoagulation lesion; Sagital section; ten day degeneration.

The lesion and resulting degeneration are summarized in Figure 4. This lesion was made by the posterior approach and the electrode tip was located caudal and

Figure 4. Two drawings to illustrate representative section of Cat J8. (1) Posterior approach with electrocoagulation needle (grid) only minimal degeneration in a few ascending fibers is noted (stipple). (2) Infarction of the lateral part of the dorsal subthalamic nucleus with resulting degeneration in the ascending fibers (stipple).

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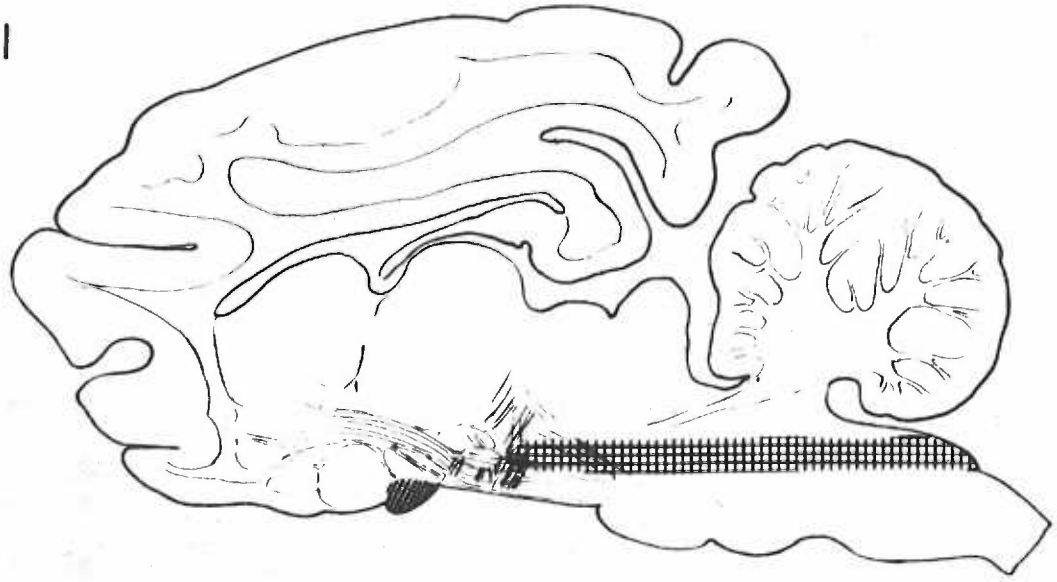

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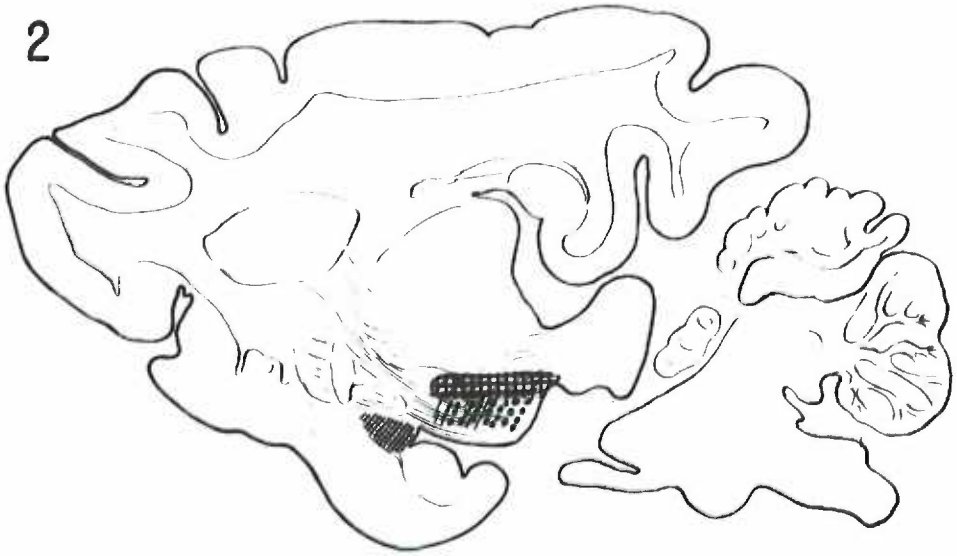


dorsal to the left ventral subthalamic nucleus. The ascending pathway from the peduncle can be seen as described in Cat J21. At the lateral extent of the lesion, diffusely spread fibers can be seen ascending from the peduncle to the dorsal tegmental area through the caudal subthalamic region and also through the substantia nigra.

Cat XP1. Electrocoagulation lesion; Transverse section; twelve day degeneration.

The lesion was placed along the left putamen and lateral globus pallidus. The primary electrocoagulation destroyed the entire putamen and lateral globus pallidus. There was both macroscopic and microscopic evidence of a vascular infarction of the adjacent internal capsule and head of the caudate nucleus. Extensive degeneration is noted in the homolateral entopeduncular nucleus. The subthalamic nucleus on the involved side has a moderate loss of neuropil and loss of afferents from the entopeduncular nucleus is evident coursing through the peduncle. There are degenerating fibers noted in the fasciculus lenticularis also. There was evidence of degeneration in the lateral aspect of the thalamus on the homolateral side which was secondary to the primary electrocoagulation.

Cat J16. Electrocoagulation lesion; Transverse section; six day degeneration.

The lesion and resulting degeneration are summarized in Figure 5. The lesion is very similar to Cat XP1 with the primary electrocoagulation involving the left putamen,

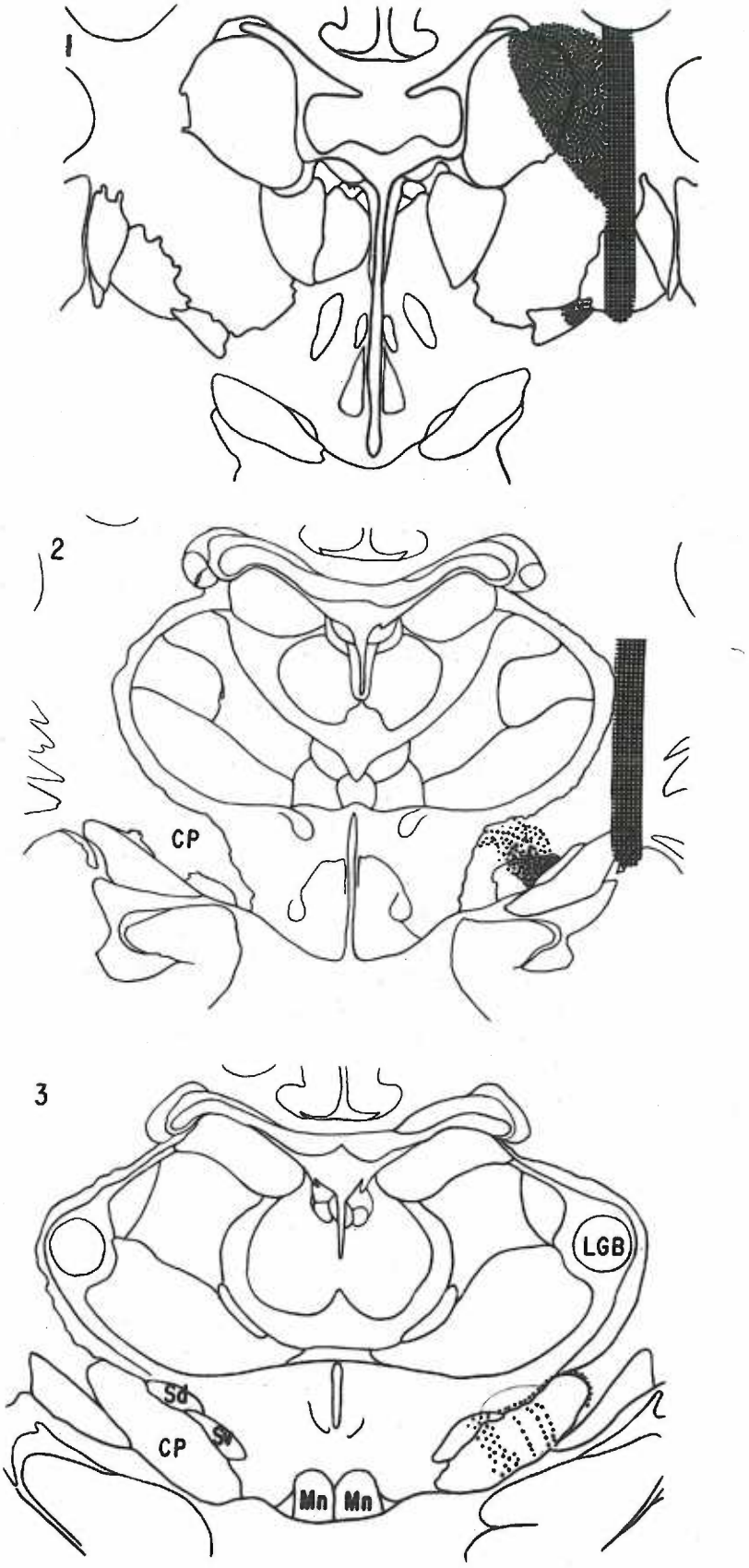
caudate and only the lateral tip of the lateral globus pallidus. This lesion was made from the vertical approach in contrast to Cat XP1, which was made from the posterior approach. Again, the vascular infarction is noted in the internal capsule and lateral aspect of the thalamus. Degeneration in the homolateral entopeduncular nucleus is slight compared to Cat XP1 and limited to the middle and lateral aspects of this nucleus macroscopically. Microscopically, however, the entire nucleus has loss of cellularity and degenerative qualities. Again, homolateral degeneration is noted in the fasciculus lenticularis and only minimal loss of neuropil is noted in the dorsal and ventral subthalamic nuclei.

Cat J37. Electrocoagulation lesion; Sagital section; seven day degeneration.

The electrode was placed in the left lateral globus pallidus from the vertical approach. The needle tract had minimal infarction surrounding it and passed into the basal part of the lateral globus pallidus destroying it completely. A very small portion of the internal capsule at its lateral-most extension was interrupted with very minimal loss of internal capsule fibers noted. No infarction was noted in the thalamus.

After careful search, no degeneration is noted in the ventral subthalamic nuclei. Very slight degeneration is noted in the rostral dorsal subthalamic nucleus. The fascicles that course through the nucleus previously

Figure 5. A series of three drawings to illustrate representative sections of Cat J16. (1) Forward extent of the vertical lesion (grid) into the lateral globus pallidus. Note secondary infarction of the needle tract into the lateral aspect of the thalamus (coarse stipple). Degeneration noted in the lateral entopeduncular nucleus (fine stipple). (2) The lesion is marked with very little secondary infarction. Note degenerated entopeduncular nucleus and "comb" fibers coursing through the peduncle to the subthalamic region (fine stipple). (3) Degeneration in the fasciculus lenticularis (stipple) noted with some loss of fibers in the peduncle. Only slight loss of neuropile in the subthalamic nucleus.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explained are intact.

On the contralateral side to the lesion, no degeneration was noted in the subthalamic nuclei.

Cat J36. Electrocoagulation lesion; Transverse section; fourteen day degeneration.

The lesion and resulting degeneration are summarized in Figure 6. This lesion was made by vertical approach. The electrode passed through the cortex into the lateral globus pallidus. There was no thalamic infarction macroscopically or microscopically. The needle tip made a lesion on the medial extent of the lateral globus pallidus with secondary vascular infarction of the lateral entopeduncular nucleus. Degenerating fibers can be traced through the peduncle (entopedunculo fugal) into the ventral subthalamic nucleus. The ventral subthalamic nucleus has loss of cellular detail and argyrophilic degeneration is present.

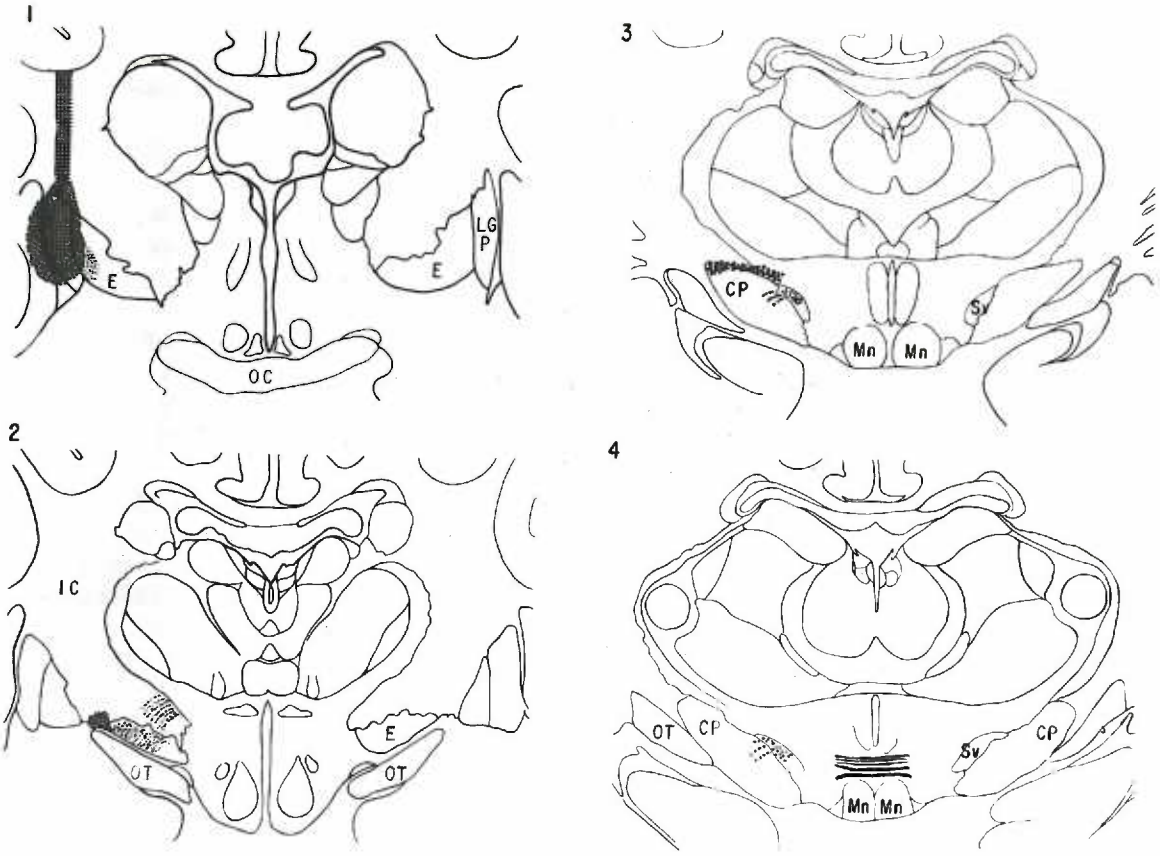
The fasciculus lenticularis shows slight degeneration; also there is slight loss of cellular clarity and degeneration in the dorsal subthalamic nucleus. On cross section, one is able to see the many fascicles passing through the subthalamus that are so easily seen on sagital section in other brains. In this case they are intact.

The supramamillary decussation shows minimal degeneration with a few finely myelinated, tortuous, swollen fibers noted.

Cat J7. Electrocoagulation lesion; transverse section; eight day degeneration.

The lesion and resulting degeneration are summarized

Figure 6. A series of four drawings to illustrate representative sections in Cat J36. (1) Anterior extent of the lesion with electrode tract, slight secondary infarction (coarse stipple). Note small infarction secondary to lesion in lateral entopeduncular nucleus (fine stipple). No part of the thalamus was infarcted secondarily. (2) Tip of electrode and secondary degeneration (fine stipple) noted in entopeduncular nucleus. (3) Degenerating fibers coursing into the subthalamic nucleus with loss of cellularity (fine stipple). Also, the fasciculus lenticularis is degenerated with some loss into the dorsal subthalamus (coarse stipple). (4) Minimal degeneration is noted in supramamillary decussation, (solid lines).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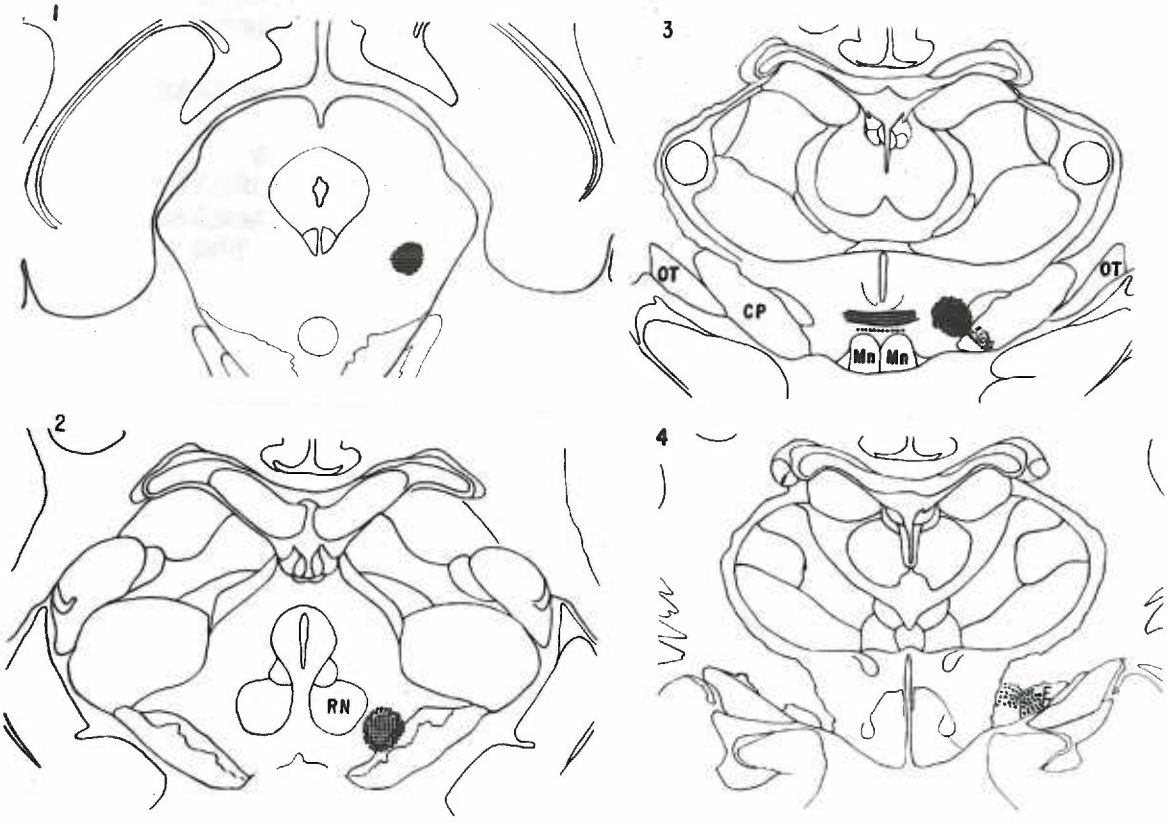
in Figure 7. The electrode was inserted from the posterior approach, its tip passing into the medial ventral subthalamic nucleus. Limited cellular reaction is noted around the electrode path and no gross infarction occurred along its path. There are degenerating fibers noted coursing through the peduncle with loss of cellular detail, loss of neuropil and debris is noted in the homolateral entopeduncular nucleus. There is minimal degeneration in the supramamillary decussation, characterized by swollen, finely myelinated fibers. There is also a change in cellularity and loss of neurons in the contralateral medial ventral subthalamic nucleus.

