PROJECTIONS OF THE SUPERIOR COLLICULUS TO THE THALAMUS IN THE MONKEY, MACACA MULATTA. A LIGHT AND ELECTRON MICROSCOPIC STUDY

by

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THESIS

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ABSTRACT

The projections of the superior colliculus to the thalamus have been studied in the monkey, Macaca mulatta, with light and electron microscopic techniques. Lesions of various size and location were placed in the superior colliculus of seventeen animals to study the pattern of anterograde degenerating fibers in the thalamus, with the Wiitanen silver method. Massive lesions were placed in the superior colliculus of ten other animals, which were allowed to survive one to seven days and then perfused with a buffered formaldehyde-glutaraldehyde mixture and postfixed with osmium tetroxide. Samples from the inferior nucleus of the pulvinar and from the paracentral nucleus were sectioned and stained with lead citrate and uranyl acetate for electron microscopy. The results have demonstrated that the superior colliculus projects to the inferior nucleus of the pulvinar in a topographical manner with the lower visual field represented dorsomedially and the upper field ventrolaterally. The periphery is located along the medial border and the fovea at the dorsolateral border adjacent to the lateral geniculate nucleus. The superior colliculus also sends an important projection to the ipsilateral intralaminar complex, i.e., the parafascicular, central lateral and paracentral nuclei, and a lesser projection to the corresponding contralateral intralaminar nuclei. The paracentral nucleus is the main site of termination of these fibers. Degenerating tectal fibers were also found in the ventral lateral geniculate nucleus. Four types of vesicle-containing profiles were observed in the inferior pulvinar and paracentral nucleus, the RLP, RSD, F and P. The large RLP and small RSD terminals contain round vesicles of uniform size and form asymmetric contacts mainly with large and small dendrites respectively. The F terminal contains a mixture of small round and flat vesicles. It forms symmetric contacts with dendrites and cell somata. The P profile is very pale and contains a relatively sparse population of vesicles showing a great variation in size. It forms symmetric contacts with medium to large dendrites. It was frequently found postsynaptic to the other types, especially the RLP, was interpreted as a presynaptic dendrite and was regularly seen as the intermediate element of serial and triadic synaptic arrangements. The experimental electron microscopic study has shown that the fibers from the superior colliculus terminate mainly as RLPs on large proximal dendrites in both the inferior pulvinar and the paracentral nucleus. They undergo direct dense degeneration.

LITERATURE REVIEW

I. Introduction

Recent evidence indicates that two visual pathways carry visual information to telencephalic centres in reptiles, birds and mammals (Ingle and Schneider '70). The first is the well-known geniculostriate pathway, extending from the retina, through the lateral geniculate nucleus to the primary visual cortex (or its equivalent telencephalic structure). It has been extensively studied both anatomically and physiologically, and is well-known to play a fundamental role in form and pattern recognition, at least in mammals.

The existence of a second visual pathway has been described in many vertebrates (e.g., in the frog, Ingle '73; in the turtle, Hall and Ebner '70; in the pigeon, Revzin and Karten '66; in the cat, Sprague and Meikle '65, Garey and Powell '68, Graybiel '72 ; in the hamster, Schneider '69; in the tree shrew, Snyder and Diamond '68, Casagrande et al. '72). It is more prominent in lower vertebrates and gradually diminishes in relative size from reptiles to primates with the concomitant development of the primary visual system (Diamond and Hall '69). In reptiles and birds, it extends from the retina, through the optic tectum, to the nucleus rotundus, and hence to the dorsal ventricular ridge (Hall and Ebner '69, Revzin and Karten '66). In lower mammals, and up to the tree shrew, it passes from the retina, through the superior colliculus and lateral posterior nucleus to the extrastriate visual cortex. In simian primates, at least one part of the pulvinar is believed to replace the lateral posterior nucleus as the thalamic relay of this pathway. However, the anatomical evidence for this pathway in primates is still somewhat incomplete.

Projection of the retina to the superior colliculus has been well described in many primates, including the macaque (see e.g., Wilson and Toyne '70). Although Clark ('30) had suggested a long time ago that the pulvinar of primates is comparable to the lateral posterior nucleus of lower mammals, and although the projection of the pulvinar to visual cortical association areas had been shown by retrograde cell degeneration studies (e.g., Chow '50), no one had yet demonstrated the postulated tectopulvinar projection in primates at the time the present study was initiated. Since then, two anatomical studies have shown that the superior colliculus in the monkey projects to the inferior nucleus of the pulvinar. These are a short communication by Mathers ('71) in the squirrel monkey and a recent abstract by Benevento and Fallon ('74) in the macaque.

The lack of information on the second visual pathway in primates is all the more surprising since it has been mentioned even in textbooks (Mountcastle '69) to explain the relative functional independence of the secondary visual cortical area in monkeys (and presumably in man). This independence is quite remarkable in primitive primates like the tree shrew in which simple pattern recognition is maintained after removal of the primary visual cortex (Snyder and Diamond '68, Killackey et al. '72, Ware et al. '74). Although pattern recognition is not maintained in the monkey after a similar lesion, Kluver ('42), Denny-Brown and Chambers ('58), Humphrey and Weiskrantz ('67) and Schilder et al. ('72) have demonstrated that rhesus monkeys in which the striate area has been removed, discriminate changes in luminous flux and carry out gross movements of the eyes toward moving objects (although visual fixation and tracking movements are lost). The residual visual functions in both the tree shrew and the monkey disappear on removal of the secondary visual areas (Ware et al. '74, in the tree shrew; Denny-Brown and Chambers '58, Pasik and Pasik '71, in the monkey).

Similar findings in the cat (Winans '67, Dow and Dubner '69) suggest that visual information reaches the extrastriate cortex through direct projections from the lateral geniculate nucleus, a pathway described in the cat by many authors (Garey and Powell '67, Glickstein et al. '67, Wilson and Cragg '67, Colonnier and Rossignol '69, Sprague and Niimi '70, Rossignol and Colonnier '71). Such a pathway, however, does not exist in primates, in which the lateral geniculate nucleus projects exclusively to area 17 (Wilson and Cragg '67, Hubel and Wiesel '72). The most reasonable alternate anatomical pathway is the previously described second visual pathway relaying through the superior colliculus and the pulvinar to the visual cortex.

The present study will deal with this second visual pathway, specifically with the tectothalamic projection. Before specifying the problem formulation more precisely, a brief review of the literature on this projection is necessary.

II. Superior Colliculus

The superior colliculus is generally considered to be a reflex centre involved in the orientation of the eyes towards a stimulus, so that the image is projected on the fovea, the most discriminative part of the retina. This mechanism has been called foveal acquisition (Kluver '42, Schiller and Koerner '71). It includes maintainence of visual targets at the centre of gaze in such activities as tracking moving objects and reading.

The superior colliculus is also involved in visual attention, presumably through connections with the reticular formation. This view derives from studies in the cat (Sprague and Meikle '65, Dow and Dubner '69), hamster (Schneider '69), tree shrew (Casagrande et al. '72, Casagrande and Diamond '74) and monkey (Denny-Brown '62) in which ablation of the colliculus results in visual neglect of events in the contralateral visual field. Denny-Brown ('62) described a monkey with unilateral destruction of the superior colliculus, staring aimlessly into space with a totally expressionless face. When an object moved into the intact visual field, the eyes looked in the direction of the object, but the animal seemed to lose the object of his interest quickly.

Evidence indicates that these two functions may occur in different layers of the superior colliculus. Humphrey ('68) has suggested that the stratification of the different afferents to the various layers of the superior colliculus may reflect the importance of the upper layers in the location of a moving visual stimulus and of the deeper layers in the detection of a "new" stimulus. In agreement with this, Schiller ('72) found that the neuronal response to visual stimuli in the superficial layers did not alter in the unanesthetized or anesthetized monkey, but was affected in the deeper layers by anesthesia.

A. The Layers of the Mammalian Superior Colliculus

The dorsal surface of the midbrain consists of four rounded elevations, the paired inferior and superior colliculi. These structures form the roof or "tectum" of the midbrain, overlying the cerebral aqueduct. The mammalian superior colliculus, situated rostrally, plays an important role in visual functions and is considered to be homologous to the submammalian optic tectum (Huber and Crosby '43). In the present text, the terms "optic tectum" (or the abbreviated form, "tectum") and "superior colliculus" are interchanged synonymously.

The superior colliculus is a complex laminated structure consisting of seven alternating layers of white matter and gray matter (Fig. 1). They have been given a variety of names in the literature, and these have been reviewed in detail by Crosby and Lauer ('59). The most popular terminology is the following. The most superficial layer is called the "stratum zonale". It is a poorly defined layer characterized by the presence of tangentially oriented myelinated fibers. The next layer, the "stratum griseum superficiale" or superficial gray layer, contains numerous small cells irregularly scattered in clusters and some myelinated axons usually oriented perpendicularly or obliquely to the pial surface. The cells tend to increase in numbers and size in the deeper parts of this layer. Golgi preparations reveal that the dendritic arborization of many of these fusiform and pyramidal-shaped cell bodies also orient themselves perpendicular to the surface. Other dendritic fields have random patterns of orientation. The axons of cells in the superficial gray layer usually appear to descend to deeper sites, although collaterals may terminate in the same layer (Sterling '71). The third layer, the "stratum opticum", receives its name because of the presence of retinal fibers entering through the brachium of the superior colliculus. The layer consists of myelinated axons running predominately rostrocaudally, amongst scattered large neuronal cell bodies. When the optic input is small, as in the bat or mole (Huber and Crosby '43), the optic layer is correspondingly reduced. These upper three strata are often loosely termed the superficial layers of the superior colliculus.

The next four strata are referred to as the "deep" layers of the superior colliculus. The first three are not clearly separated from each other, especially in primates, because these limits are obscured by affer-

Figure 1 Transverse section of the right superior colliculus of the Macaca mulatta. Magnification 25X.

Layer 1	Stratum zonale
Layer 2	Stratum griseum superficiale
Layer 3	Stratum opticum
Layer 4	Stratum griseum intermediale
Layer 5	Stratum album intermediale
Layer 6	Stratum griseum profundum
Layer 7	Stratum album profundum

Fig. 1a Heidenheim fiber stain

Fig. 1b Cresyl violet cell stain

Figure 1

ent fascicles which distribute widely within them (e.g., the spinotectal tract). The "stratum griseum intermediale" is made up of multipolar cells of medium to large size. Deep to this layer is the "stratum album intermediale". It consists mainly of fibers, with no specific pattern of orientation. It also contains a few cells similar to those found in the stratum griseum intermediale. The sixth layer, the "stratum griseum profundum" is an ill-defined layer consisting of scattered cells and a few fibers. The deepest layer, the "stratum album profundum" is well-defined. It is composed almost entirely of efferent and commissural fibers.

B. The Afferent Connections of the Mammalian Superior Colliculus

The retinotectal fibers project predominantly to the contralateral superior colliculus in all mammals studied. In some species, it has even been suggested that this projection is entirely crossed (Lashley '34, in the rat; Tigges '66, in the tree shrew). Siminoff et al. ('66) and Lane et al. ('71) provided neurophysiological evidence in these same species, to support this view. However, many other investigators have obtained direct anatomical evidence for an ipsilateral, albeit sparse projection to the superior colliculus of the rat (Nauta and Van Straaten '47; Lund '69) and the tree shrew (Campbell et al. '67, Laemle '68). The results reported in other species indicate that at least some retinal fibers always project to the ipsilateral superior colliculus.

