SOME NEOCORTICO-AMYGDALOID CONNECTIONS IN THE CAT

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A THESIS

Submitted to the School of Graduate Studies
in Partial Fulfilment of the Requirements
for the Degree of Doctor of Philosophy.

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Ottawa, February 1971

ACKNOWLEDGEMENTS

I wish to thank, Professor E. Hall, for her guidance and patience throughout this investigation.

ACKNOWLEDGEMENTS

I wish to thank the staff members and the technicians of the Department of Anatomy for their advice and assistance during this project.

ACKNOWLEDGEMENTS

This investigation was supported financially by the University of Ottawa and the Medical Research Council, Grant MT-870.

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INTRODUCTION

Phylogenetic and Ontogenetic Studies

Among the earliest investigations of the amygdala were those of Herrick (1891, 1893) and Kollicker (1896) (see Hall, 1960). The former investigator recognized the presence of a cellular mass in the occipito-basal area of the cortex of the reptile. The latter demonstrated that these cells could be divided into four small groups, one of which he called the nucleus amygdalae. A group of cells similar to that described by Herrick was observed in mammals by Volsch (1906, 1911, see Johnston, 1923), who identified seven subdivisions in this region. Further studies on the ventrobasal region of the hemispheres were reported by Crosby (1917) who described the forebrain of the alligator and by Herrick (1921) who studied amphibians. However, the most substantial contribution to the study of the forebrain during the early part of this century was undoubtedly that of Johnston (1923).

Johnston described and classified the nuclei of the forebrain in reptiles and mammals (Johnston, 1923). The terminology which he used and the classification which he postulated have formed the basis for most subsequent

studies on the amygdala. Only minor modifications have been introduced since by more recent investigators. He identified six nuclei in the ventrobasal region of the mammalian hemispheres: the central, the medial, the lateral, the basal and the accessory basal nuclei, and the nucleus of the lateral olfactory tract. He hypothesized, on the basis of the presence or the absence of these nuclei in fishes, amphibians, reptiles and mammals, that the amygdala is composed of two groups of nuclei: a phylogenetically older and a phylogenetically younger group. He traced the older group, which is constituted of the central, medial, and cortical nuclei and nucleus of the lateral olfactory tract, through various categories of fishes and tetrapods. The younger group is composed of the basal and lateral nuclei. According to Johnston (1923), the first of these nuclei has its beginning in reptiles while the second is present only in mammals. A third amygdalar subdivision was later introduced by Gurdjian (1928). She described the area located between the well-defined amygdalar nuclei and the tuberculum olfactorium as the anterior amygdaloid area. Later, Humphrey (1936) modified the terminology by naming the group of older nuclei, the corticomedial complex because of its

position in the ventromedial part of the amygdala, and the newer nuclei the basolateral complex because of its location in the ventrolateral part of the amygdala. Thus Johnston's classification remains as the basic division of the amygdaloid nuclei.

In addition to his description and classification of the amygdaloid nuclei, Johnston (1923) elaborated a theory on the development of these structures. He postulated that the formation of the phylogenetically older nuclei results from the proliferation of cells of the primitive olfactory centres because these regions of the temporal cortex receive olfactory fibres from the more anterior olfactory centres. He suggested that the younger group is formed by a migration of cells from an infolding in the pyriform lobe because the cells of the pyriform cortex are in continuity with those of the basal nucleus. However some modification to his theory was reported recently in the embryological studies of Macchi (1951) and Humphrey (1968). From his studies, Macchi (1951) pointed out that the basolateral complex arises directly from the striatal ridges and not from an infolding along the brain wall. Humphrey (1968) confirmed Macchi's statement and described more

accurately the cellular migration which gives rise to the basolateral complex as well as to the other parts of the amygdala.

Humphrey (1968) identified a thickening in the ventrocaudal wall of the interventricular foramen in the brain of the human embryo. This agglomeration of cells, seen in the early embryonic stages, has been called the primitive striatum, or more specifically, the primitive lateral striatal ridge. According to Humphrey, cells of this ridge migrate outward to form the primordial amygdala from which the three amygdaloid subdivisions differentiate and form groups distinct from the surrounding nuclear areas. However, a region of continuity remains between the basal and cortical nuclei and the pyriform cortex. This is the cortico-amygdaloid transitional area which Humphrey believed to represent the region where cell migration has not progressed outward to the cortical surface. Thus she concluded that the basolateral complex is not the product of an infolding along the brain wall.

The Nuclei of the Amygdala

Johnston's description (1923) of the amygdala in the opossum, rabbit, bat, monkey and human foetus was confirmed by Berkelbach van der Sprenkel (1926) in the opossum, by Young (1936) in the rabbit, by Humphrey (1936) in the bat and by Lauer (1945) in the monkey. Additional investigations have been carried out in the rat by Gurdjian (1928) and Brodal (1947), in the cat by Fox (1940), in the human by Crosby and Humphrey (1941) and in the guinea pig by Johnson (1957). Since the cat was the experimental animal used in the present study, Fox's description (1940) of the cat amygdala will be reviewed in detail.

In the cat, the amygdala lies medial to the pyriform cortex, posterior to the diagonal band of Broca and anterior to the hippocampus (fig. 1). Because of their position and fibre connections, the nucleus of the lateral olfactory tract and the intercalated masses are joined with the anterior amygdaloid area to form the anterior amygdaloid group of nuclei. The corticomedial group is composed of the central, the medial and the cortical nuclei, and the basolateral complex of the basal and lateral nuclei.

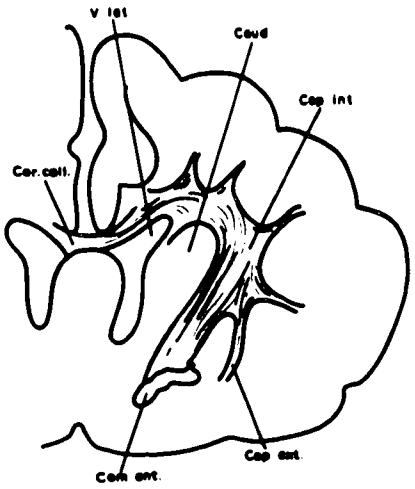
FIGURE

FIGURE I

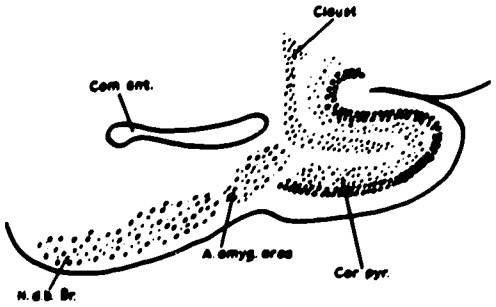
Diagrams of the Amygdaloid Nuclei at Three Different Levels.

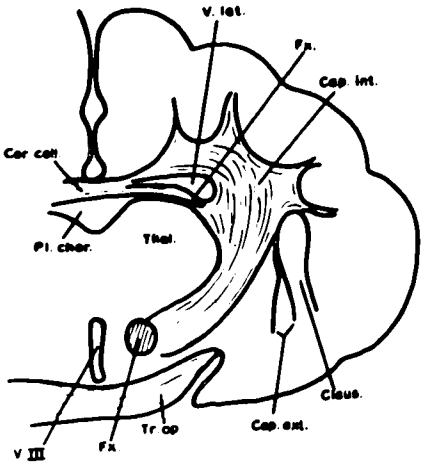
The column on the right illustrates the nuclei. The column on the left illustrates the fibre tracts bounding the amygdaloid complex.

Cat Brain

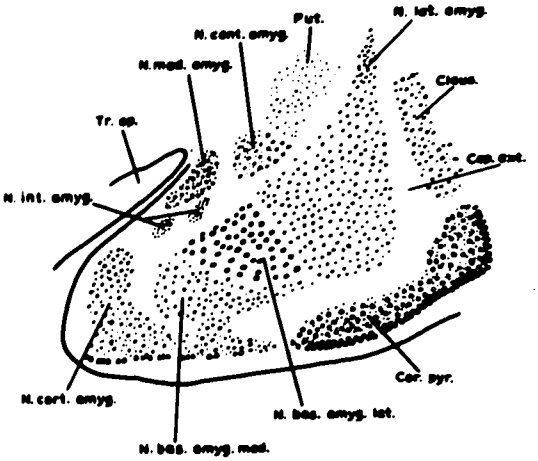


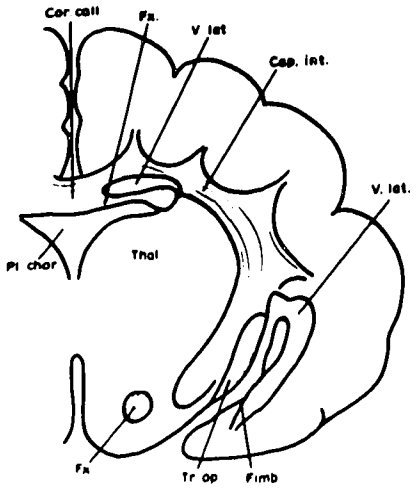
Anterior



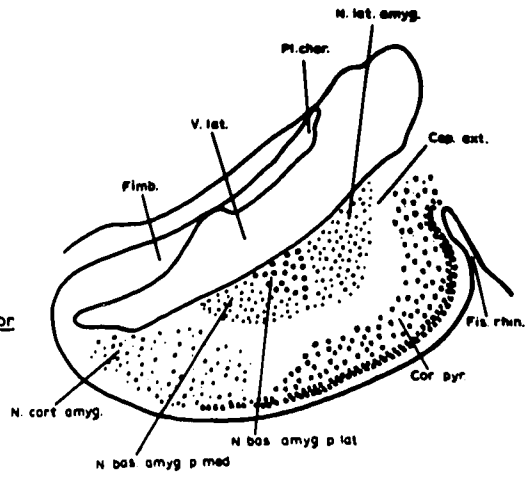


Middle





Posterior



The anterior amygdaloid group consists of the anterior amygdaloid nucleus, the nucleus of the lateral olfactory tract and the intercalated masses. The anterior amygdaloid nucleus (fig. 1) is that region immediately in front of the corticomedial and basolateral complexes. It is continuous laterally and inferiorly with the pyriform cortex, and medially with the diagonal band of Broca. The cells within this region are both small and large in size and are arranged in a diffuse manner. The nucleus of the lateral olfactory tract is a small agglomeration of darkly stained cells containing much Nissl substance. It overlies the medial side of the lateral olfactory tract and is completely surrounded by the anterior amygdaloid area. The intercalated masses are islands of small cells located between the basal and central nuclei, and the basal and medial nuclei. More anteriorly they are located above the basal and the lateral nuclei. One of these masses enlarges in the anterior amygdaloid area and reaches the level of the lateral part of the anterior commissure.

The corticomedial complex is made up of the central, medial and cortical nuclei (fig. 1). The

central nucleus is composed of a small celled part which is lateral to and a large celled part which is medial to the longitudinal association bundle. The medial group is easily determined by its relatively large cells but the cells of the lateral group are so similar to those of the putamen that it is difficult to identify the supero-lateral limit of that part of the central nucleus. In fact, Fox (1940) called the lateral part of the central nucleus the putamino-central nucleus. In general, a bundle of fibres which crosses the most inferior part of the putamen is taken as the superior boundary of the lateral part of the central nucleus. Immediately medio-ventral to the central nucleus lies the medial nucleus. It is located medial to the basal nucleus and lateral to the optic tract. The medial nucleus is composed of small and medium sized cells. The cortical nucleus is the most ventral and superficial of the amygdaloid nuclei. It extends to the surface of the hemisphere and is considered a modified cortex (Hall, in preparation). The nucleus is composed primarily of small and medium pyramidal cells forming a corrugated layer near the surface of the cortex.

The basolateral complex is made up of the lateral and basal nuclei. The lateral nucleus is limited laterally and ventrally by the external capsule, medially by the basal nucleus and dorsally by the central nucleus and the putamen (fig. 1). More posteriorly, it is bounded medially and dorsally by the lateral ventricle. Anteriorly, it is completely surrounded by the external capsule. Koikegami (1963) distinguished a medial and a lateral part in the lateral nucleus of the cat. The lateral portion is that segment which is wedged between the putamen and the external capsule dorsally. The remainder of the nucleus forms the medial portion. Both subdivisions are composed of small and medium sized cells. The basal nucleus (fig. 1) is located medial to the lateral nucleus, dorsal to the cortical nucleus, lateral to the medial nucleus and the stria terminalis, and at more posterior levels, lateral to the lateral ventricle. The dorsal boundary is formed by the central nucleus and the longitudinal association bundle. The basal nucleus consists of a more dorsal large celled group and a more ventral small celled group.

Cortico-Amygdaloid Connections

The subject of this description is concerned with those amygdaloid afferents which arise in the cortex. The cortico-amygdaloid afferents have been the object of investigations on normal as well as experimental material. These studies have suggested that the amygdala receives fibres from both the paleocortex and the neocortex.

A. Paleocortical Projections to the Amygdala

Cajal (1911) was among the first to describe fibres from the pyriform cortex entering the amygdala through its posterior and lateral aspects. However, Johnston (1923), in his exhaustive study of the forebrain was the first author to describe carefully a group of fibres which arises from all parts of the pyriform cortex and converges over the basolateral complex to form a bundle. This group of fibres was described as an association bundle between the pyriform cortex and the amygdala as well as a projection tract.

Fox (1940) gave a more detailed account of the longitudinal association bundle in the cat.

He stated that the bundle is formed from fibres of the pyriform cortex and the lateral and basal nuclei. These fibres ascend through the amygdala and come to lie dorsal to the basolateral complex underneath the central nucleus where they form the longitudinal association bundle. They travel in the bundle anteriorly from the level where the stria terminalis ends to the anterior limit of the basal nucleus. More recently Valverde (1965) recognized in Golgi preparations of cats and rats that the pyriform component of the longitudinal association bundle in the cat had three divisions at its origin. He described a medial system ascending dorsally into the basal nucleus, an intermediate or diffuse system composed of small bundles entering the lateral nucleus and a lateral system fusing with the intermediate system, and ascending through the external capsule to the lateral nucleus.

In a recent discussion on the connections of the amygdala in the rat, Cowan, Raisman and Powell (1965) demonstrated the presence of an antero-posterior organization to the longitudinal association bundle. They determined that the bundle could be divided into two parts: an anterior part which consists of a group

of fibres coursing from the pyriform lobe to the basolateral complex, and a posterior part which projects primarily to the hypothalamus but also includes fibres ending in the basolateral amygdaloid complex. They also noted that ablations immediately above the orbital sulcus did not cause any degeneration in the bundle.

B. Neocortical Projections to the Amygdala

i) Temporo-Amygdaloid Connections

Information on the neocortico-amygdaloid afferents has been gathered from studies on normal as well as experimental material. Investigations on normal human brain have revealed the existence of bundles interconnecting the neocortex with the basolateral amygdaloid nucleus (Klingler and Gloor, 1960). Klingler and Gloor (1960) observed that the uncinate and inferior fronto-occipital fasciculi, which travel in the inferior half of the external capsule, and the superior longitudinal fasciculus which courses in the superior half of the external capsule, carry fibres that pass into the basolateral amygdaloid complex. In addition they demonstrated the presence of two short fascicles, the amygdalo-temporal and amygdalo-

insular fascicles, connecting the amygdala with the temporal and the insular cortex. The amygdalo-temporal fascicle is described as beginning to form as it emerges from the lateral surface of the amygdala and bends in an antero-inferior direction to enter the white matter of the temporal pole. The amygdalo-insular fascicle is first observed at the anterior part of the amygdala and can be followed through the external capsule into the medullary lamina of the long insular gyrus where the fibres become dispersed in the gray matter. However from this study, no conclusion could be reached concerning the direction of these fibres with regard to the amygdala.

The application of silver impregnation techniques for degenerating axons has determined the existence and terminations of temporo-amygdaloid fibres in monkeys and cats. After ablating several small areas of the temporal lobe of the monkey, Whitlock and Nauta (1956) determined that only the rostral part of the inferior temporal gyrus projects to the amygdala. Degenerated fibres entered the white matter of the temporal cortex and continued in the external capsule into the amygdala where most of the

preterminals were observed in the basal and lateral nuclei. Only a few preterminals were reported in the central nucleus. Although Whitlock and Nauta (1956) were unable to trace temporo-amygdaloid fibres from other regions of the temporal cortex, Showers and Lauer (1961) stated that area 22 in the superior temporal gyrus is also connected to the amygdala. Using the Marchi method, the latter investigators observed fibres from the superior temporal gyrus in the white matter of the temporal lobe joining the inferior longitudinal fascicle and the fibres of the temporal limb of the anterior commissure terminating in the amygdala. The projections from the superior temporal gyrus were traced only to the basal and lateral nuclei.

Investigations of the temporo-amygdaloid projections in the cat agree in part with those described in the monkey. Using the Nauta technique, Lammers and Lohman (1957) (see Gastaut and Lammers, 1961) reported that the inferior part of the posterior sylvian gyrus, which is homologous to the temporal pole in monkeys (Papez, 1929), projects to the dorsal part of the lateral amygdaloid nucleus and to the lateral

part of the central nucleus. More recently, Powell (1964) stained degenerated fibres in the amygdala following lesions in the middle ectosylvian gyrus. He reported that most fibres reach the amygdala via the external capsule. However, he also noted that some fibres course in the stria terminalis.

Thus in man, monkeys and cats, there is evidence indicating that temporal fibres reach the basolateral complex and the central nucleus.

ii) Orbito-Amygdaloid Connections

In their investigation of the insulo-temporal cortex in monkeys, Showers and Lauer (1961) discussed amygdaloid afferents from the frontal and parietal opercular region and the orbital gyrus. They observed that degenerated fibres from the orbital gyrus enter the extreme capsule and penetrate the amygdala where some of the fibres end. Degenerated products stained with the Marchi method were identified only in the basolateral complex. However it should be noted that Nauta (1962) did not report any orbito-amygdaloid fibres in monkeys.

More recently, several investigations in the cat have revealed the presence of orbito-amygdaloid fibres. These experimental degeneration studies were

carried out with the Nauta staining technique. Koikegami (1963) stated briefly in his review article that some fibres connected the anterior orbital gyrus to the corticomedial division. However little supporting data was provided. It should be noted that Koikegami employed the terms anterior orbital gyrus and orbito-sylvian gyrus or posterior orbital gyrus for the more widely accepted terms orbital gyrus and anterior sylvian gyrus. The latter terminology is used in this dissertation.

In a more detailed description of the subcortical projections of the orbital surface of the cat, Hirata (1965) observed a remarkably extensive distribution of orbito-amygdaloid projections. He observed degenerated fibres from the anterior orbital area proceeding posteriorly into two bundles, one within the external capsule and the other one outside it. These two fibre bundles distributed mainly in the anterior amygdaloid area and in both parts of the basal nucleus. However, some degeneration was also observed in the ventral part of the lateral nucleus and in the corticomedial complex. In addition, Hirata (1965) carried out ablations on the orbito-

sylvian area. According to him, the orbito-amygdaloid fibres from this region coursed only in the external capsule. Moreover, he observed that the degenerated fibres were distributed only to the corticomedial complex and the parvocellular basal nucleus.

In his investigation of the pyriform lobe, Valverde (1965) reported on lesions in the orbital cortex of the cat. In his Nauta study, he also noted the presence of the two orbito-amygdaloid bundles. In addition, the sections obtained with the Nauta method contained fine degenerated fibres in the anterior amygdaloid area, in the central nucleus and in the basolateral complex. The latter finding also confirmed Koikegami's and Hirata's results. As well, Valverde described some fibres entering the central nucleus and continuing into the stria terminalis.