Cat J20. Electrocoagulation lesion; Transverse section; seven day degeneration.

This lesion is identical with that of Cat J7. Again the posterior approach was used; the electrode tip is well localized in the medial ventral subthalamic nucleus. The lesion was well localized and only minimal hemorrhage beyond the needle tract was noted. This lesion was slightly more medial than Cat J7, thereby not injuring the ventral subthalamic as extensively. No thalamic degeneration is noted after careful examination. The commissure of the fornix is noted to be more grossly degenerated in this case with the finely myelinated fibers showing swollen and distorted qualities. There is argyrophilic debris and beading within the thin terminal neuropil. The decussation of the fornix is located ventral

Figure 7. A series of four drawings to illustrate representative sections of Cat J7. (1) Electrode tract (grid) with minimal cellular necrosis beside the tract. (2) Electrode tract continued involving the substantia nigra lateral and ventral to the red nucleus. (3) Medial ventral subthalamic nucleus destroyed by lesion. Degeneration noted in the peduncle leading retrograde into the entopeduncular nucleus (fine stipple). Note slight degeneration of the commissure of the fornix. (4) Degeneration noted especially in the medial aspect of the entopeduncular nucleus. Also degeneration noted in the peduncle (fine stipple).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to the supramamillary decussation and just dorsal to the mamillary nuclei.

Cat J23. Electrocoagulation lesion; Transverse section; twenty-two day degeneration.

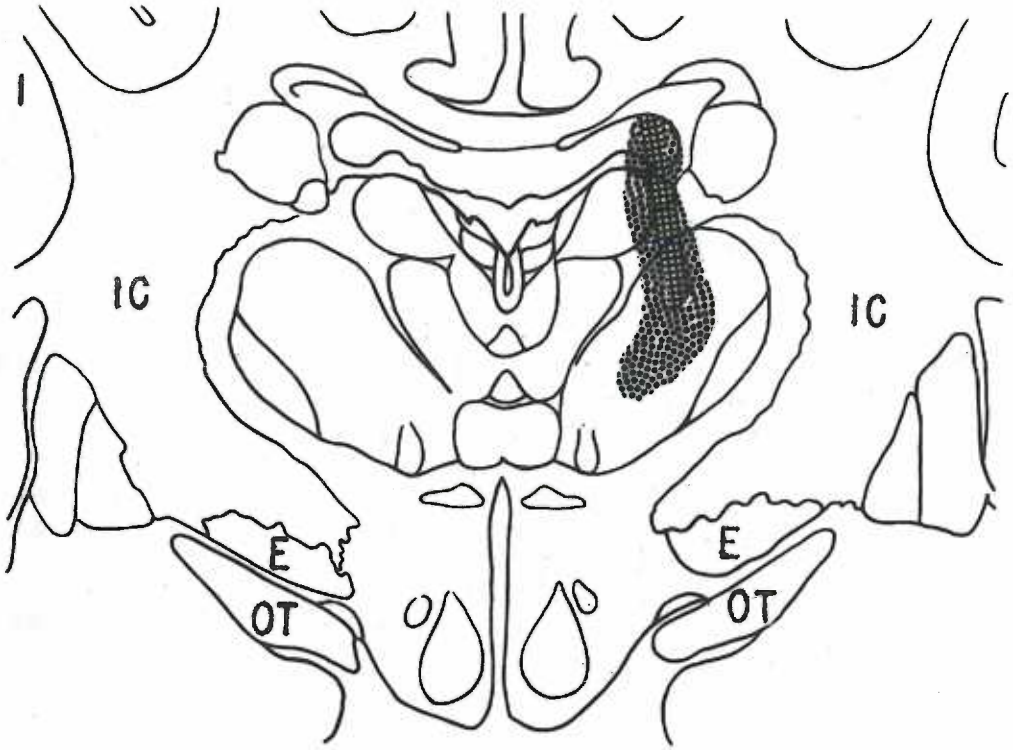
The lesion and resulting degeneration are summarized in Figure 8. The lesion was made by the vertical insertion of the electrode with slight posterior angulation into the medial aspect of the dorsal subthalamus, injuring the fasciculus lenticularis and only the dorsal tip of the ventral subthalamic nucleus. The lesion extended into the prerubral field of Forel. The electrode tract passed through the lateral thalamic nucleus and a portion of the fornix.

Degeneration was observed in the homolateral fasciculus lenticularis coursing in the direction to the lateral globus pallidus. These fibers were grossly distorted and argyrophilic debris is noted in many areas. The contralateral fasciculus lenticularis is intact with no degeneration noted. The heavily myelinated fibers of the supramamillary decussation show minimal degeneration.

Cat J15. Electrocoagulation lesion; Transverse section; Seven day degeneration.

The lesion and resulting degeneration are summarized in Figure 9. This lesion was made by the posterior approach similar to Cat J20, but this lesion was more extensive. The tip of the electrode made a lesion involving the entire subthalamic complex and vascular infarction extended into the dorsal peduncle ventrally

Figure 8. Two drawings to illustrate representative sections in Cat J28. (1) Forward extension of electrode tract (grid) with minimal vascular infarction around electrode tract (coarse stipple). (2) Electrode tract with minimal vascular infarction noted. a) Degeneration in homolateral fasciculus lenticularis b) Degeneration in supramamillary decussation (dotted line) c) Normal fibers in the contralateral fasciculus lenticularis (lines).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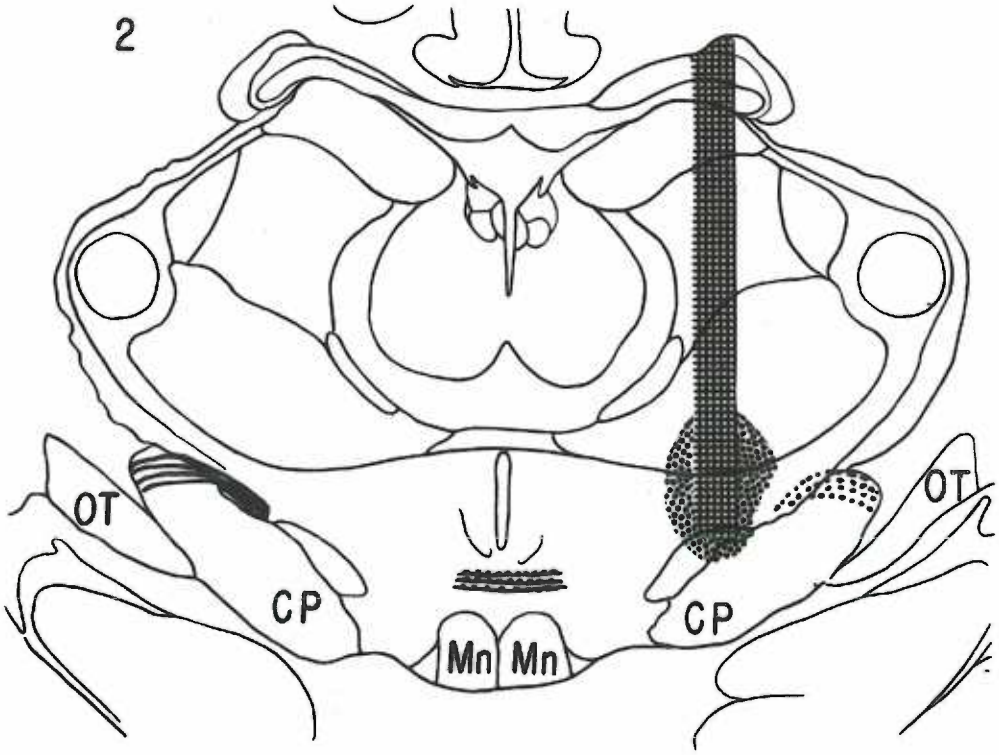
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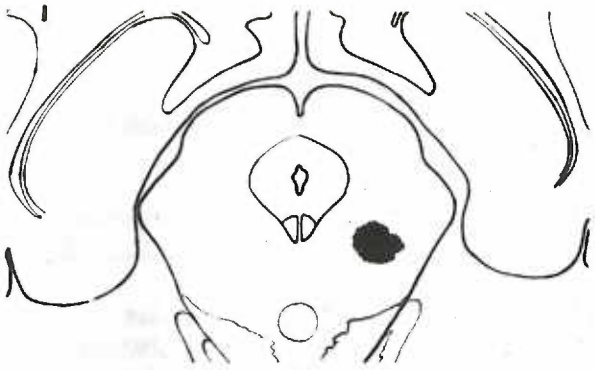
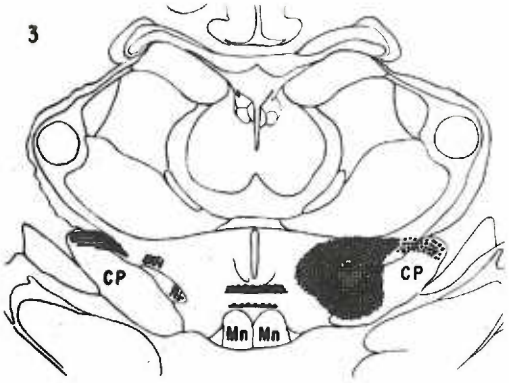
Figure 9. A series of four drawings to illustrate representative sections of Cat J15. (1) Electrode tract (grid) slight extension by vascular infarction (coarse stipple). (2) Electrode tract continued, again minimal surrounding vascular infarction. (3) Lesion involving the dorsal subthalamic nucleus, the peduncle and prerubral field. Note degeneration in the supramamillary decussation, contralateral subthalamic, homolateral fasciculus lenticularis (dotted line) and note the intact contralateral fasciculus lenticularis (line). (4) Forward extension of the electrocoagulation lesion with secondary infarction.

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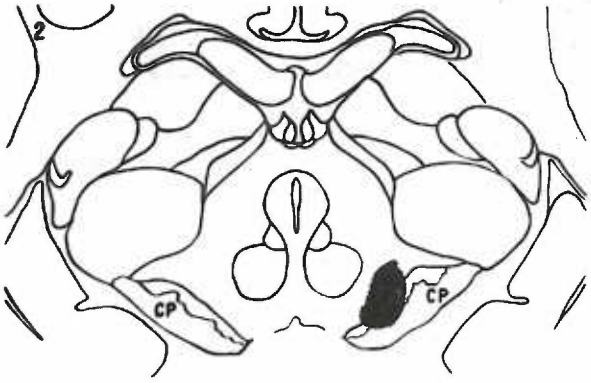
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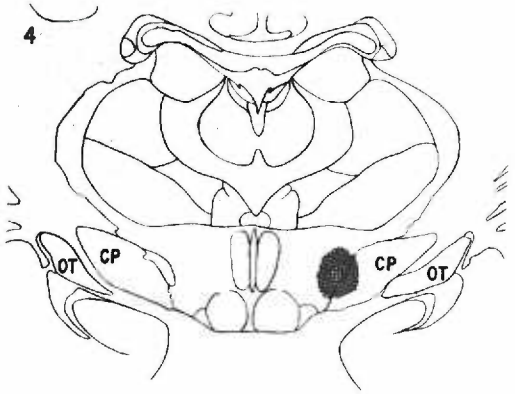
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and dorsally the lesion included the prerubral field of Forel. Medially the supramamillary decussation area was not involved primarily, but secondary degeneration is noted in the commissure of the fornix. The contralateral ventral subthalamic nucleus shows moderate loss of neuropil and loss of normal cellularity. Homolateral degeneration is noted in the fasciculus lenticularis. No thalamic degeneration is observed macroscopically or microscopically.

Cat J14. Electrocoagulation lesion; transverse section; six day degeneration.

This lesion was made by inserting the electrode vertically into the dorsal subthalamic nucleus. The electrode tip continued down through the fasciculus lenticularis and into the peduncle. The electrode tract was limited with only minimal vascular infarction. The electrode passed through the lateral thalamus en route to the subthalamic area. This lesion spared the prerubral field of Forel. There was no degeneration in the supramamillary decussation. There was slight degeneration noted in the homolateral fasciculus lenticularis.

Cat J2. Electrocoagulation lesion; Horizontal section; eight day degeneration.

This lesion was made by the conventional posterior approach with the tip of the electrode ending in the area medial to the subthalamus and posterior at the level of supramamillary decussation. The horizontal section was used to study this case. The lesion is extensive with satellite hemorrhage and secondary vascular infarction.

Some degenerative changes are noted in the contralateral entopeduncular nucleus consisting of loss of cellularity and argyrophilic debris in the medial aspect of that nucleus. There is minimal degeneration noted on the homolateral entopeduncular nucleus.

Human MS#1. Cerebro-vascular accident; Marchi technique.

For correlation with human antomy, a Marchi stained human pathologic brain is examined. This patient encountered a cerebral vascular accident involving the artery supplying the medial globus pallidus, the anterior choridal artery. The Marchi staining technique stains degenerating myelin. It is not the ideal method to follow degenerating fibers because of its sporatic and inconsistent staining characteristics, but this case shows an interesting finding. Degeneration is noted passing from the medial globus pallidus through the peduncle via the "comb" system into the subthalamic nucleus. The dark debris coursing through the peduncle into the ellipsoid-shaped subthalamic nucleus shows the pallidal-fugal fibers to the subthalamic nucleus in the human brain. The darkly stained degenerating fibers can be followed therefore, from the medial globus pallidus into the homolateral subthalamic nucleus. Degenerating myelin is spread homogeneously and diffusely throughout the subthalamic nucleus on the side of the lesion. Examination of the supramamillary decussation was impossible because the tissue of this area was not included.

Figure 10. A schematic diagram representing a partial summary of the connections of the subthalamic region in the cat. Heavy lines represent a large amount of fibers, while fine lines denote smaller contributions of fibers.

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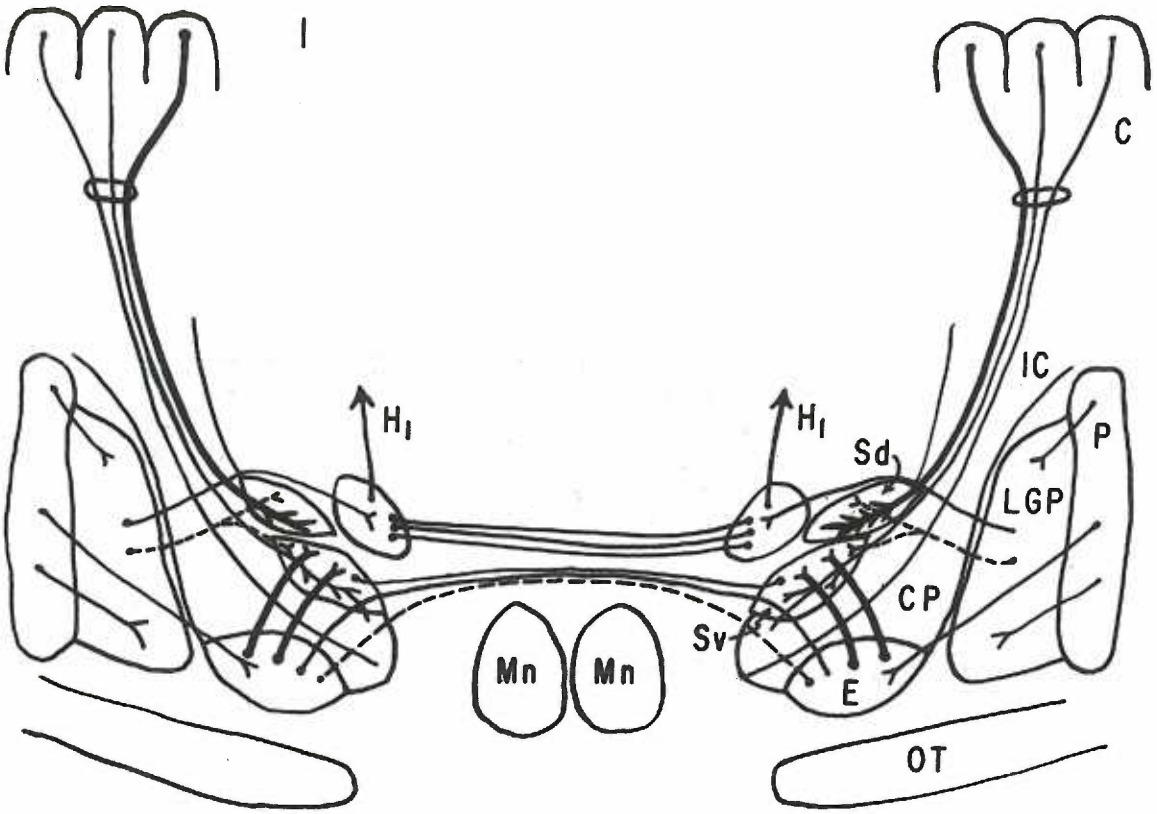