It has been estimated that 90-95% of the optic fibers are crossed in the rat (Hayhow et al. '62) and the rabbit (Giolli and Guthrie '69), and that approximately 80% are crossed in the opossum (Bodian '37) and the cat (Laties and Sprague '66). The uncrossed fibers tend to become more numerous with the increase in size of the binocular field. This progression is generally observed in the mammalian series as the placement of the eyes shifts from the lateral position (e.g., in rodents), to a more frontal location, until the optical axes become nearly parallel (e.g., in primates). Although no quantitative studies have been reported for primates concerning the number of crossed versus uncrossed fibers, it has been found in the macaque that a greater number of retinotectal fibers reach the contralateral superior colliculus (Wilson and Toyne '70).

Numerous anterograde degeneration studies have been carried out in many different species to determine the exact site of termination of retinal fibers within the layers of the superior colliculus. Some studies concluded that the mammalian retina projects to all parts of the superficial layers of the superior colliculus (Huber and Crosby '43), i.e., the stratum zonale (layer 1), the stratum griseum superficiale (layer 2) and the stratum opticum (layer 3). Many workers have not specified in which of the superficial layers the optic fibers end (Bodian '37, in the opossum; Nauta and Van Straaten '47, Hayhow et al. '62, in the rat; Giolli and Guthrie '69, in the rabbit; Schneider '70, in the hamster; Casagrande et al. '72, in the tree shrew; Truex and Carpenter '69, in the human). Other workers have attempted to define the specific lamina in which the optic fibers terminate, but differing opinions exist. For example, Tsai ('25) observed retinotectal fibers in layers 2 and 3 in the opossum, Campos-Ortega and Glees ('67) in layer 3 of the squirrel monkey and Hendrickson and her colleagues ('70) in layer 2 of the macaque. These discrepancies might be interpreted in terms of species differences. Other inconsistencies, however, cannot be explained on this basis. Singleton and Peele ('65) suggest that retinal fibers terminate mainly in layer 3 in the cat, whereas in the same species Hedreen ('69) reports that they end in layers 1 and 2. These descriptive differences may be due to differences in interpretation between fibers of passage and sites of termination when using various modified silver methods.

The limitations of other techniques have also created certain problems in the interpretation of the site of termination of these fibers. Barris et al. ('35) used the Marchi technique to describe degenerated myelinated fibers in layer 3 of the cat. Crosby and Henderson ('48) using the Weil fiber stain found normal myelinated axons in layer 3 of the macaque. Neither of these methods stain unmyelinated fibers. Hence, the presumably unmyelinated preterminals described in layers 1 and 2 by other authors would not be observed using these techniques.

Careful studies by Tigges and Tigges ('70) in the galago, Wilson and Toyne ('70) in the macaque and Tigges and O'Steen ('74) in the squirrel monkey have shown that the optic fibers enter the stratum opticum and terminate mostly in the stratum griseum superficiale and only sparsely in the stratum zonale. Electron microscope studies tend to verify this finding. Lund in the rat ('69) and macaque ('72), Sterling in the cat ('71) and Tigges et al. in the galago ('73) all found that degenerating axons are numerous in the stratum opticum and scattered in the stratum zonale, whereas degenerating terminals were present mainly in the stratum griseum superficiale.

A retinal projection to deeper layers of the superior colliculus has been suggested in some species. Although Altman ('62), Laties and Sprague ('66) and Garey and Powell ('68) found that the retinotectal fibers end mainly in layers 2 and 3, they also observed some fibers ending in the stratum griseum intermediale (layer 4). Campbell et al. ('67) found degenerating retinal fibers in layer 4 of the tree shrew, as well as in the superficial layers. Laemle ('68) even found fibers in the stratum album intermediale (layer 5) and in the stratum griseum profundum (layer 6). The majority of studies, however, conclude that the retinal fibers project to the superficial layers of the superior colliculus.

The corticotectal fibers project to the ipsilateral superior colliculus in mammals. These fibers arrive via the brachium of the superior colliculus. Most of them enter through the stratum opticum, although a few approach the stratum zonale directly. The layers in which these fibers terminate have been intensively studied by tracing anterograde degenerating fibers from different regions of the visual cortex. The site of origin of these cortical projections is not always clearly defined in many studies. When authors specify that the lesion involved only the primary visual cortex, the degenerating fibers are said to terminate mainly in the superficial layers of the superior colliculus. This was observed in the cat by Probst ('01) and Barris et al. ('35), in the tree shrew by Abplanalp ('70) and Harting and Noback ('71), in the squirrel monkey by Spatz et al. ('70) and in the galago by Tigges et al. ('73). A sparse projection to layer 4, the stratum griseum intermediale, was also observed by Nauta and Bucher ('54) and Lund ('64) in the rat, by Sprague ('63) and Garey ('65) in the cat and by Wilson and Toyne ('70) in the macaque.

When the site of the cortical lesion is not clearly defined with respect to primary and secondary visual cortices, or when the lesion clearly included more than the primary visual area (presumably association visual cortex), the evidence indicates that these sites also send a dense projection to the deeper layers of the superior colliculus. This has been demonstrated in the rat (Lund '69), cat (Poliak '27, Sprague '63), macaque (Crosby and Henderson '48) and galago (Campos-Ortega '68). It is tempting to assume that the primary visual cortex projects to the superficial layers and that the secondary visual cortex projects to the deep layers. This may be only partly correct. Giolli and Guthrie ('69) carried out a direct comparison of the projections of the primary visual cortex and association visual cortex to the superior colliculus of the rabbit. Their results demonstrate that in this species at least, the primary visual cortex projects to the superficial collicular layers, whereas the secondary visual cortex projects to both the superficial and intermediate layers.

A comparison of the retinal and cortical projection to the superior colliculus reveals that though they both terminate in the superficial layers, they may end at separate levels within these layers. The electron microscope work of Lund ('69) in the rat and Sterling ('71) in the cat indicate that the sites for these two projections are differentiated into an upper retinal layer, involving the stratum zonale and the upper portions of the stratum griseum superficiale, and a lower cortical layer, involving the lower portions of the stratum griseum superficiale and the stratum opticum. In the macaque, however, this stratification was not observed. The primary visual cortex in this species projects throughout the superficial layers of the superior colliculus (Lund '72).

Neurophysiological recordings from specific strata of the superior colliculus indicate that cells responsive to visual stimuli are found primarily in the superficial layers (Humphrey '68, in the rat; McIlwain and Buser '68, in the cat; Kadoya et al. '72, in the squirrel monkey; Goldberg and Wurtz '72, in the macaque). Most cells in these layers respond to stationary or moving objects in specific parts of the visual field. The cells are sensitive to the size of the stimulus, but rarely to its shape (Schiller and Koerner '71). Because of the readiness of most cells to respond to a variety of visual stimuli, such as flashing lights, changes in flux or moving targets, the cells have often been referred to as "event detectors" (Goldberg and Wurtz '72, Cynader and Berman '72). In the cat, three-fourths of the units are directionally selective (Sterling and Wickelgren '69), whereas only a few cells are directionally selective in the monkey (Cynader and Berman '72). It is not known whether these characteristics depend exclusively on direct retinal input or whether they are also determined by cortical influences (Humphrey '68, Wickelgren and Sterling '69, Hoffman and Straschill '71).

Other tectal inputs have been described by many authors as terminating in the deeper layers of the superior colliculus (Truex and Carpenter '69). These afferent fibers consist of descending projections from non-visual cortices and ascending projections from the spinal cord, trigeminal nuclei and inferior colliculus.

The descending non-visual cortical fibers which project to the deep layers of the superior colliculus arise mainly from the temporal and parietal lobes, including the primary and secondary auditory cortex (Poliak '27, Sprague '63, in the cat; Mettler '35, Crosby and Henderson '48, Kuypers and Lawrence '67, in the macaque; Crosby and Lauer '59, in humans). Others descend from the cortex rostral to the precentral gyrus in the macaque (Kuypers and Lawrence '67). Astruc ('71) specified that these fibers arise from the gyrus rostral to the arcuate sulcus (area 8 of Brodman), a region involved in voluntary eye movements.

Non-visual ascending projections to the superior colliculus have also been shown to end in the deeper layers. This is the case for the spinotectal projections (Jassik-Gerschenfeld '65, in the cat; Crosby and Henderson '48, Mehler et al. '60, in the macaque; Crosby and Lauer '59, in humans), for the fibers from the trigeminal nuclei (Steward and King '63, in the cat; Crosby and Henderson '48, in the macaque; Crosby and Lauer '59, in humans) and for the fibers from the inferior colliculus (Moore and Goldberg '63, Powell and Hatton '69, Syka and Straschill '70, in the cat; Crosby and Henderson '48, Moore and Goldberg '66, in the macaque; Crosby and Lauer '59, in humans).

Complimentary to these inputs to the deep layers of the superior colliculus, neurons have been found within these layers that respond to visual, tactile and auditory stimuli (Horn and Hill '66, in the rabbit; Humphrey '68, in the rat; Cynader and Berman '72, in the macaque).

C. The Efferent Connections of the Mammalian Superior Colliculus

The descending projections of the superior colliculus originate in its deep layers and terminate at various levels of the brain stem and cervical spinal cord (Huber and Crosby '43). Tectospinal, tectopontine and tectoreticular fibers have been readily identified in all mammalian species studied, i.e., in the rat (Papez and Freeman '30), cat (Bucher and Burgi '50, Altman and Carpenter '61), opossum (Martin '69, Rafols and Matzki '70), tree shrew (Martin and Harting '72, Harting et al. '73), monkey (Crosby and Henderson '48, Myers '63) and man (Crosby and Lauer '59, Truex and Carpenter '69, Barr '72). The tectospinal tract forms a prominent bundle of fibers that extends to motor nuclei of the lower brainstem and to cervical levels of the spinal cord. The tectopontine tract carries fibers to the pontine nuclei, presumably to be relayed to the cerebellum (Barr '72). The tectoreticular fibers form a diffuse array that terminates in the reticular formation of the midbrain tegmentum, pons and medulla.

Some investigators state that fibers from the superior colliculus project to the oculomotor nucleus (Papez and Freeman '30, in the rat; Crosby and Henderson '48, in the macaque; Crosby and Lauer '59, in man), whereas others have denied their existence (Tarlov and Moore '66, in the rabbit; Harting et al. '73, in the tree shrew; Truex and Carpenter '69, in man). Although Bucher and Burgi ('50) found that tectal fibers approach the oculomotor nucleus in the cat, it seems more likely that they actually terminate in the adjacent region, in the nucleus of Darkschewitsch and the interstitial nucleus of Cajal (Altman and Carpenter '61). Similar findings have been described in the rabbit (Tarlov and Moore '66), opossum (Rafols and Matzke '70) and man (Truex and Carpenter '69). Despite the anatomical evidence that the superior colliculus does not project directly to the extraocular motor nuclei, stimulation of the tectum results in conjugate deviation of the eyes in the alert monkey (Robinson '72). In agreement with this, it has been found that activity in cells of the deeper layers of the superior colliculus precedes eye movements (Straschill and Reiger '73, in the cat; Schiller and Koerner '71, Goldberg and Wurtz '72, in the macaque). The pathway responsible for these eye movements probably involves the nucleus of Darkschewitsch, the interstitial nucleus of Cajal and the brainstem reticular formation. In the investigation by Robinson ('72), the head of the monkey was restrained in a stereotaxic instrument. Presumably head and neck movements would also be elicited by tectal stimulation in freely moving animals, due to the tectospinal connections.