However, a recent study by Mizuno et al., (1969) has failed to confirm such extensive projections of the orbital gyrus. In fact hardly any fibres were seen in the amygdala. The only ones observed, coursed in the external capsule and ended in the anterior amygdaloid area. Thus the evidence for the existence of orbito-amygdaloid fibres is questionable and those

that have been reported are controversial.

C. Physiological Localization of Amygdaloid Afferents

The application of physiological techniques to the study of the connections of the amygdala has suggested that additional cortical regions project to this complex. Wendt and Albé-Fessard (1962) demonstrated that short latency responses could be recorded in the lateral nucleus after stimulation of the anterior ectosylvian gyrus (SII). Niemer et al., (1963, 1966) confirmed these results and demonstrated that stimulation of the anterior sylvian gyrus, and the coronal gyrii also produced short latency responses in the basolateral complex. These were not considered monosynaptically transmitted. However it is possible that the synapses are located within the amygdala itself. Valverde (1965) and Hall (in preparation) observed that many axons of the lateral amygdaloid nucleus give off collaterals which arborize locally within the lateral nucleus.

Functional Studies

The amygdala has been attributed a major role in expressing the emotions of fear and anger. Attention was brought to this forebrain structure as a modulator of emotional responses by the reports of Klüver and Bucy (1939) on bilateral temporal lobectomized monkeys. The behavioural pattern exhibited by these monkeys was characterized by a loss of fear and anger responses, psychic blindness, marked oral tendencies, a tendency to attend and react to all visual stimuli, and an increase in sexual behaviour. The analysis of this syndrome demonstrated that some of its components could be identified with particular structures. Weiskrantz (1956) was the first to demonstrate in monkeys that removal of the amygdala produced docility. Jameson et al., (1957) confirmed these results by implanting radioactive material in the amygdala. This method permitted the ablation of the amygdala with minimal involvement of the surrounding structures. Their results demonstrated that, as long as the lesion was confined to the amygdala, the monkeys exhibited only a loss of anger and fear reactions, but whenever the lesion extended into the surrounding structures

other signs of the syndrome made their appearance.

However, early attempts at analyzing the function of the cat amygdala by ablation led to entirely opposite results. Spiegel et al., (1940) and Bard and Mountcastle (1947) reported that cats became extremely aggressive following bilateral removal of the temporal lobe. The discrepancy between the results in the monkey and the cat cannot be accounted for by a difference in species since Schreiner and Kling (1954) and Green et al., (1957) were able to produce docility in the cat following bilateral amygdalectomy. Moreover, loss of anger and fear reactions was also reported in other animals following ablations of the amygdalae (Anand and Brobeck, 1952, in rats and Martin et al., 1958, in dogs). It is possible to explain this discrepancy by the fact that the lesion may have extended into the hippocampus (Green et al., 1957), or by the presence of a region in the amygdala inhibiting anger responses (Kaada, 1967).

Stimulation of the amygdala in experimental animals and in humans has confirmed the role of this structure in the modulation of fear and anger. However, attempts at localizing these emotions to specific

nuclei have led to some controversies. MacLean and Delgado (1953), Fernandez de Molina and Hunsperger (1959), and Hunsperger and Bucher (1967) maintained that the corticomedial complex modulates the fear and anger responses. Furthermore, Hunsperger and his collaborators (1959, 1967) reported that stimulation of the stria terminalis produces the same emotional reaction. On the other hand, Kaada et al., (1954) and Ursin and Kaada (1960) considered that the basolateral complex is primarily responsible for the control of fear and anger. However, these views are not mutually exclusive because the small-celled part of the basal nucleus sends fibres to the stria terminalis. Other workers, Hilton and Zbrozyna (1963), showed that the defence reaction can be induced by the longitudinal association bundle and that severance of the bundle abolishes the defence reaction. Lissak and Endrőczi (1967) supported this statement by demonstrating that stimulation of the anterior part of the basolateral complex, and the anterior part of the amygdala also evokes fear and rage reactions. Furthermore, in a combination of stimulation and ablation experiments, Ursin (Ursin and Kaada, 1960,

and Ursin, 1965) claimed that the rostral half of the basolateral complex, the central nucleus and the preamygdaloid area are regions controlling fear responses and that the ventromedial and caudal parts of the basolateral complex are the regions for the defence reactions. Thus, these experiments suggest that the amygdala regulates the fear and anger responses. However it is not definite whether one part has more importance for anger and another for fear.

The influence of the neocortex on the control of fear and anger reactions produced by the amygdala has always remained ill-defined. Klüver and Bucy (1939) concluded that bilateral removal of the first or second and third temporal convolutions has no effect on the behaviour of monkeys. Although no information of this nature exists in the cat, the removal of the entire neocortex bilaterally has been reported to produce docility (Bard and Mountcastle, 1947 and Rothfield and Harmann, 1954). Moreover Rothfield and Harmann (1954) reported that whenever the dorsolateral and dorsomedial parts of the neocortex were removed, no changes in the rage threshold were observed. Thus they concluded that at least part

of the more ventrally located fronto-temporal cortex must be removed alone or with the rest of the neocortex in order to produce docility. Bard and Mountcastle adopted the following proposition (p. 396, 1947): "that the amygdala exerts a sole direct suppressing action and this is facilitated by impulses from the midline cortex and neocortex." That part of the neocortex sends facilitatory impulses to the amygdala was shown to be true by Sawa et al., (1960). The latter author demonstrated that stimulation of the temporal neocortex facilitates the cells of the lateral nucleus in cats. In addition, Sawa and Delgado (1963) have also shown that sensory stimulation facilitates most cells of the lateral nucleus but can inhibit some of them. This facilitation of amygdalar cells by peripheral stimulation is not unrelated to that produced by the cortex because Wendt and Albé-Fessard (1962) showed that somatic impulses recorded in the amygdala are relayed by the secondary sensory area. In summary, the functional studies suggest that the neocortex, mainly its fronto-temporal region, facilitates fear and anger responses from the amygdala. Thus it may be anticipated that the neocortical pro-

jections to the amygdala arise from the fronto-temporal region.

Problem Formulation

The review of the anatomical and physiological literature indicates the existence of conflicting results in regard to the origin and sites of termination of neocortico-amygdaloid projections so that further investigation of these projections is required. More specifically, it would be of interest to determine whether neocortico-amygdaloid projections follow some form of organization and if so, whether sites of termination could be correlated with functionally distinct regions in the amygdala.

In the few experimental anatomical studies reported in the literature, only the orbital and temporal regions of the neocortex have been investigated. Thus it is not known whether other areas of the neocortex project to the amygdala, and if so, whether these projections are of equal extent and density to those already described.

Most of the previous studies were based

on the use of the Nauta technique only. In order to demonstrate the amygdaloid afferents more adequately, both the Nauta (1957) and the Fink and Heimer techniques (1967) have been employed.

MATERIAL AND METHODS

Operative Procedures

Sixty-two adult cats, varying in weight from 1.7 kg to 4.5 kg were used in this investigation. In all, twelve different cortical areas were ablated. All of them were situated in the neocortex except for one region situated in the paleocortex. In each ablation, which was made in the left hemisphere, the same procedure was followed.

The cat was anesthetized with an intraperitoneal injection of 40 mg of Nembutal per kilogram of body weight. The head was secured in a stereotaxic apparatus of the Kopf type, shaved, and disinfected with iodine and alcohol. The skin was incised along the orbital border of the frontal bone, from the midline to the front of the helix of the ear, then posteriorly from the ear to a point above the nuchal line. The L-shaped skin flap was reflected and the temporalis muscle exposed. The left temporal muscle was incised at its origin and reflected inferiorly. The region of the calvaria overlying the intended lesion site was identified with the help of coordinates

from the Atlas of Jasper and Ajmone-Marsan, (1954). An opening was made with a dental drill and then enlarged sufficiently with a rongeur to expose clearly the lesion site. The coagulating electrode, described below, was then placed on the intact dura mater and the current applied. Following the coagulation, the operative site was rinsed with warm physiological saline, the extent of the damage estimated, and the bony defect filled with gelfoam. The temporal muscle was sutured and the skin edges were approximated with metal Michel clips. The operative site was once more disinfected and then coated with collodion. In addition, 0.5 cc to 1.0 cc of penicillin (300,000 i.u. per cc) was given intramuscularly as further prevention of infection.

Electrodes. Three different electrodes were employed in these experiments. The first electrode consisted of a copper disc 5 mm in diameter mounted on the end of a copper rod insulated with asbestos. After a few usages, the disc became oxidized to a paper thin plate of copper and it had to be replaced. A second electrode was made with the same specifications but of stainless steel. This electrode

proved to be far more durable while being just as easy to handle. The electrode was connected to the negative pole of an instrument called a Lesion Generating Device manufactured by Stoelting Co. of Chicago while the positive pole was attached to the temporal muscle close to the site of the lesion. The electrode was held manually on the dura mater. A direct current of 15 milliamperes was applied for 20 seconds. This amount of current was usually enough to coagulate the outer five cortical layers. However, one region of the cortex could not be reached with this type of electrode and here, a third electrode was employed. It consisted of a fine silver wire, 0.01 inch in diameter insulated in a straight capillary glass tubing. A tip of 1.0 mm was left exposed beyond the point of fusion of the glass to the metal. The electrode, held on a carrier, was set in position according to the coordinates of the Atlas of Snider and Niemer (1961). A direct current of a 3 milliampere strength was delivered for 10 seconds from the same apparatus as mentioned above.

Post-Operative Period

The post-operative period was uneventful except in a few animals which had to be fed by hand for the first day. The duration of the post-operative period was governed by two variables: the portion of the axon to be impregnated and the staining technique used. Electron microscopic studies (Colonnier, 1964) have shown that the first part of the axon to degenerate is the bouton, and then the axonal segment. In this study only a few preterminals were observed in the amygdala with the Nauta technique, although fibres of passage could be seen distinctly. On the other hand, the Fink and Heimer II procedure revealed numerous terminals in the amygdala where few or none could be detected with the Nauta method. It was thus considered advantageous to combine both techniques to study the course and distribution of degenerated fibres. In this particular series of experiments (Table 1), a survival period of ten days gave the best results with the Nauta method. However, some well-impregnated sections were obtained with a five day survival period. For the Fink and Heimer II method, a survival of five days yielded more degenerated

terminals in the amygdala than any other survival time. A few animals were sacrificed also at three days, as recommended by Wiitanen (1969), but this was discontinued because the latter technique could not be adjusted properly to obtain good impregnation.

Histological Preparations

A. Perfusion. Fixation. Cutting.

For the perfusion, the animals were anesthetized with Nembutal as previously discussed. After clipping away the fur over the anterior chest wall, an opening was made in the thoracic cage large enough to expose the pericardium. The pericardium was incised and the heart exposed. The right auricle was opened, the thoracic aorta was clamped at the mid-thoracic level, and a fifteen gauge needle was introduced into the left ventricle. Five to six hundred cc of physiological saline were perfused through the left ventricle followed by the same quantity of 10% formalin. In order to obtain a good perfusion, the perfusing fluid flowed from bottles suspended at about five feet above the animal. The brain was removed and stored in at least ten times its own volume of

TABLE I

Summary of the Schedule of the Post-Operative Period and Staining Procedure Employed for each Animal.

TABLE 1

Summary of Procedure for Each Experiment

Cat No.	Post.–Op. Survival	Plane of Section	Staining Method
C–12	10 DAYS	FRONTAL	NAUTA
C–14	5 "	"	" & FINK–HEIMER II
C–15	5 "	"	FINK–HEIMER II
C–20	5 "	"	" "
C–21	5 "	"	" "
C–22	5 "	"	" "
C–23	5 "	"	" "
C–30	10 "	"	NAUTA
C–31	10 "	"	
C–32	5 "	"	F.–H. II
C–37	10 "	"	" " " & NAUTA
C–39	10 "	"	" " " "
C–40	5 "	"	" " " "
C–41	5 "	"	" " " "
C–44	5 "	"	" " "
C–45	5 "	"	" "
C–51	3 "	"	WIITANEN
C–52	3 "	"	"
C–53	3 "	"	" & F.–H. II
C–55	3 "	"	F.–H. II
C–56	3 "	"	F.–H. II
C–58	5 "	"	F.–H. II
C–59	5 "	SAGITTAL	F.–H. II
C–60	5 "	FRONTAL	F.–H. II

10% formalin. The Nauta method requires a minimum of two weeks of fixation in 10% formalin to obtain "occasional satisfactory results" (Nauta, 1957), and a period of 4 to 6 months is said to be preferable (Nauta, 1957). In this group of experiments, the tissue to be stained with the Nauta method was fixed in formalin for 5 to 8 weeks. The Fink and Heimer method is most effective on tissue fixed for 1 to 3 weeks (Fink and Heimer, 1967). With this latter method, the author used the prescribed fixation time. Following the respective fixation periods, several brains were placed in 30% sucrose solution to improve the preservation of the tissue and to facilitate the cutting procedure (Fink and Heimer, 1967). Within three to five days, the brains had sunk to the bottom of the jar. They were trimmed and sectioned at 30/u on a freezing microtome. The tissue could be kept in sucrose for up to 9 days without influencing the quality of the impregnation. The sections were stored in 2% formalin for the Fink and Heimer II method and in 10% formalin for the Nauta procedure.

B. Staining Methods

i) Nissl Stain

Sections from the region of the lesion and the amygdala were mounted on slides with albumin and stained with cresyl echt violet to demonstrate the extent of the lesion as well as to provide confirmation of the nuclei containing terminal degeneration.

ii) Silver Impregnation Methods and their Biochemical Mechanisms

As already mentioned, degenerated axons were stained with two methods: the Nauta method (1957) and the Fink and Heimer II procedure (Fink and Heimer, 1967) which is a modification of the original Nauta procedure. The Nauta method which impregnates degenerated fibres well, was supplemented by the Fink and Heimer II method for the reason mentioned in the description of the post-operative procedure and because terminal portions of axons can be impregnated with the Heimer technique (Heimer and Peters, 1968). Therefore, it seemed that the distribution of terminals could be observed with more precision with the Fink and Heimer method than the conventional Nauta methods. These two techniques are based on similar principles.

The Fink and Heimer method and the Nauta

method can be divided into three steps: the first step consists in subjecting the tissue to a pre-treatment of potassium permanganate-phosphomolybdic acid or potassium permanganate-uranyl nitrate to increase the argyrophilia of degenerated axons and to diminish that of the normal axons: the second step consists in the impregnation of degenerated structures with silver which leads to the formation of what Nauta (1957) has termed "submicroscopic silver nuclei": and the third step is the further deposition and reduction of metallic silver on degenerated fibres thus making them microscopically visible. Because of the variation in the impregnation that can be obtained by minor changes in these techniques, it was deemed relevant to review the role of the different constituents of both methods.

1) Pretreatment Step

Potassium permanganate. Oxidation of tissue is necessary for the staining of normal as well as degenerated fibres (Eager and Barnett, 1966) and it is also necessary for selective impregnation of degenerated fibres (Nauta and Gygax, 1954). It seems that the role of potassium permanganate in the silver

techniques is that of an oxidizing agent (Eager and Barnett, 1966). Its replacement by other known oxidizing agents such as formalin, hydrogen peroxide and periodic acid yields a silver impregnation comparable to that obtained by the regular Nauta method. The selectivity imparted by potassium permanganate or other oxidizing agents is dependent mainly on the time of exposure of the tissue to the oxidant and also on the degree of myelination of the axons. Short oxidation time brings out the fine fibres maximally, degenerated as well as normal ones; longer oxidation brings out thicker, heavier myelinated axons of both the normal and the degenerated types but suppresses the finer ones, and very prolonged oxidation suppresses the staining of all axons (Eager and Barnett, 1966).

The reactive site of the oxidizing agent on the axis cylinder has not yet been elucidated. However, the evidence available seems to indicate the lipid portion of axonal membranes and myelin sheath as the active point (Evans and Hamlyn, 1956). Furthermore, the blocking of the unsaturated fatty acid fraction of these lipids abolishes silver impregnation (Giolli, 1965 and Eager and Barnett, 1966). The

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latter investigators have thus suggested that oxidation transforms ethylene bonds of unsaturated acids into carbonyl groups where silver ions can be deposited. Heimer (1967) considered, on the other hand, the possibility that lipid extraction enhances the suppressing effect of $KMnO_4$ rather than diminishing the argyrophilic sites on normal fibres. Wherever the site of predilection for the oxidative agent may be, the fact that degenerated fibres are more sensitive to oxidation than normal fibres accounts in part for the selectivity of the stain.

Hydroquinone - Oxalic Acid. This mixture is solely a decolorizing agent. If non-coloring agents are used, such as hydrogen peroxide, this step is unnecessary.

Phosphomolybdic Acid. Uranyl Nitrate. The role of phosphomolybdic acid is even more problematic than that of $KMnO_4$. It seems that it has a dual role: first, it is necessary for the staining of normal as well as degenerated fibres (Eager and Barnett, 1966), and second, it increases the argyrophilia of degenerated axons to the detriment of normal ones. Contrary to the effect of $KMnO_4$, prolonged exposure to the acid

never abolishes the argyrophilia of degenerated fibres. Moreover, the acid is active either in the presence of an oxidizing agent (whether this agent comes before or after the acid) or in the presence of carbonyl groups (Eager and Barnett, 1966).

Some tentative explanations have been forwarded to explain this complex mechanism of the acid. Lund and Westrum (1966) have suggested that phosphomolybdic acid acts by combining with sites on the filaments that would otherwise have been occupied by silver ions. Eager and Barnett (1966) have extended this idea by suggesting that the acid provides negative ions to add on to double bonds of unsaturated fatty acids. Perhaps the best concluding remarks are those of Rossignol (Thesis, 1969, p. 66): "Whether the role of phosphomolybdic acid is passive as proposed by Lund and Westrum, 1966) or active (as proposed by Eager and Barnett, 1966), it remains that all silver techniques use in their pretreatment a heavy metal, whether it is molybdenium (Nauta, 1957), uranium (Nauta, 1957, and Fink and Heimer, 1967) or

tungsten (Johnstone and Bowsher, 1969)."

2) Impregnation Step

Silver Nitrate. This is the central step in the silver impregnation methods used. Its omission abolishes the staining of fibres (Eager and Barnett, 1966). However, this does not hold for all silver methods, because Rossignol described a modified Fink and Heimer method which does not employ a silver nitrate step. During the silver nitrate stage, "submicroscopic silver nuclei" are deposited on the fibres (Nauta and Ryan, 1952), or more precisely, on the carbonyl groups produced from the oxidation of unsaturated fatty acids (Eager and Barnett, 1966). In one technique used, the Fink and Heimer II procedure, the silver nitrate solution is mixed with pyridine. The value of adding pyridine lies in its ability to increase the argyrophilia of the finest fibres (Johnstone and Bowsher, 1969).

3) Deposition and Reduction Step

Ammoniacal Silver Nitrate. This step is the most critical of the entire procedure. It is concerned with the deposition of silver ions, from

an ammoniacal silver solution, on the "submicroscopic silver nuclei". This silver deposition is dependent on the availability of free silver, Ag^+, in the solution. The quantity of silver ions available, (Ag^+), is the result of a precarious balance between a weak base, ammonium hydroxide, and a strong base, sodium hydroxide. Nauta and Gygax (1951) have explained clearly the biochemical mechanism underlying the deposition of free silver on the fibres.

The addition of ammonium hydroxide to silver nitrate forms a complex cation, $[Ag(NH_3)_2^+]$ which liberates silver easily. This complex ion is found only in small quantity because most of the silver exists in the form of the complex salt $Ag(NH_3)NO_2$ of a strong base $Ag(NH_3)OH$. The further addition of a base should break down the salt. However ammonium is too weak to break down $Ag(NH_3)OH$ into its salt and thus liberate more free silver. In order to liberate silver ions, Ag^+, a strong base such as sodium hydroxide is required. Sodium hydroxide decomposes $Ag(NH_3)OH$ and liberates the complex cation $Ag(NH_3)^+$ which in turns frees silver ions, Ag^+. This complex mechanism is necessary in order to deposit silver ions

on the "submicroscopic silver nuclei".