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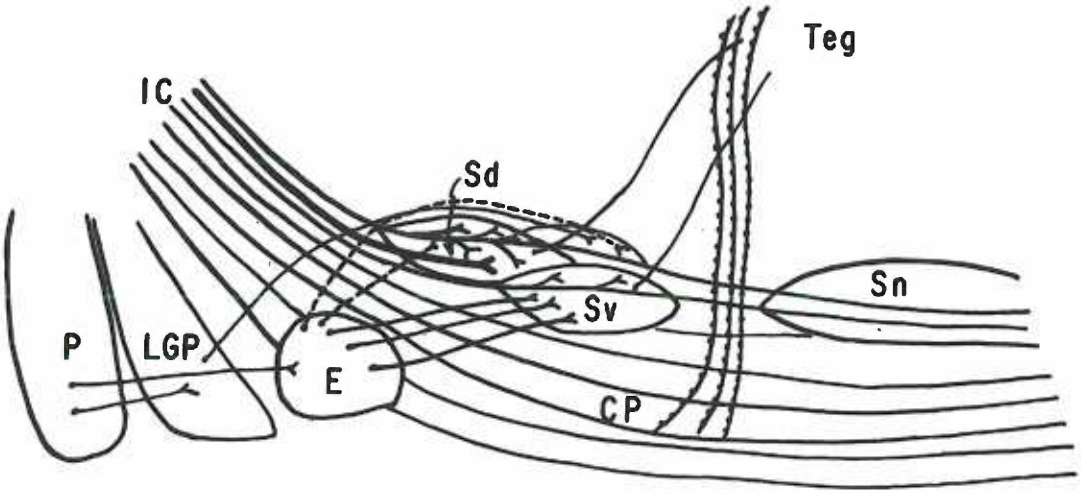

Cortical Subthalamic Fibers

An anatomical curiosity relating to the subthalamic nucleus was reported in human material by Winkler (46) who described a remarkable aberrant bundle gathering rostral to the subthalamic nucleus. These fibers apparently originated in the internal capsule and perforating fibers were described that coursed caudally through its very central part exchanging fibers and becoming smaller. These fibers then continued on into the substantia nigra, according to Winkler. He considered this group or fascicle of fibers to be abnormal in the human brain. This fascicle began in the medial part of the rostral part of the internal capsule above the optic chiasm. He also believed that this fascicle became stronger by contributions from the "comb" system. He observed that this fascicle entered the nucleus in the fronto-dorsal part and passed in a caudal direction. He also noted that the fibers split and went into the medial and intermediate area of the substantia nigra. It then formed two bundles or fascicles and proceeded into the lateral pontine field. He claimed these two fascicles reunited in the pons and then proceeded back to the peduncle. At the time of description, he also believed that von Monakow was aware of this group of fibers and considered it difficult to trace them beyond this point, but he believed that they went into the spinal cord.

After pre-frontal leucotomy, gliosis and pathologic changes in neurons were observed in two of eight cases by Meier, Beck and McCarty (24). They confirmed in the human brain that a pre-fronto pontine tract or Arnold's bundle at least existed. They tentatively suggested that it had its origin in area ten of the cerebral cortex. Through anatomical studies, they traced it down the medial aspect of the anterior limb of the internal capsule and believed that it terminated in the dorsal medial situated cells of the anterior pons. They also mentioned fiber terminations of this tract in the subthalamic nucleus and the substantia nigra.

Mettler (22) described a cortical subthalamic tract in the baboon and monkey. They reached the corpus subthalamicus after traveling for some distance with the fasciculus thalamicus. Earlier, Mettler (21) described the cortico-subthalamic fibers arising from the middle and inferior frontal gyri. He believed that these fibers proceeded and penetrated partially with the pallidal fibers and partially as fibers accompanying the thalamic fasciculus. Mettler (20), while working on the monkey, also described the cortical original of this tract in Brodmann area nine.

In 1935, Levin (18) could find no degeneration to the subthalamic nucleus after frontal lobe lesions in the monkey. In his publication, he denied any cortical subthalamic fibers, as did Wilson (44). Wilson found no

experimental proof of cortical subthalamic fibers in apes as described by previous workers such as Dejerine (5). The presence of a direct cortical connection with the basal ganglion has never been generally accepted. Glees (8) described a direct cortical striate connection in the cat. He noted degeneration in the caudate nucleus resulting from ablation of the cortical suppressor strip area but his demonstration seems far from conclusive.

Dejerine (5), in 1901, studied the subthalamic nucleus. He noted a few cortical fibers from the internal capsule proceeding into the back part of the nucleus. He also noted at that time, decussating subthalamic fibers to the contralateral side in the supraoptic decussation of Ganzer.

In summary, Dejerine (5) said this:

> "le corps de luys depend essentiellement du corps strie: il degenere chaque fois que le globus pallidus, le putamen et le noyau caude sont detruits. Il envoie quelques fibers dans la substance grise interpedonculaire et recoit de la corticalite cerebrale quelques tres rares fibers qui passent par les lames medullariu du globus pallidus."

In his research he noted cortico-subthalamic fibers infrequently. He could not demonstrate these fibers using the Weigert-Pal technique, but was able to demonstrate them using the Marchi technique of staining degenerating myelin.

Kodama (16), in 1928, after the examination of two adults and two embryonic human brains, also described the abnormal bundle that Winkler had previously described. He

also thought that these were cortical in origin.

Cajal (32) described collateral fibers which he thought were most likely cortical in origin coming from the internal capsule and ending in the subthalamic nucleus. In 1925, Foix and Nicolesco (6) could not demonstrate cortico-subthalamic fibers in the human brain.

Shaner (37) worked on the development of the finer structures and fibers of the connections of the globus pallidus and subthalamic nucleus in the pig. He thought the pallidal fibers ran with the cortical fibers into the subthalamic nucleus; these fibers breaking into a terminal felt around the cells of that nucleus. Shaner found no collateral fibers as described by Cajal. He belived that the fibers coming in the posterior subthalamic nucleus could be ascending fibers from a caudal source, but was unable to determine their origin.

Morgan (26), using the dog and the metalic staining technique, thought that it was possible that most, if not all cortical fibers to the region of the thalamus and subthalamus entered the thalamus and zona incerta from the lateral side and did not lay in close proximity to the subthalamic nucleus. He believed that they probably passed dorsal and ran perpendicular to the descending fibers of the subthalamic nucleus.

In cat 357 and Cat 358, cortical extirpation was performed and resulted in secondary degeneration of the afferents to the subthalamic nucleus. Degeneration was noted by loss of fascicles through both the dorsal and

ventral part of the subthalamic nucleus and also marked loss of cellularity in the lateral dorsal part of the nucleus. In both of these cats, the globus pallidus and entopeduncular nucleus were intact, by evidence of an intact "comb" system; only the cortex was destroyed unilaterally. The dorsal subthalamic nucleus receives a larger cortical projection than does the ventral subthalamic nucleus in the cat.

In summary, the cortical subthalamic fibers are derived from the cortex and run in the dorsal internal capsule until they come to the subthalamic nucleus where they form fascicles and proceed into the nucleus, both ventral and dorsal parts in the cat, and course through in a caudal direction. These fascicles get smaller as they pass through the nuclei and degeneration is noted in the size of the fascicle and in the cellular detail of these nuclei when the cortical area is removed surgically.

Cortico-reticular Fibers

In cats 357 and 359, and in all other cats with internal capsular lesions, it was noted that degenerating fibers ascended from the caudal inferior portion of the ventral subthalamic nucleus in the direction of the tegmentum. These fibers run in an ascending direction rostral to the substantia nigra. The degeneration noted is proportional to the amount of cortex removed. Marked to moderate degeneration was noted in all cats with unilateral cortical extirpations. In the cats with only a small lesion

in the internal capsule, minimal degeneration was noted in these ascending fibers. It was impossible to follow these ascending fibers into their termination in the tegmentum. No conclusion can be drawn as to the termination of these fibers, except that they appeared to be in the direction of the tegmentum and reticular formation.

The only mention of this fiber tract that I was able to find was that of Kimmel (15). He worked with the cat and described a nigrostriatal tract. He detected degenerating fibers coursing rostrally in the basis pedunculi and internal capsule following Horsely-Clark electrocoagulation lesions in the substantia nigra. He followed degeneration to the level of the entopeduncular nucleus and globus pallidus where many fibers ended. Some degenerated fibers extended rostrally within the internal capsule beyond the globus pallidus but technical difficulty prevented him from determining their termination. He may have destroyed some of the cortico-reticular fibers with his electrode.

In summary, it appears that this ascending pathway has its origin in the cerebral cortex and runs in the internal capsule and then peduncle until it ascends into the tegmental region at the subthalamic area. This ascending pathway is referred to in this paper as the cortico-reticular pathway.

The Pallido-subthalamic Fibers

For many years it has been known that the subthalamic nucleus had its primary afferent connection with the globus

pallidus. Cajal, Deferine, Foix and Nicolesco and all the early workers on this particular area of the brain were in agreement that the subthalamic nucleus received fibers from the globus pallidus. The polarity of the fibers from the globus pallidus to the subthalamic nucleus has been disputed for the past fifty years. Also, the origin of the pallido-subthalamic fibers has been disputed. Ranson and Ranson (34), using experimental material, and Papez, Bennett and Cash (30), using human material, considered the connections between the lateral globus pallidus to be stronger than those from the medial globus pallidus to the subthalamic nucleus. Mettler (22, 23) and Papez (29), from experimental material, considered the medial segment of the globus pallidus to be the strongest, if not the sole projection to the subthalamic nucleus. Many workers in the past half a century have thought that connections from the globus pallidus were supplemented by fibers from the putamen and caudate nucleus.

Using the silver impregnation technique, Johnson and Clemente (13), carried out an experimental study of the fiber connections between the putamen and globus pallidus in the cat. After ablation of the putamen and lateral globus pallidus, they noted degeneration in the ansa lenticularis and the "comb" system. They observed degeneration in the homolateral subthalamic nucleus. With a lesion isolated in the putamen only, they observed no degeneration past the medial and lateral globus pallidus.

It was of interest that Johnson and Clemente did not describe the dorsal part of the subthalamic nucleus as described in this paper.

Ranson and Ranson (33) described fine strio-fugal fibers which they thought probably arose in the caudate nucleus and putamen and partially from the lateral division of the globus pallidus and traced these fibers into the subthalamic nucleus. The Ransons used monkeys in their experiment and used the Weil method of staining the fibers and the cresyl violet stain for the cells. Laursen (17), in 1955, did an experimental study of the pathways of the basal ganglion. He used the monkey and the Marchi technique of staining degenerating myelin. He did not share the same opinion as others as to the origin of the ansa lenticularis being entirely from the internal segment of the globus pallidus. He placed lesions in the lateral part of the globus pallidus and noted degeneration in the ansa lenticularis as well as the fasciculus lenticularis. He also concluded that the ansa lenticularis received fibers from the putamen. In his work, he could not document that any particular portion of the subthalamic nucleus was responsible for the termination of any particular part of the afferents from the globus pallidus. He noted that there were pallido-incertal fibers which were from the fasciculus lenticularis and proceeded into the zona incerta. He considered their termination as the nucleus

of the field of Forel. He also concluded that the two segments, both medial and lateral part of the globus pallidus, were inter-connected.

Morgan (26) in his experimental study of secondary degeneration following lesion in the corpus striatum in man and acute degeneration studies in the corpus striatum of cats, concluded the following: In his cat experiments, he found that finely degenerated fibers from both divisions of the globus pallidus traveled obliquely through the cerebral peduncle and ended directly upon the cells in the subthalamic nucleus. He found that lesions in the lateral globus pallidus and the medial globus pallidus developed degeneration in Meynert's supraoptic commissure. He noted, after a lesion in the lateral globus pallidus and the putamen of a cat, sparing the entopeduncular nucleus, that degenerating fibers could be traced to the subthalamic nucleus and also into the substantia reticularis hypothalami, or as he put it, Forel's field. In this same lesion he also noted a few finely myelinated fibers which terminated in the subthalamic nucleus. He noted a great many terminations in the caudal subthalamic region. There is no reference in his paper as to the divisions of the subthalamic nucleus. He does not have a dorsal and ventral subthalamus as in this paper. He also gave no mention to cortical afferents to the subthalamic nucleus. He noted, after electrocoagulation of the lateral globus pallidus, that he found only a few degenerating fibers in the

subthalamic nucleus. Also, only slight degeneration in an area that he called the caudal subthalamus was seen. In his human material, he noticed that the lateral globus pallidus proceeded into the lateral part of the subthalamic nucleus. In man, he concluded that all fibers that terminated in the subthalamic nucleus passed through the ansa lenticularis or the fasciculus lenticularis. He also noted that the lateral globus pallidus sent decussating fibers across the supramamillary decussation to the contralateral field of Forel and lateral globus pallidus of the contralateral side. Another conclusion that he reached was that the medial globus pallidus, plus the ventral part of the lateral globus pallidus, went to the subthalamic nucleus on the homolateral side. These particular fibers from his observation, had to do with general body movement, whereas those fibers from the lateral part of the lateral globus pallidus proceeded to the pons and medulla and had to do with voice, masticating food and swallowing.

Fox and Schmidt (7), in an experimental study in the cat using a toluidine blue staining technique, studied the substantia nigra and entopeduncular nucleus. They noted that the entopeduncular nucleus degenerated completely with a lesion medial to the entopeduncular nucleus. The lateral globus pallidus remained intact during this experiment. These two workers pointed out the homology of the entopeduncular nucleus in the cat with that of the

medial segment of the primate globus pallidus, as did Ariens Kappers (1). Holmes (12) described subthalamic fibers going to both medial and lateral globus pallidus, in 1901. Papez (31), in 1942, described subthalamic fibers going to the putamen. Glees and Wall (10) described subthalamic fibers to the globus pallidus.

Foix and Nicolesco (6), in 1925, using a human brain specimen, described an interesting case report. In the brain of a human with the putamen completely injured, they found no degeneration of fibers into the subthalamic nucleus on the homolateral side; the pallido-subthalamic fibers were still intact. Therefore, they concluded that the fibers going to the subthalamic nucleus were not from the putamen, but rather from the globus pallidus. Woodburne, Crosby and McCotter (47, 4), working experimentally with the monkey using the Weigert stain, described the connections from the globus pallidus into the subthalamic nucleus. They concluded that the fasciculus subthalamicus arose in the external and internal segments of the globus pallidus and a small part from the putamen. They concluded that the fasciculus lenticularis, for the most part, entered the lateral pole of the subthalamic nucleus where it terminated. They also commented that they could not determine the direction of the connections under investigation; whether they were pallido-fugal or pallido-petal.

In the cat, the medial globus pallidus is oval and

completely imbedded in the cerebral peduncle. It is homologous to the medial segment of the globus pallidus as mentioned before. In Cat XP1, electrocoagulation of the left putamen and lateral globus pallidus resulted in secondary degeneration in the homolateral entopeduncular nucleus. Degeneration in the fasciculus lenticularis was noted, but only minimal degeneration was noted in the subthalamic nucleus on the homolateral side. However, degeneration from the secondarily degenerated entopeduncular nucleus was noted through the corpus pedunculi into the area at the subthalamic nucleus. Similar results were seen in Cat J16. A very discrete lesion was made in Cat J37, in the lateral globus pallidus, destroying it completely. There was very minimal infarction related to this lesion. After careful search, no degeneration was noted in the homolateral subthalamic nucleus. There was no degeneration in the contralateral subthalamic nucleus. In Cat J36, a discrete lesion was made in the lateral globus pallidus and the entopeduncular nucleus on one side. Degenerating fibers could be traced through the peduncle into the ventral subthalamic nucleus. The homolateral fasciculus lenticularis also showed slight degeneration.

In summary, the studies just reported seem to indicate that few fibers from the lateral globus pallidus project to the subthalamic nucleus on the homolateral side. The greater proportion of the afferents to the subthalamic nucleus from the globus pallidus come by way of the medial

globus pallidus or entopeduncular nucleus in the cat. The lateral globus pallidus projects mainly to the prerubral field of Forel by way of the fasciculus lenticularis. The impression from the present study was that no major projection occurred from the lateral globus pallidus into the subthalamic nucleus, either dorsal or ventral, in the cat. From study of a human pathologic brain, it can be said that fibers arise in the medial globus pallidus and end in the homolateral subthalamic nucleus.

Connections of the Subthalamic Nucleus via Decussations

Various fiber pathways have been considered to cross between the subthalamic nucleus and certain contralateral structures. Mainly the opposite subthalamic nucleus, the contralateral pallidum and the contralateral tegmentum have been considered. Most authors agree that the crossing fibers pass via the supramamillary decussation and have recognized this decussation in their writings. The supraoptic decussation of Meynert is located on the dorsal aspect of the optic chaism. It is finely myelinated. The supramamillary decussation is located dorsal to the mamillary nuclei and is more heavily myelinated. Foix and Nicolesco (6) noted fibers from the subthalamic nucleus crossing in the decussation to the contralateral subthalamic nucleus. They also noted fibers terminating in the globus pallidus on the contralateral side and in the midbrain tegmentum, notably to the nucleus profundus mesencephali.

Gurdjian (11), while studying the diencephalon of the albino rat, noted and described a commissure from the subthalamic nucleus crossing the decussation which is sometimes referred to as the decussation of Forel. This commissure terminated in the contralateral subthalamic nucleus, contralateral globus pallidus and contralateral tegmentum. Papez, Bennett and Cash (30) described similar fiber tracts while working on human brains in their study of hemichorea. Mettler (23) confirmed their findings. Morgan (26), after lateral globus pallidus and medial globus pallidus lesions in the cat, described degeneration in Meynert's supraoptic commissure, and concluded that it ended in the contralateral medial and lateral globus pallidus. He thought that the entopeduncular nucleus sent fibers in the supramamillary decussation and believed that a small part of these fibers accompanied the fasciculus lenticularis on the contralateral side.