Other terminal sites of descending tectal fibers have also been described, although general agreement for these projections is lacking. Tectal projections have been reported to the red nucleus and to the substantia nigra of the opossum (Martin '69), macaque (Crosby and Henderson '48) and man (Crosby and Lauer '59, Barr '72). A sparse tectal input to the inferior olive has been described in the opossum (Martin '69), tree shrew (Harting et al. '73) and monkey (Myers '63). Harting and his colleagues ('73) also found tectal fibers to the parabigeminal nucleus and inferior colliculus of the tree shrew.

Commissural fibers, joining the superior colliculi, have been shown to exist in all mammalian species arising and terminating in the deeper layers.

The ascending projections of the superior colliculus terminate in various nuclei of the thalamus. Comparison of these nuclei from species to species is difficult because the thalamic areas concerned have been differently subdivided and labelled in various species. Homologies are often difficult to establish. The tectothalamic connections themselves, however, can help in clarifying these problems.

Comparative morphological studies have demonstrated that the major tectothalamic projection is the nucleus rotundus in reptiles (Hall and Ebner '70, Butler and Northcutt '71) and the lateral posterior nucleus of non-primate mammals. Tectal fibers to this nucleus have been described in the hedgehog (Hall and Ebner '70), opossum (Martin '69, Benevento and Ebner '70, Rafols and Matzke '70), squirrel (Abplanalp '70) and cat (Altman and Carpenter '61, Graybiel '72). In the tree shrew, Abplanalp ('70) referred to the site of major tectal projection as the lateral posterior nucleus whereas Casagrande et al. ('72) and Harting et al. ('73) referred to the same site as the pulvinar. This is not surprising since the tree shrew is often considered phylogenetically transitional between insectivores and lower primates (Harting and Noback '71). It has been suggested by Clark ('30) that the lateral posterior nucleus of most non-primates and the pulvinar of primates are homologous structures. In the cat, however, this homology is confusing because of the existence of a pulvinar as well as a lateral posterior nucleus that receives tectal fibers (Altman and Carpenter '61). Graybiel ('72) found that the lateral posterior nucleus receives a major projection from the superior colliculus whereas the pulvinar receives only a few fibers. On the basis of the predominant input, one might suggest that the lateral posterior nucleus of the cat is equivalent to the lateral posterior nucleus of other non-primate mammals.

Glendenning et al. ('72) and Harting et al. ('72) have reported a tectal projection to the inferior or caudal portion of the pulvinar in the galago. At the time the present study was undertaken, no reports of tectal fibers to the pulvinar of higher primates were available. In a short communication, Mathers ('71) recently demonstrated the presence of tectal fibers in the inferior pulvinar of the squirrel monkey. This projection has been verified recently in the macaque, as reported in an abstract by Benevento and Fallon ('74).

Another important thalamic projection of the superior colliculus terminates in the intralaminar nuclear complex. These fibers have been described in the cat (Graybiel and Nauta '71), opossum (Martin '69, Benevento and Ebner '70), tree shrew (Martin and Harting '72, Casagrande et al. '72, Harting et al. '73) and galago (Harting et al. '72). It was specified that the tectal fibers terminate in the parafascicular and paracentral nuclei of the intralaminar complex in the opossum (Benevento and Ebner '70), whereas they terminate in the parafascicular-centromedian region in the tree shrew (Harting et al. '73). Altman and Carpenter ('61) cautioned that fibers terminating in the intralaminar complex may arise from the periaqueductal gray rather than from the superior colliculus. Such fibers were observed mainly after very large lesions of the superior colliculus that included the periaqueductal gray. The only reference to tectointralaminar fibers in higher primates prior to this study was given in an abstract by Myers ('63) for the "monkey". The author did not define the species. Recently, Benevento and Fallon ('74) reported a tectointralaminar projection in the macaque.

Tectopretectal fibers have been described in the hedgehog (Hall and Ebner '70), opossum (Martin '69, Benevento and Ebner '70, Rafols and Matzke '70), rabbit (Tarlov and Moore '66), cat (Altman and Carpenter '61), tree shrew (Abplanalp '70, Casagrande et al. '72, Harting et al. '73), squirrel (Abplanalp '70) and monkey (Myers '63). In these same species, as well as in the galago (Harting et al. '72), tectal projections have also been observed in the suprageniculate nucleus and/or the magnocellular division of the medial geniculate nucleus (the posterior nuclear group of Harting et al. '73, in the tree shrew). The ventral division of the lateral geniculate nucleus is also said to receive fibers from the superior colliculus in all species which have been studied in some detail.

A pathway from the superior colliculus to the dorsal lateral geniculate nucleus has been identified in some, but not all mammalian species. It cannot be decided whether these differences reflect real variations between species or differences in technique. Hall and Ebner ('70) expressed their uncertainty as to the existence of this projection in the hedgehog, while Martin and Harting ('72) verified it in the tree shrew. In the cat, Altman and Carpenter ('61) concluded that these fibers are absent, whereas Graybiel and Nauta ('71) observed them to be present. Myers ('63) refers to collicular fibers to the dorsal lateral geniculate nucleus in the "monkey" and yet Mathers ('71) states that these fibers do not exist in the squirrel monkey. One must conclude, therefore, that fibers to this nucleus, if they exist, must be very sparse indeed.

The zona incerta and field H of Forel receive fibers from the superior colliculus in the hedgehog (Hall and Ebner '70), opossum (Martin '69, Rafols and Matzke '70), cat (Bucher and Burgi '50, Altman and Carpenter '61), tree shrew (Casagrande et al. '72, Harting et al. '73) and monkey (Myers '63).

There also has been a suggestion of tectal fibers in the medial dorsal nucleus of the cat (Graybiel and Nauta '71), tree shrew (Harting et al. '73) and monkey (Myers '63). However most investigators do not recognize such fibers.

Recent evidence suggests that the efferent fibers of the superior colliculus can be divided into two groups according to their lamina of origin. This functional distinction of the lamination of the superior colliculus has been postulated by Morest ('65) in the opossum and by Graybiel ('72) in the cat. By placing discrete lesions in the superficial or in the deep layers of the superior colliculus, Casagrande et al. ('72) and Harting et al. ('72, '73) agree that, at least in the tree shrew and galago, the upper layers project to the pulvinar, pretectum and dorsal and ventral lateral geniculate nuclei, whereas the deeper layers project to the intralaminar nuclei, suprageniculate and magnocellular medial geniculate nuclei, subthalamic regions, plus various parts of the brain stem.

III. The Pulvinar

A. The Subdivisions of the Primate Pulvinar

The pulvinar in the primate occupies the most caudal part of the thalamus. Its posterior extremity overhangs the medial and lateral geniculate bodies. Medial to this, its free border overlies the superior colliculus of the mesencephalon.

The nuclei of the pulvinar have been described on the basis of a) cytoarchitectural criteria of cell size, shape and staining characteristics; b) myeloarchitectural criteria of general texture and fiber pattern; c) the results obtained from retrograde cell degeneration studies. In spite of the fact that different authors use different terminologies, there is general agreement in the literature concerning the subdivisions of the pulvinar into its main nuclear groups (Table 1).

Most investigators divide the pulvinar into at least three main nuclei, a medial pulvinar, a lateral pulvinar and an inferior pulvinar (Crouch '34, Walker '38, Chow '50, in the macaque; Mathers '72a, in the squirrel monkey). At the more rostral limit where the medial and lateral nuclei of the pulvi-

TABLE I The Subdivisions of the Primate Pulvinar

Walker, 1938 Chow, 1950 Mathers, 1972a	Olszewski, 1952 Eidelberg & Saldias, 1960 Snider & Lee, 1961 Emmers & Akert, 1963	Crouch, 1934	Hassler, 1959	Vogt, 1909 Friedeman, 1912 Clark & Boggon, 1935 Clark & Northfield, 1937	Clark, 1930 Aronson & Papez, 1934 Atlas & Ingram, 1937
Pulvinaris lateralis	pulvinaris pars lateralis	pulvinar lateralis pars superior	pulvinaris lateralis superior	pu	P2
		pars inferior	inferior	pn	
Pulvinaris medialis	pulvinaris pars medialis	pulvinar medialis pars medialis	pulvinaris medialis internus	pB	P3
		pars superior	dorsalis		
		pars intermedius	zentralis		
		pars inferior	ventralis		
Pulvinaris inferior	pulvinaris pars inferior	pulvinar inferior	pulvinaris intergeniculatus griseus	pd	P1
(part of pulv. lat.)	(part of pulv. pars lat.) (Emmers & Akert, only)	(part of pulv. lat. pars inferior)	fasiculosus	(part of pn)	(part of P2)
Posterior nucl. (Mathers, only)			pulvinaris suprabrachialis	pY_1 ?	
	pulvinaris pars oralis		pulvinaris oralis	puB	
(distinct from pulv.) (Walker, only)		(part of pulv. med. pars superior)	pulvinaris superficialis	pa	P4

nar blend, many authors have defined an additional subdivision, the "nucleus pulvinaris oralis" (Olszewski '52, Snider and Lee '61, in the macaque; Emmers and Akert '63, in the squirrel monkey; Eidelberg and Saldias '60, in the cebus monkey). A fifth nucleus of the pulvinar, the "nucleus pulvinaris superficialis" has been recognized by a few authors (Hassler '59, compare with Friedeman '12, Clark '30) and yet apparently ignored by others (Chow '50, Olszewski '52, Snider and Lee '61).

Some authors have used a numerical nomenclature. This was first introduced by Clark ('30) for the nuclei of the pulvinar in the primitive primate "Tarsius". Aronson and Papez ('34) and Atlas and Ingram ('37) followed Clark's terminology with some modifications in their studies of the rhesus monkey.

The main nuclei have been further subdivided by a number of authors. Vogt ('09) used myelin patterns to determine the subnuclei of the pulvinar in the cercopithecoid family of monkeys. Friedeman ('12) independently described similar subdivisions in the same species, on the basis of cytoarchitectonic characteristics. Both authors used non-descriptive Greek symbols to name these subdivisions. This terminology was followed by Clark and Boggon ('35) and Clark and Northfield ('37) for the macaque monkey. An extensive study was also carried out by Crouch ('34) in the macaque and by Hassler ('59) in the human who used a more descriptive topographic terminology (see Table I).

Very early it was recognized that the painstaking effort to divide the nuclei into subnuclei may not be relevant (Friedeman '12). It is still true today that no morphological or functional data have been provided to clarify this issue. In the further discussion of the pulvinar, only the main nuclear groups will be described in detail and illustrated.