The reduction of free silver ions, Ag^+, into metallic silver, thus making the fibres microscopically visible, is controlled by a weak acidified reducer, a 10% alcoholic solution of dilute formalin in the presence of citric acid. In addition, the weak acid, citric acid, contributes to improve the selectivity of the impregnation.

Sodium Thiosulfate. The "submicroscopic silver nuclei" which are deposited on normal axons are soluble in sodium thiosulfate while those on degenerated fibres are not. The role of the sodium thiosulfate appears to be the removal of undesired silver compounds from the normal fibres.

C. Staining Protocol

i) Nauta method (1957) - using phosphomolybdic acid

1. Wash sections in double distilled water (DD).
2. Transfer sections to 0.5% phosphomolybdic acid for 30 mins.
3. Transfer sections directly to 0.05% $KMnO_4$ for 5, 10 or 15 mins. depending on the amount of oxidation desired.

4. Transfer sections to 1% oxalic and 1% hydroquinone for a period of $2\frac{1}{2}$ mins.
5. Rinse sections in three baths of DD for not less than 15 mins.
6. Transfer sections to a 1.5% silver nitrate solution for 10 or 15 mins. depending on the amount of silver deposition desired.
7. Rinse sections in three baths of DD for not less than 15 mins.
8. Transfer sections individually into Laidlaw's solution.
9. Transfer into two baths of reducing solution for 1 minute in each bath. Agitate the sections constantly in the first bath.
10. Wash sections in a bath of DD.
11. Transfer sections into a 1% solution of sodium thiosulfate.
12. Rinse sections in two baths of DD and mount sections.

ii) Nauta method (1957) (modified) - using uranyl nitrate

1. Rinse sections in DD.
2. Treat sections with 5% aqueous solution of uranyl nitrate for half an hour.
3. Wash sections thoroughly in several volumes of

DD for a total time not less than 15 mins.

4. Transfer sections to a 0.05% aqueous solution of $KMnO_4$ for 30, 45, or 60 mins. depending on the amount of oxidation necessary.
5. Wash sections briefly in DD.
6. Decolorize sections in a mixture of equal parts of 1% oxalic acid and 1% hydroquinone for about 2 mins.
7. Wash sections thoroughly in three volumes of DD for a total time of not less than that of 15 mins.
8. Transfer sections to 1.5% silver nitrate for 20 or 30 minutes depending on the degree of silver impregnation required.
9. Wash briefly in DD and pass sections individually through the carbonated silver nitrate solution of Laidlaw for one minute. If the sections are too dark, a few drops of ammonia are added. (Laidlaw's solution was prepared according to the method given by Nauta, 1957).
10. Pass the sections in two baths of reducer, one minute in each bath. The sections should be agitated constantly in the first bath.
11. Wash sections briefly in DD.

12. Place sections in 1% sodium thiosulfate for one minute.
13. Wash in two baths of DD.
14. Mount sections.

iii) Fink and Heimer method II (1967)

1. Rinse sections in DD.
2. Transfer sections into 0.025% solution of $KMnO_4$ for 5 mins.
3. Rinse sections in DD.
4. Transfer sections into a mixture of equal part of 1% oxalic acid and 1% hydroquinone.
5. Rinse sections in three baths of DD for not less than 15 mins.
6. Transfer sections for 5, 10 or 15 mins. to a 2.5% solution of uranyl nitrate. The time depends on the amount of suppression needed.
7. Rinse sections in three volumes of DD for not less than a total period of 15 mins.
8. Transfer sections for 1 or 2 hours in a 0.2% solution of silver nitrate. The time depends on the amount of impregnation required. The addition of 0.2 ml of pyridine to every 10 ml of silver nitrate may improve the results. The

sections are then transferred into this bath by groups of three.

9. Transfer sections into a freshly prepared ammoniacal silver nitrate solution for 2 to 5 minutes. A period of 3 mins. was satisfactory. Composition of ammoniacal silver nitrate solution. Note that the components should be added in the same order as they are listed:

1.5%	silver nitrate	-	20 ml
95%	ethyl alcohol	-	12 ml
	strong ammonia water	-	2 ml
2.5%	sodium hydroxide	-	1.6 to 1.8 ml

10. Transfer sections into two baths of Nauta reducers, usually one minute in each bath. Agitate the sections in the first bath.
11. Rinse sections in DD.
12. Transfer sections for 1 min. to 0.5% sodium thiosulfate.
13. Rinse sections in two volumes of DD.
14. Mount sections.

iv) Preparation of ammoniacal silver nitrate solution and reducer

Preparation of Laidlaw's Solution

1. Dissolve 24 grams of $AgNO_3$ in 40 cc of DD in a 500 cc graduated cylinder.
2. Add 460 cc of saturated (1.33%) lithium carbonate solution. Shake vigorously and let the precipitate settle to the 140 cc mark.
3. Carefully decant the supernatant fluid, refill to 500 cc with DD, shake and let the precipitate settle to 140 cc. Decant as before, repeating this washing procedure three times.
4. Again let the precipitate settle to the 140 cc, decant and add slowly 24 - 26 cc of 2% ammonia water with constant shaking until the solution is almost clear, or when you can see the window bars through the blackish precipitation. Avoid excess of ammonia. The solution when clear should have only a slightly ammoniacal smell.
5. Dilute to total volume of 240 cc. Filter, and store in a chemically clean bottle exposed to daylight for at least two weeks before use. A silver mirror will form on the glass of the bottle, indicating a good solution. This solution is

now very stable. Filter before use.

Preparation of the Nauta Reducer

10% alcohol	-	27 cc
1% citric acid	-	27 cc
95% alcohol	-	90 cc
Double distilled water	-	800 cc

Preparation of Ammoniacal Silver Nitrate - (Fink and Heimer II method)

The components of this solution should be added in the order listed:

1.5%	silver nitrate	- 20 ml
95%	ethyl alcohol	- 12 ml
	strong ammonium hydroxide	- 2 ml
2.5%	sodium hydroxide	- 1.6 to 1.8 ml

v) Mounting Procedure

The sections were mounted on slides from a warm gelatin bath. The mounted sections were dehydrated in alcohol and then taken through xylene solutions to remove completely the alcohol. After removing the excess of xylene, two drops of permount were placed on the slide and a coverslip was applied.

Illustrations of Degeneration

Drawings of the lesions and of the amygdala were made directly from sections enlarged with a photographic enlarger (Hansa Photographic Enlarger). The course and pattern of degeneration were drawn free hand while examining the sections under the microscope. Representative drawings of the lesions and of the amygdala were collected together to provide a comprehensive view of the origin, course and distribution of the degenerated fibres.

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Abbreviations:

Aaa	anterior amygdaloid area.
AEC	anterior ectosylvian gyrus.
A S	anterior sylvian gyrus.
B M	magnocellular part of the basal nucleus.
B P	parvocellular part of the basal nucleus.
C L	lateral part of the central nucleus.
C M	medial part of the central nucleus.
C O	cortical nucleus.
E C	external capsule.
ECA	anterior ectosylvian sulcus.
ECP	posterior ectosylvian sulcus.
EXC	extreme capsule.
I C	internal capsule.
L	lateral nucleus.
M	medial nucleus.
MEC	middle ectosylvian gyrus.
O G	orbital gyrus.
O T	optic tract.

PEC	posterior ectosylvian gyrus.
P S	posterior sylvian gyrus.
PSS	pseudosylvian sulcus.
PUT	putamen.
S C	coronal sulcus.
SCR	cruciate sulcus.
S D	diagonal sulcus.
S L	lateral sulcus.
SLP	posterior lateral sulcus.
S O	orbital sulcus.
SPCR	posterior cruciate sulcus.
SRH	rhinal sulcus.
SSA	anterior suprasylvian sulcus.
SSM	middle suprasylvian sulcus.
SSP	posterior suprasylvian sulcus.
S T	stria terminalis.

OBSERVATIONS

Before describing the results of these experiments, it appears appropriate to define the terms "degenerated fibres" and "degenerated terminals".

The term "degenerated fibres" applies to axons whenever they show rectilinear arrangements of "drop-like disintegration" (Nauta and Ryan, p. 179, 1952). In addition, the black drop-like fragments are interconnected by lighter brown narrow bridge which are also part of the original axons. Although degenerated fibres are not recognized as well with the Fink and Heimer II procedure as with the Nauta method (Fink and Heimer, 1967), the term "degenerated fibres" can be applied to the rows of spherules stained with the latter method. This is based on the fact that the spheroidal structures impregnated with the Fink and Heimer II procedure are found in regions where degenerating axons can be stained with the Nauta technique.

The term "degenerated terminals" denotes the presence of small black staining spheres which are the products of degenerated axons located near the soma or the dendrites of neurons. This term will be used to describe the black granules seen with the

Fink and Heimer II technique and also the pericellular axon fragments seen with the Nauta technique. According to Nauta (1957) his method impregnates only preterminals and degenerating fibres of passage (Nauta, 1957). However, it still seems justified to use the term because the presence of preterminal degeneration implies the presence of a degenerating terminal bouton in the vicinity. Furthermore, Guillery and Ralston (1964) have demonstrated that the Nauta technique is able to stain terminal boutons.

Unfortunately, the dots observed are not exclusively degenerated fibres. Some of the dots seen with the Nauta method and the Fink and Heimer II procedure are glial structures. Thus an awareness of the inherent limitations of these methods is useful for the correct interpretation of the stained tissue. In the Nauta sections, the commonest artifact is the "artificial deformities of normal axons" (Glees and Nauta, p. 82, 1955). The artifact consists in "spindle-shaped or rhomboid varicosities" (Glees and Nauta, p. 82, 1955) along the axon. The distinction between this artifact and true degeneration has been established on the basis of two criteria. First, the artifact is present in every region of the section.

Second, there is an absence of the characteristic "drop-like disintegration" (Nauta and Ryan, p. 179, 1952) of axonal degeneration. Another frequent source of misinterpretation which is inherent in both the Nauta and Fink and Heimer methods, is incomplete impregnation of normal axons. The impregnated fibres appear as broken black lines longer than true degenerated axonal fragments. A further source of error which is restricted to the Fink and Heimer method is the impregnation of perivascular structures. The latter structures appear as cylinders of oval or spherical black dots. This artifact is found in the external capsule, in the amygdala and in many areas of the cortex. These pseudodegenerated axons can be recognized by the uniformity of their rows and also by the proximity of blood vessels. According to Heimer (1967), it represents the impregnation of glial elements. The last source of misinterpretation is the presence of dust-like silver particles. These particles can be recognized by the fact that they are usually smaller and more uniformly distributed than true degenerated terminals and they are located bilaterally.

To clarify the description of the results, it was found useful to determine the antero-posterior extent of the terminal degeneration in the amygdala. The regions of degeneration were compared for the purpose of identification with the frontal planes of the Atlas of Jasper and Ajmone-Marsan (1954). In addition, the lateral amygdaloid nucleus was subdivided arbitrarily into three parts. The first part begins at the rostral portion of the lateral nucleus and ends at the beginning of the lateral part of the central nucleus. This region, which will be referred to as the anterior segment of the lateral nucleus, spans the area between Frontal 14.5 and 13.0. The middle segment of the lateral nucleus extends from Frontal 13.0 to Frontal 10.0. The posterior segment begins at the termination of the medial part of the central nucleus and ends at the caudal part of the amygdala. Thus it lies between Frontal 10.0 and Frontal 8.5. The lateral part of the central nucleus begins at Frontal 13.0 and ends at the caudal part of the amygdala, Frontal 8.5.

Investigation of the Temporo-Amygdaloid Connections

The temporal cortex was investigated first by removing the entire temporal region in one animal, and secondly by parcelling the temporal cortex into smaller regions and removing them separately. Thus, smaller lesions were placed in the following subdivisions (fig. 2, p. 57): the temporal polar area, the inferior part of the posterior ectosylvian gyrus, the inferior part of the posterior sylvian gyrus, the entire auditory area and the primary auditory region. Each region was removed successfully in at least two animals with the exception of the primary auditory region where the lesion was satisfactory in only one animal.

A. Lesions of the Whole Temporal Region (C-15, fig. 3, p. 58).

The lesion involves the middle and posterior ectosylvian gyrii as well as the posterior sylvian gyrus. It extends through the gray matter and encroaches slightly on the underlying white matter (fig. 3, p. 58). Degenerated axons proceed from the lesion into underlying white matter and from there into the lateral two thirds of the internal capsule.

The fibres either turn downward from the internal capsule into the external capsule (fig. 4, p. 59) or reach the latter directly by coursing through the inferior part of the extreme capsule. From the external capsule, the fibres bend in an infero-medial direction and enter the amygdala throughout its entire rostro-caudal extent. A heavy projection also reaches the putamen via the external capsule.

Degenerated terminals are distributed in three amygdaloid nuclei, two of which receive a heavy projection while the third receives only an occasional fibre (fig. 5, p. 60). Fibre terminals are scattered throughout the entire extent of the lateral nucleus, that is, medio-laterally as well as antero-posteriorly, but a much greater concentration is observed in the dorso-lateral part of the lateral nucleus. The lateral part of the central nucleus also receives many terminals, but the quantity is less than that in the lateral nucleus. The fibres enter the central nucleus through the ventral part of the putamen, the dorsal part of the lateral nucleus and the medial limb of the external capsule. The medial limb is that part of the external capsule interposed between the ventral segment of the putamen and the dorsal

segment of the lateral nucleus. The basal nucleus receives only a few fibers which are confined to its magnocellular part. The efferent bundles of the amygdala, the stria terminalis and the longitudinal association bundle, remain free of degeneration.

Fibres reach the contralateral external capsule via the anterior commissure. Although some of the external capsule fibres pass near the amygdala, no degeneration is observed in that nucleus. The site of termination of these fibres is the contralateral temporal cortex.

FIGURE 2

Localization of Lesions in the Temporal Lobe. (See the Chapter on Material and Methods for list of Abbreviations).

FIG. 2

Lesions of The Temporal Lobe

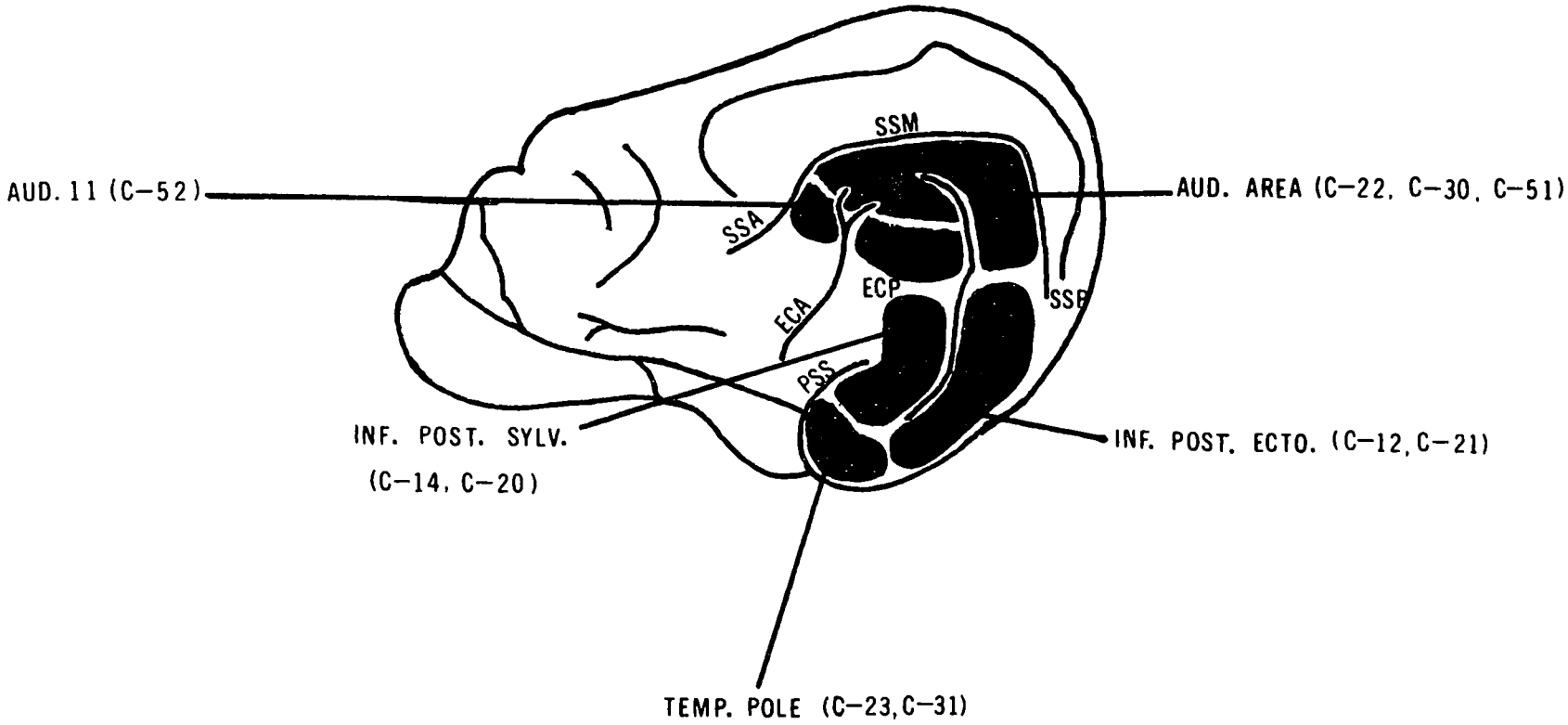


FIGURE 3

Localization of Lesion of the Entire Temporal Lobe.

FIG. 3

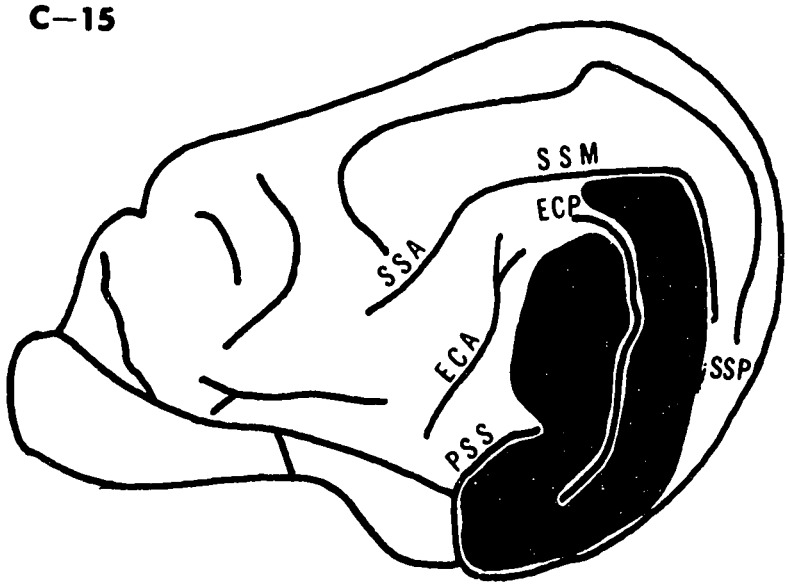


FIGURE 4

Depth of Lesion of the Entire Temporal Lobe and Distribution of Degeneration. Note the Presence of Degeneration in the Lateral Part of the Central Nucleus, the Lateral Nucleus and the Magnocellular Basal Nucleus.