Shaner (37), while studying the fiber connections of the globus pallidus and corpus of Luys in the pig, used the silver impregnation technique. Shaner described a large nucleus of Meynert's commissure located between the cerebral peduncle and the optic tract. It developed from cells that are continuous with the globus pallidus. He stated that the nucleus of Meynert's commissure was connected with the subthalamic nucleus in the pig. He concluded that the supraoptic decussation was primarily

a hypothalamic decussation. He said that the dorsal commissure of Ganzer or the supramamillary decussation connected the zona incerta and the peri-peduncular nuclei. He concluded that the ventral or Meynert's decussation received fibers from the corpus of Luys through the cerebral peduncle and also the peri-peduncular nucleus. Shaner's work was done on pig embryos. He believed that in later stages, Meynert's commissure possibly could include pallidal fibers.

Johnson and Clemente (13), using the silver impregnation technique, investigated the midbrain tegmentum in the cat. After ablation of the lateral globus pallidus and putamen, among other findings they noted fiber degeneration in supramamillary decussation or Ganzer's commissure. They also found degeneration in the lateral part of the nucleus profundus mesencephali. After a lesion of the zona incerta and the prerubral field of Forel, but sparing the entopeduncular substantia nigra and subthalamic nucleus, they noted slight degeneration across the supramamillary decussation. They noted that most of the fibers that crossed the midline descended in the midbrain tegmental area and terminated in the nucleus profundus mesencephali. Another observation that was made by these two men was that a direct pallido-fugal connection existed. Degeneration was noted in the nucleus of Darkshewitch and the interstitial nucleus of Cajal, following a lesion in the ipsilateral or homolateral globus pallidus. The concluded, because of this connection, that the globus pallidus exerted a direct

influence on the activity of the medial longitudinal fasciculus.

Rioch (35), in studies of the diencephalon of the carnivore, also noted commissure connections via the supramamillary decussation with much of the contralateral side of the brain.

In the series of electrocoagulation lesions, it appears that many decussations or commissures are present in this area of the cat brain. In Cat J36, mild degeneration was noted in the supramamillary decussation following a lesion in the entopeduncular nucleus. In Cat J7 and J20, a lesion was made by the posterior approach and destroyed the medial ventral subthalamic nucleus. There was only minimal degeneration in the supraoptic decussation. The fornix was secondarily infarcted and this resulted in mild degeneration in the commissure of the fornix. The commissure of the fornix is located ventral to the supramamillary decussation. In Cat J15, the lesion was more extensive, involving the peduncle, field of Forel and subthalamus. The supramamillary decussation is degenerated. In Cat J14, the vertical approach was used and the resulting lesion involved the fasciculus lenticularis but not the prerubral field of Forel or the ventral subthalamic nucleus. The supramamillary decussation showed no degeneration. No degeneration was noted in the supramamillary decussation after a lesion in the lateral globus pallidus, as seen

in Cat J16 and Cat XP1. In Cat J7, an extensive lesion involving the subthalamic nuclei resulted in contralateral degeneration in the medial half of the ventral subthalamic nucleus.

From this study there is little evidence that the lateral globus pallidus sends commissural fibers to the contralateral side, although the entopeduncular nucleus does. The subthalamic nucleus receives crossed fibers from the contralateral subthalamic nucleus. It appears from these studies, that many fibers cross and terminate in the midbrain tegmentum of the contralateral side. This is an interesting possibility and warrants further experimental investigation.

SUMMARY AND CONCLUSIONS

The fiber connections of the subthalamic region in the cat brain have been studied by the experimental method. In a series of cats, various nuclear components including the cerebral cortex, subthalamic nucleus, entopeduncular nucleus and globus pallidus were destroyed by electrocoagulation using a stereotaxic instrument. After a survival period of seven to fourteen days, the animals were sacrificed and histologic sections prepared by the intensified protargol technique.

Analysis of the histologic preparations yielded the following results:

1. On the basis of the anatomical appearance in the cat, the subthalamus has been divided into two main divisions; ventral and dorsal. The ventral nucleus is the nucleus which is usually thought of as the main subthalamic nucleus of Luys, seen in the monkey and the human. The dorsal nucleus is that accessory nuclear area located dorsal-lateral to the ventral nucleus, but in close continuity, separated only by a fascicle of fibers.

2. Extirpations of the frontal cortex, anterior to the middle ectosylvian sulcus, produce degeneration in the subthalamic nuclei, particularly the lateral dorsal subthalamic nucleus. The degree of degeneration is proportional to the amount of cortical afferents destroyed.

3. Cortical extirpation results in degeneration of

a lightly myelinated fiber tract ascending from the cerebral peduncle just caudal to the subthalamic region. It was not possible to follow these fibers to their termination.

4. Lesions in the lateral globus pallidus produce only minimal degeneration in the homolateral or contralateral subthalamic nuclei.

5. Lesions in the entopeduncular nucleus produce marked degeneration in the homolateral subthalamic nucleus, particularly the ventral subthalamic nucleus.

6. Lesions in the subthalamic nuclei produce degeneration in the supramamillary decussation. No degeneration is noted in the supraoptic decussation following these lesions.

7. Lesions in the subthalamic nuclei produce degeneration in the contralateral subthalamic nuclei, particularly the ventral subthalamic nucleus.

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TABLE OF ABBREVIATIONS

C	Cerebral Cortex
Co	"Comb" System (Pallido-subthalamic Fibers)
CP	Cerebral Peduncle
CR	Cortico-reticular Fibers
E	Entopeduncular Nucleus
F	Commissure of the Fornix
f	fascicles
H	Prerubral Field of Forel
Hl	Fasciculus Thalamicus
IC	Internal Capsule
L	Lesion
La	Lateral Ventral Subthalamic Nucleus
LGB	Lateral Geniculate Body
LGP	Lateral Globus Pallidus
Me	Medial Ventral Subthalamic Nucleus
Mgp	Medial globus pallidus, human
Mid Ecto	Middle Ectosylvian Gyrus
Mn	Mamillary Nucleus
OC	Optic Chiasm
Olf. Bulb	Olfactory Bulb
OT	Optic Tract
P	Putamen
RN	Red Nucleus
S	Subthalamic Nucleus, Human.

Sd	Dorsal Subthalamic Nucleus, Cat
Sn	Substantia Nigra
SM	Supramamillary Decussation
Sv	Ventral Subthalamic Nucleus, Cat
Teg	Tegmentum

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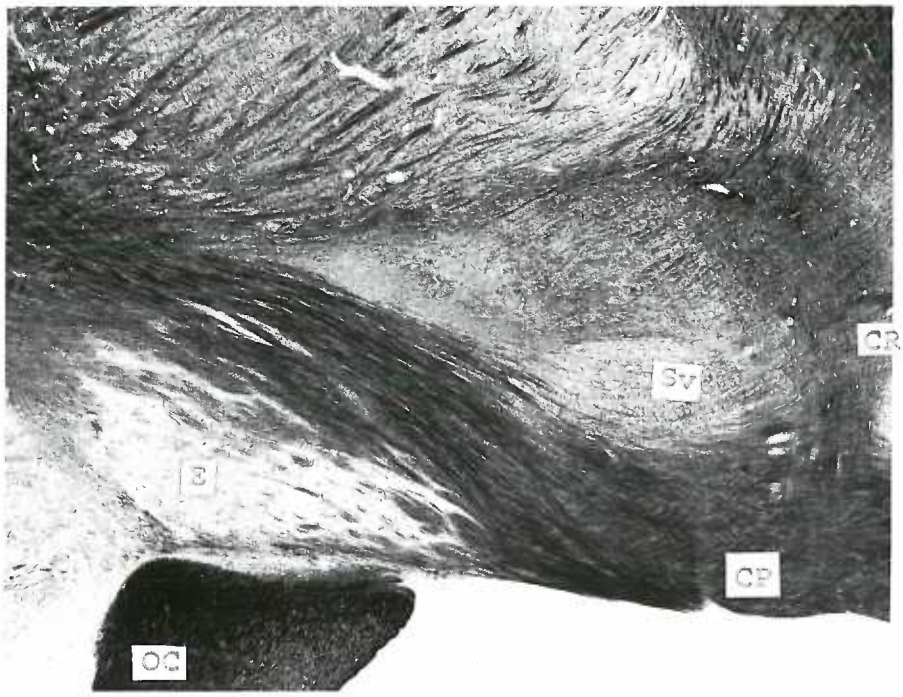

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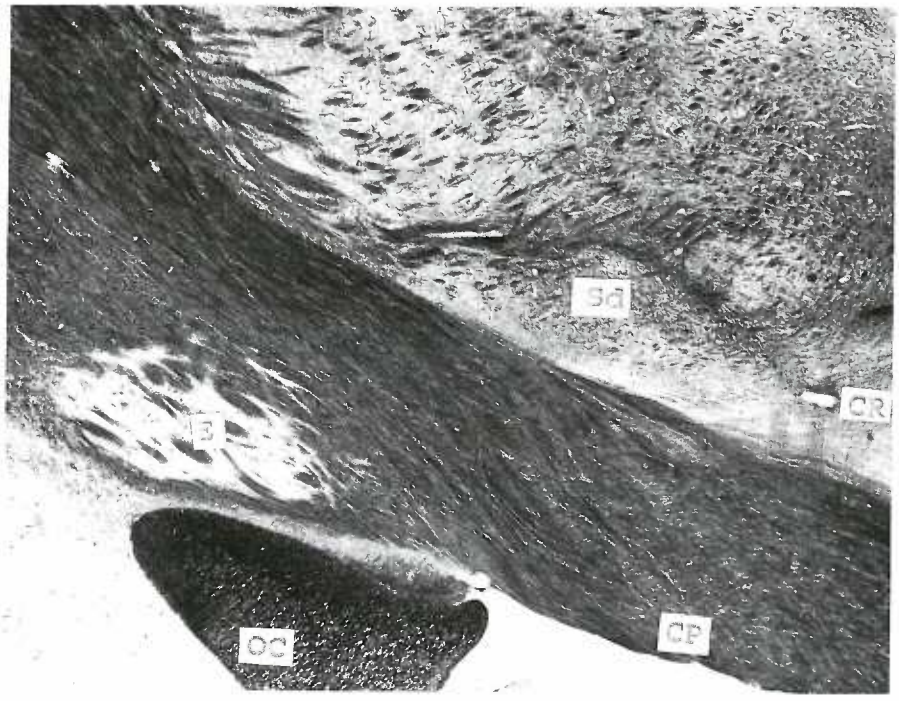

PLATE I.

Figure 11. Photomicrograph illustrating a mid-sagital section of a normal cat brain. Structures are identified. Low power. Weigert stain.

Figure 12. Photomicrograph illustrating a more lateral sagital section of a normal cat brain. Structures are identified. Note lightly myelinated ascending cortico-reticular tract (CR). Low power. Weigert stain.

PLATE II.

Figure 13. Photomicrograph illustrating a transverse section of a normal cat brain. Note supramamillary decussation (SM) and mamillary nuclei (MN). Low power. Weigert stain.

Figure 14. Photomicrograph illustrating a transverse section through the subthalamic nucleus of a normal cat. Note dorsal subthalamic nucleus (SD), ventral subthalamic nucleus (SV) and cerebral peduncle (CP). Low power. Weigert stain.

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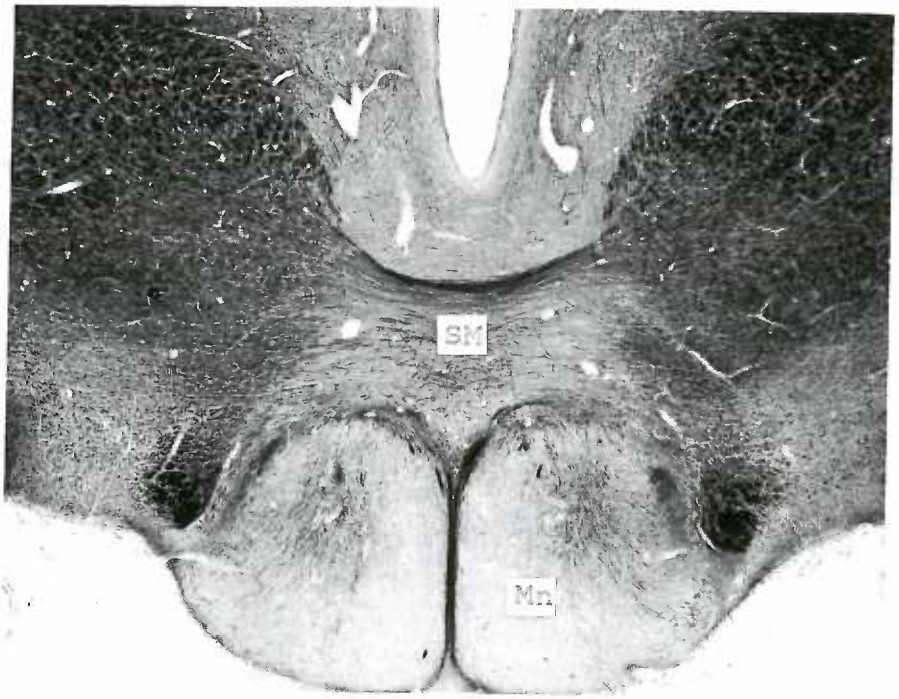

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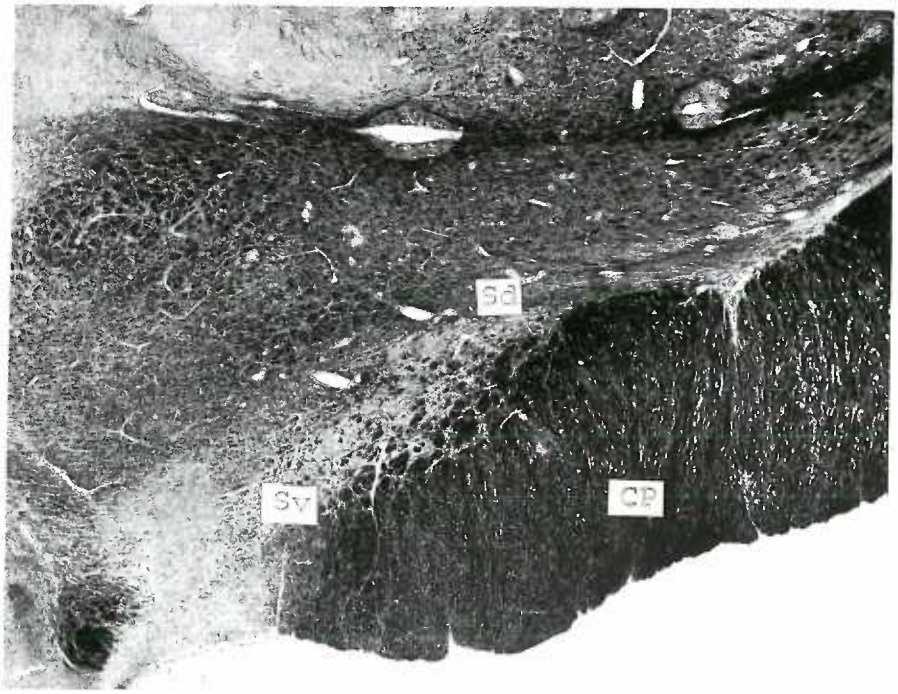

PLATE III.

Figure 15. Photomicrograph of a normal cat brain, sagital section. In this section, one can see the normal dorsal and ventral subthalamic nuclei with the normal fascicles coursing through these nuclei. The normal ascending cortico-reticular pathway is seen (CR). The normal substantia nigra is showing (SN). The internal capsule is intact (IC). Low power. Intensified protargol stain.

Figure 16. Cat 358. Photomicrograph showing gross degeneration in internal capsule (IC) and peduncle. Also note degeneration in rostral part of the dorsal subthalamic nucleus (SD). Note degeneration in ascending cortico-reticular pathway (CR). Low power. Intensified protargol stain.

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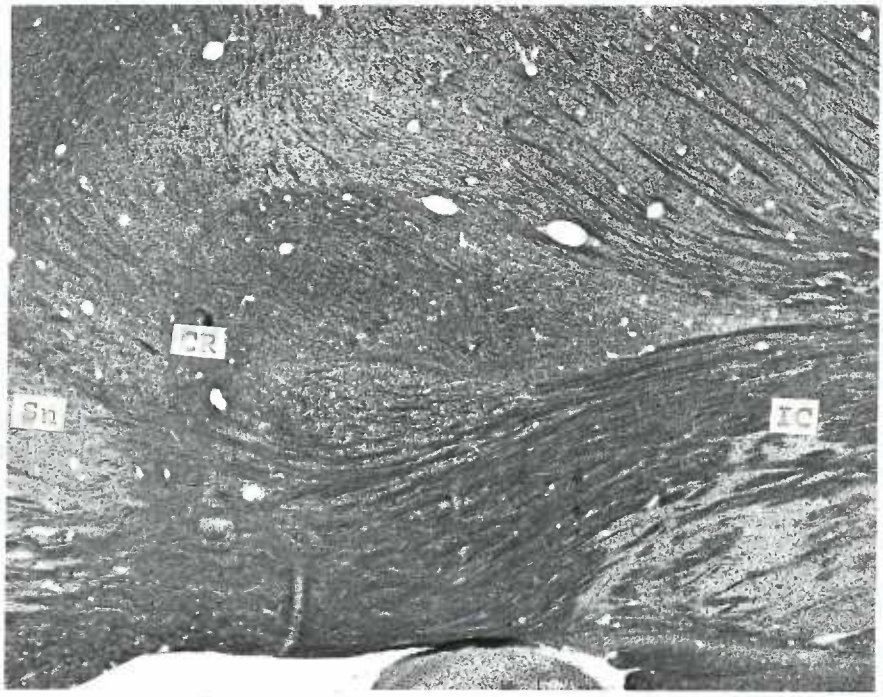

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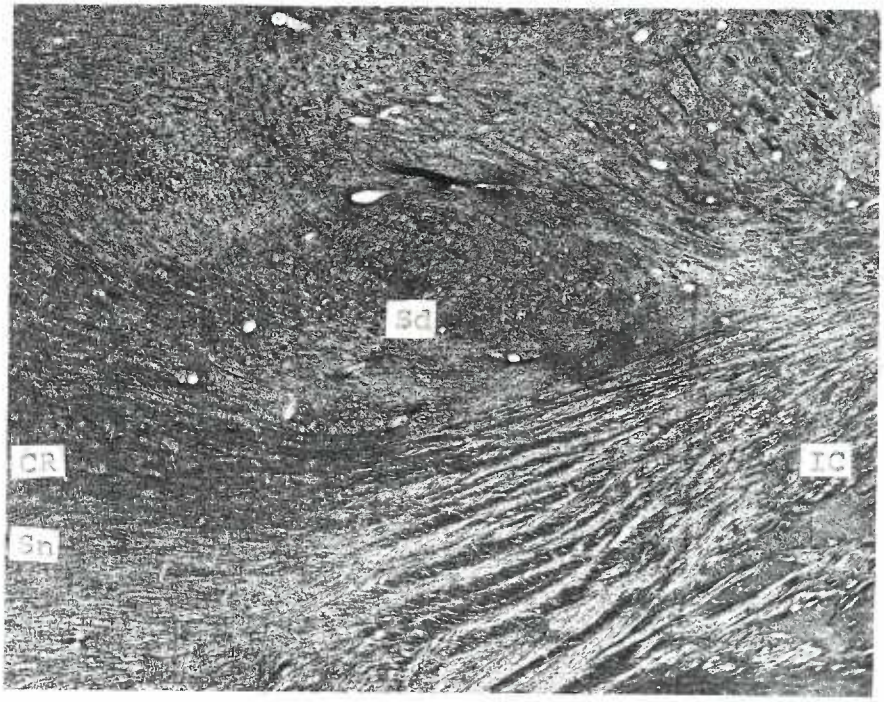

PLATE IV.