The medial nucleus of the pulvinar (see RESULTS, Figs 6, 7) is the largest subdivision of the pulvinar. It takes up two-thirds of the dorsomedial area anteriorly (Fig. 7) and the main part of the caudal region (Fig. 6a). The nucleus extends rostrally to the centromedian nucleus, dorsally to the lateral ventricle and caudally to the posterior limit of the thalamus. It is bordered medially by the medial dorsal nucleus, ventrolaterally by the lateral nucleus of the pulvinar and ventrally by the inferior nucleus of the pulvinar and the medial geniculate nucleus. Friedeman ('12) refers to this nucleus as pB and Clark ('30) as P3.

The medial nucleus of the pulvinar is composed of evenly dispersed, medium-sized cells. No large cells are seen. Myeloarchitectonically, it is characterized by a light network of dispersed fibers.

The lateral nucleus of the pulvinar extends rostrally, medial to the external medullary lamina of the thalamus, towards the level of the centromedian nucleus. The nucleus is bordered dorsomedially by the medial nucleus of the pulvinar and ventrally or ventromedially by the inferior nucleus of the pulvinar (Fig. 6). Some discrepancy in the literature exists concerning the latter relation. Friedeman ('12), Crouch ('34) and Walker ('38) indicate that the lateral nucleus of the pulvinar extends along the external medullary lamina to form the lateral border of the inferior nucleus of the pulvinar (Fig. 7a). Friedeman ('12) subdivided the lateral nucleus of the pulvinar into a dorsal portion, pu and a ventral portion, pn. These same subnuclei were called pulvinar lateralis, pars superior and pars inferior by Crouch ('34). Clark ('30) and others termed the entire nucleus P2. Olszewski ('52) and Hassler ('59) suggest that the posteroventral part of the lateral nucleus of the pulvinar, lying immediately lateral to the inferior nucleus of the pulvinar, really belongs to the inferior nucleus.

The lateral nucleus of the pulvinar consists of rather small, lightly stained cells, with some large, darker cells in the more ventral portions.

The distinguishing characteristic of this nucleus, however, is the arrangement of cells in wide, horizontal strips, separated by numerous fiber bundles which extend medially inwards from the external medullary lamina. On the basis of this latter characteristic, it seems more reasonable to include the posterior fascicular portion of the pulvinar with the lateral nucleus (Friedeman '12, Crouch '34, Walker '38) and not with the inferior nucleus (Olszewski '52, Hassler '59).

The <u>inferior nucleus of the pulvinar</u> occupies a ventral position and extends rostrally like a blunt arrow between the medial and lateral geniculate bodies (Friedeman '12), best seen in the horizontal plane (Fig. 6b). Because of these relations, Hassler ('59) has named it the nucleus "pulvinaris intergeniculatus". The nucleus was termed "pd" by Vogt ('09) and Friedeman ('12), and Pl by Clark ('30). In the most caudal portion, the inferior nucleus is separated from the rest of the pulvinar dorsally and laterally by the large fiber bundles of the brachium of the superior colliculus (Fig. 6c). Ventrally, the nucleus forms the lower free border of the thalamus. On the medial side, the inferior nucleus is bounded by the medial geniculate body (Figs 7, 8). More anteriorly, the brachium is replaced on the lateral side by the lateral nucleus of the pulvinar (Crouch '34, Walker '38). As stated earlier, Olszewski ('52) and Hassler ('59) referred to this lateral portion as part of the inferior nucleus. Despite this, however, Hassler recognizes the distinction between a compact cellular area medially and a fibrous area laterally, labelling them as separate subdivisions, "pars griseus" and "pars fasciculosus" of the pulvinaris intergeniculatus. The pars fasciculosus corresponds to a portion of pu of Friedeman ('12) or part of the lateral pulvinar, pars inferior of Crouch ('34). Most anteriorly the lateral geniculate nucleus replaces the lateral nucleus of the pulvinar as a lateral relationship (Fig. 8).

In its most caudal part, the inferior nucleus of the pulvinar has a small medial projection extending as a wedge dorsal to the medial geniculate nucleus (Fig. 7a). It has been identified as a separate subnucleus on the basis of cytoarchitecture by Friedeman ('12) who referred to this area as "py", and by Hassler ('59) who labelled it "pulvinaris suprabrachialis". Using degeneration studies, Mathers ('71) also recognized it as a separate subdivision and labelled it the "posterior nucleus". Short slender fiber bundles travel horizontally from the brachium through this region into the inferior nucleus proper.

The inferior nucleus of the pulvinar can be recognized because of its densely packed cells and the presence of a limited number of distinctly larger and darker cells, scattered among the medium-sized cells typical of the pulvinar.

The <u>oral nucleus of the pulvinar</u> is formed by the gradual blending of the lateral and medial nuclei of the pulvinar as they continue rostrally. Thus, Friedeman ('12) appropriately named this area puB, where pu is the lateral nucleus and pB the medial nucleus of the pulvinar. The nucleus is bordered laterally by the ventroposterior lateral nucleus (Fig. 8b) and medially by the centromedian nucleus. The most rostral extent (Fig. 8c) is difficult to demarcate as it merges with the lateral posterior nucleus (Aronson and Papez '34, Olszewski '52).

The nucleus consists of small, lightly stained cells. The cell density is irregular, and generally this area is less cellular than other parts of the pulvinar. No large fiber bundles are present.

A fifth nucleus of the pulvinar has been described by some authors, occupying the dorsomedial angle of the medial nucleus of the pulvinar, immediately underlying the transverse fissure of the brain. Clark ('30) and others have referred to this area as "P4". Friedeman ('12) labelled it "pa", while Hassler ('59) called it "pulvinaris superficialis". Walker ('38) considered it as being distinct from the pulvinar.

B. Afferent Connections of the Pulvinar

Tectal projections in the hedgehog, tree shrew and galago (Harting et al. '72) provide strong evidence that the lateral posterior nucleus of non-primates is homologous with the pulvinar of primates (refer to the review of "tectal afferents"). This view coincides with the earlier work of Clark ('30) who found that the pulvinar and lateral posterior nucleus are identical in their topographical relations to adjacent nuclei and in their various afferent and efferent connections. Harting et al. ('72) even suggested on the basis of Mather's work ('71), that only one of the subdivisions of the simian pulvinar is the true homologue of the lateral posterior nucleus, i.e., the inferior nucleus of the pulvinar.

Although tectal afferents to this nucleus provide the main subcortical input, other connections have been described. Walker ('66) reported fibers from the adjacent dorsal lateral geniculate nucleus to the pulvinar. This has been supported by the work of Clark ('30) in Tarsius and that of Altman ('62) in the cat.

Retinopulvinar projections have also been reported. Many early works, cited by Singleton and Peele ('65), indicate that these fibers exist but more recent authors deny them. Altman ('62) and Meikle and Sprague ('64) state that retinopulvinar fibers could not be found in the lateral posterior nucleus of the cat but a few were observed in the pulvinar or posterior nucleus in this species. Campos-Ortega et al. ('70) described degenerating fibers in the pulvinar of the baboon and macaque using the Glees method ('46) but could not find these fibers in the same material using the Nauta and Gygax ('54) or Fink and Heimer ('67) technique. Polyak ('57) and Laemle ('68) are uncertain of their existence. Many other workers have suggested that these fibers do not exist (Clark '30, Lashley '34, Hayhow et al. '62, in the rat; Barris et al. '35, Singleton and Peele '65, in the cat; Laemle '67, Campos-Ortega and Glees '67, in the squirrel monkey; Campos-Ortega and Cluver '68, in the galago; Brouwer '27, in the macaque).

The pulvinar of primates and its homologue in non-primates also receives a cortical input, but the specific areas of origin are not well-defined. In non-primates, most investigators agree that the primary visual cortex projects to the lateral posterior nucleus (Nauta and Bucher '54, in the rat; Alplanalp '70, in the squirrel; Giolli and Guthrie '71, in the rabbit; Altman '62, Meikle and Sprague '64, in the cat). Some workers conclude, however, that these fibers do not exist (Abplanalp '70, in the tree shrew; Barris et al. '35, Beresford '61, in the cat). In many studies, the site of the lesion for these projections included both primary and secondary visual cortices (Benevento and Ebner '70, in the opossum; Heath and Jones '70, Graybiel and Nauta '71, Graybiel '72, in the cat). One is not certain from these reports whether the cortical fibers arise from the primary or the secondary visual cortex or both. Giolli and Guthrie ('71) specified that in the rabbit both projections exist.

In primates, Ferrier and Turner ('97) were the first to describe projections from the occipital lobe to the pulvinar. Since that time, many investigators have attempted a more precise description of these projections. The primary visual cortex projection to the pulvinar is controversial. Brouwer and Zeeman ('26), Mettler ('35) and Polyak ('57) expressed doubt concerning the existence of these fibers. Recent evidence indicates, however, that they exist at least in some species (e.g., Tigges et al. '73, in the galago). Spatz et al. ('70) found that these fibers project to the medial nucleus of the pulvinar of the squirrel monkey whereas Myers ('62) and Campos-Ortega and Hayhow ('72) observed in the macaque, that they project mainly to the inferior nucleus and to a lesser extent to the lateral nucleus of the pulvinar.

Projections from secondary visual and non-visual cortical areas to the primate pulvinar have also been described. In the macaque, the secondary visual cortex projects mainly to the lateral nucleus of the pulvinar (Beresford '62) and to a lesser extent to the inferior nucleus of the pulvinar (Campos-Ortega and Hayhow '72). In the squirrel monkey, it has been reported that the secondary visual cortex projects mainly to the inferior pulvinar (Mathers '72a). The anterior temporal cortex projects mainly to the medial nucleus of the pulvinar (Whitlock and Nauta '56, Chow '61) and perhaps to the inferior nucleus (Siqueira '65). The posterior temporal cortex projects to the inferior nucleus and the posterior parietal cortex projects to the lateral nucleus of the pulvinar (Mathers '72a).

C. The Efferent Connections of the Pulvinar

The efferent fibers of the pulvinar, or its homologue, the lateral posterior nucleus in non-primates, project to areas between the primary visual and the primary auditory cortex. The area can generally be described as secondary visual cortex and parts of the temporal association cortex. This has been observed in the hedgehog (Harting et al. '72), rat (Clark '30), cat (Heath and Jones '70, Burrows and Hayhow '71, Graybiel '70, '72, Chalupa et al. '73), squirrel (Diamond and Hall '69, Kaas et al. '72), tree shrew (Snyder and Diamond '68, Diamond et al. '70, Harting et al. '72, '73) and galago (Harting et al. '72, Glendenning et al. '73). In higher primates, the various subdivisions of the pulvinar project to different but overlapping sites of this same region, i.e., the association cortex adjacent to the primary auditory, somatosensory and visual sensory fields. The medial nucleus of the pulvinar projects mainly to the anterior temporal cortex and the superior temporal gyrus (Clark and Northfield '37, Chow '50, Simpson '52, Locke '60). The lateral nucleus of the pulvinar projects mainly to the posterior parietal cortex and the temporooccipital cortex (Walker '38, '66, Chow '50), including part of the secondary visual cortex (Mettler '35, Clark and Northfield '37, Lashley '48, Hassler '67). Denny-Brown and Chambers ('58) state that the lateral nucleus of the pulvinar projects specifically to area 19 of Brodman. The inferior nucleus of the pulvinar also projects to the secondary visual cortex (Mettler '35, Clark and Northfield '37, Lashley '48, Chow '50, Walker '66, Hassler '67), specifically to area 18 of Brodman according to Denny-Brown and Chambers ('58). It has been noted that fibers from the pulvinar do not extend to the striate cortex (Cragg and Ainsworth '69). Hence, the striate cortex projects to the inferior pulvinar but does not receive fibers from it. With this exception, it appears that the nuclei of the pulvinar projecting to the cortex receive reciprocal connections.