C-15

FIG. 4

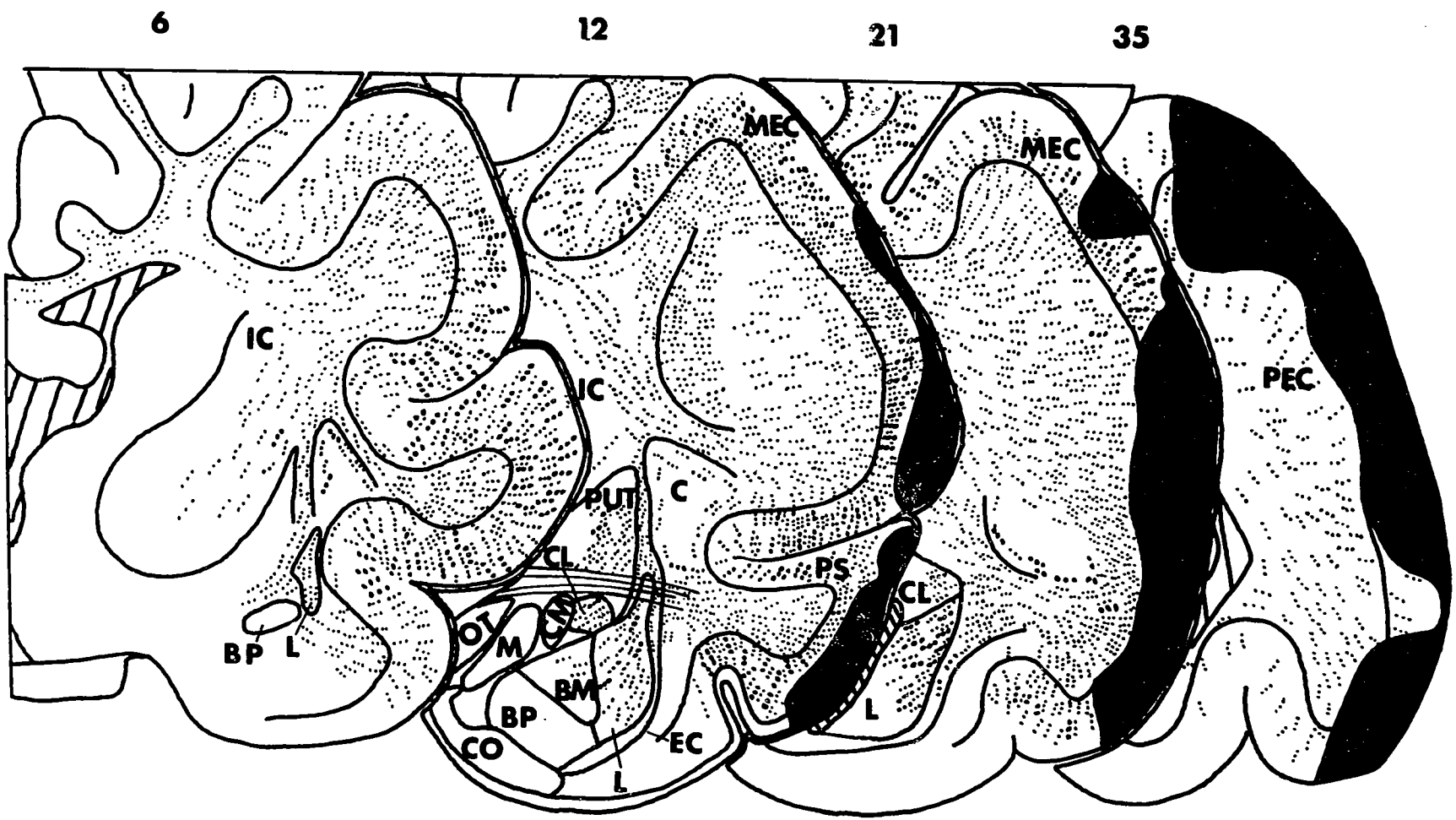
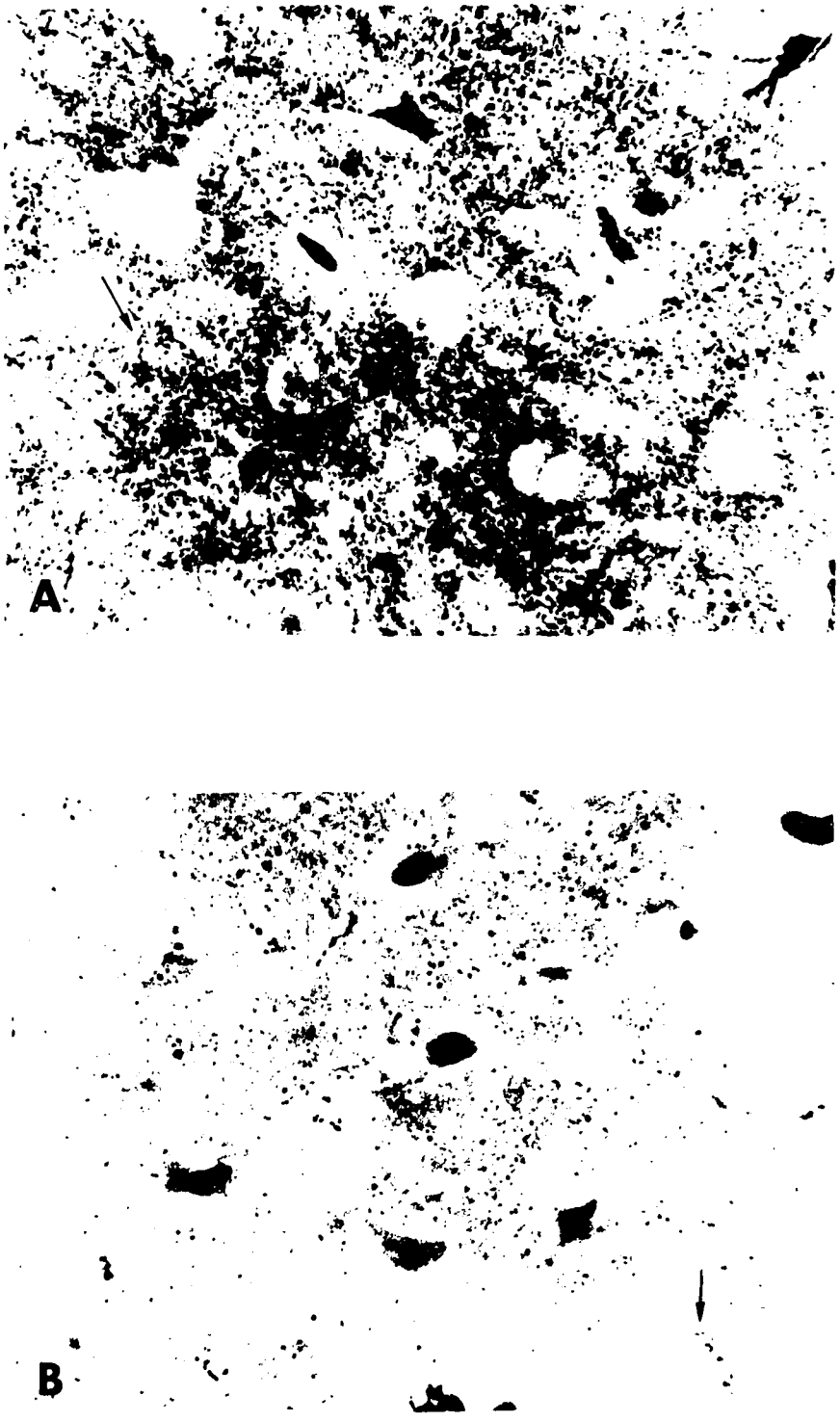


FIGURE 5

A. Fine Degeneration Products (Arrow) in the Ipsilateral Lateral Nucleus (C-15). Fink and Heimer II Procedure. Mag. X 400.

B. Absence of Degeneration in the Contralateral Lateral Nucleus. Arrow indicates a blood vessel. Fink and Heimer II Procedure. Mag. X 400.

FIG. 5



B. Lesions of the Temporal Polar Region (C-23, C-31, fig. 2, p. 57).

The lesion in C-31 involves the entire gray matter and encroaches slightly on the underlying white matter. In C-23, (fig. 6), the lesion is shallower encroaching barely on the underlying white matter. A group of degenerated fibres emerging from the posterior part of the lesion (C-23, fig. 6) courses anteromedially in the white matter and enters the external capsule. This group of fibres becomes diffuse as it reaches the caudal part of the amygdala. Fibres from the anterior part of the lesion course directly medially in the white matter to enter the external capsule at the level of the middle segment of the lateral nucleus. Some of these fibres end in the amygdala while others continue their anterior course in the external capsule, cross the midline in the anterior commissure and are distributed to the contralateral temporal cortex. No degenerated fibres were observed in the contralateral amygdala.

In the ipsilateral amygdala, terminals are confined to two nuclei: the lateral nucleus and the lateral part of the central nucleus. Fibre terminals are scattered throughout the anterior

FIGURE 6

Depth of Lesion in the Temporal Polar Region and Distribution of Degeneration. Degenerated Fibers are Present only in the Lateral part of the Central Nucleus and Lateral Nucleus.

FIG. 6

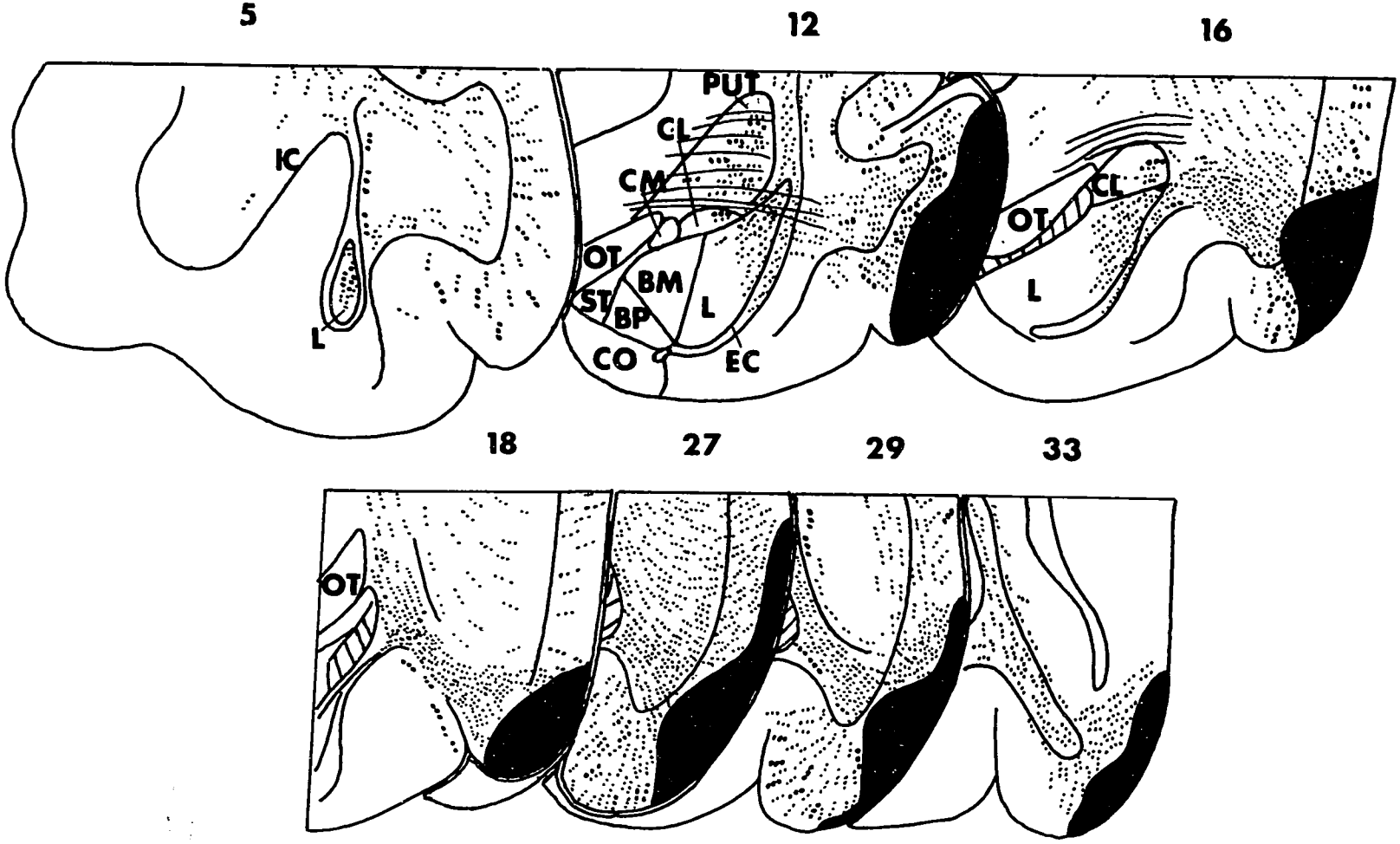


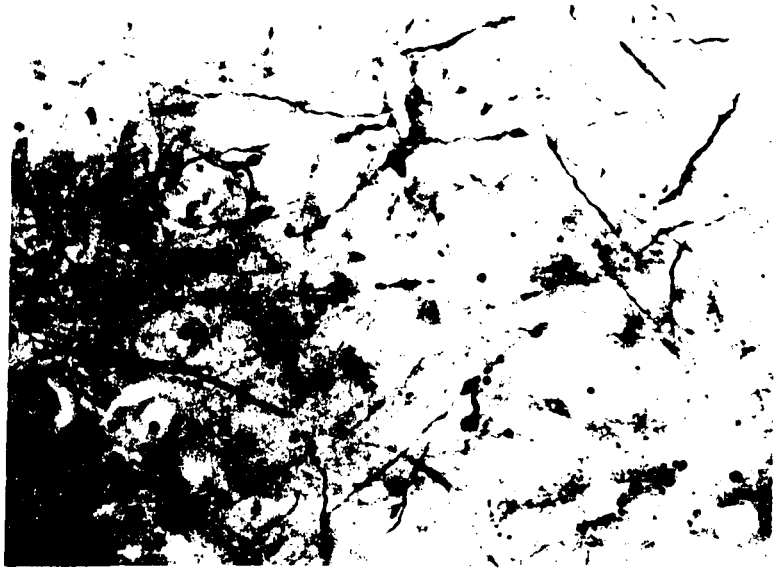
FIGURE 7

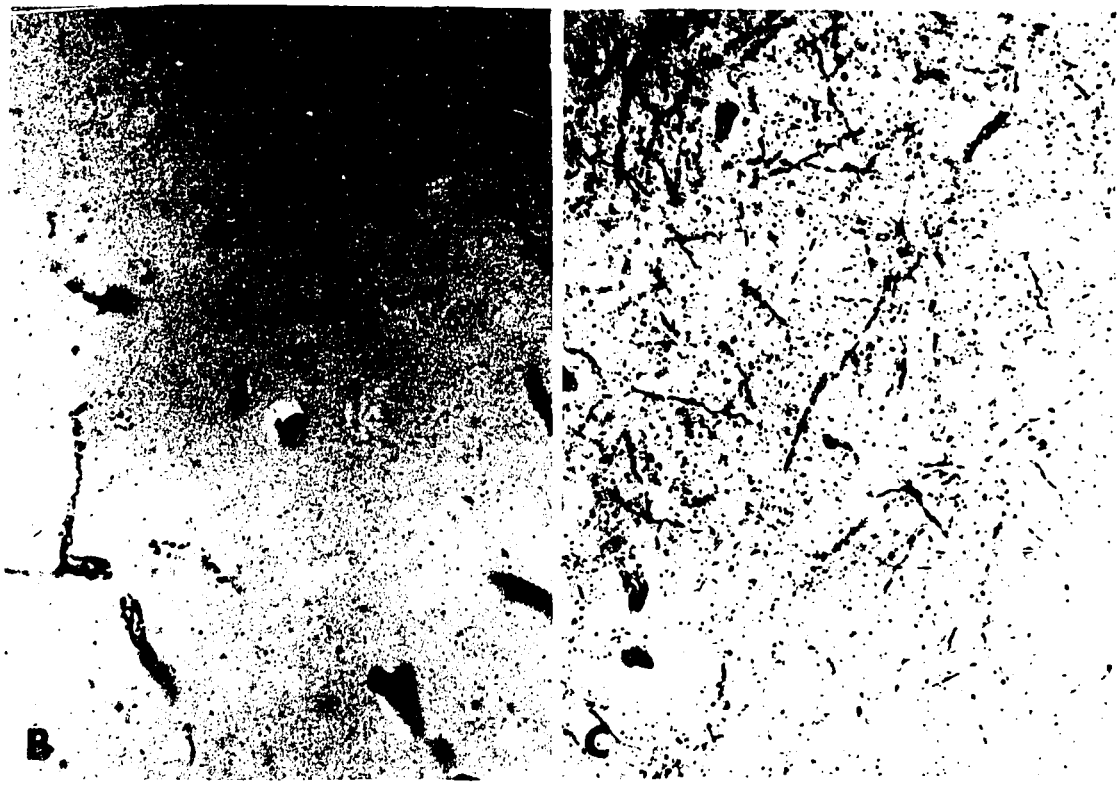
A. Degenerated Fibres in the Dorsal Part of the Lateral Nucleus (C-31). Nauta Method. Mag. X 540.

B. Contralateral Lateral Part of Central Nucleus (C-23). Fink and Heimer II Procedure. Mag. X 340.

C. Ipsilateral Lateral Part of Central Nucleus (C-23). Fink and Heimer II Procedure. Mag. X 340.

FIG. 7





segment of the lateral nucleus and the superolateral region of its middle and posterior segments (Fr. 13 to Fr. 8.5) (fig. 7). Somewhat fewer terminals are distributed to the lateral part of the central nucleus. The fibres ending in this nucleus pass through the ventral part of the putamen and medial limb of the external capsule.

C. Lesions of the Inferior Part of the Posterior Ectosylvian Gyrus (C-12, C-21, fig. 2, p. 57).

In C-12, the lesion penetrates through the gray matter into the white matter. However, in C-21 (fig. 8), the lesion is restricted to the deeper layers of the gray matter. Degenerated fibres from the lesion (C-21) pass posterior to the claustrum and mingle with the fibres of the lateral half of the internal capsule. These fibres, while coursing anteriorly, descend from the internal to the external capsule. Degenerated fibres then turn ventromedially and enter the putamen and the amygdala (fig. 10).

As in the previous lesion, (C-23, C-31), two amygdaloid nuclei are the seat of terminal degeneration: the lateral nucleus and the lateral part of the central nucleus. Terminals are found

throughout the entire anterior segment of the lateral nucleus. The middle and posterior segments also receive degeneration but only in their dorsolateral portions (fig. 9). A few fibres of passage course dorsoventrally through the lateral nucleus. Their site of termination could not be identified. The lateral part of the central nucleus also receives terminals but in a smaller quantity than the lateral nucleus. The fibres ending in the central nucleus pass through either the ventral part of the putamen or the dorsal part of the lateral nucleus and the medial limb of the external capsule. It is interesting to note that the quantity of degenerated fibres in the amygdala is less than in the previous lesion, even though the lesions are larger in size and just as deep. A few fibres are seen in the anterior commissure, in the contralateral external capsule and in the contralateral posterior ectosylvian gyrus, but none end in the contralateral amygdala.

FIGURE 8

Depth of Lesion in the Posterior Ectosylvian Gyrus and Distribution of Degeneration.