Figure 17. Cat 357. Photomicrograph showing the lateral subthalamus. Note degeneration in dorsal subthalamic nucleus (SD) and the cerebral peduncle (CP). Low power. Intensified protargol stain.

Figure 18. Cat 357. Photomicrograph showing the ventral subthalamic nucleus (SV) with marked loss of fascicles. Note degeneration in the dorsal cerebral peduncle (CP). Low power. Intensified protargol stain.

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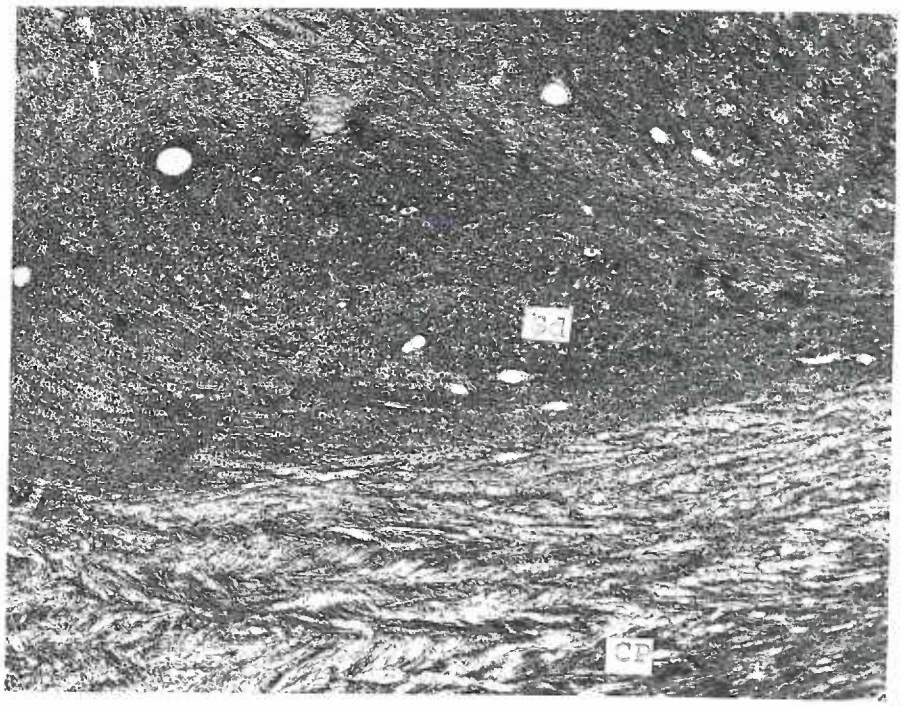

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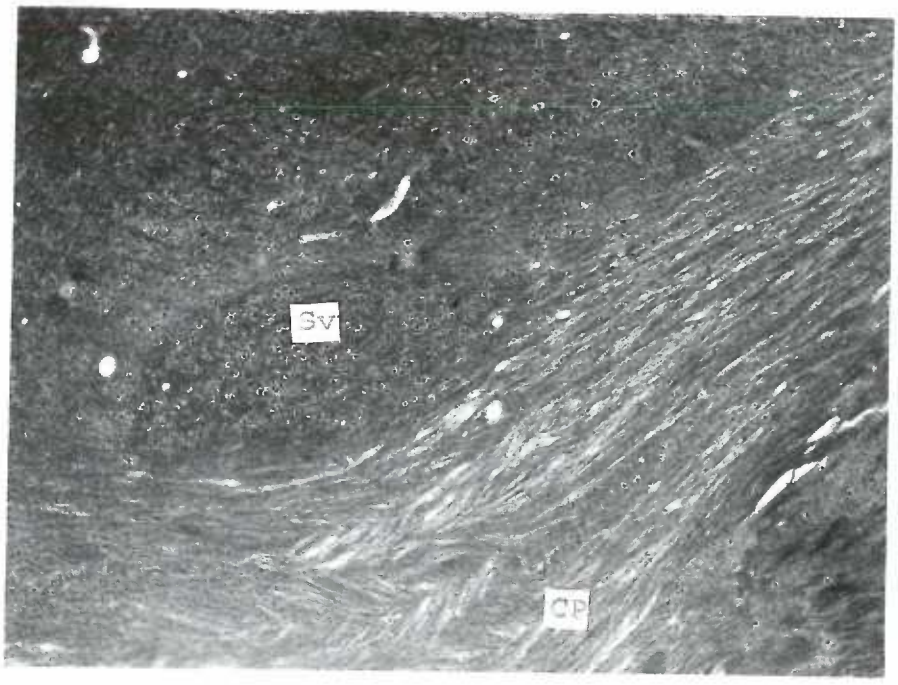

PLATE V.

Figure 19. Cat 357. Photomicrograph showing degeneration in dorsal subthalamic nucleus. Note loss of distinct cellularity. High power. Intensified protargol stain.

Figure 20. Cat 357. Photomicrograph showing very high power of Figure 19. Note loss of neuropil, distortion of intercellular fibers and degeneration of terminals around cells in the dorsal subthalamic nucleus. Oil immersion. Intensified protargol stain.

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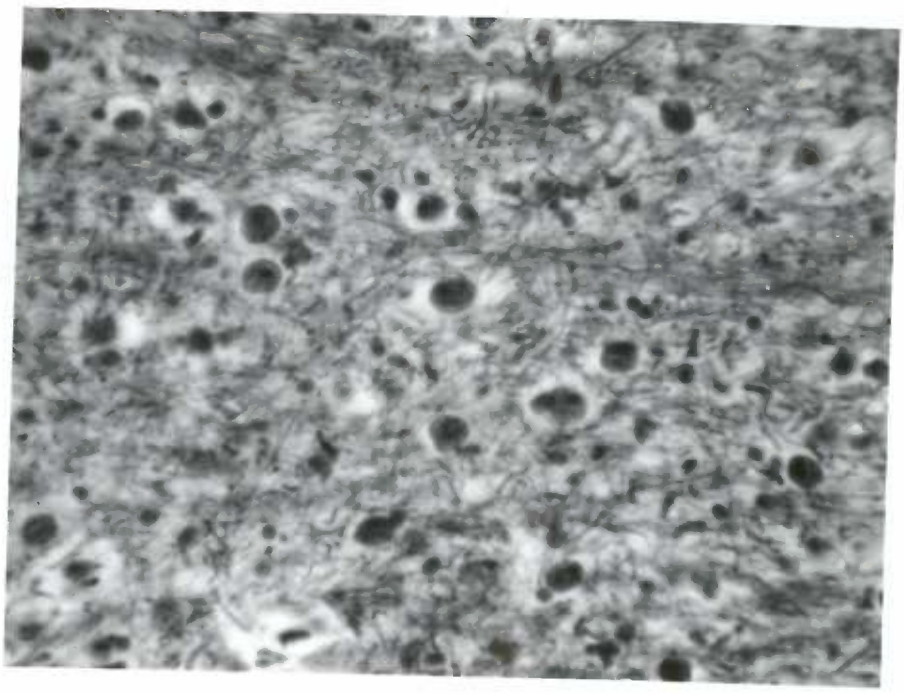

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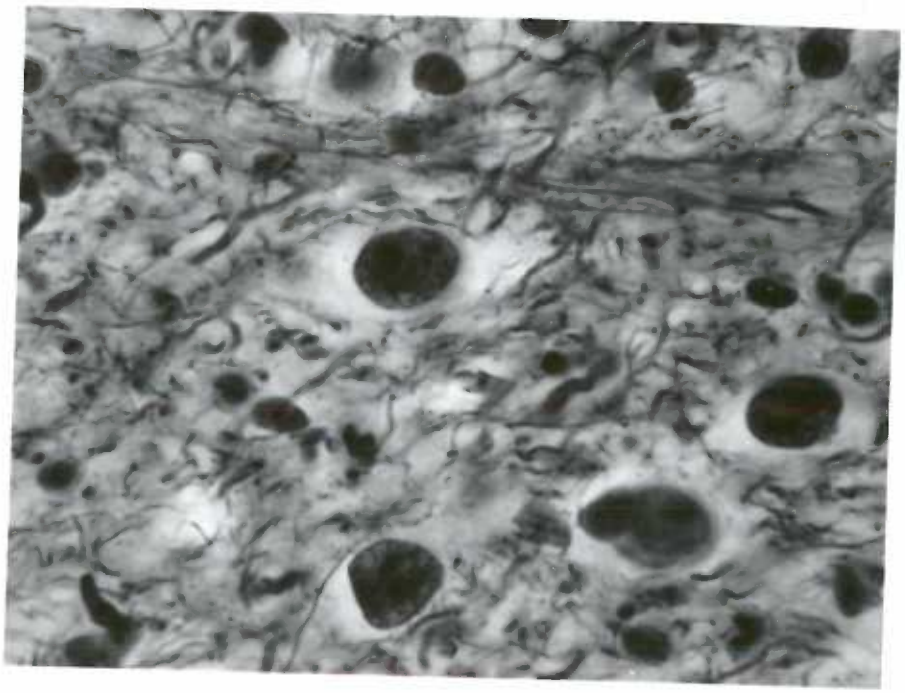

PLATE VI.

Figure 21. Cat 357. Photomicrograph showing the degenerating ascending cortico-reticular tract (CR). Note degenerated cerebral peduncle (CP). High power. Intensified protargol stain.

Figure 22. Cat 357. Photomicrograph showing the degenerated ascending cortico-reticular fibers (CR) high above the peduncle. Note tortuous and argyrophilic fibers. Oil immersion. Intensified protargol stain.

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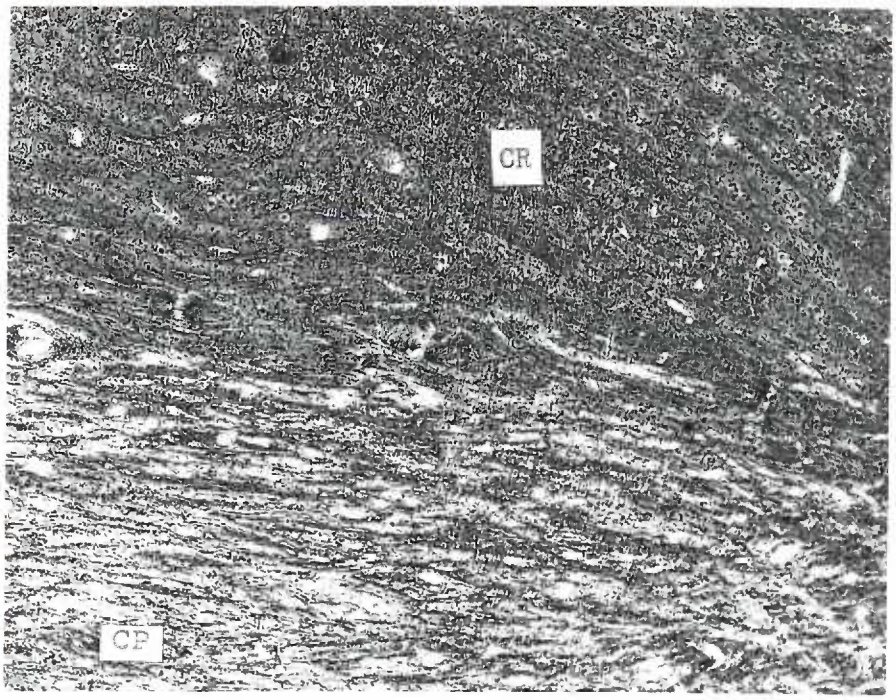

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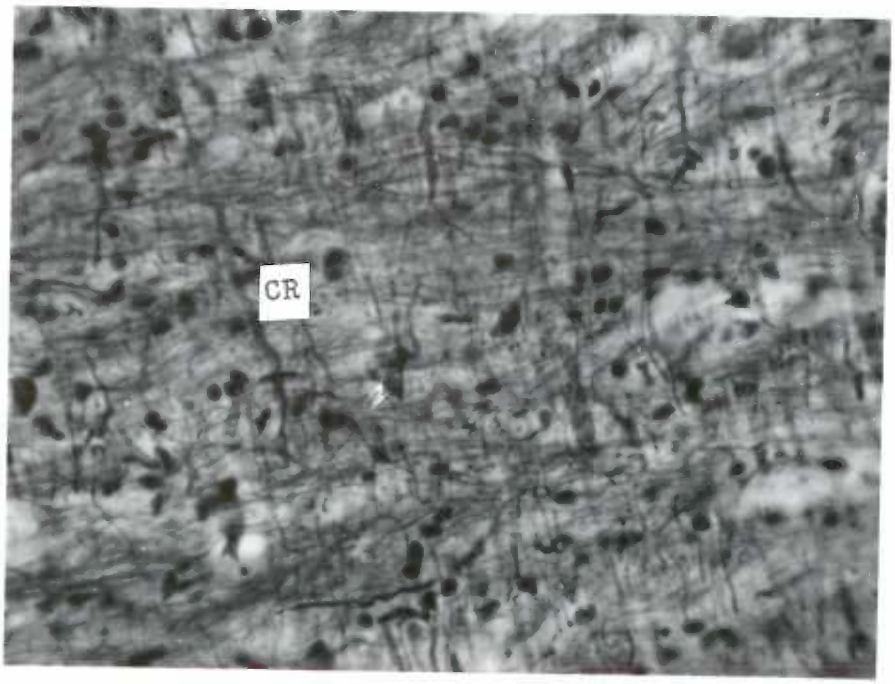

PLATE VII.

Figure 23. Cat 357. Photomicrograph showing intact entopeduncular nucleus (E) and intact lateral globus pallidus (LGP). Note degenerated internal capsule (IC). Low power. Intensified protargol stain.

Figure 24. Cat 357. Photomicrograph showing the intact entopeduncular nucleus (E) and intact lateral globus pallidus (LGP). Note intact internal capsule (IC) in sharp contrast to the degenerated internal capsule in Figure 23. Low power. Intensified protargol stain.

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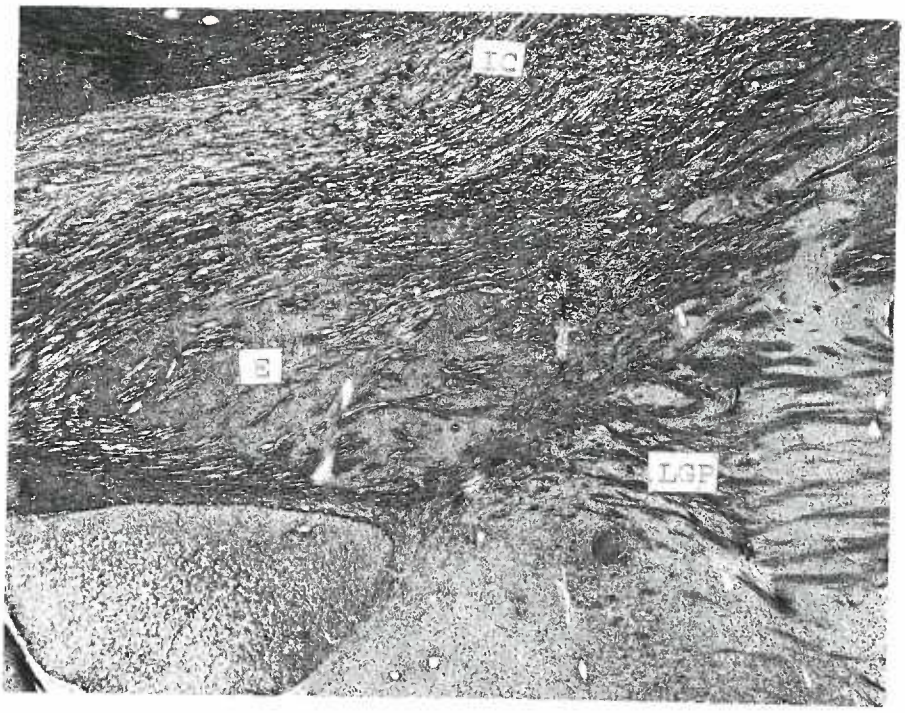

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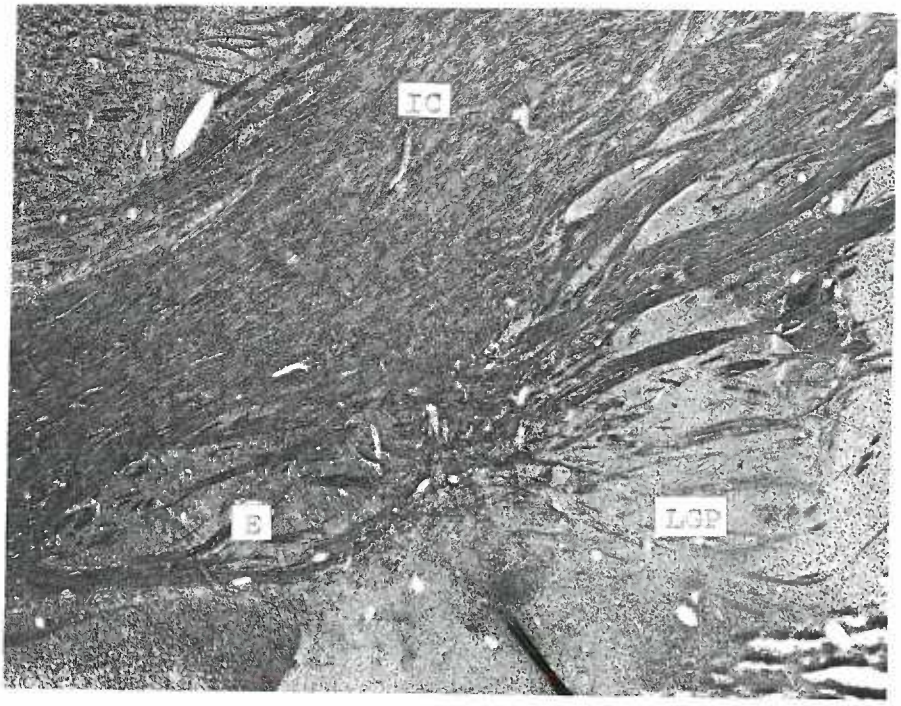

PLATE VIII.