IV. The Intralaminar Nuclei

The intralaminar nuclei are cell groups located within the fibers of the internal medullary lamina separating the medial and lateral thalamic masses. These nuclei have been identified in primates as the centromedian-parafascicular complex extending most caudally, the central lateral nucleus and the paracentral nucleus rostrally (Figs 9a, b, c). Some authors refer to a central medial nucleus as part of the intralaminar complex (Truex and Carpenter '69, Ebner '73) while others consider it as one of the midline nuclei (Walker '38, Toncray and Krieg '46).

The centromedian nucleus consists of small, loosely-arranged, ovoid cells (Walker '38) located in the middle third of the thalamus. It is bordered above and medially by the dorsomedial nucleus throughtout its extent. Below and laterally it is adjacent to the ventral posterior nucleus anteriorly (Figs 8c, 9a, b) and to the pulvinar posteriorly (Figs 8a, b). It is a large, sharply-defined cell group very prominent in the primate (Clark '32) and relatively small in the mouse (Scheibel and Scheibel '66). In its rostral portion, the centromedian nucleus extends medially toward the midline, whereas in its more caudal portion, it is separated from it by the parafascicular nucleus. The centromedian nucleus is almost completely surrounded by fibers of the internal medullary lamina except along its medial border where it merges indistinguishably with the parafascicular nucleus to form the centromedian-parafascicular complex.

The parafascicular nucleus can be distinguished from the centromedian nucleus by its larger and darker cells (Olszewski '52). It is a well-defined group of cells situated medial to the centromedian nucleus, and ventral to the caudal part of the dorsomedial nucleus (Figs 8, 9a). The parafascicular nucleus partially surrounds the habenulo-interpenducular tract, so that its cells lie both medial and lateral to the tract.

The central lateral nucleus is characterized by small clusters of medium to large-sized dark cells, with small oval cells also present (Olszewski '52). It extends vertically between the centromedian nucleus ventrally and the lateral dorsal nucleus dorsally (Figs 8a, b). The nucleus blends anteriorly with the paracentral nucleus at the rostral extent of the centromedian nucleus. It is bordered medially by the dorsomedial nucleus and laterally by the ventral nuclear complex and lateral posterior nucleus.

The cells of the paracentral nucleus are large, dark and multipolar, grouped into small clusters among the fiber bundles of the internal medullary lamina (Walker '38). They form the anterior continuation of the central lateral nucleus dorsally, and replace the centromedian nucleus ventrally (Fig. 9c). The nucleus extends rostrally and medially to surround the anterior part of the dorsomedial nucleus. The paracentral nuclei are joined anteriorly by the midline nuclei (Snider and Lee '61). Laterally the nucleus is bordered by area X and the ventrolateral nucleus (Olszewski '52).

A. Afferent Connections of Intralaminar Nuclei

The main afferent connection of the intralaminar nuclei consists of fibers from the reticular formation of the brainstem and involves these nuclei in mechanisms of wakefulness and arousal (Brodal '69). Other pathways to the intralaminar nuclei have been described from the spinal cord, globus pallidus, cerebellum, superior colliculus and various regions of the cortex.

A direct input from the reticular formation originates in the medial two-thirds of the brainstem. It projects via the central tegmental fasciculus (Nauta and Kuypers '58) and appears to terminate throughout the intralaminar complex (Scheibel and Scheibel '66).

The other pathways to the intralaminar complex project more specifically to the different nuclei. Spinothalamic fibers have been traced to the parafascicular and central lateral nuclei in the monkey by Mehler et al. ('60) and Bowsher ('61). The globus pallidus projects to the centromedian nucleus in monkeys (Carpenter and Strominger '67, Mehler '71, Harding '73). The cerebellum also projects to the intralaminar complex, mainly to the central lateral nucleus although there is some disagreement to which other nuclei (Carpenter '59, Mehler '71, Kievit and Kuypers '72, Harding '73, Szabo '74, '75). Some investigators indicate that the site of termination varies according to the origin from different cerebellar nuclei but agreement is lacking (Thomas et al. '56, Cohen et al. '58, in the cat).

Tectal fibers to the intralaminar nuclei have been reviewed above. Scheibel and Scheibel ('66, '67) described tectointralaminar fibers, as a general pattern in mammals, although most of their work was carried out in the mouse. Martin ('69) and Benevento and Ebner ('70) found that these fibers terminate in the paracentral and parafascicular nuclei in the opossum, whereas Harting et al. ('72) described them in the parafascicular-centromedian complex of the tree shrew.

Cortical projections to the intralaminar nuclei arise from widespread regions of the cortex rostral to the central sulcus (Scheibel and Scheibel '67). Fibers from different parts of this area have been described in the monkey, terminating in the paracentral, central lateral, parafascicular and centromedian nuclei (Petras '64, '69, Mehler '66, Kuypers and Lawrence '67, Powell and Cowan '67, DeVito '69, Astruc '71). In the cat, association cortex posterior to the cruciate sulcus (equivalent to Brodman's area 5 and 7) also projects to the intralaminar nuclei (Szabo and Cobus '72).

B. Efferent Connections of the Intralaminar Nuclei

The efferent fibers of the intralaminar nuclei project to the thalamus, caudate, putamen and perhaps to the cortex. The parafascicular-centromedian complex projects to the ventral nuclear group of the thalamus (Nauta and Whitlock '54, Mehler '66, Scheibel and Scheibel '67) and the putamen (Clark and Russell '39, Nauta and Whitlock '54, Mehler '66, Bowsher '66, Powell and Cowan '67), but not, according to most authors, to the cerebral cortex (Nauta and Whitlock '54, Mehler '66, Powell and Cowan '67). The more rostral intralaminar nuclei centralis lateralis and paracentralis project to the caudate (Nauta and Whitlock '54, Powell and Cowan '67), the ventral nuclear group of the thalamus (especially ventralis anterior) and the rostral part of the thalamic reticular nucleus (Nauta and Whitlock '54, Scheibel and Scheibel '67).

A cortical projection from these rostral intralaminar nuclei is somewhat controversial, although recent evidence indicates that such projections exist. Neurophysiological experiments have demonstrated that stimulation of the intralaminar nuclei cause profound changes in the cortical electrical activity (Morison and Dempsey '42, Jasper '49), but anatomical evidence in the past was not convincing that direct connections exist. It was generally held that intralaminar nuclei do not project to the cortex because of the finding that hemidecortication in primates caused no retrograde cell changes in the intralaminar nuclei (Walker '35, '38). Scheibel and Scheibel ('67) have recently cautioned, however, that extensive collateral patterns of intralaminar cells to the striatum and cortex might protect the cells from the usual retrograde events following cortical lesions. Evidence is now available that the intralaminar nuclei project diffusely to the orbitofrontal cortex of the mouse (Scheibel and Scheibel '66), rat (Jones and Leavitt '74) and cat (Murray '66); the "limbic" cortex of the cat (Nauta and Whitlock '54, Murray '66) and rat (Jones and Leavitt '74); the parieto-occipital cortex of the cat (Murray '66); and the parietal cortex of the opossum, hedgehog (Killacky and Ebner '72) and rat (Jones and Leavitt '74). Jones and Leavitt ('74) have also reported that the central lateral nucleus of the intralaminar complex projects to the sensorimotor cortex of the squirrel monkey.

V. Topography of the Second Visual Pathway

A. Topographical Representation in the Superior Colliculus

A retinotectal map has been demonstrated in a variety of species, and these maps display a remarkable similarity in all mammals, including primates. Regardless of the position of the vertical meridian, the upper visual field (lower retina) is represented medially and somewhat anteriorly in the superior colliculus, and the lower visual field (upper retina) is represented laterally and somewhat posteriorly (Fig. 2). The horizontal meridian dividing the two regions has a slightly oblique anterolateral to posteromedial orientation (e.g., in the rat, Lashley '34; cat, Apter '45; tree shrew, Abplanalp '70; macaque, Wilson and Toyne '70). In animals in which the retinal projection is totally or almost totally crossed, the entire visual field of each eye is represented in the contralateral superior colliculus. In these species, the "vertical meridian" crosses at right angles to the horizontal-meridian, dividing the colliculus into a rostral and caudal area. The nasal field (temporal retina) is represented rostrally and the temporal field (nasal retina) is represented caudally (Fig. 3a). This pattern is found in the rat (Lashley '34, Siminoff et al. '66), rabbit (Schaefer '66), tree shrew and squirrel (Abplanalp '70, Lane et al. '71).

In animals with increasing overlap of the visual fields, the part of the temporal retina sharing the binocular field projects to the ipsilateral superior colliculus; the more nasal areas continue to project to the contralateral colliculus (e.g., the opossum, Bodian '37). As the degree of binocular overlap increases, the number of fibers from the temporal retina projecting to the contralateral superior colliculus decreases. The representation of the nasal field to the contralateral colliculus must thus also decrease. This brings the vertical meridian to a more anterior position. When the binocular overlap is sufficient for the two eyes to have the same fixation point, all of the temporal retinal fibers project to the ipsilateral colliculus. The visual fields become represented homo-