C–21

FIG. 8

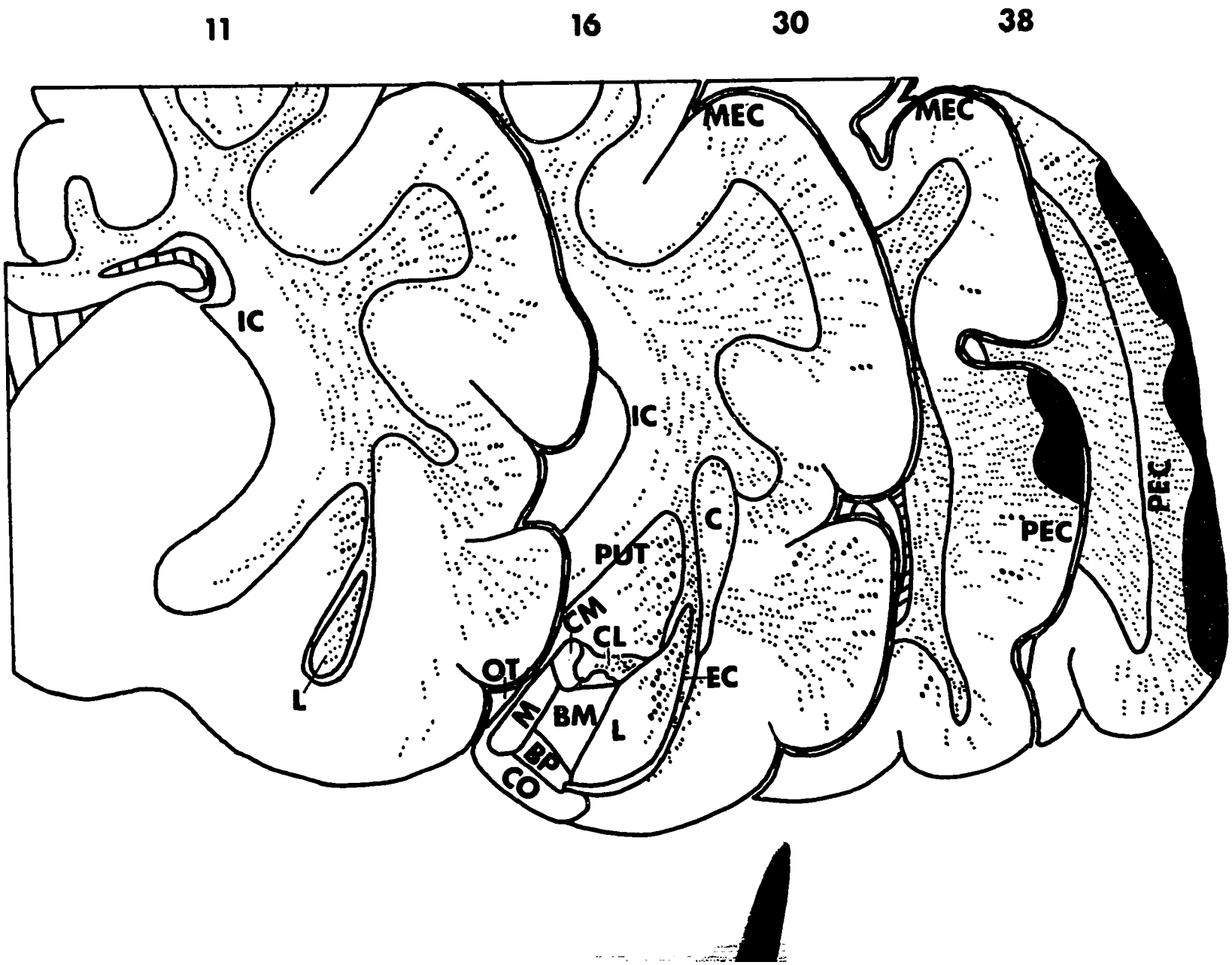


FIGURE 9

Degenerated Products in the Ipsilateral Lateral Nucleus (C-12). Nauta Method. Mag. X 600.

FIG. 9

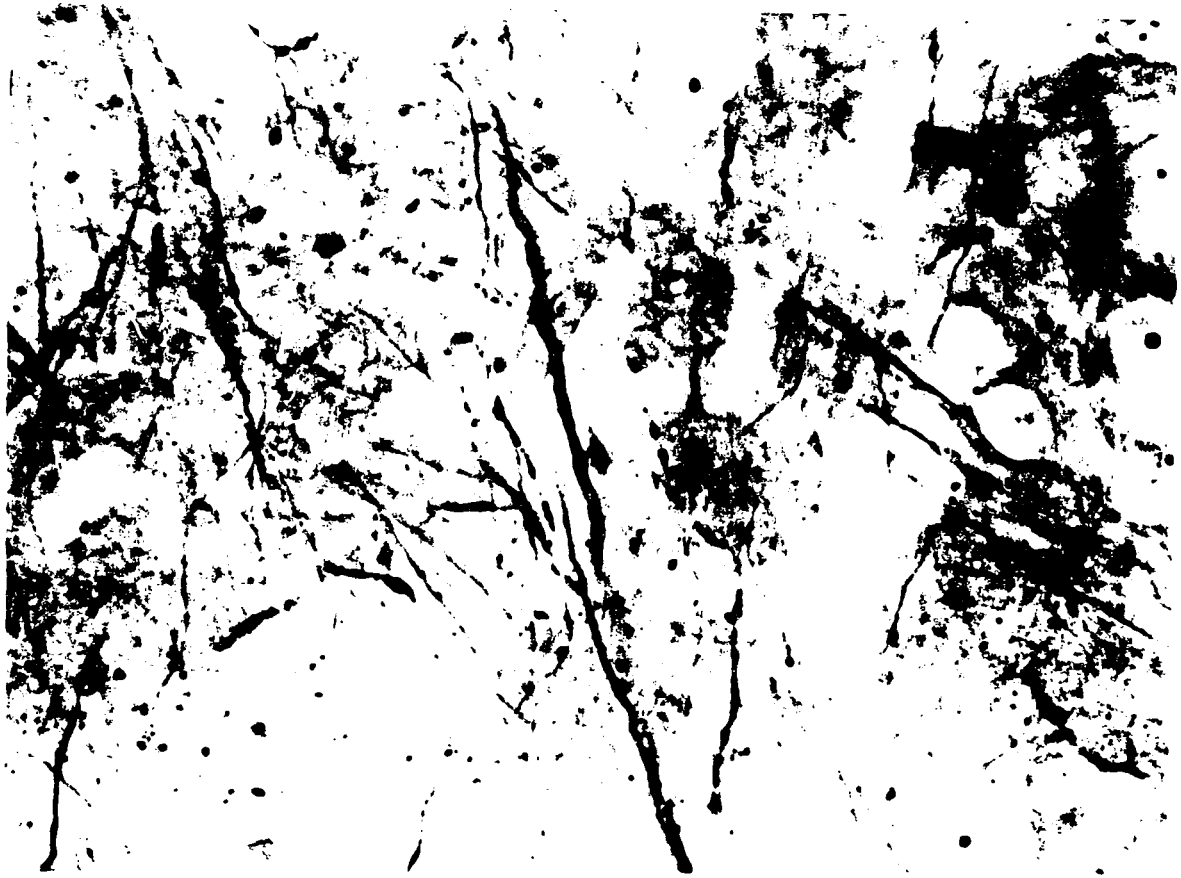
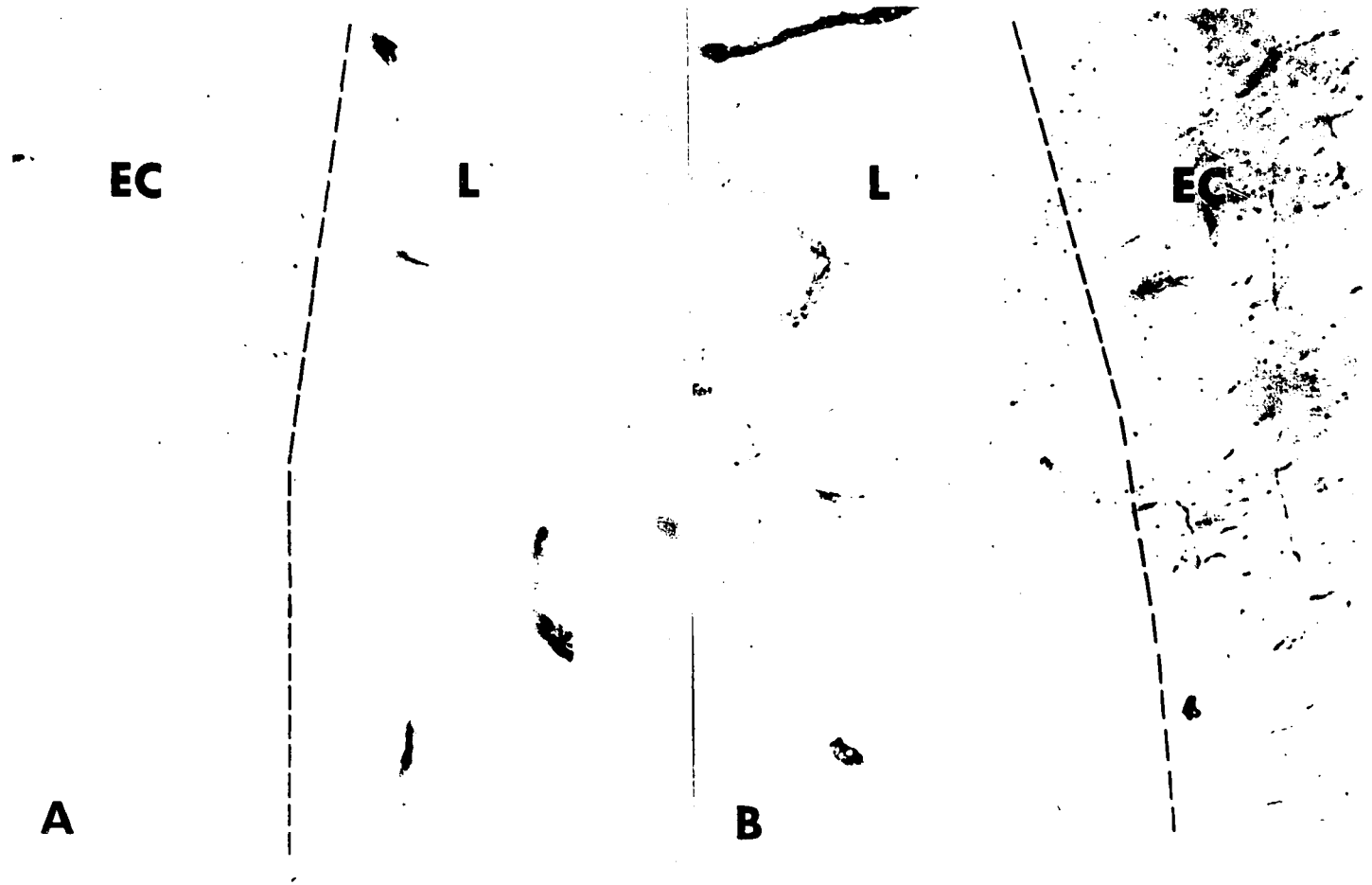


FIGURE 10

A. Contralateral External Capsule and Lateral Nucleus (C-21). Fink and Heimer II Procedure. Mag. X 250.

B. Ipsilateral External Capsule and Lateral Nucleus (C-21). Fink and Heimer II Procedure. Mag. X 250.

FIG. 10



D. Lesions of the Inferior Part of the Posterior Sylvian Gyrus (C-14, C-20, fig. 2, p. 57).

In these two animals, the lesions are restricted to the gray matter (fig. 11 illustrates C-20 only). In both brains, the fibres from the upper part of the lesion (fig. 11) leave the site of injury by coursing directly in the white matter underlying the lesion. They then travel in an antero-inferior direction along the lateral half of the internal capsule. After turning into the posterior part of the external capsule, these fibres join degenerated axons from the inferior portion of the lesion. The degeneration arising from the inferior part of the lesion passes in the extreme capsule inferior to the body of the claustrum and into the external capsule. The claustrum receives a heavy projection throughout its anteroposterior extent. Degenerated fibres, coursing anteriorly in the external capsule, incline in a ventromedial direction to enter the putamen and the amygdala.

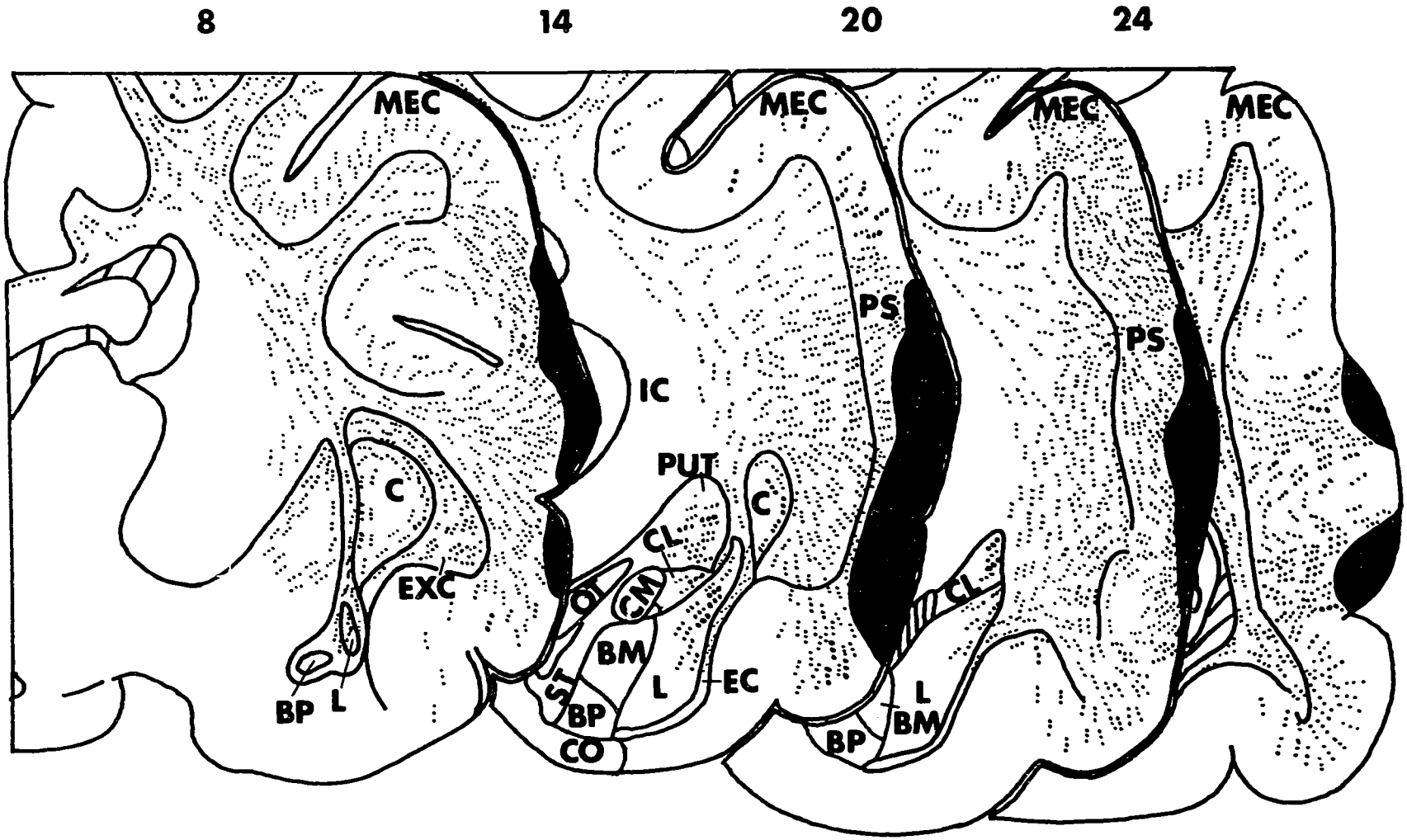
In the amygdala, the same two nuclei again receive terminal degeneration. The entire anterior segment and the dorsolateral part of the middle and posterior segments of the lateral nucleus are the

FIGURE 11

Depth of Lesion in the Posterior Sylvian Gyrus and Distribution of Degeneration.

C–20

FIG. 11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main sites of terminal degeneration (fig. 12). Fewer terminals end in the lateral part of the central nucleus. Degenerated axons are observed in the anterior commissure and in the contralateral external capsule. These fibres end in the posterior sylvian gyrus of that side. The volume of degeneration observed in the amygdala is comparable to that obtained from a lesion of the posterior ectosylvian gyrus. It should be emphasized that the superior horizontal levels of the posterior sylvian and ectosylvian gyri are identical.

E. Lesions of the Auditory Area (C-30, C-35, C-51 C-52, fig. 2, p. 57).

As mentioned previously, the auditory area was studied in two parts. The entire auditory region was removed in C-30, C-35 and C-51 (fig. 13), then a smaller lesion was made in the primary auditory region C-52 (fig. 2, p. 57). In all cases, the lesions destroyed the entire thickness of the gray matter and extended slightly in the white matter.

From the lesions of the entire auditory region (C-30 is illustrated in fig. 13), some degenerated fibres leave the lesion site, pass superior

main sites of terminal degeneration (fig. 12). Fewer terminals end in the lateral part of the central nucleus. Degenerated axons are observed in the anterior commissure and in the contralateral external capsule. These fibres end in the posterior sylvian gyrus of that side. The volume of degeneration observed in the amygdala is comparable to that obtained from a lesion of the posterior ectosylvian gyrus. It should be emphasized that the superior horizontal levels of the posterior sylvian and ectosylvian gyri are identical.