Figure 25. Photomicrograph of a pathologic human brain. This brain had a vascular accident involving the arterial supply to the middle globus pallidus. Note the dark staining degenerated myelin coursing through the cerebral peduncle via the "comb" system (Co). Note the homogenous degeneration in the homolateral subthalamic nucleus (S). Low power. Marchi stain.

Figure 26. Photomicrograph of human brain, same as Figure 25. Degeneration is noted in the "comb" system (Co). Low power. Marchi stain.

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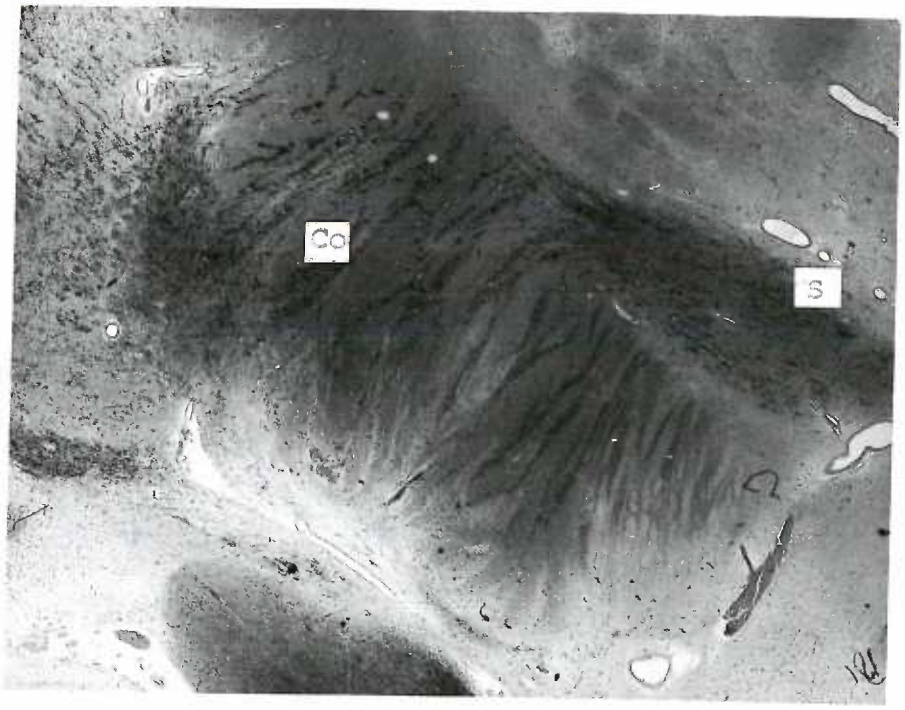

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PLATE IX.

Figure 27. Cat J36. Photomicrograph showing degeneration in entopeduncular nucleus (E). Note degenerating fibers coursing through the cerebral peduncle, "comb" system (Co). Low power. Intensified protargol stain.

Figure 28. Cat J36. Photomicrograph showing degeneration and loss of "comb" system (Co). As these fibers approached the homolateral ventral subthalamic nucleus. High power. Intensified protargol stain.

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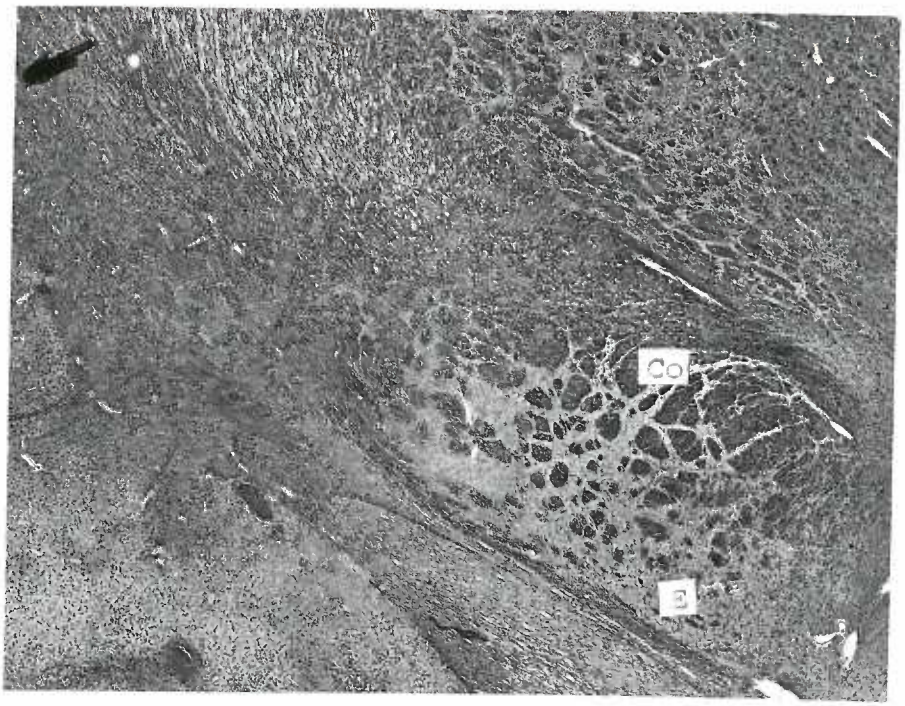

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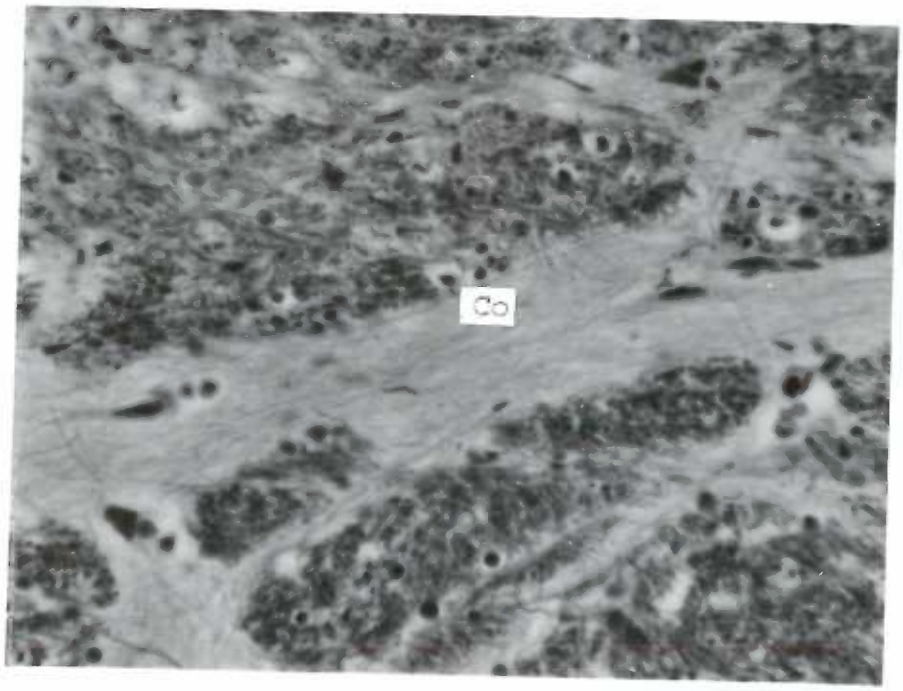

PLATE X.

Figure 29. Cat XP1. Photomicrograph showing lesion (L) and secondary degeneration in entopeduncular nucleus (E). Note loss of "comb" fibers through the cerebral peduncle. Low power. Intensified protargol stain.

Figure 30. Cat XP1. Photomicrograph showing loss of cellularity in homolateral ventral subthalamic nucleus. Note disruption of normal cellularity and clarity of cells. There is minimal loss of neuropil. High power. Intensified protargol stain.

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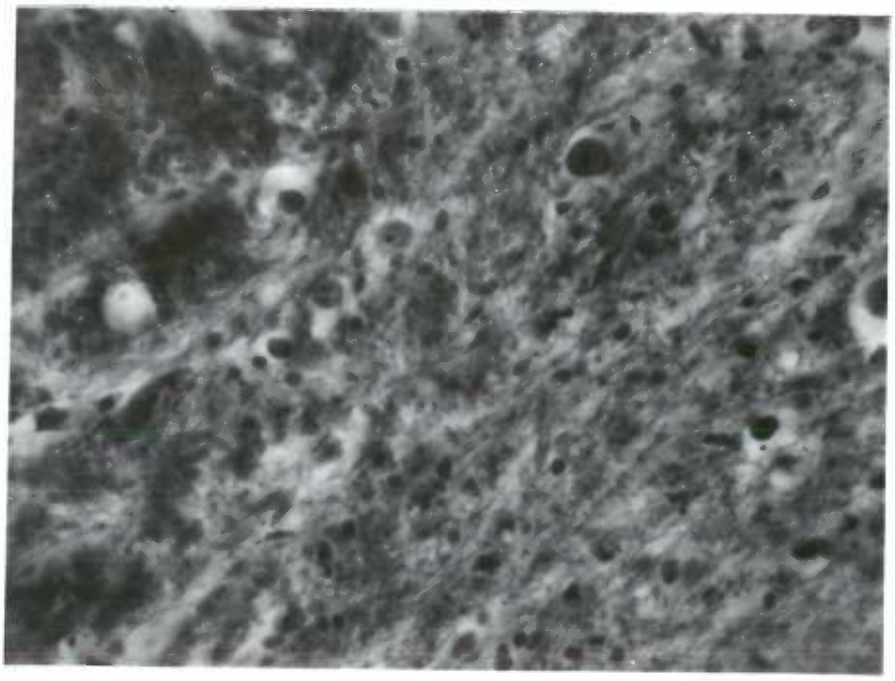

PLATE XI.

Figure 31. Photomicrograph showing the normal cat brain in horizontal section. Note the position of the ventral subthalamic nucleus (SV) and its angled position. Note the entopeduncular nucleus (E) in this section. Note the supramamillary decussation. Low power. Weigert stain.

Figure 32. Photomicrograph showing the normal supramamillary decussation (SM) as seen in the horizontal section. Note the lightly myelinated commissure of the fornix (F). High power. Weigert stain.

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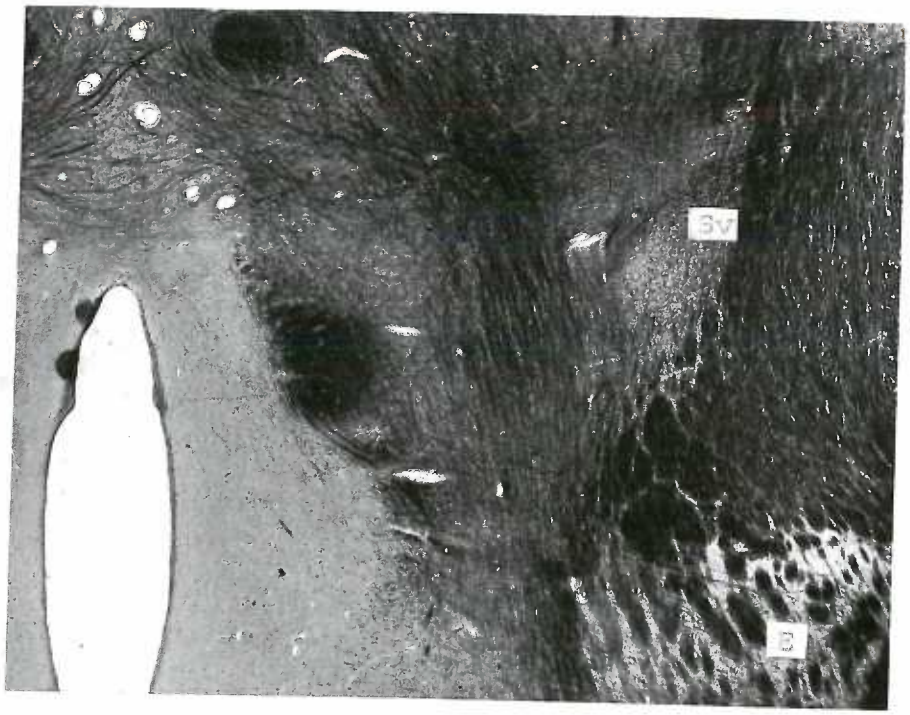

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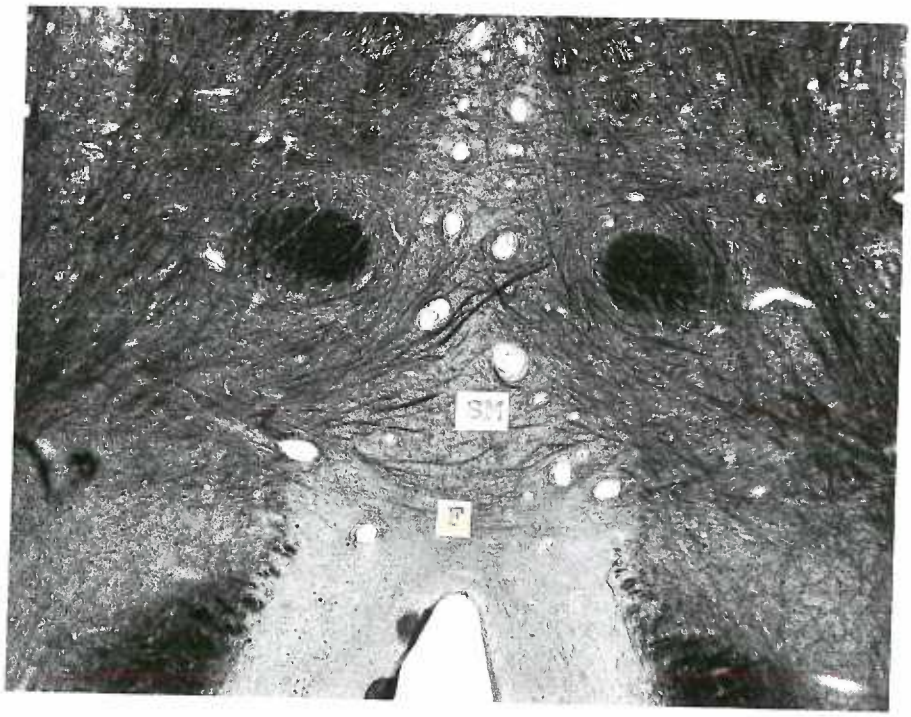

PLATE XII.

Figure 33. Cat J13. Photomicrograph showing gross lesion (L) in the cerebral peduncle. Note the minimal reaction around the electrode tract. Low power. Intensified protargol stain.

Figure 34. Cat J13. Photomicrograph showing degeneration of afferents into homolateral ventral subthalamic nucleus. Note loss of normal cellularity and debris. High power. Intensified protargol stain.

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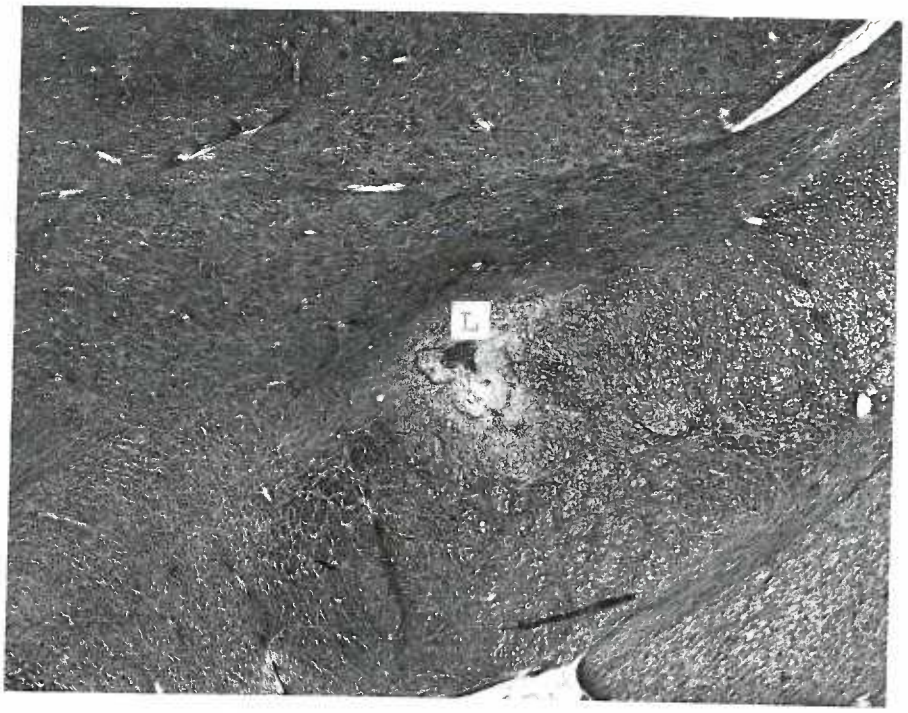

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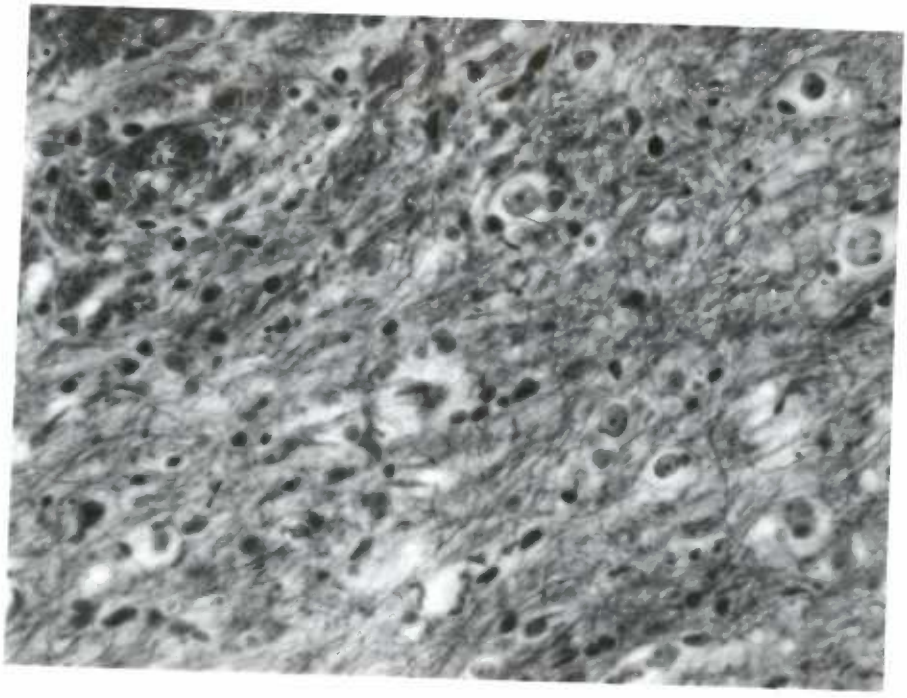

PLATE XIII.