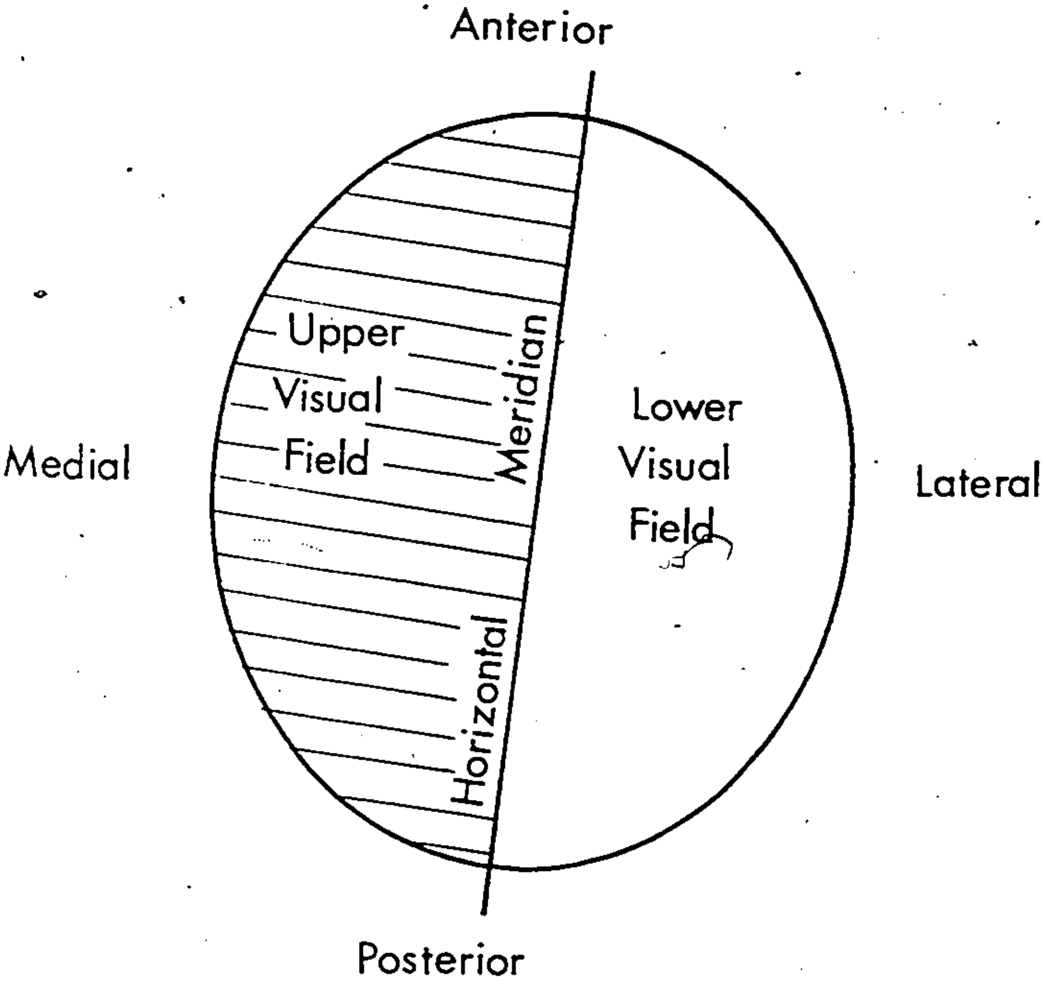
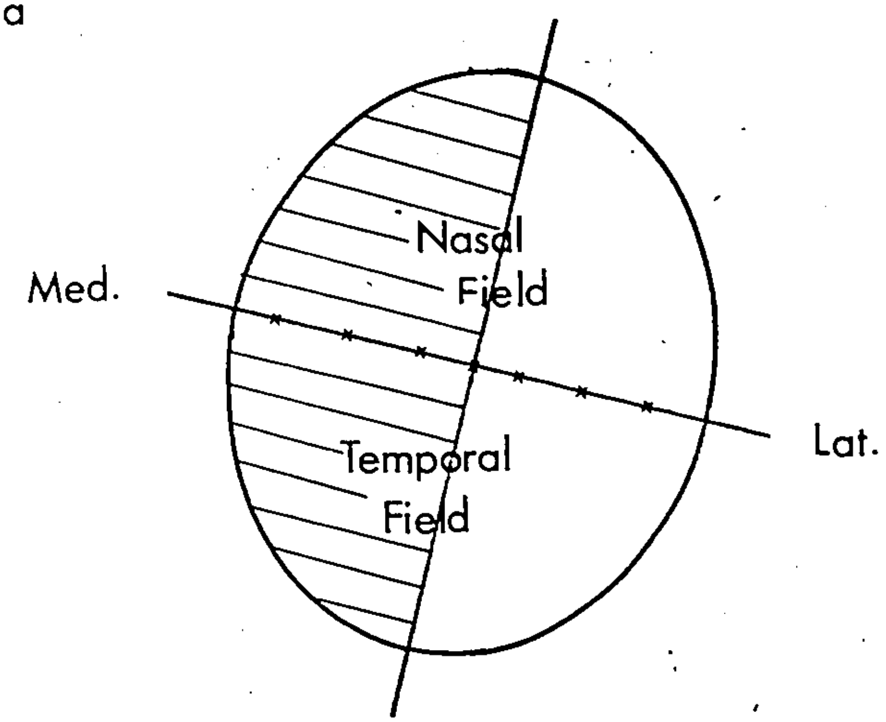


Figure 2: Dorsal view of the right superior colliculus of both non-primates and primates to show the generalized topographical pattern of the retinotectal projection. Note the vertical meridian has been omitted from this diagram.

3a



3b

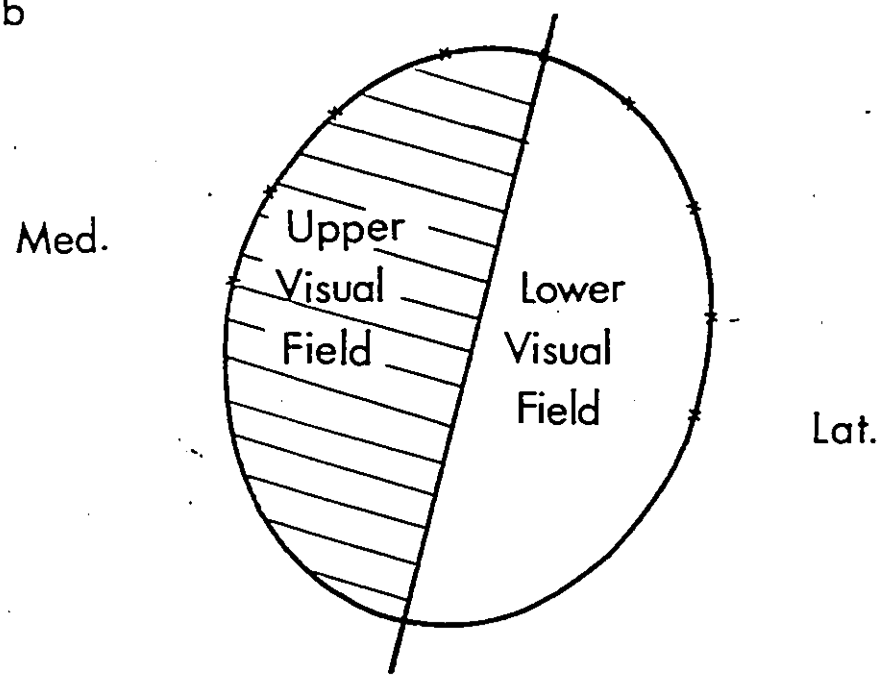


Figure 3: Dorsal view of the right superior colliculus to illustrate a) animals in which both the nasal and temporal visual fields are represented in the contralateral superior colliculus; and b) animals in which only the contralateral hemifield is found in the superior colliculus. The vertical meridian is represented by X's. The upper field is shaded.

nymously in each colliculus and the vertical meridian then occupies its most anterior border (Fig. 3b).

This situation exists in primates where the nasal retina projects entirely to the contralateral superior colliculus and the temporal retina, to the ipsilateral superior colliculus. Only the contralateral visual hemifield is represented in each superior colliculus (Fig. 4). The fovea is represented at the rostral pole of the superior colliculus, with the lower vertical meridian of the visual field extending along the rostral and medial border of the colliculus, and the upper vertical meridian extending along the rostral and lateral border (Figs 3b, 4). The peripheral visual field is represented caudally. This general pattern of the retinotectal projection has been described in the squirrel monkey (Kadoya et al. '72), galago and owl monkey (Lane et al. '73) and macaque (Wilson and Toyne '70, Schiller and Koerner '71, Goldberg and Wurtz '72, Cynader and Berman '72).

The monocular crescent of the peripheral visual field is represented in the most nasal part of the retina, and projects to the caudal pole of of the contralateral superior colliculus. Thus, the temporal retina does not project to the most caudal region (Wilson and Toyne '70, Tigges and Osteen '74, in the macaque; Kadoya et al. '71, in the squirrel monkey; Lane et al. '73, in the galago and owl monkey).

Although neurophysiological recordings have demonstrated a foveal representation in the colliculus of the macaque (Goldberg and Wurtz '72, Cynader and Berman '72), surprisingly no retinal projections from the fovea to the superior colliculus have been found (Brouwer and Zeeman '26, Wilson and Toyne '70). After removal of the eye, the most anterior portions of the colliculi do not have degeneration. It is probable that the neurons driven by the foveal area are activated by corticotectal projections since

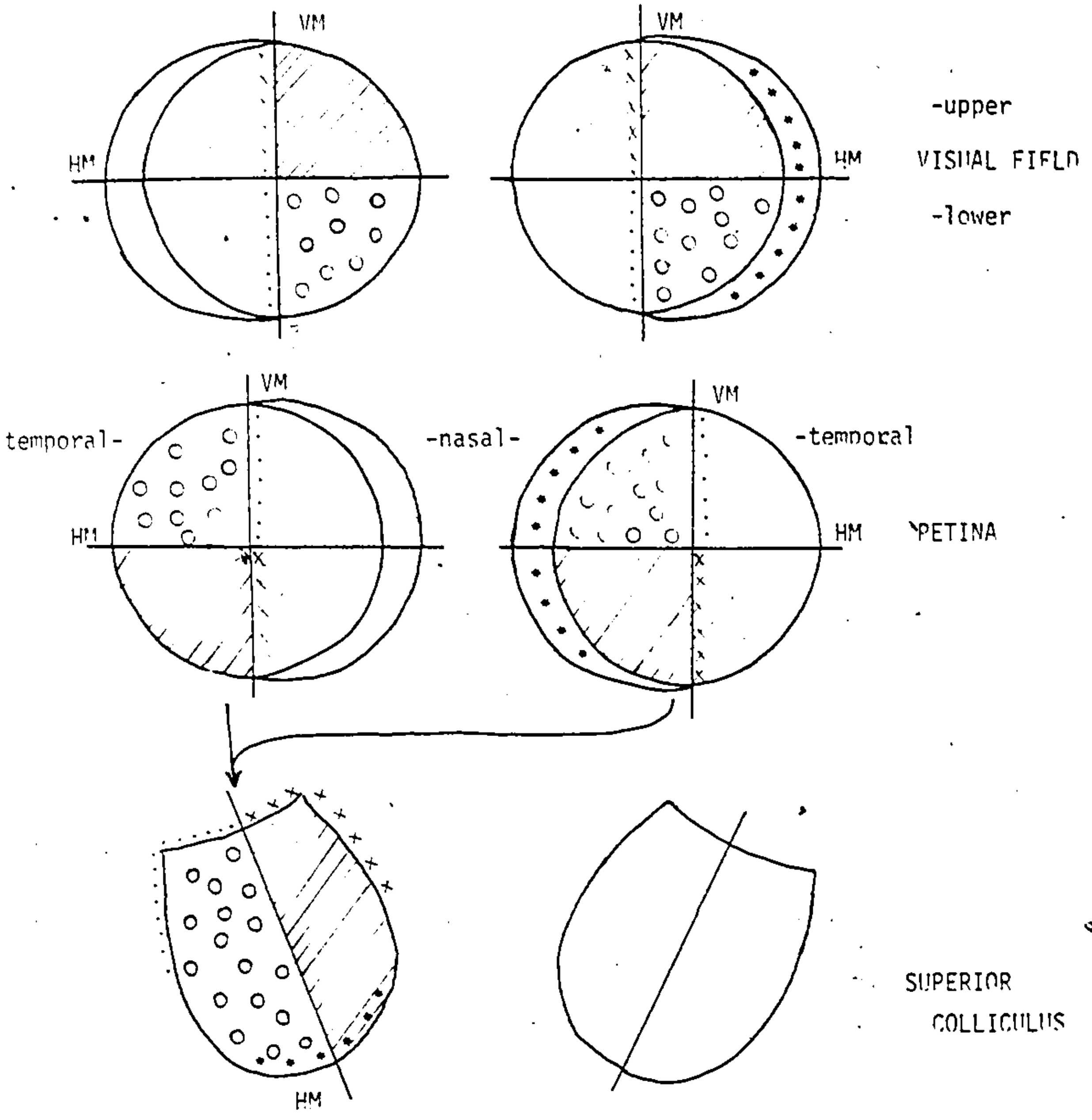


Figure 4 Schematic representation of the projection of the contralateral visual hemifield onto the surface of the superior colliculus in primates. VM signifies vertical meridian, HM horizontal meridian, * monocular region of the contralateral peripheral field.

the visual cortex projects to the superior colliculus in a corespondingly topographical manner (Wilson and Toyne '70), with the foveal area of the cortex projecting most anteriorly. It has been shown in several species that sites in the visual cortex having a specific retinal representation project to sites in the superior colliculus with corresponding retinal representation (Lund '64, in the rat; Garey and Powell '68, in the cat; Giolli and Guthrie '71, in the rabbit; Harting and Noback '71, in the tree shrew; Kadoya et al. '71, in the squirrel monkey; Crosby and Henderson '48, Wilson and Toyne '70, in the macaque).