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From the lesions of the entire auditory region (C-30 is illustrated in fig. 13), some degenerated fibres leave the lesion site, pass superior

FIGURE 12

A. Fine Degenerated Products in the Ipsilateral Lateral Nucleus (C-20). Fink and Heimer II Procedure. Mag. X 400.

B. Absence of Degeneration in Contralateral Lateral Nucleus (C-20). Fink and Heimer II Procedure. Mag. X 400.

FIG. 12

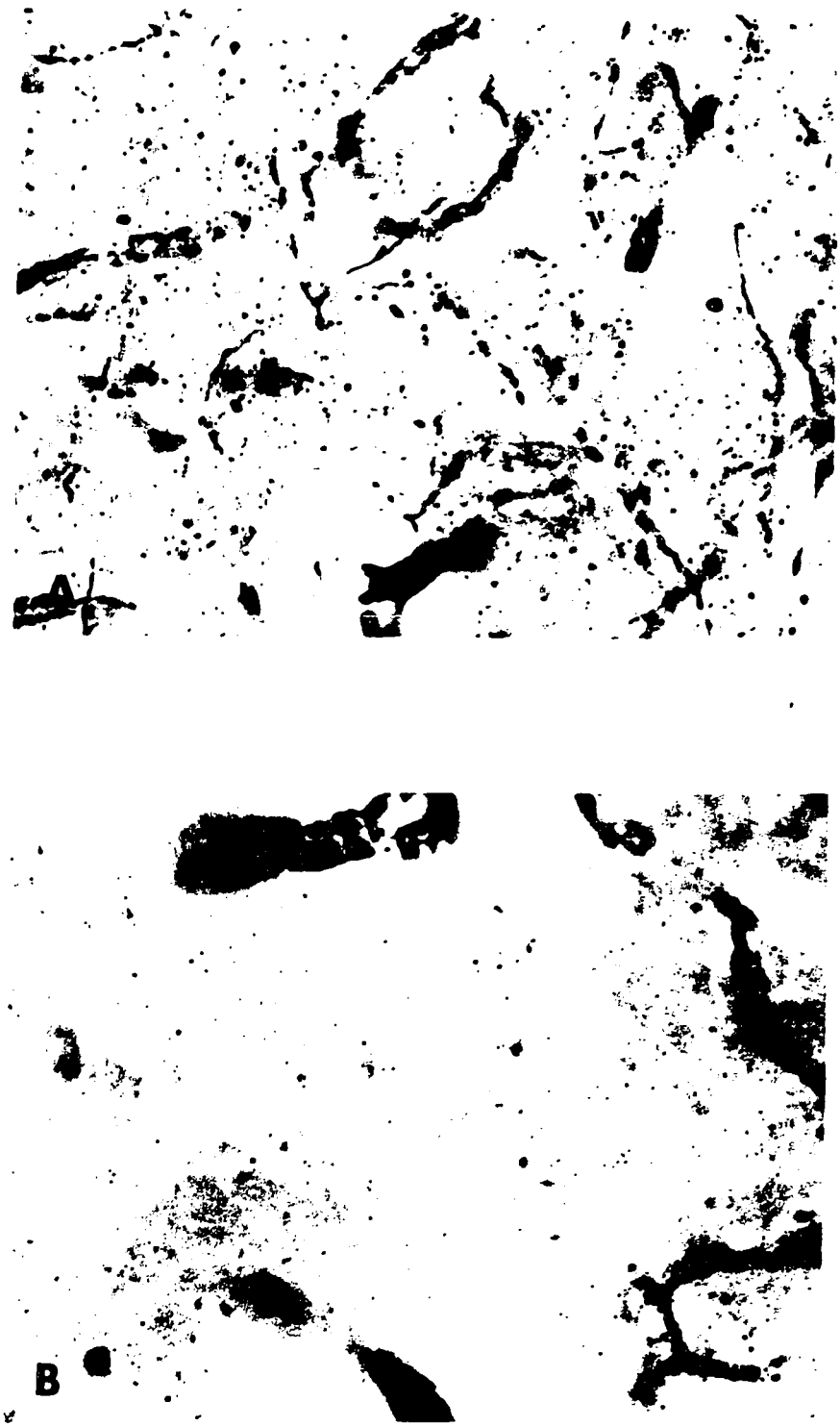
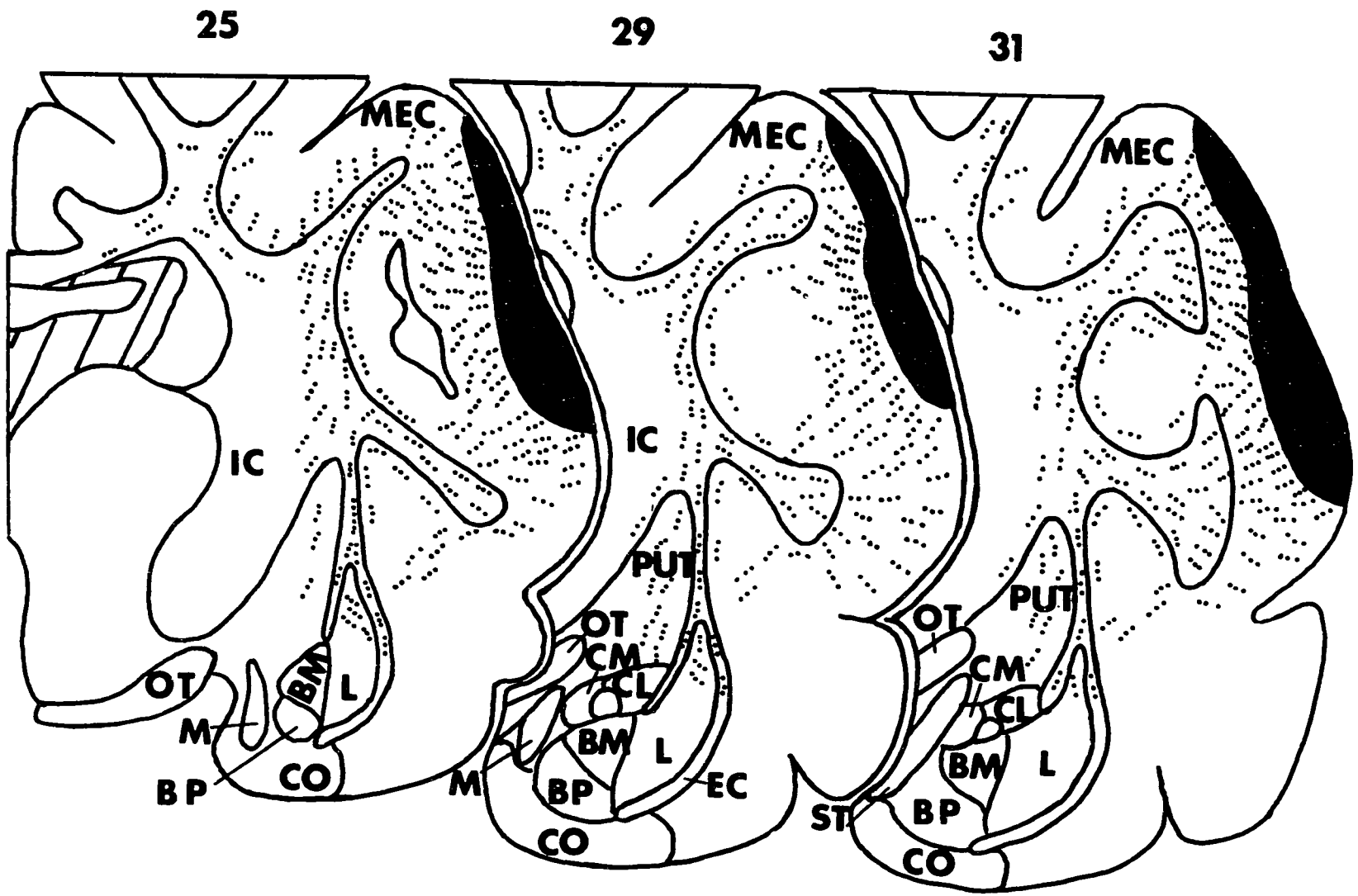


FIGURE 13

Depth of Lesion in the Entire Auditory Area and Distribution of Degeneration. Note the Presence of Degeneration Only in the Dorsal Part of Lateral Nucleus.

FIG. 13



to the claustrum and merge with the fibres of the external capsule. Others pass directly into the extreme capsule, and then inferior to the claustrum into the external capsule. At the level of the anterior and middle part of the lateral nucleus, a few fibres pass from the ventral part of the putamen and from the medial limb of the external capsule into the amygdala. Coarse degenerated products are found in the dorso-lateral part of the anterior and middle segment of the lateral nucleus (fig. 14). The lateral part of the central nucleus receives very few terminals. Another point of interest is that the auditory area located at a horizontal level superior to that of the posterior sylvian and ectosylvian gyrii, sends a smaller projection to the amygdala than the inferior part of the posterior sylvian or posterior ecto-sylvian gyrii.

From the lesion in the primary auditory area (C-52, fig. 2, p. 57) degenerated axons are seen in the cortex surrounding the lesion, in the internal capsule and in the putamen. But very few fibres reach the dorsal part of the lateral amygdaloid nucleus. So few fibres were found that it is doubtful whether

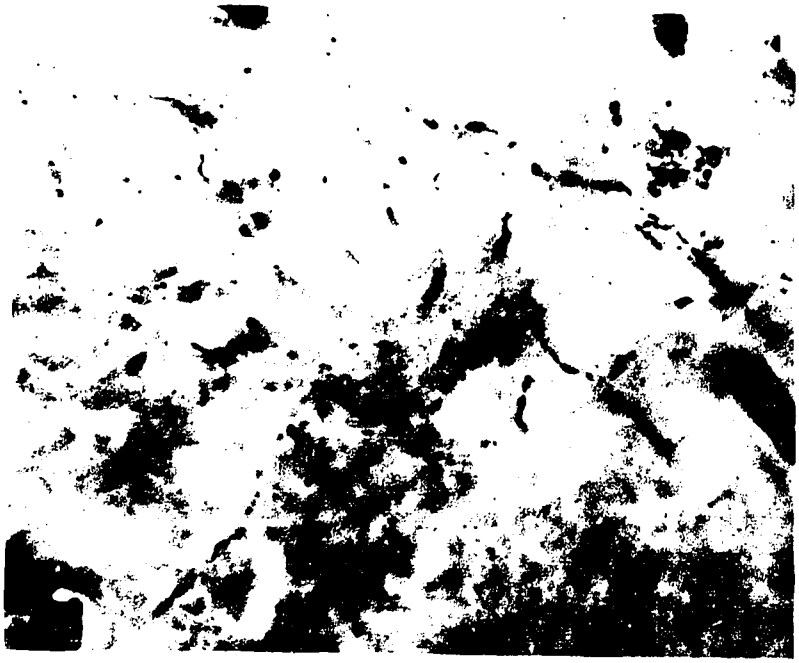
any auditory projection to the amygdala originate in the primary auditory area. It is considered that most of the degeneration from the lesion of the entire auditory area originates in the secondary auditory region.

FIGURE 14

A. Coarse Degenerated Products in Dorsal Part of the Ipsilateral Lateral Nucleus After Ablation of the Auditory Area (C-30). Fink and Heimer II Procedure. Mag. X 400.

B. Absence of Degeneration in Contralateral Lateral Nucleus. Fink and Heimer II method. Mag. X 400.

FIG. 14



B

Investigation of the Frontal Connections to the Amygdala

In this investigation, the term frontal lobe includes the cortical areas medial to and in front of the coronal gyrus (Papez, 1929). In addition, the orbital gyrus, which is a continuation of the sylvian gyrus, has been included with the frontal lobe. Three different areas were removed in the frontal lobe: the primary sensory area, the primary motor area and the orbital gyrus (fig. 15). Two animals were used for the lesions of the primary sensory area and two for the orbital gyrus, but only one lesion was placed in the primary motor area.

A. Lesions of the Primary Sensory Area (C-32, C-39, fig. 15).

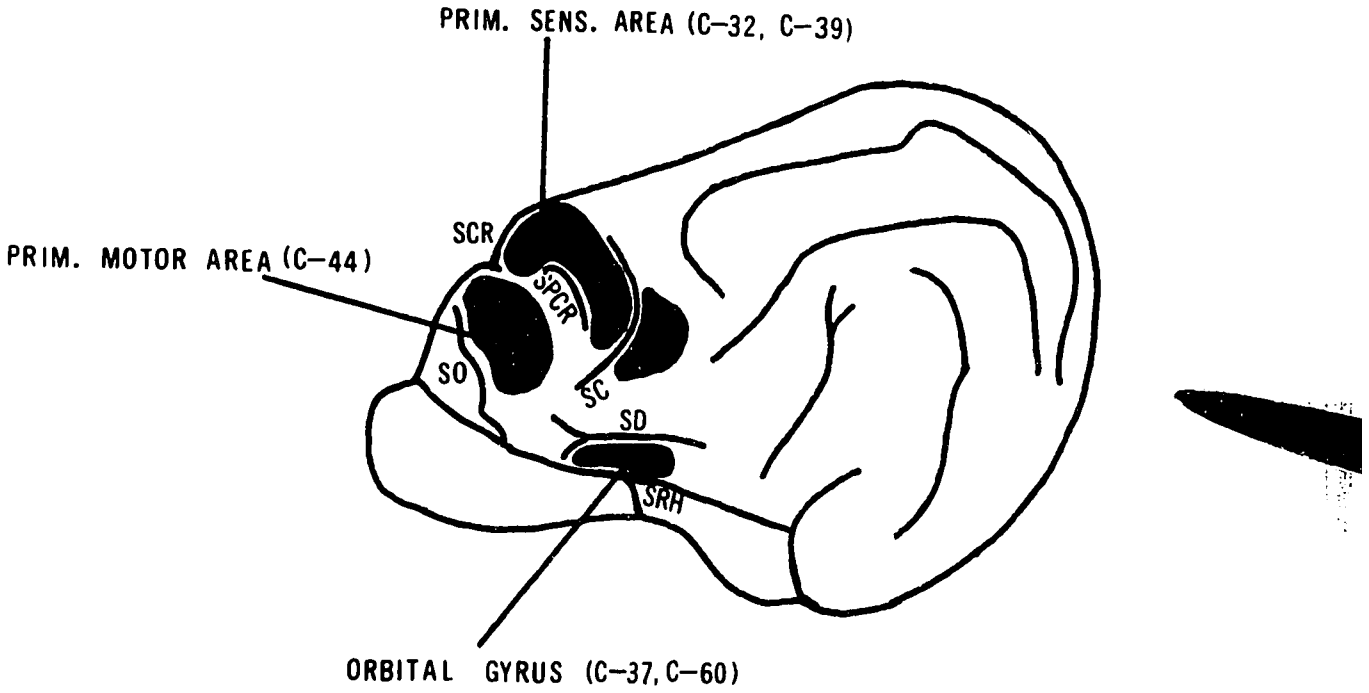
The lesions in both of these animals penetrate deeply through the gray matter into the underlying white matter. Degenerated fibres were observed in the cortical areas surrounding the lesion, such as the secondary sensory area, in the internal capsule and in the putamen, but no fibres were observed in the amygdala.

FIGURE 15

Localization of Lesions in the Frontal and Orbital Cortex.

FIG. 15

Lesions of The Fronto-orbital Cortex



B. Lesions of the Orbital Gyrus (C-37, C-60, fig. 15).

The lesion in C-37 (fig. 16) was made with a fine electrode directed vertically through the cortex and the white matter of the frontal lobe. Three descents were made, one at Frontal 23, another at Frontal 21, and one at Frontal 19. The lesion involves the entire gray matter and encroaches slightly on the underlying white matter. In C-60, the lesion was made under direct vision by removing the bone in the posterior part of the orbit. This lesion is shallower, involving only the gray matter.

Degenerated fibres course posteriorly in the ventrolateral part of the internal capsule in a position immediately superior to the claustrum (fig. 16). Some of the fibres turn inferiorly into the external capsule where they continue their course in a posterior direction. Fibres from the internal capsule and others from the external capsule are distributed to the ventrolateral part of the putamen in an area just medial to the external capsule. Fibres course inferiorly through the putamen, merge with fibres descending from the medial limb of the external capsule and enter the amygdala.

Coarse degenerated products are distributed again in the same two amygdaloid nuclei: the lateral nucleus and the lateral part of the central nucleus. Within the lateral nucleus, however, the fibres are distributed to the ventromedial part of the anterior and middle segments rather than to the dorsolateral part of that nucleus (fig. 17). Terminal degeneration was observed between Frontal 14.0 and Frontal 12.0. The quantity of degeneration is slightly less than that obtained from the lesions of the inferior part of the posterior ectosylvian gyrus. The lateral part of the central nucleus also receives several terminals. No fibres terminate in the contralateral amygdala.

C. Lesion of the Primary Motor Area (C-44, fig. 14 p. 76).

The lesion in this cat extended deeply through the gray matter into the underlying white matter. The cortical areas surrounding the lesion, the internal capsule, and the putamen are invaded with degenerated fibres but none reaches the amygdala.

FIGURE 16

Depth of Lesion in the Orbital Gyrus (C-37) and Distribution of Degeneration. Note the Presence of Degeneration in the Ventromedial Part of the Lateral Nucleus and in the Lateral Part of the Central Nucleus. Also the Presence of Degeneration in the External Capsule above the Amygdala and in the Part of the Capsule Between the Amygdala and the Putamen.

FIG. 16

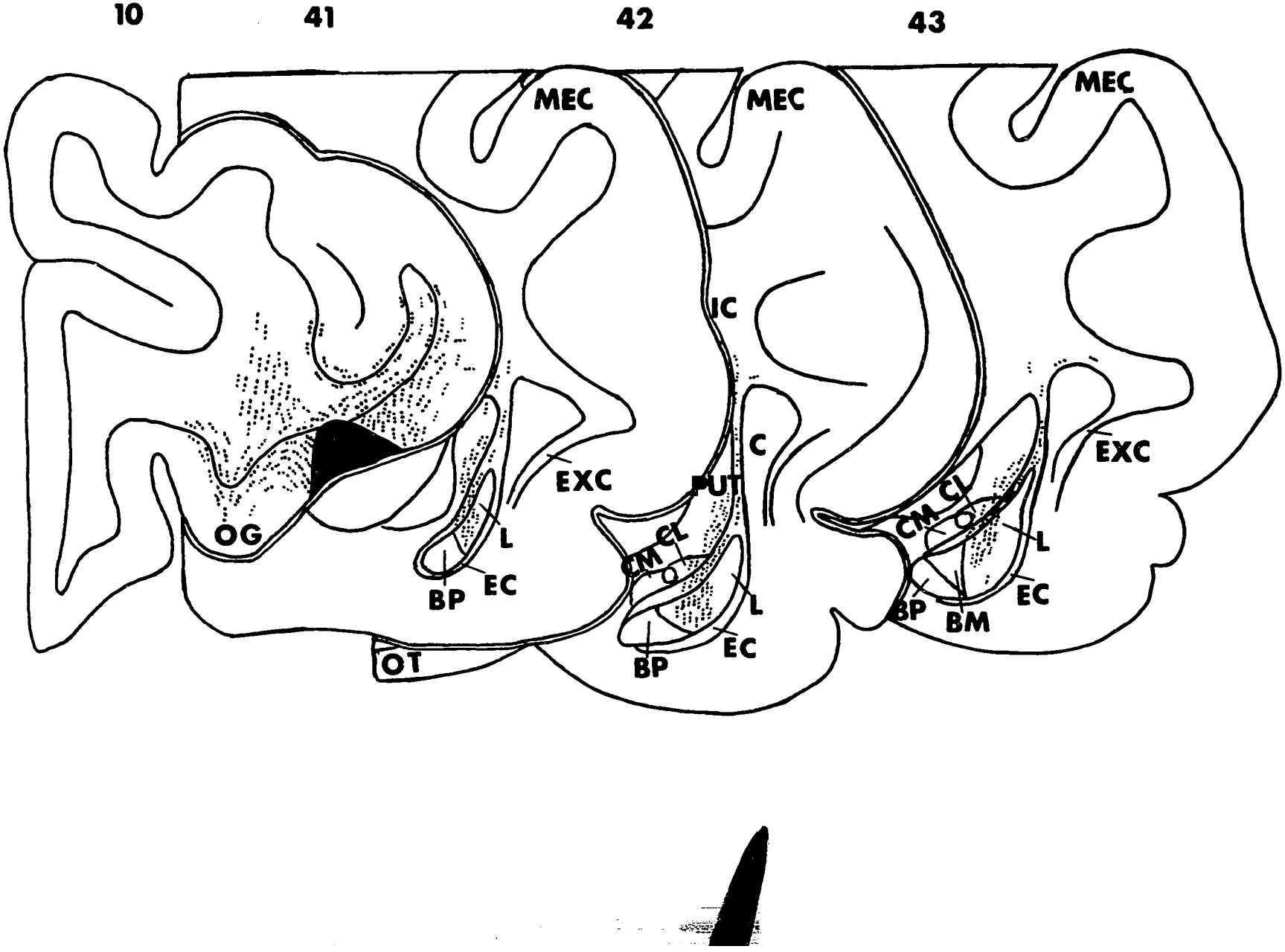

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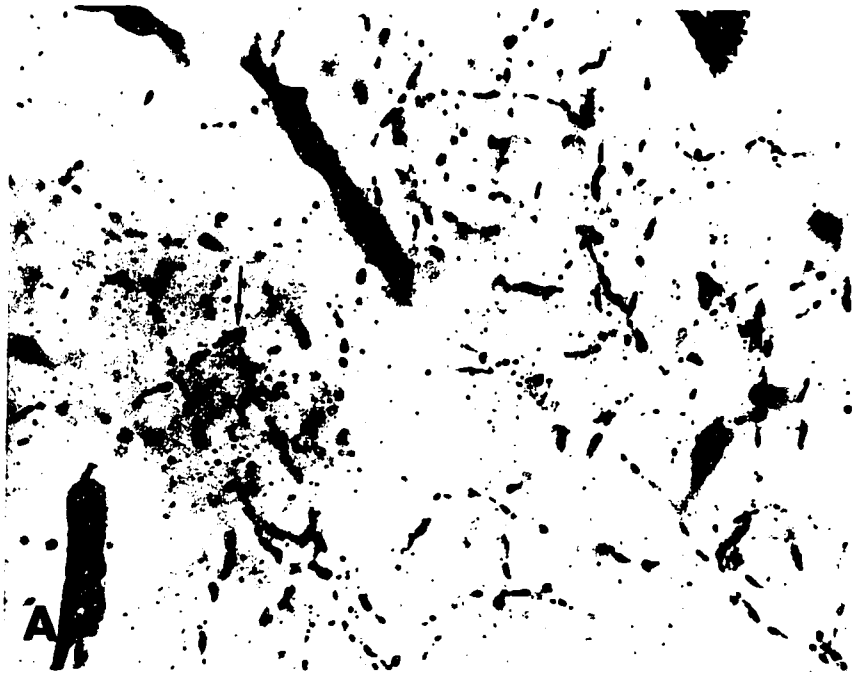
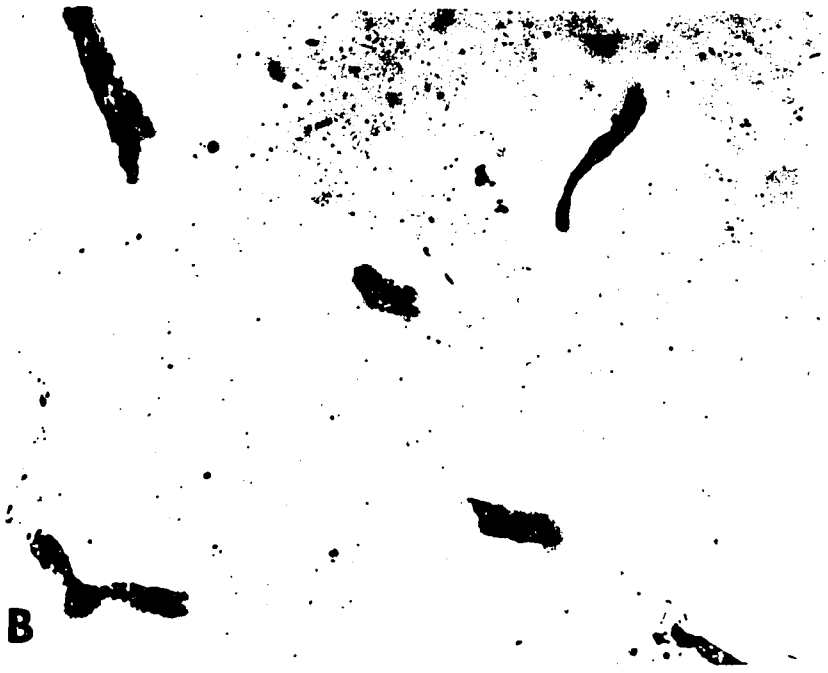
FIGURE 17