Figure 35. Cat J37. Photomicrograph showing the electrode tract and lesion (L) from the vertical approach. Note lesion is confined to lateral globus pallidus (LGP) with no primary damage to the entopeduncular nucleus (E). Very minimal involvement in the internal capsule (IC). Low power. Intensified protargol stain.

Figure 36. Cat J37. Photomicrograph showing no degeneration in the dorsal or ventral subthalamic nuclei. Note the dark fascicles coursing from the intact internal capsule into the subthalamic nuclei (f). Low power. Intensified protargol stain.

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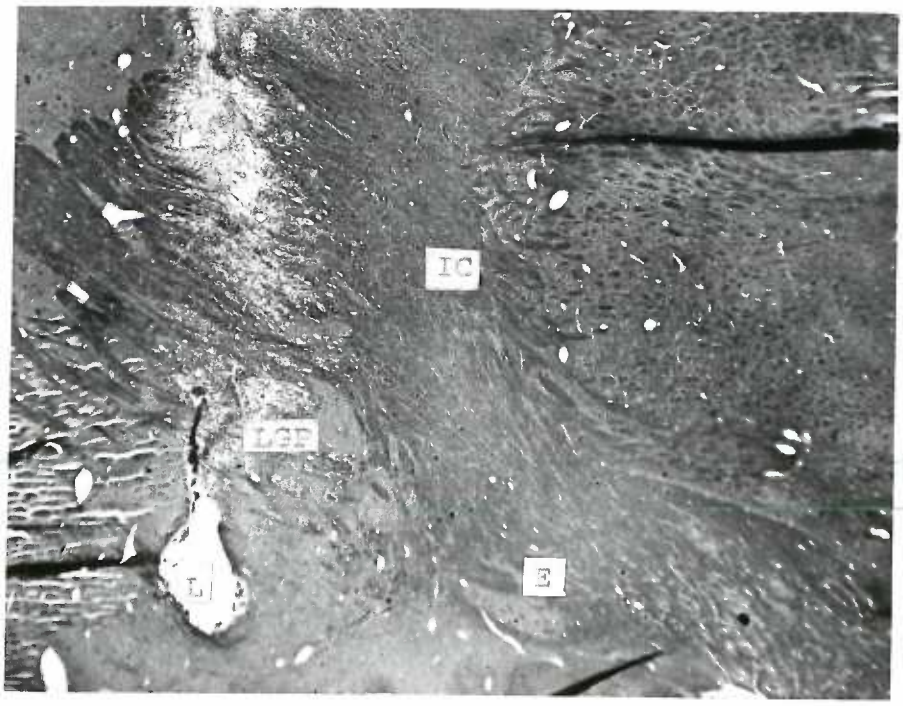

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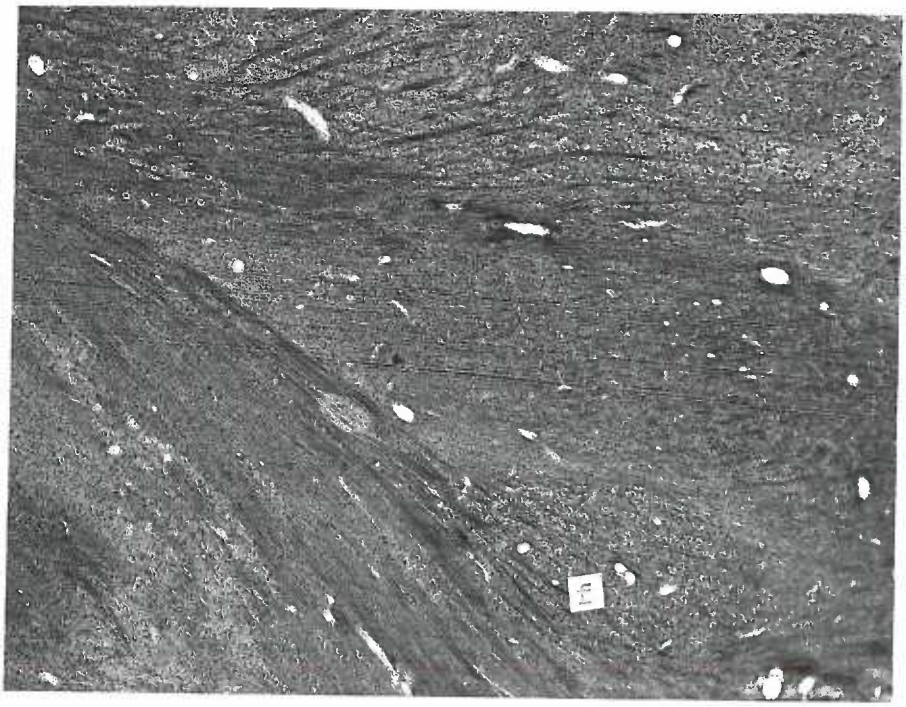

PLATE XIV.

Figure 37. Cat J16. Photomicrograph showing marked degeneration in entopeduncular nucleus (E) with degeneration into the homolateral "comb" system. Low power. Intensified protargol stain.

Figure 38. Cat J16. Photomicrograph showing normal intact entopeduncular nucleus on contralateral side to Figure 37. Low power. Intensified protargol stain.

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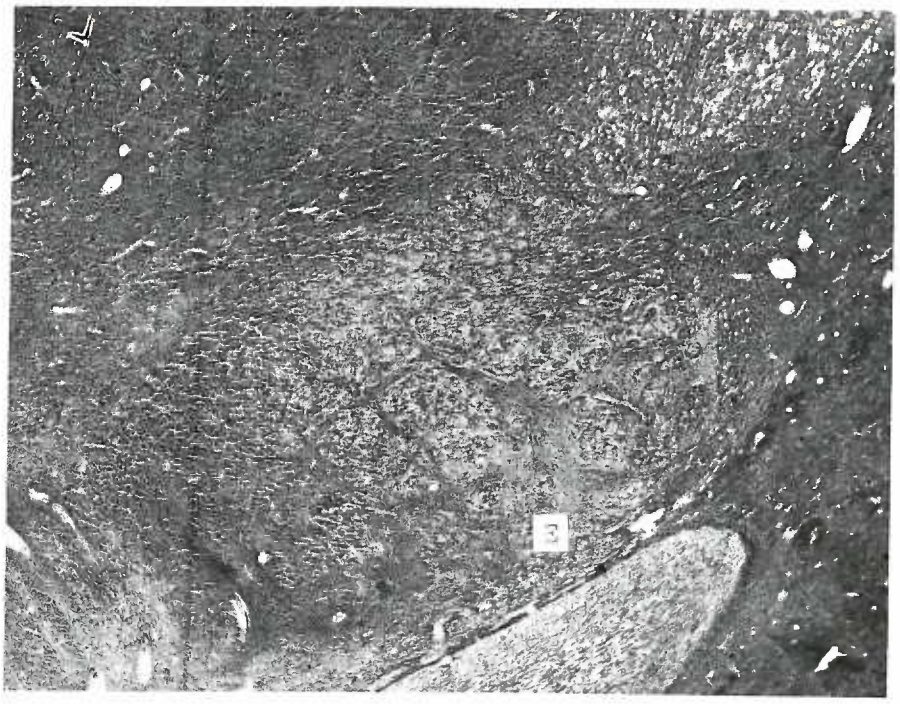

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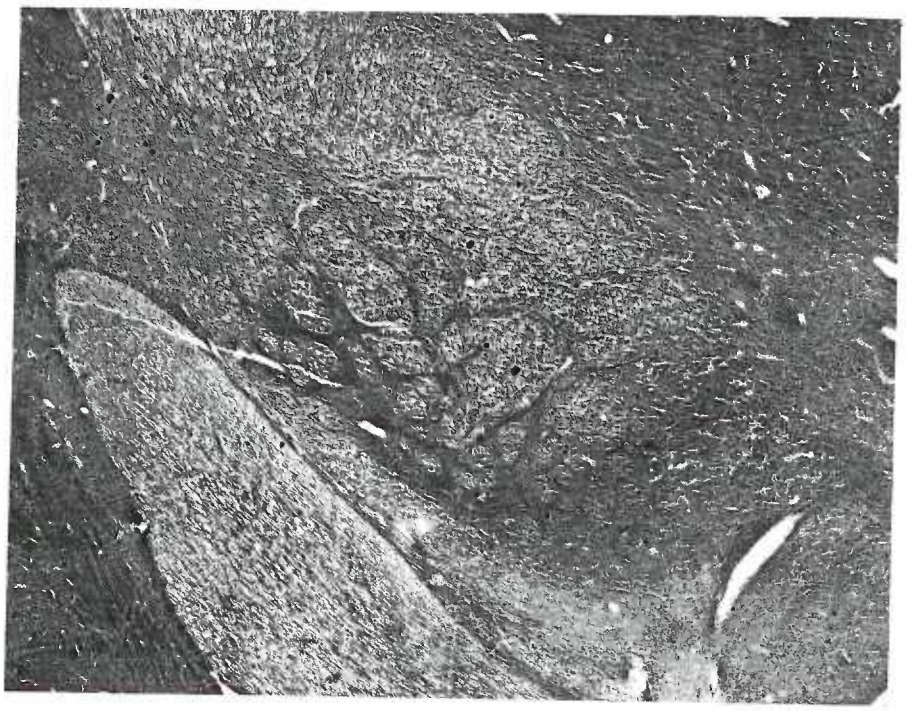

PLATE XV.

Figure 39. Cat J7. Photomicrograph showing gross lesion (L). The lesion destroyed most efferent nerve fibers to the contralateral side. Note location of supramamillary decussation (SM). Low power. Intensified protargol stain.

Figure 40. Cat J7. Photomicrograph showing the difference in medial (Me) and lateral (La) parts of the ventral subthalamic nucleus after a lesion in the contralateral subthalamus. Low power. Intensified protargol stain.

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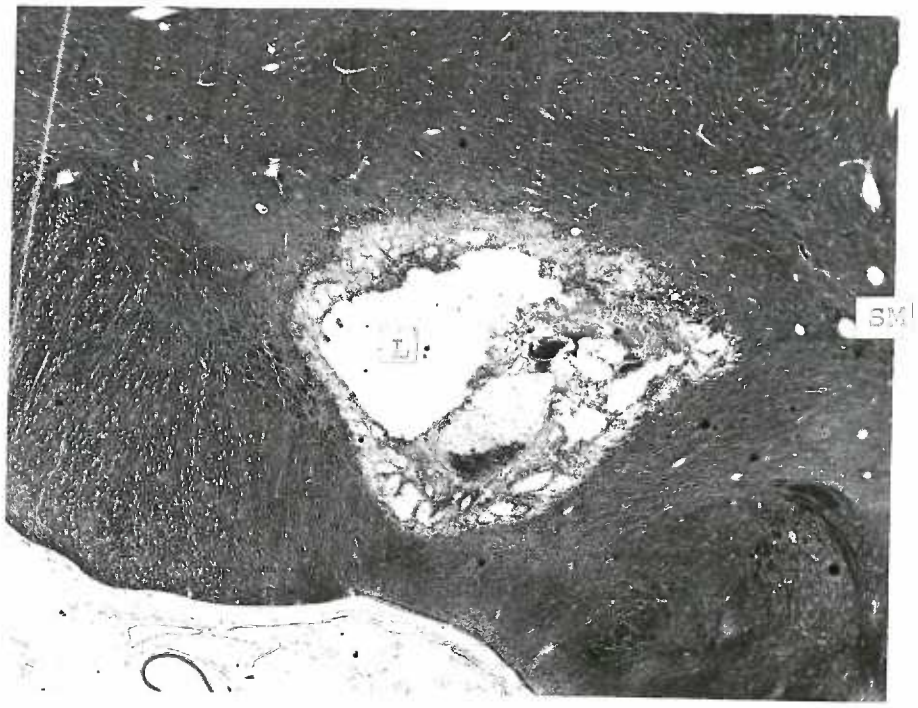

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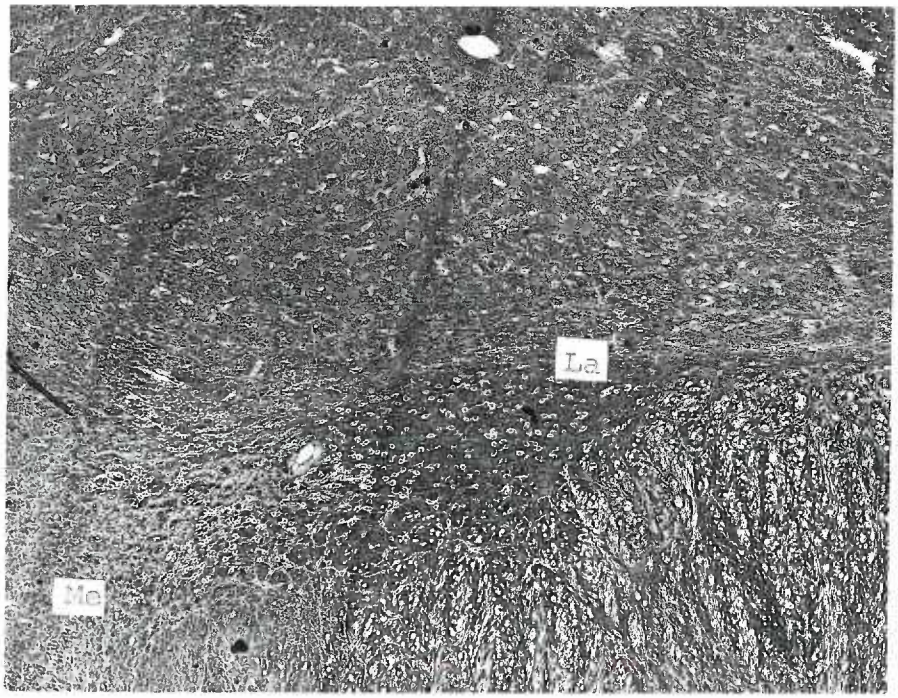
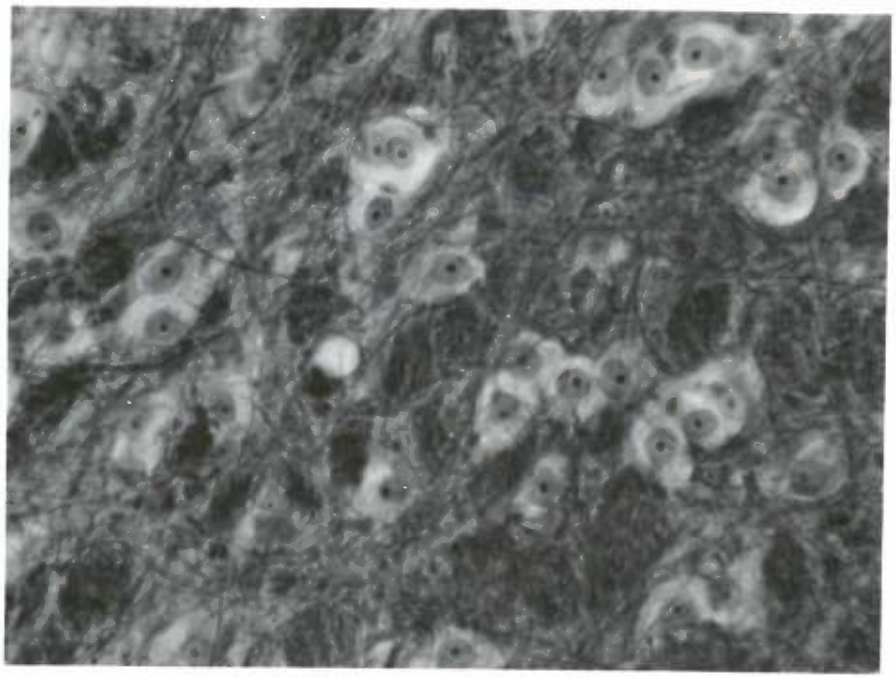


PLATE XVI.

Figure 41. Cat J7. Photomicrograph showing the lateral part of the ventral subthalamic nucleus. Refer to Figure 40. Note the normal appearance with no loss of cellular detail. Oil immersion. Intensified protargol stain.

Figure 42. Cat J7. Photomicrograph showing the medial aspect of the ventral subthalamic nucleus. Note the loss of cellular detail and degenerated fibers in this picture. Refer to Figure 40. Oil immersion. Intensified protargol stain.