Most investigators have found that the visual field near the "centre of gaze" receives an expanded representation in the superior colliculus, at the intersection of the horizontal and vertical meridian (Laties and Sprague '66, Garey and Powell '68, Feldon et al. '70, in the cat; Lane et al. '71, in the squirrel and tree shrew; Wilson and Toyne '70, Goldberg and Wurtz '72, in the macaque; Lane et al. '73, in the owl monkey). A disproportionate amount of tissue is devoted to central vision, to the extent that a third of the collicular surface is devoted to representing the central ten degrees of the visual field in the macaque (Cynader and Berman '72). The degree of magnification appears to follow the histology of the retina, so that a greater area of the colliculus is devoted to parts of the field with finer retinal grain (Humphrey '68).

In the studies so far discussed, the topographical projections represent the sensory visual input to the superior colliculus, as determined by physiological and anatomical techniques. Since the functions of the superior colliculus can be subsumed under the general concept of foveal acquisition, one should be able to predict the direction of eye movements elicited on stimulation of its different parts. That this is the case has been shown by Apter ('46) and Straschill and Reiger ('73) in the cat, and Robinson ('72) in the macaque.

[illegible]. Topographical Representation in the Pulvinar

Prior to the onset of this study, evidence was available that a crude topographical representation of the visual field was present in the pulvinar of the tree shrew (Diamond et al. '70, Harting et al. '73) and in its homologue, the lateral posterior nucleus of the cat (Garey et al. '68). In higher primates, there was some evidence of a topographical arrangement in the inferior nucleus of the pulvinar. Clark and Northfield ('37) and Chow ('50) determined the projections of the inferior nucleus of the pulvinar to the extrastriate visual cortex in the macaque by means of retrograde degeneration studies following cortical lesions.

Since the initiation of the present study, Campos-Ortega and Hayhow ('72) have mapped the projection of the primary visual cortex (area 17) to the inferior nucleus of the pulvinar in the macaque using anterograde degeneration studies. The representation of the visual field in the inferior nucleus of the owl monkey has also been determined by Allman et al. ('72) by electrophysiological recordings in the inferior nucleus while stimulating different parts of the visual field. The results of these various findings correspond closely for both Old World (macaque) and New World (owl monkey) species.

VI. Electron Microscope Review

A. Criteria for Identification of Synapses

The expression "synapse" was introduced by Sherrington in 1897, to signify the site of functional contact between neurons. "Synapses" were first described in electron microscopic studies by Palade and Palay ('54) and DeRobertis and Bennett ('54). They are identified as morphologically specialized contacts between neurons in which one profile contains an agglomeration of vesicles towards a differentiated membrane, the membranes at the site of contact being thicker and denser than elsewhere (DeRobertis and Bennett '55, Palay '56, '58, DeRobertis '59, Gray '59, Whittaker and Gray '62, Gray and Guillery '66). DeRobertis and Bennett ('55) were the first to describe the axonal vesicles and coined the expression, "synaptic vesicles". Two types of vesicles have been described, the first is small, 300-500 A in diameter, with a clear centre (Palay '58); the second varies from 500 to 1500 A in diameter, with a characteristic dense core (Grillo and Palay '62, Pappas et al. '66). In the appropriate plane of section, the "pre-" and "postsynaptic" membranes are separated by approximately 200 A. The space is referred to as the "synaptic cleft" (Palay '58) and typically contains a dense osmiophylic material. It has been postulated that these specialized sites of contact may serve both as points of adhesion and as sites for synaptic transmission (Palay '56). There is evidence that these membranes adhere strongly to each other (Gray '59). The agglomeration of synaptic vesicles in the presynaptic element towards the synaptic membrane and the speculation that synaptic vesicles may contain the chemical transmitter substance (Palay '56, DeRobertis '59, Whittaker and Gray '62), lends support to the second view.

B. Morphological Classification of Synaptic Terminals

Recently a wide variety of synaptic terminals has been described on the basis of the morphological characteristics of their synaptic vesicles and of their differentiated membranes. Not only can the synaptic vesicles be separated into two types on the basis of the presence or absence of a central dense core but the shape of synaptic vesicles can vary from one terminal to the next. These different shapes seem to be dependent to some extent upon the fixative used. They appear, however, to be specific for different types of endings and therefore provide useful criteria for categorizing different types of boutons. It is reasonable to assume that such differences may reflect differences in function.

Since synaptic vesicle morphology depends on fixation procedures, it seems worthwhile to consider briefly some of the fixatives used in electron microscopic studies. The first important fixative to appear was buffered osmium tetroxide (according to Palade '52). With this type of fixative, synaptic vesicle populations consisted of uniformly round vesicles (DeRobertis and Bennett '55, Palay '56, '58, Gray '59).

With the introduction of a buffered formaldehyde fixation prior to immersion in osmium tetroxide, it became apparent that two types of synaptic vesicle populations could be distinguished, a population with predominantly round vesicles and a mixed population of round and flattened or ellipsoidal vesicles (Uchizono '65, Walberg '65, Hirata '66, Lund and Westrum '66). Bodian ('66) and Walberg ('66) observed similar results using buffered glutaraldehyde instead of buffered formaldehyde. It was concluded that aldehyde fixation was responsible for this differentiation. Uchizono ('65) and Lund and Westrum ('66) noted that the vesicles in the "flat" population were smaller than the others, and Lenn and Reese ('66) and Larramendi et al. ('67) further determined that the two vesicle populations could be differentiated by size alone, regardless of aldehyde fixation.

In the above studies, Uchizono ('65), Hirata ('66) and Walberg ('66) state that sucrose was used in the fixative solutions but the significance of the sucrose and the osmolarity of the buffer solutions was not mentional. Bodian ('70) reported that the critical factor responsible for the flattened vesicle population was a half-hour wash in the sucrose-containing buffer solution between the steps of primary fixation in aldehydes and secondary fixation in osmium tetroxide. It has now been shown, however, that the morphology of synaptic vesicles is dependent on the osmotic effect of the buffer during primary fixation as well as the subsequent rinse (Valdivia '71). In the extensive study of the effects of fixation, Valdivia ('71) considered many possible variables, such as the concentration of the aldehydes, pH, temperature and the osmolarity of the various solutions. Neither the concentration nor the osmolarity of the aldehydes affected the shape of synaptic vesicles. Rather, the osmolarity of the buffer in which the aldehydes are dissolved is the crucial factor. In buffered solutions below 200 milliosmoles, nearly all synaptic vesicles are round; in solutions above 800 milliosmoles an excessive number of vesicles are flat in both populations. Buffered solutions between 200 and 800 milliosmoles result in two clearly defined populations of synaptic vesicles.

Dennison ('71) further subdivided the "flat" vesicle population. By viewing these vesicles stereoscopically, it was found that one type of profile contained cylindrical vesicles and another type contained discoid vesicles. (This topic is further elaborated below).

C. Classification of Synaptic Terminals According to Membrane Specializations

Another characteristic used to classify synaptic types was the appearance of the synaptic membranes. On this basis, Gray ('59) observed two types of synapses in the cerebral cortex: type 1 synapses in which the opacity of the postsynaptic membrane is more pronounced than that of the presynaptic membrane; and type 2 synapses in which the opacity at the pre- and postsynaptic membrane is more closely similar. In the type 1 synapse, the synaptic cleft is wider than the nonsynaptic interneuronal regions and contains an electron dense material. The synaptic cleft at type 2 synapses has the same width as the rest of the extracellular space, and contains little or no electron dense material. In the above study, osmium tetroxide served as the primary fixative. When aldehyde fixation precedes this step, a distinction is not easily made between the two types of contacts on the basis of the width of the synaptic cleft and the interlemmal opacity. The membranous specialization, however, is still present. Indeed, the increased postsynaptic density of Gray's type 1 synapse is then shown to be mainly an increase in opacity of the postsynaptic cytoplasm adjacent to the synaptic membrane. Because of this uneven opacity at the synaptic contact, Colonnier ('68) referred to this type of contact as "asymmetrical". In Gray's type 2 contact, the postsynaptic cytoplasmic opacity is absent and, therefore, the synaptic contact appears "symmetrical" (Colonnier '68).

The first suggestion that a correlation may exist between the shape of synaptic vesicles and the thickness of the synaptic membranes, was given by Hirata ('66). He observed that the synaptic profile containing flattened vesicles formed a contact in which the membrane thickenings were less obvious. In an elaborate presentation, Colonnier ('68) firmly established the concept that terminals with mainly round synaptic vesicles are usually associated with the asymmetric synaptic contact. On the other hand, terminals with the population of flattened vesicles are associated with the symmetrical contact. A similar relationship has also been observed by Price ('68) and Ralston ('68a).

Several investigators attempted to attribute functional significances to these different characteristics. Physiologically it has been determined that inhibitory contacts are situated on the soma of the cerebellar Purkinje cell (Andersen et al. '63) and on the soma of hippocampal pyramids (Andersen '64). In parallel, electron microscopic studies have shown that type 2 synapses (symmetrical) often occur on the cell body of pyramidal cells (Gray '59). On this basis Eccles ('64) suggested that the type 2 synaptic contact was inhibitory, and that consequently, the type 1 synapse found on dendrites and their spines was probably excitatory. Uchizono ('65) then related these findings to the morphology of synaptic vesicles in the cerebellum. It was found that the soma of the Purkinje cell is contacted exclusively by boutons containing flattened vesicles, whereas the dendrites and their spines were contacted mainly by terminals containing round synaptic vesicles. Through similar studies in various parts of the central nervous system, there has been mounting circumstantial evidence that terminals with round vesicles associated with asymmetrical differentiations may be excitatory and terminals with flat vesicles with symmetrical differentiations would be inhibitory (e.g., Lenn and Reese '66, Larramendi et al. '67, Colonnier '68, Gray '69). Atwood et al. ('72) have found in the crayfish that stimulation of the excitatory axon to the opener muscle, in the presence of a metabolic inhibitor, results in depletion of synaptic vesicles from terminals containing round vesicles. Stimulation of the inhibitory axon to the muscle, under these same conditions, produces depletion of vesicles from other terminals containing flattened vesicles thereby providing more direct evidence to relate round vesicle populations to excitation and flattened vesicle populations to inhibition.