A. Coarse Degenerated Products (Arrow) in the Ipsilateral Ventromedial Part of the Lateral Nucleus (C-37). Fink and Heimer II Procedure. Mag. X 375.

B. Absence of Degenerated Products in the Contralateral Lateral Nucleus (C-37). Fink and Heimer II Procedure. Mag. X 375.

FIG. 17





Investigation of the Parietal Connections with the Amygdala

The parietal lobe was defined by Papez (1929) as the region comprising the cortex of the lateral, suprasylvian, coronal and anterior ectosylvian gyrii. In this investigation, the anterior sylvian gyrus is included with the parietal lobe for descriptive purposes. The parietal cortex was also investigated in three parts. Lesions were placed in the anterior sylvian gyrus, in the anterior ectosylvian gyrus and in the inferior part of the posterior lateral and suprasylvian gyrii (fig. 18). For each subdivision, a satisfactory lesion was made in two animals.

A. Lesions of the Anterior Sylvian Gyrus (C-41, C-55, fig. 18, p. 85).

The lesions in both animals penetrate the gray matter and encroach slightly on the underlying white matter. Degenerated fibres (fig. 19) follow the superior part of the claustrum and turn inferiorly into the external capsule. Very few fibres can be traced in the extreme capsule ventral to the body of the claustrum. Fibres are also found in the lateral third of the internal capsule.

In the amygdala, fine degeneration invades the same two nuclei as in the previous lesions; the lateral nucleus and the lateral part of the central nucleus (fig. 20). Terminals are scattered throughout the anterior segment of the lateral nucleus and in the dorsolateral part of its middle segment (Frontal 14.5 to Frontal 10.0). A few fibres from the medial limb of the external capsule and from the dorsal part of the lateral nucleus end in the lateral part of the central nucleus. The density of the degeneration in these two nuclei is almost the same as that obtained from lesions of the posterior ectosylvian gyrus.

FIGURE 18

Localization of Lesions in the Parietal Cortex.

FIG. 18

Lesions of The Parietal Cortex

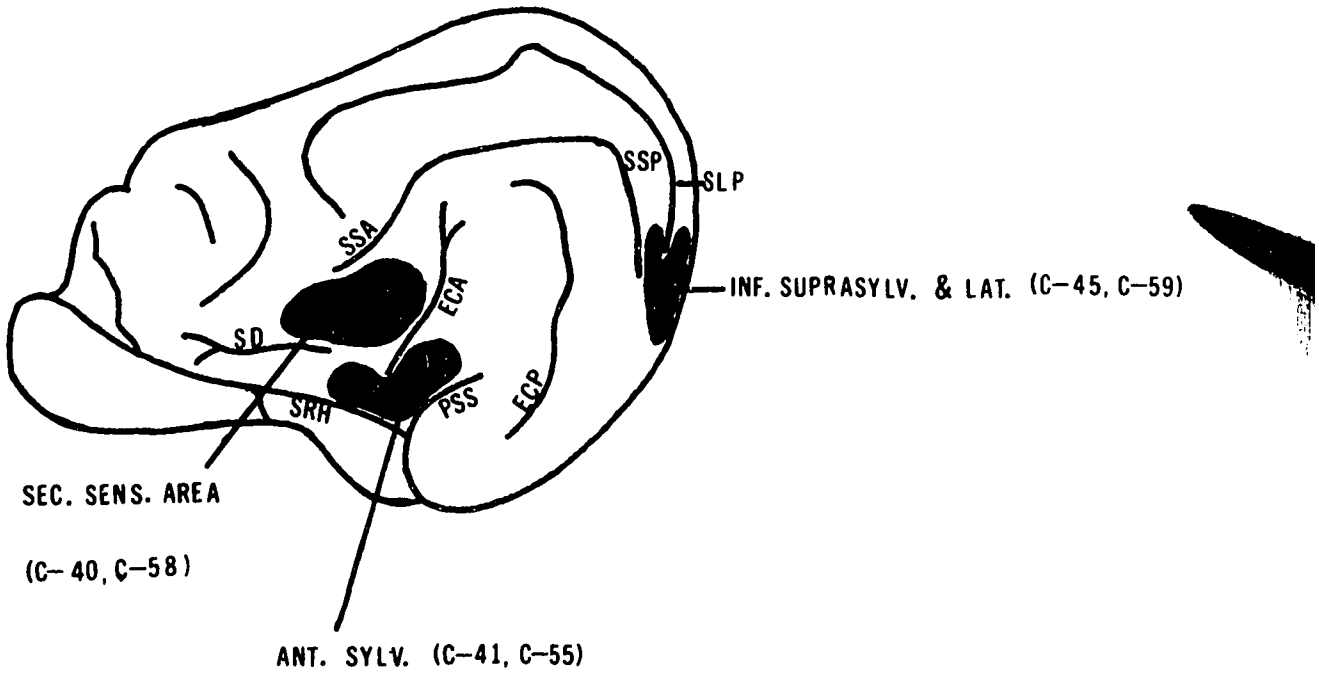


FIGURE 19

Depth of Lesion of Anterior Sylvian Gyrus (C-41) and Distribution of Degeneration.

C–41

FIG. 19

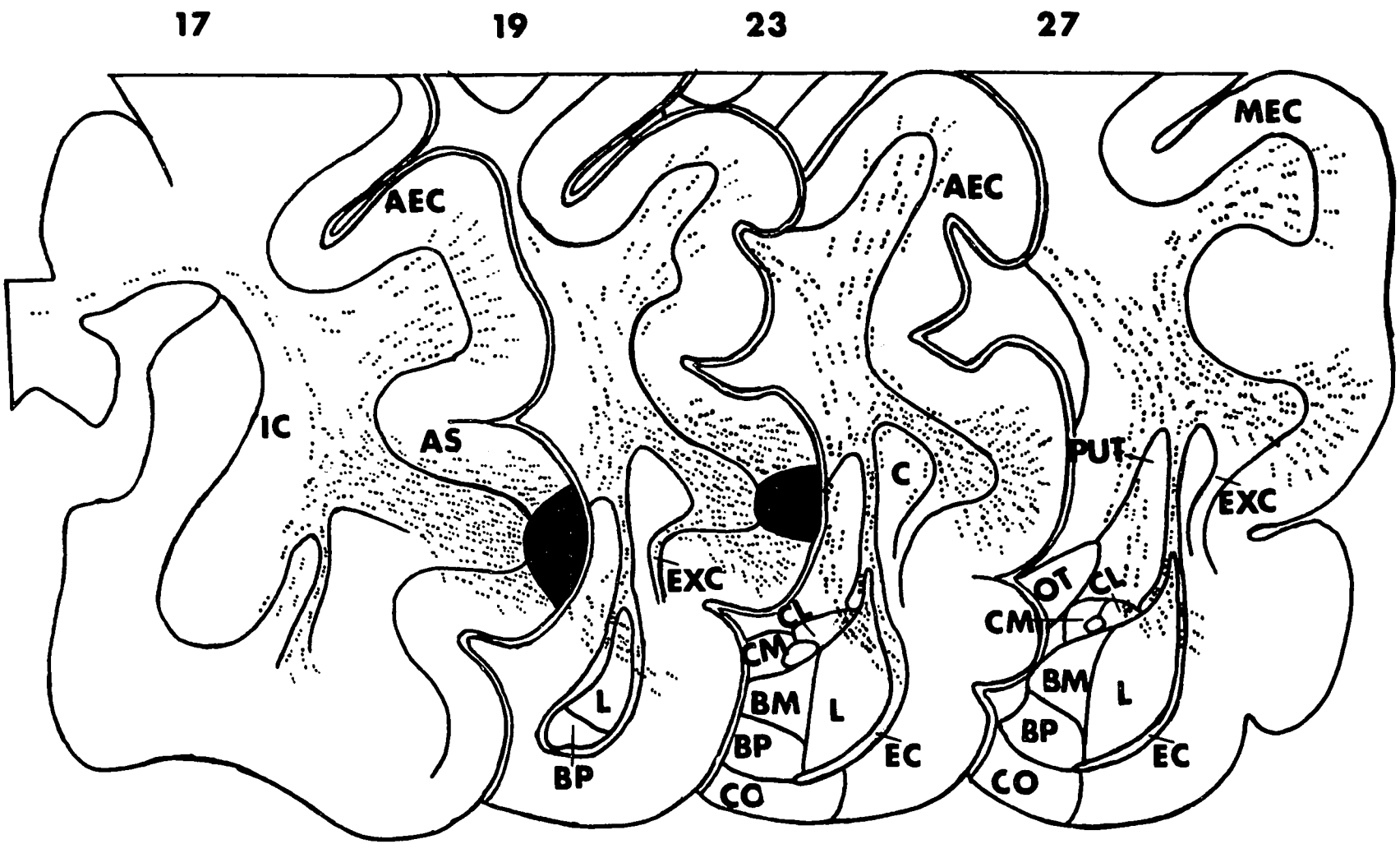

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FIGURE 20

A. Degenerated Products in Dorsal Part of the Lateral Nucleus (C-41). Fink and Heimer II Procedure. Mag. X 600.

B. Absence of Degeneration on the Contralateral Lateral Nucleus. Fink and Heimer II Procedure. Mag. X 600.

FIG. 20

B. Lesions of the Anterior Ectosylvian Gyrus - Secondary Sensory Area (C-40, C-58, fig. 18, p. 85).

The lesion in this animal encroaches slightly on the underlying white matter (fig. 21). Fibres proceed from the lesion into the internal capsule and from there some of them incline inferiorly to enter the ipsilateral external capsule. In one animal (C-40), some of the fibres from the external capsule turn medially into the anterior commissure, cross the midline and descend posteriorly in the contralateral external capsule.

In the homolateral side, fibres course in a posterior direction, enter the amygdala, and terminate from the more anterior part of the lateral nucleus to its more posterior limits. Two nuclei definitely receive fine degeneration, the lateral nucleus and the lateral part of the central nucleus. In the lateral nucleus, the entire anterior segment receives terminals while only the dorsolateral part of the middle and posterior segments receive fibres (fig. 22, A and B). It can be noted here that somewhat more degeneration could be observed in the middle and posterior segments than in the anterior segments of the lateral nucleus. A few terminals were found in the lateral part of the

central nucleus. The quantity of degeneration in these two nuclei is slightly less than that obtained from the lesions in posterior ectosylvian gyrus. In addition to these two nuclei, the anterior amygdaloid area receives a few terminals. As in the previous lesions, no degenerated fibres were seen in the contralateral dorsolateral part of the lateral nucleus or in the lateral part of the central nucleus.

A diffuse group of coarse fibres can be seen in the region of the middle segments of the lateral nucleus of both amygdalae in one animal (fig. 21, double arrows). Some fibres from the more inferior part of the homolateral external capsule turn in a superomedial directions and cross the ventral part of the lateral nucleus and the magnocellular part of the basal nucleus. Then the fibres continue medial and inferior to the ventral amygdalofugal bundle (longitudinal association bundle of Johnston) and enter the medial part of the central nucleus where the fibres could not be followed any farther. Whether these fibres terminate in the medial part of the central nucleus, the magnocellular part of the basal nucleus and the ventral part of the lateral nucleus

could not be resolved with the technique used. Other fibres leave the inferior part of the external capsule and disperses themselves in the plexiform layer of the pyriform cortex from the level of the anterior amygdaloid area to the middle segment of the lateral nucleus (frontal 14.5 to frontal 10.5).

On the contralateral side, degenerated fibres descend to the more inferior portion of the external capsule, turn in a superomedial direction and follow the same course as those described in the ipsilateral amygdala.

FIGURE 21

Depth of Lesion in the Anterior Ectosylvian Gyrus (S II, C-40) and Distribution of Degeneration.

C-40

FIG. 21

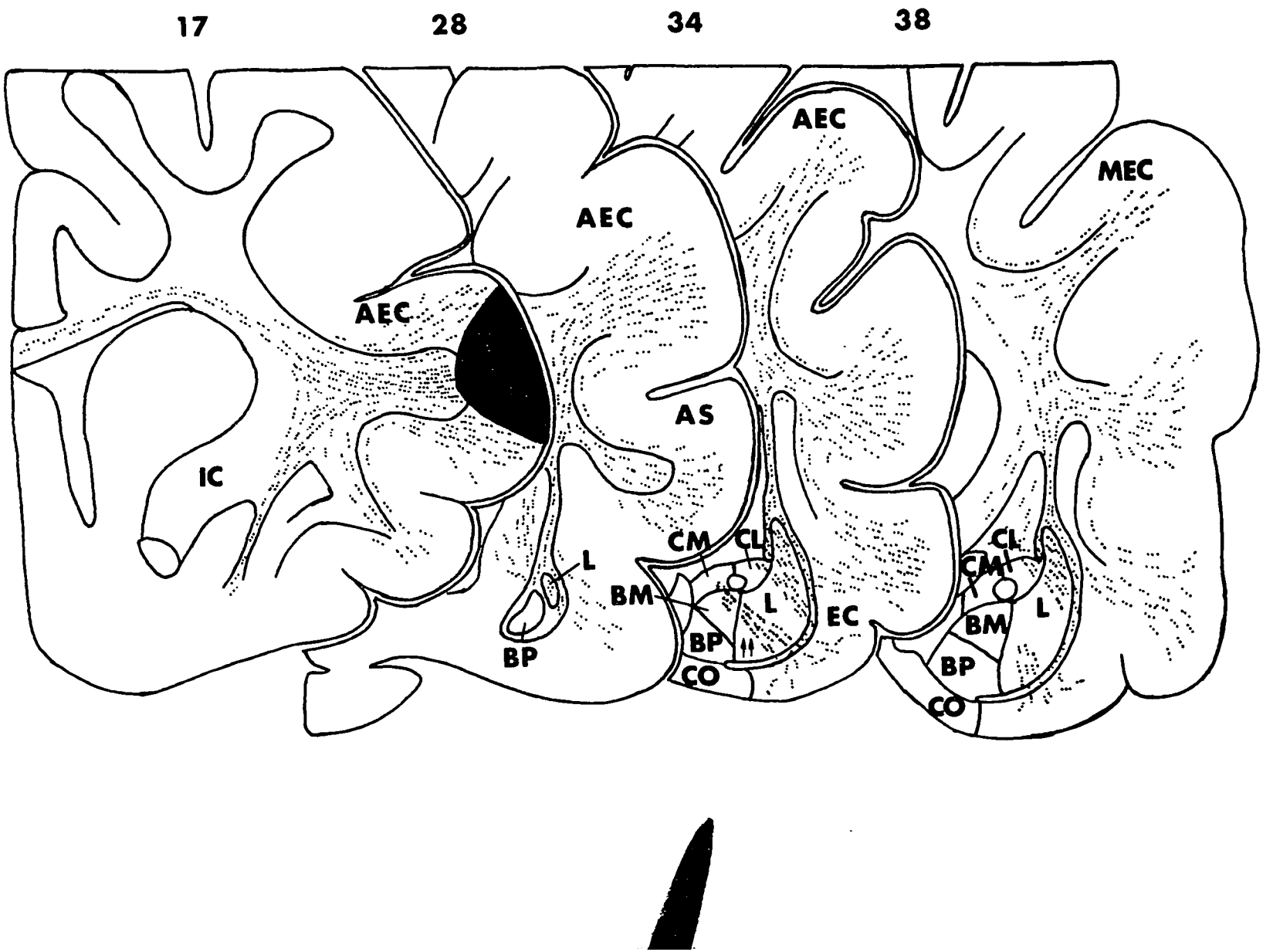


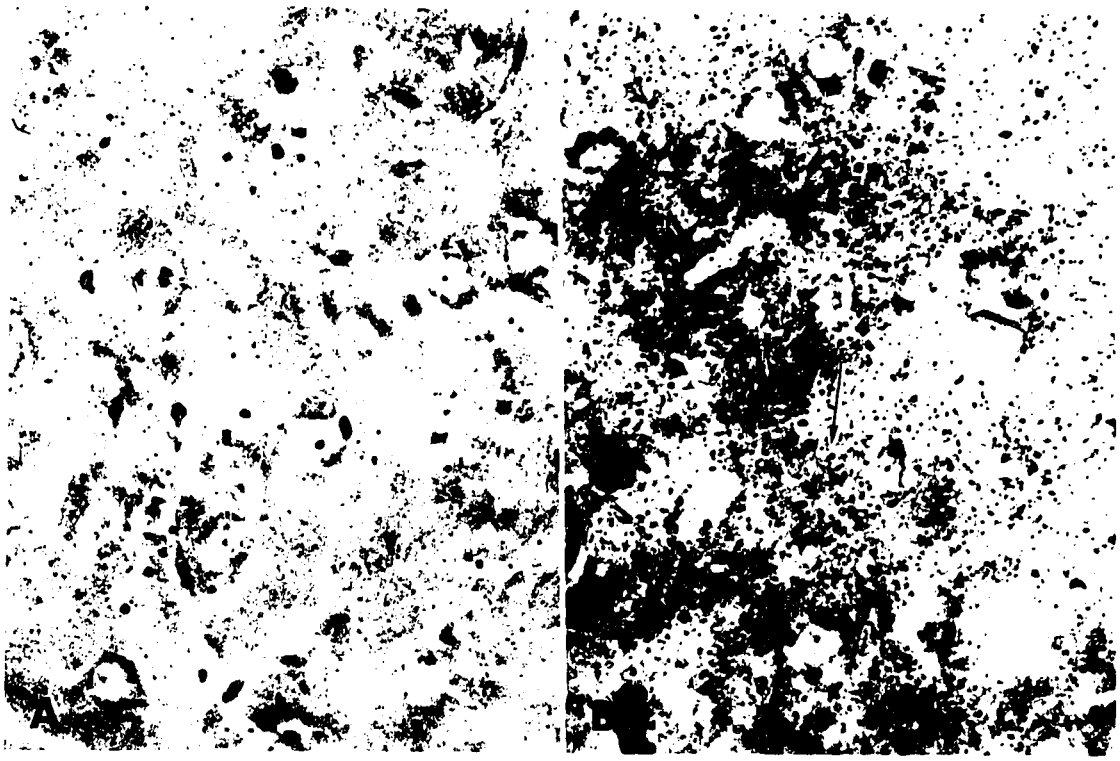
FIGURE 22

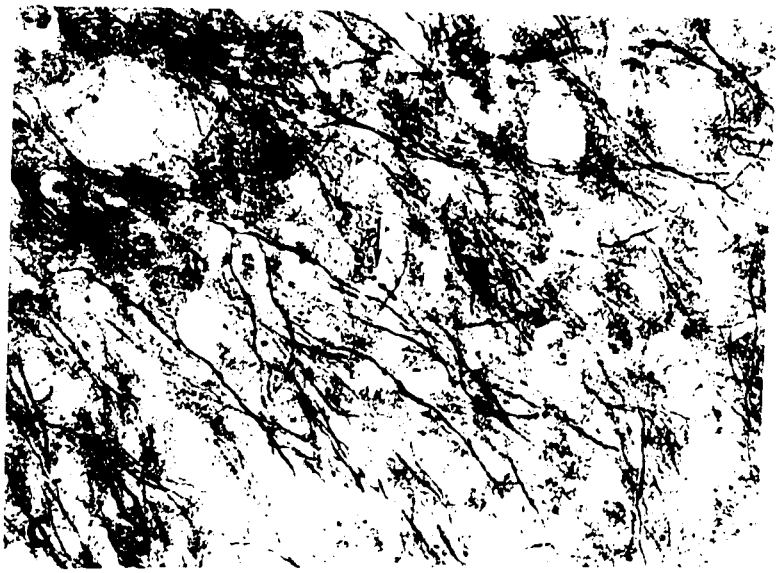
A. Absence of Degeneration in the Contralateral Lateral Nucleus (C-40). Fink and Heimer II Method. Mag. X 340.