41



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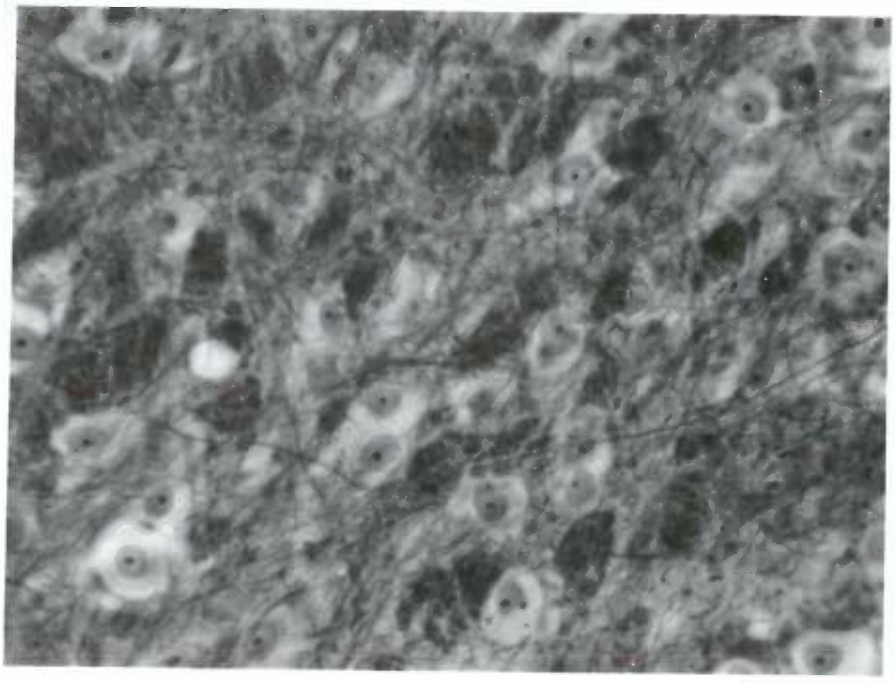
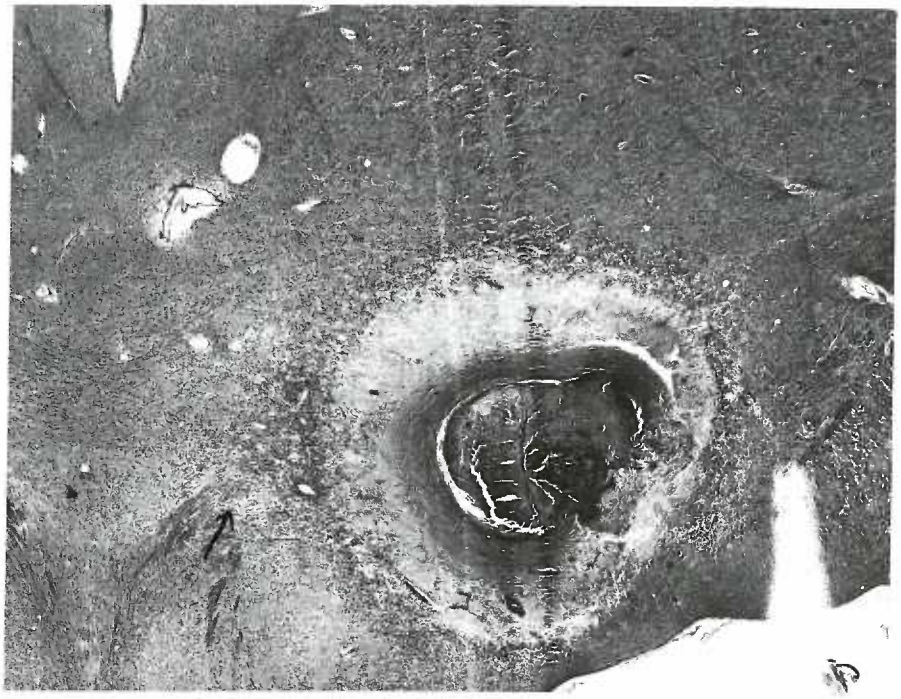


PLATE XVII.

Figure 43. Cat J20. Photomicrograph showing very gross lesion of subthalamic area, peduncle and surrounding area. By secondary infarction the homolateral fornix was involved (arrow). Low power. Intensified protargol stain.

Figure 44. Cat J20. Photomicrograph showing degeneration in the finely myelinated fibers of the commissure of the fornix. Argyrophilic debris is noted inside the axonal membrane. (arrow). High power. Intensified protargol stain.

43



44

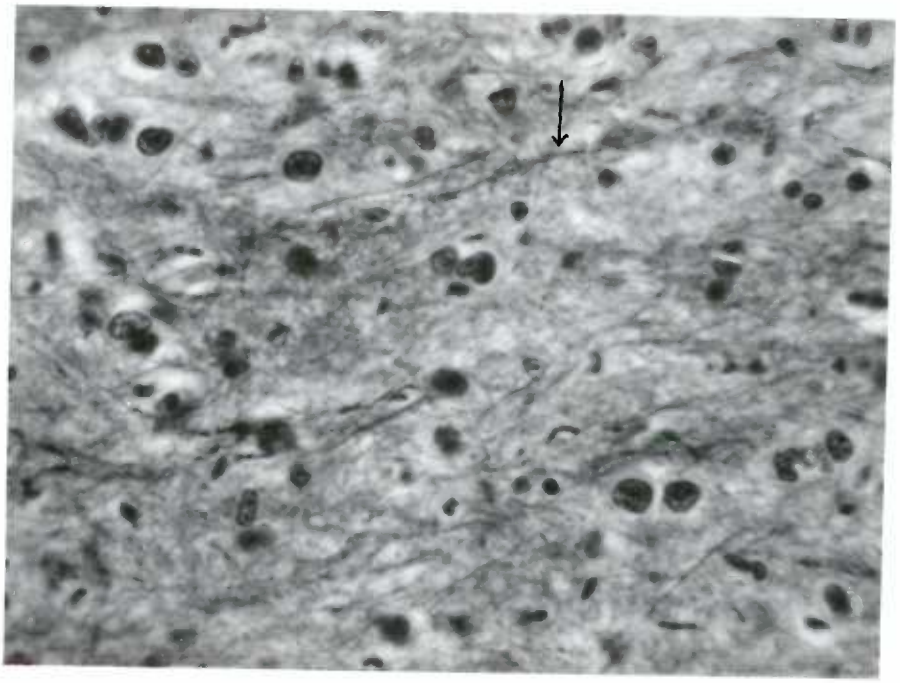
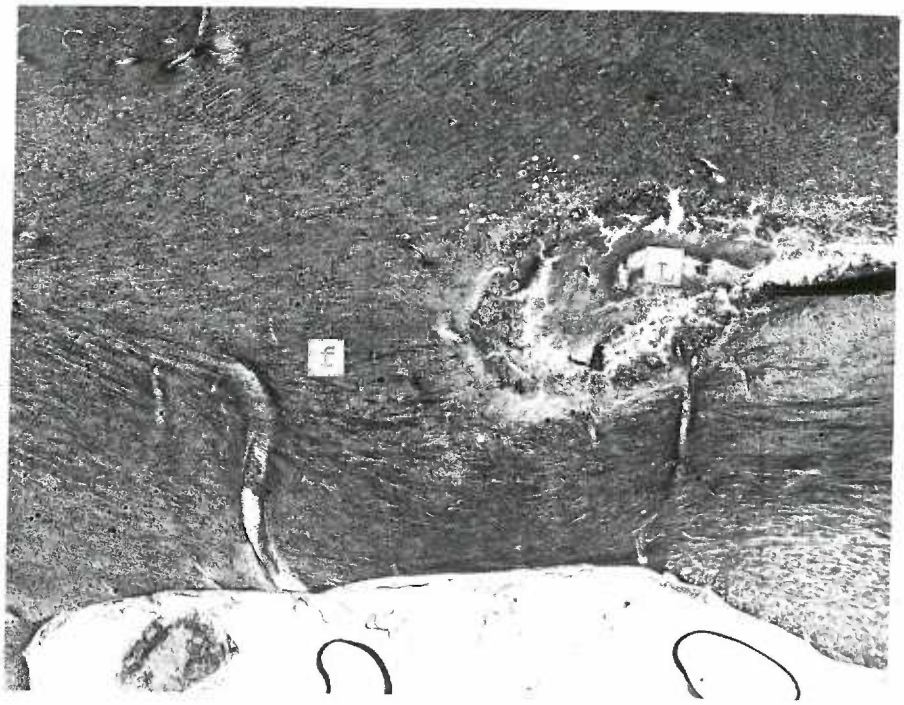


PLATE XVIII.

Figure 45. Cat J21. Photomicrograph shows posterior lesion (L). This is a sagital section. Note position of subthalamic nucleus, also note intact fascicles passing through the subthalamic nucleus (f). Low power. Intensified protargol stain.

Figure 46. Cat J21. Photomicrograph showing the ascending cortico-reticular tract. Most of these fine fibers are intact with only very minimal degeneration. Oil immersion. Intensified protargol stain.

45



46

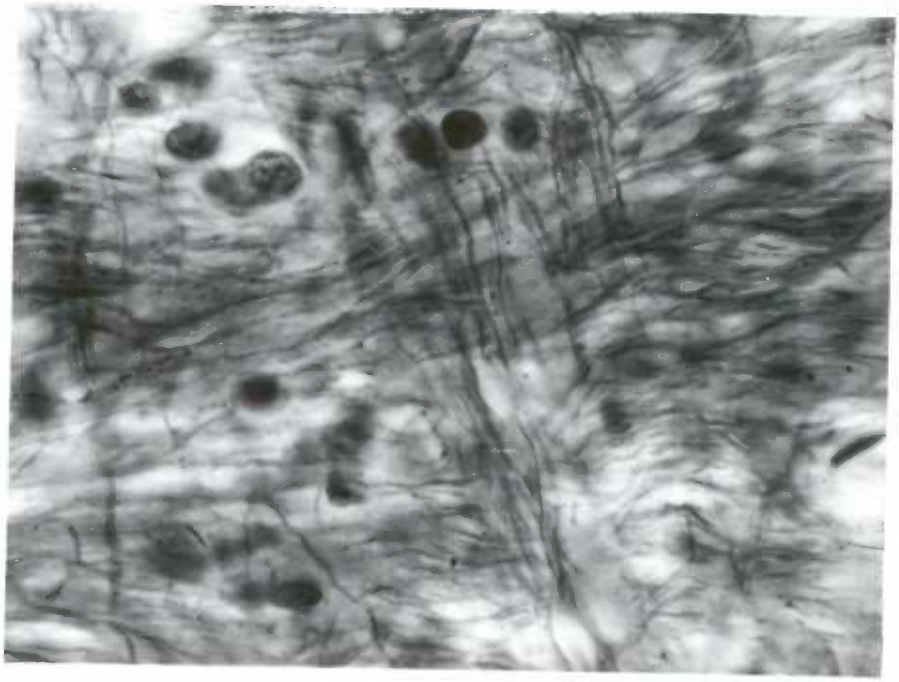
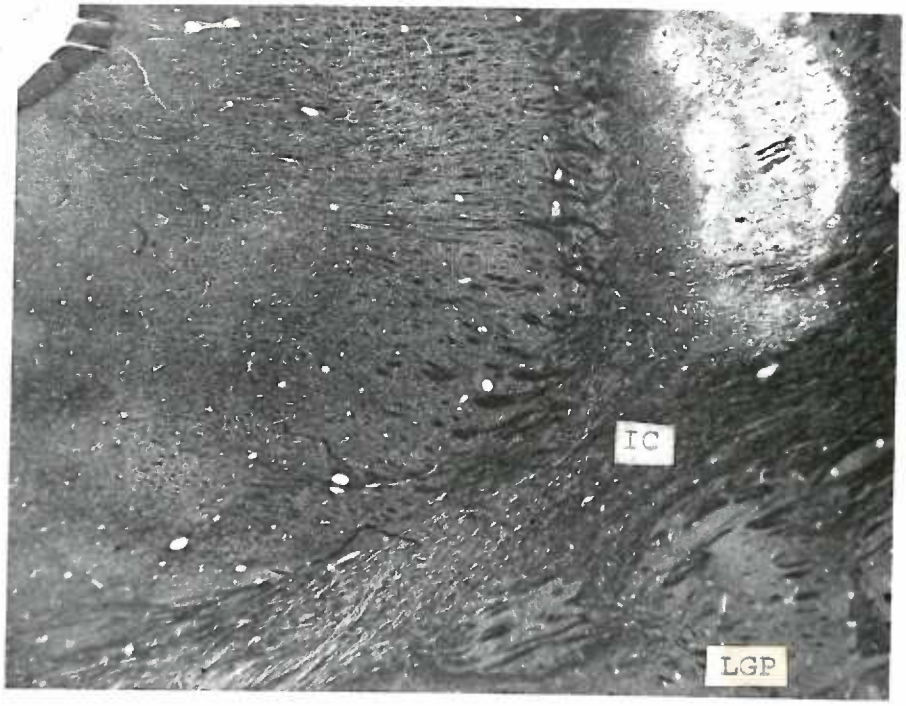


PLATE XIX.

Figure 47. Cat J33. Photomicrograph showing a combination lesion of lateral globus pallidus (LGP) and internal capsule (IC). Note degeneration in internal capsule beneath the subthalamic area. Also loss of fascicles passing through the subthalamic nuclei and loss of cellular detail. Low power. Intensified protargol stain.

Figure 48. Cat J33. Photomicrograph showing loss of cellular detail and loss of neuropil in lateral dorsal subthalamic nucleus. Oil immersion. Intensified protargol stain.

47



48

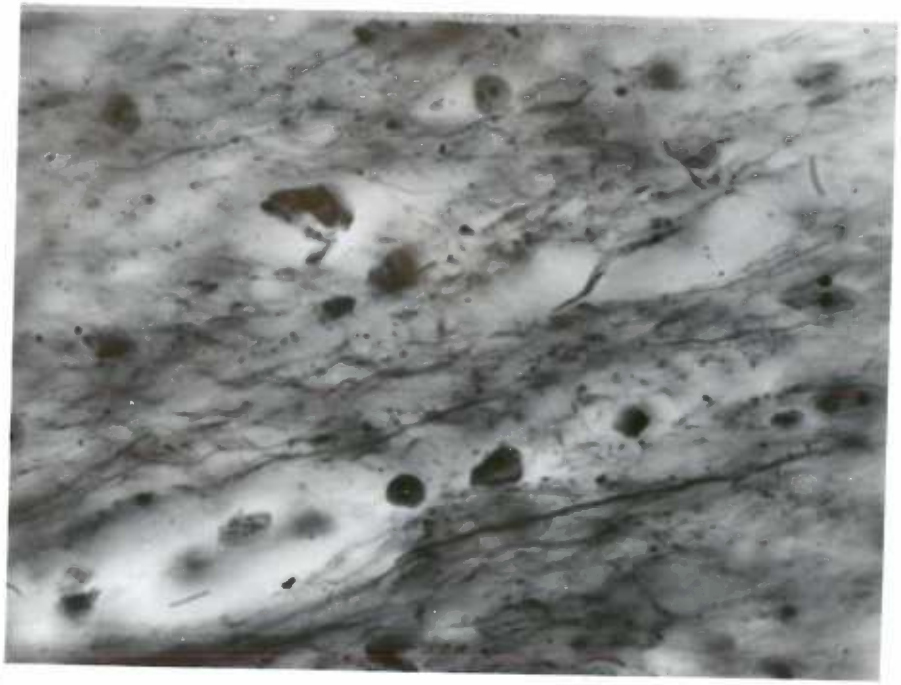
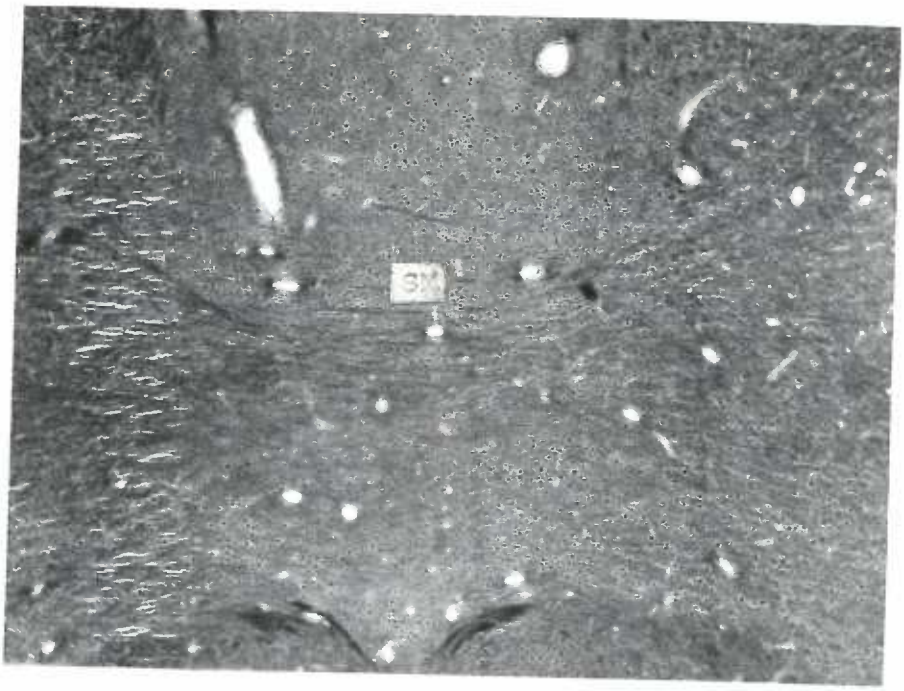


PLATE XX.

Figure 49. Cat J15. Photomicrograph showing heavily myelinated supramamillary decussation (SM) with degeneration. Low power. Intensified protargol stain.

Figure 50. Cat J15. Photomicrograph showing the degenerated supramamillary decussation. Note distorted and tortuous argyrophilic fibers with granular debris. Oil immersion. Intensified protargol stain.

49



50