B. Degenerated Products in Ipsilateral Lateral Nucleus (C-40). Arrow indicates fine degeneration. Fink and Heimer II Method. Mag. X 340.

C. Degenerated Fibers in Ipsilateral Basal Nucleus (C-40). Arrow indicate coarse fibres. Nauta Method. Mag. X 250.

FIG. 22





C. Lesions of the Inferior Part of the Suprasylvian and Lateral Gyrii (C-45, C-59, fig. 18).

Both lesions in these two animals extend deeply into the white matter. Although degenerated fibres can be followed to the caudate and putamen, no degeneration is present in the amygdala.

Summary of Observations

In summary, lesions have been made in three different neocortical regions, the temporal, the frontal and the parietal cortices (Table 2).

The temporal cortex was investigated by making lesions of the entire temporal cortex, the temporal polar region, the inferior part of the posterior sylvian and of the posterior ectosylvian gyrii, the entire auditory area and the primary auditory area. All the lesions of the temporal cortex project to the lateral nucleus and to the lateral part of the central nucleus except the auditory area which projects only to the lateral nucleus. Within the lateral nucleus, fine degenerated terminals are found throughout its anterior segment and in the dorsolateral part of its middle and posterior segments. The projections from the auditory area, however, can be observed only in the dorsolateral part of the anterior and middle segments of the lateral nucleus. Comparing the density of the projections from these different regions, the temporal polar region has been found to send the heaviest projection, the inferior part

of the posterior sylvian and the posterior ectosylvian gyrii a lighter projection, and finally the auditory area the lightest projection.

The amygdaloid afferents from the fronto-orbital cortex were investigated by removing the anterior sigmoid gyrus which is the primary motor area, the posterior sigmoid gyrus which is the primary sensory area and the orbital gyrus. Only the orbital gyrus projects to the amygdala. Both the lateral nucleus and the lateral part of the central nucleus receive fibres. Within the lateral nucleus, however, only the ventromedial part of the anterior and middle segments of the lateral nucleus receive any projections. Comparing the density of the projection with that of the previous lesions, the lateral nucleus receives somewhat less degeneration than from the inferior part of the posterior ecto-sylvian gyrus.

The investigation of the parietal cortex followed the same plan as the one for the orbital gyrus. The anterior sylvian, anterior ectosylvian, and inferior part of the posterior lateral and suprasylvian gyrii were removed. Only the anterior

sylvian and anterior ectosylvian gyrii project to the amygdala. The degeneration is scattered in the lateral nucleus and in the lateral part of the central nucleus. Within the lateral nucleus, the anterior segment is filled with fine degeneration while in the middle and posterior segment, fibres occupy the dorsolateral part. In addition, the anterior ectosylvian gyrus sends a bundle of coarse fibres bilaterally which enters the amygdala medial and inferior to the longitudinal association bundle. This group of fibres then traverses the medial part of the central nucleus, the magnocellular part of the basal nucleus and the ventral part of the lateral nucleus. These fibres join a group of fibres in the fifth layer of the pyriform cortex. Their terminals are scattered in the periamygdaloid cortex. The density of the projections to the lateral amygdaloid nucleus from the parietal cortex is approximately equal to that obtained from the orbital cortex.

TABLE 2

Summary of Location of Degenerated Products Following the Various Ablations in the Neocortex.

TABLE. 2

Terminal Degeneration in Amygdaloid Nuclei After Neocortical Lesions.

Symbols: +, terminal degeneration; ++, massive terminal degeneration;
—, no evidence of degeneration; ?, uncertain.

Lesions	Cat.	Ipsilateral Nuclei						
		Lat.	B.M.	B.P.	C.L.	C.M.	C.O.	Aaa.
TEMPORAL CORTEX								
ENTIRE TEMPORAL LOBE	C-15	++	+	—	+	—	—	+
INF. POST. SYLVIAN GYR.	C-14, C-20	++	—	—	+	—	—	—
INF. POST. ECTOSYL. GYR.	C-12, C-21	++	—	—	+	—	—	—
TEMPORAL POLE	C-23, C-31	++	—	—	+	—	—	—
ENTIRE AUDITORY AREA	C-22, C-30	+	—	—	—	—	—	—
PRIMARY AUDITORY AREA	C-51, C-52	—	—	—	—	—	—	—
FRONTO-ORBITAL CORTEX								
PRIMARY MOTOR AREA	C-44	—	—	—	—	—	—	—
PRIMARY SENS. AREA	C-32, C-39	—	—	—	—	—	—	—
ORBITAL GYRUS	C-37, C-60	+	—	—	—	—	—	—
PARIETAL CORTEX								
ANT. SYLVIAN GYRUS	C-41, C-55	+	—	—	+	—	—	—
ANT. ECTO. GYRUS	C-40, C-58	++	?	?	+	?	—	—
INF. POST. SUPRASYL. GYR.	C-45, C-59	—	—	—	—	—	—	—

Note: no evidence of degeneration in the medial nucleus.

DISCUSSION

The results of these experiments have confirmed and extended previous descriptions of the neocortico-amygdaloid fibres. Moreover it has been possible to study the pathways and the specific regions where these afferents end.

Before discussing the various results, an objection concerning the methods of staining might be raised. Reciprocal connections between the amygdala and neocortex have been described in man by Klingler and Gloor (1960), in monkeys by Nauta (1962) and in cats by Valverde (1965). Consequently it might be questioned whether retrograde degeneration could account for some of the degeneration which has been interpreted as neocortico-amygdaloid projections. This appears to be unlikely as in the present series of experiments no retrograde cellular changes have been observed.

As it was mentioned in the introduction, the better defined neocortico-amygdaloid projections are those arising in the temporal neocortex. Whitlock and Nauta (1956) and Showers and Lauer (1961) reported that in the monkey the temporo-amygdaloid fibres could

be followed to the lateral and basal nuclei, and, in addition, the former authors observed that some fibres also end in the central nucleus. The projection these authors described appeared to be of equal density in both the lateral and basal nuclei and without any preference for either part of the basal nucleus. The present study indicates that in the cat temporo-amygdaloid fibres end mainly in the lateral nucleus and to a lesser extent in the central nucleus. These results are in agreement with those described by Lammers and Lohman in the cat (1957). No degeneration was observed in the basal nucleus except when the lesion extended over the entire surface of the temporal lobe. The discrepancy between the observations in the monkey and those in the cat can be explained by the difference in species. The presence of more degeneration in the basal nucleus of the monkey as compared to that of the cat may reflect a progressive influence of the neocortex on the amygdala.

The present series of experiments in the fronto-orbital regions have confirmed the existence of orbito-amygdaloid projections. Direct afferent

fibres from the orbital gyrus to the amygdaloid complex were found only in the ventromedial part of the lateral nucleus and the lateral part of the central nucleus. Some indication of degeneration in the anterior amygdaloid area was also noted. These findings agree in part with those of Valverde (1965), Hirata (1965) and Mizuno et al., (1969). However, Valverde (1965) and Hirata (1965) described afferents ending in both the basolateral and corticomedial complexes. Valverde (1965) attributed the presence of degeneration in the corticomedial complex to a vascular lesion in the stria terminalis. A more plausible explanation might be that the lesion extended into the prepyriform cortex and olfactory tubercle or lateral olfactory tract and produced degeneration in the medial, central and cortical nuclei (Mizuno et al., 1969).

The lesions in the parietal cortex have also resulted in degeneration in the amygdala. In agreement with Koikegami (1963) and Hirata (1965), it was observed that the projections from the anterior sylvian gyrus terminate in the lateral and central nuclei. However, Hirata (1965) has reported

that the projection extends not only to these two nuclei but also to the cortical, medial and basal nuclei. As suggested by Mizuno et al., (1969), the interruption of fibres in the prepyriform cortex and possibly of the olfactory tubercle or the lateral olfactory tract may have been the origin of such a diffuse projection.

The present study demonstrates the existence of fibres from the secondary sensory area crossing the basal nucleus. These fibres course in the inferior aspect of the external capsule, then bend sharply in a superomedial direction to enter the posterior portion of the medial system of the longitudinal association bundle. Some of the fibres could also be followed from the secondary sensory area across the corpus callosum to the contralateral white matter. Some of these fibres were observed to enter the contralateral basal nucleus and then join the longitudinal association bundle. Thus the longitudinal association bundle is not solely composed of fibres from the paleocortex but also of the neocortex. It is interesting to note that Valverde (1965) has described fibres coursing along the medial side of the lateral part of the central

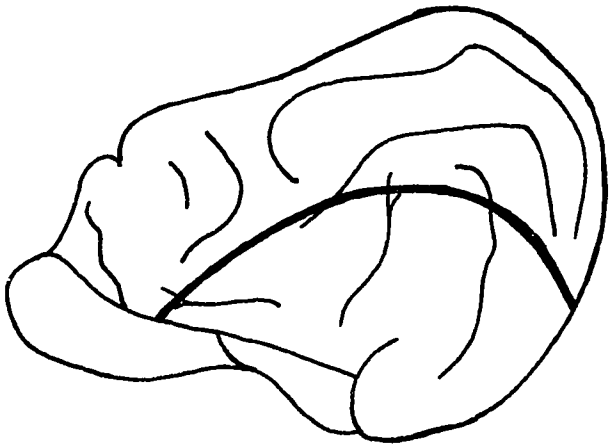
nucleus after a lesion in the external capsule. However, he concluded that these fibers were not part of the longitudinal association bundle.

It was mentioned in the introduction that the neocortical projections reach the amygdala via the external capsule, via a small bundle located between the putamen and the lateral nucleus and via the stria terminalis. The temporo-amygdaloid fibres observed in the stria terminalis by Powell (1964) were not seen in this series of experiments, nor was the external capsule component of the orbito-amygdaloid fibres that Valverde (1965) and Hirata (1965) described. However, the present results confirm that all neocortico-amygdaloid fibres course in the external capsule, except the orbito-amygdaloid projections which travel only in a fascicle between the putamen and the amygdala (as Hirata, 1965, and Valverde, 1965, also observed). The present investigation provides no information concerning the distinct fascicles connecting the cortex and the amygdala that were described by Klingler and Gloor (1960) in the human.

The collection of findings in these experiments

has allowed the plotting of a line demarcating the neocortical areas projecting to the amygdala (the areas inferior to the line) from the areas which do not project to the amygdala (the areas superior to the line) (fig. 23). A correlation can be made between the cytoarchitecture of these areas projecting to the amygdala and the density of these projections.

FIGURE 23



According to Sanides (1969), the cytoarchitecture of the neocortical regions inferior to this line exhibits an "insular character" which is distinguished by darkly staining medium-sized pyramidal cells and by a small fourth layer of granule cells. These features are signs of a relatively primitive neocortex. The present findings show that the neocortical regions

exhibiting this insular character to a higher degree, that is the regions closer to the amygdala, have heavier projections than those further away. This would argue in favour of including the orbito-insulo-temporal cortex in the limbic system on the basis of connections and cytoarchitecture. However it must be remembered that stimulation or ablation of neocortical regions does not give rise to changes in emotional behaviour as they do with the amygdala. In addition it would appear unjustified to include the secondary sensory area within the limbic system because it is a region which is concerned with the integration of somatic sensation, and on ablation or stimulation it does not cause any emotional changes.

Can the existence of these projections allow the development of a concept concerning the role of the neocortex in relation to the amygdala? Some answers to this question have been forthcoming from Golgi studies and preliminary studies with the electron microscope after ablation of the temporal cortex. Golgi studies have revealed that the dendrites of modified pyramidal cells in the lateral nucleus and the cells of the lateral part of the central nucleus

carry a dense spine population in comparison with the cells in the medial nucleus and medial part of the central nucleus (Hall, in preparation). In addition, the dendrites of the modified pyramidal cells in proximity of the external capsule extend into that capsule. There exists also a group of small neurons in the lateral nucleus whose dendrites are free of spines (Hall, in preparation, and Valverde, 1965). Electron microscopic studies of experimental degeneration after ablation of the entire temporal cortex (Hall, unpublished information) has given an indication of sites of terminals of the fibres. These terminals were located mostly on spines, a few were located on dendrites but none were found on somata. Moreover, the degenerated terminals were of the B_1 and B_2 types, that is they contained round to oval vesicles (Hall, 1968) which have been associated with excitatory synapses in the cerebellum (Uchizono, 1967). These findings thus suggest strongly that the temporo-amygdaloid fibres are excitatory in nature. It might be inferred that the other neocortico-amygdaloid fibres are also excitatory.

An interesting observation has been that the frontal, parietal and temporal projections to the amygdala all converge on the lateral nucleus and the lateral part of the central nucleus. Thus the projections are not topographically arranged as are those for example to the caudate-putamen complex (Carman et al., 1963). This pattern of distribution provides an anatomical basis for the convergence of impulses of various sensory modalities (somatic, auditory, visual) in the basolateral complex and lateral part of the central nucleus (Machne and Segundo, 1956, and Wendt and Albé-Fessard, 1962). It also explains the fact reported by the latter group of investigators that somatic stimulation of widely divergent areas of the body can be recorded on a cell of the basolateral complex. In addition the morphological connections described in this series of experiments confirm the existence of the pathway postulated by Wendt and Albé-Fessard (1962) for the mediation of the somatic stimulation to the amygdala. These investigators hypothesized that a stimulus from a limb was relayed by the secondary sensory area to the basolateral complex of both

amygdalae. Thus the neocortical projections into the lateral nucleus and lateral part of the central nucleus are non-topographic in nature, and according to the physiological investigators just mentioned, those projections from the secondary sensory area carry heterotopic sensation.

One important question remains to be answered; can the present anatomical results contribute to the subdivision of the amygdala into functionally different regions? In his extensive review of the literature, Gloor (1960) concluded that the amygdala was a modulatory region without any functionally distinct areas. More recently, Brodal (1969) suggested that the divisions of the amygdala into functional regions was premature because the effects produced by stimulation or ablation could also be obtained from many other cortical areas. However, good evidence supporting the subdivision of the amygdala into functional regions has been reported in the literature. As mentioned previously, Ursin (1960, 1965) has distinguished two distinct regions modulating distinct emotional responses. First, there is an anterodorsal and lateral region

controlling fear behaviour and second, there is a postero-ventral and medial region modulating anger responses. Other evidence comes from histochemical and anatomical studies of the cat brain. Dithizone and sulphide silver stains of the amygdala have demonstrated that the dorsolateral part of the amygdala, that is, the area of termination of the neocortical projections, does not react with the staining chemicals while the ventromedial part of the lateral nucleus is intensely positive (Hall et al., 1969). In addition, the efferent connections of the lateral nucleus course in the longitudinal association bundle (Hall, 1960) while the basal nucleus is connected to both the stria terminalis and the longitudinal association bundle. Thus the amygdalar zone receiving the neocortical projections could be considered a functionally distinct region by virtue of its physiological, histochemical and anatomical properties. However, further studies with the electron microscope would be helpful in order to clarify the synaptic distribution of the various neocortical projections and thus define the organization of such a zone. Moreover, an analysis of the other amygdaloid afferents

would contribute to the determination of other cortical and subcortical influences on the amygdala.

SUMMARY

1. Small lesions were placed in the temporal, frontal and parietal cortices of 60 cats.

2. The animals were sacrificed three, five and ten days post-operatively and the brains were fixed in formalin for one to eight weeks. The duration of post-operative period and the fixation time depended on the method of staining.

3. All brains were sectioned on a freezing microtome. The brains with a three or five day post-operative survival period were stained with the Fink and Heimer II procedure. The brains with a ten day post-operative survival period were stained with the Nauta method.

4. The results have shown that the lateral nucleus receives degenerated fibres via the external capsule and via a fascicle coursing between the ventral part of the putamen and the amygdala. The temporal polar region, the posterior sylvian and posterior ectosylvian gyrii, the anterior sylvian and ectosylvian gyrii, and the

orbital gyrus project to the lateral nucleus. The terminals are located throughout the anterior part of the nucleus, and the dorsolateral part of the middle and posterior segments. The orbital gyrus projects to the ventromedial part of the lateral nucleus.

5. The basal nucleus receives a small amount of degeneration and then only when the lesion involves the entire temporal cortex. Fibres of passage were seen bilaterally crossing that nucleus in the posterior portion of the medial system of the longitudinal association bundle. However, no terminals were observed from these bundles in the basal nucleus.

6. The lateral part of the central nucleus also receives fibres via the external capsule and the fascicle coursing between the ventral part of the putamen and the amygdala. These projections arise from the temporal polar area, the posterior sylvian and ectosylvian gyrii, the anterior

sylvian and anterior ectosylvian gyrii and the orbital gyrus. However, no projections originate in the auditory area.

7. These observations demonstrate that the neocortico-amygdaloid projections are not topographically organized but rather are converging on a specific area of the amygdala. In addition, they support the functional and anatomical studies that favour distinct regions of the amygdala modulating specific emotional responses.

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