D. Synaptic Organization of the Thalamus

i) Synaptic Types

In the thalamus, electron microscope studies have recently described further subdivisions and classifications of vesicle-containing neuronal profiles. These classifications have been based upon the synaptic relationship to other neuronal elements and upon the appearance of the cytoplasm, mitochondria and vesicles within the profile. The descriptions of the different synaptic types are strikingly similar for the various specific relay nuclei, i.e., the lateral geniculate nucleus (Colonnier and Guillery '64, Szentagothai et al. '66, Peters and Palay '66, Campos-Ortega et al. '68, Pecci-Saavedra and Vaccarezza '68, Guillery '69a, Jones and Powell '69a, Guillery and Colonnier '70, LeVay '71, Wong-Riley '72a, Famiglietti and Peters '72, Lieberman and Webster '72), in the medial geniculate nucleus (Majorossy and Rethelyi '68, Jones and Powell '69a, Morest '71, Jones and Rockel '71), the ventrobasal complex (Ralston and Herman '69, Jones and Powell '69a) and the ventrolateral nucleus (Harding '71, '73).

Two types of terminals with round vesicles have been described in the thalamus. In the first type, the terminal is rather large in size, irregular in outline and contains loosely-packed round vesicles of uniform size and several mitochondria (Ralston and Herman '69). The profile forms the presynaptic element of an asymmetric contact but is also involved in another type of specialized membrane junction with a dendrite or soma. In this latter type, the opposing membranes at the site of the differentiation present a wavy outline, such that the extracellular space between them is extremely irregular. This gives the impression that the junctional site consists of a series of several individual contacts. The subjacent cytoplasm contains patches of electron-dense amorphous material, being more extensive in the dendritic than the axonal component. Networks of neurofilaments are particularly obvious in the underlying cytoplasm of the dendrite or soma, after primary osmium fixation and phosphotungstic staining. These fibrils are found lying adjacent to and occasionally embedded in the localized dense patches. It has been suggested that this type of contact does not take part in synaptic transmission because no synaptic vesicles are associated with the membrane differentiation (Peters and Palay '66, Pappas et al. '66, Guillery '67, '69a). Rather it is probably involved in the adhesion of two neuronal components (Peters and Palay '66, Ralston and Herman '69, Jones and Powell '69a) perhaps in order to produce and maintain specific neuronal relationships (Colonnier and Guillery '64, Jones and Rockel '71). This type of junction has been termed a "filamentous" contact as opposed to the "regular" contact, according to Colonnier and Guillery ('64), or an "adhesive plaque" versus a "true synaptic contact", according to Peters and Palay ('66).

The profile described above has been termed RLP by Guillery ('69a) and others (Guillery and Colonnier '70, LeVay '71), where "R" signifies the round vesicles, "L" the large terminal and "P" the fact that the mitochondria sometimes appear somewhat pale in certain preparations. The RLP profile is similar to the LP axon of Colonnier and Guillery ('64), the type 1 axon of Szentagothai et al. ('66) and Majorossy and Rethelyi ('68), the "central" axon of Peters and Palay ('66), Campos-Ortega et al. ('68) and Pecci-Saavedra and Vaccarezza ('68), the "large dark terminal" of Jones and Powell ('69) and the RL axon of Wong-Riley ('72a).

In the second type of terminal containing round vesicles, the profile is rather small, containing tightly-packed vesicles of uniform size, and only occasionally one or two mitochondria (Ralston and Herman '69). The profile forms the presynaptic component of an asymmetric contact but never takes part in a filamentous contact. The terminology RSD has been applied by Guillery ('69a) and others, to signify the "round" vesicles, "small" size of the profile and rather "dense" mitochondria. The RSD profile is similar to the SD axon of Colonnier and Guillery ('64), part of the type 3 axons of Szentagothai et al. ('66), the "simple synaptic contact" of Peters and Palay ('66), the "small dark terminal" of Jones and Powell ('69a) and the RS axon of Wong-Riley ('72a).

The other main category of synaptic terminals is those containing flattened or irregular-shaped synaptic vesicles forming symmetric synaptic contacts and occasionally filamentous contacts. They have been referred to as F profiles by many authors (e.g., Guillery and Colonnier '70, LeVay '71). The F profile varies greatly in size, but is usually smaller than the largest RLP profile. It contains one to several dark mitochondria. The vesicles are often smaller than those found in populations of round synaptic vesicles and the compactness of the vesicle population varies considerably. Two types of F profiles have been described by Guillery ('69a) and Wong-Riley ('72a), the F1 and F2 axon. In the F1 terminal, the vesicles are smaller and more closely packed and the overall appearance of the profile is usually darker. In the F2 terminal, the vesicles are usually fewer and more dispersed. The profile often contains small vacuoles of smooth endoplasmic reticulum. The F1 axons are apparently similar to part of the type 3 axons of Szentagothai et al. ('66) and the IA profile of Famiglietti and Peters ('72). The F2 axon is similar to the type 2 axon of Szentagothai et al. ('66). All the elements described above, containing flattened synaptic vesicles, were considered to be axons until recently.

It has become evident, however, that some of the vesicle-containing F profiles exhibit dendritic characteristics, i.e., they contain clusters of free ribosomes, arrays of microtubules and small patches of granular endoplasmic reticulum (Ralston and Herman '69, Famiglietti '70). These vesicle-containing profiles are distinguished by the paleness of their cytoplasm, the sparseness of synaptic vesicles and the irregular shape of these vesicles: "pleomorphic" according to Harding ('71) and Wong-Riley ('72a); "polymorphic" according to Famiglietti and Peters ('72) or "discoid" according to Dennison ('71), Lieberman and Webster ('72) and Colonnier ('74). It has been termed a P-bouton by Lieberman and Webster ('72), ID terminal by Famiglietti and Peters ('72) or Fd profile by Wong-Riley ('72a) and is synonymous to the F2 "axon" of Guillery ('69a) according to LeVay ('71), Lieberman and Webster ('72) and Famiglietti and Peters ('72). These neuronal elements often form the presynaptic component of a synaptic contact. Such "presynaptic dendrites" have now been described in other parts of the central nervous system as well as in the thalamus, e.g., in the cerebral cortex (Sloper '71), superior colliculus (Lund '69, Sterling '71) and olfactory bulb (Rall et al. '66, Price '68). This type of profile seems to be such a basic element in the synaptic organization of the thalamus that it has even been described in the reptilian lateral geniculate nucleus (Manohar '73).

In summary, four types of synaptic profiles have been described in the specific relay nuclei of the thalamus, i.e., following the terminology of Guillery ('69a), the RLP, RSD, F2 and F1 profile.

Similar types of terminals have been described in the lateral posterior-pulvinar complex of the cat (Majorossy et al. '65, Hajdu et al. '74) and in the inferior nucleus of the pulvinar of the monkey (Mathers '72a, Campos-Ortega and Hayhow '73). Hajdu et al. described four types that resemble those of Guillery ('69a), the RL, RS, F1 and F2 (dendritic). Three types of axonal profiles were described in the primate pulvinar, the RL, RS and F types of Mathers ('72a) and the corresponding type I, type III and type II of Campos-Ortega and Hayhow ('73). Their F category or type II apparently included the F2 "presynaptic dendrite" although such a distinction was not made.

ii) Synaptic Interrelationships

The various neuronal components of the specific thalamic nuclei are found either in localized aggregations or clusters involved in specific synaptic interrelationships or distributed throughout the surrounding neuropil where similar synaptic relationships occur separately. In the cat, the clusters of neuronal elements are usually isolated, to a greater or lesser extent, from the surrounding neuropil by a thin glial lamella. These synaptic zones have been called "glomeruli" by many authors (Szentagothai '63, Szentagothai et al. '66, Peters and Palay '66, Jones and Powell '69a, Jones and Rockel '71). In the monkey, the glial element is rather incomplete or absent, so that the synaptic aggregations merge with the surrounding neuropil or other aggregations and hence a more appropriate terminology, "synaptic islands" was introduced by Colonnier and Guillery ('64). The distinction between the "glomerulus" and "synaptic island" is not always clear-cut in different nuclei, nor in different species. Other terminologies have been applied to indicate the transitional types (Guillery '67, '69a, Majorossy and Rethelyi '68, Ralston and Herman '69, Morest '71).

These synaptic aggregations are usually made up of one or two RLP profiles, one or two dendrites and several F profiles (predominantly F2 when the distinction between the two F types is made). The F1 and RSD profiles are infrequently found at the periphery of these "glomeruli" (Szentagothai et al. '66, Jones and Powell '69a, Guillery '69a).

The RLP profile takes part in several asymmetric contacts, always as the presynaptic component (Guillery '69a, Wong-Riley '72a), with large, presumably more proximal dendrites and also with F2 profiles. The F2 profile forms symmetrical contacts with dendrites of all sizes and to a lesser extent with terminals similar to itself (Famiglietti and Peters '72). When synaptic contacts occur between two vesicle-containing profiles the F2 terminal is usually the postsynaptic element taking part in serial or triadic synaptic arrangements.

The serial synaptic relationship was first observed by Kidd ('62) and Gray ('62) who found that a vesicle-containing profile terminating on a dendrite could itself be postsynaptic to another vesicle-containing profile. Gray ('62) suggested that the intermediate profile was an axon resulting in an axo-axo-dendritic arrangement. Several investigators have reported similar synaptic arrangements (Pappas et al. '66, Hirata '66, Szentagothai et al. '66, Peters and Palay '66, Pecci-Saavedra and Vaccarezza '68, Jones and Powell '69a). The description of vesicle-containing dendrites has raised the possibility that the second element of the serial synapse may be a dendrite. In some situations the intermediate component is in fact axonal in nature (Ralston '68b, Westrum and Black '68), but recent evidence indicates that many serial synapses are axo-dendro-dendritic arrangements in which the intermediate component is a presynaptic dendrite (Lieberman and Webster '72, Lieberman '73). These axo-dendro-dendritic serial synapses have been described in the thalamus by many investigators (e.g., Ralston and Herman '69, LeVay '71, Morest '71, Famiglietti and Peters '72, Wong-Riley '72a).

The triadic synaptic arrangement consists of an axo-dendro-dendritic relationship in which the axon contacts not only the intermediate presynaptic dendrite, but also the same common target dendrite contacted by the intermediate element. The triadic arrangement was first described by Colonnier and Guillery ('64) and later by Peters and Palay ('66), LeVay ('71) and Famiglietti and Peters ('72). It has been referred to as a "triplet" arrangement by Jones and Powell ('69a), Harding ('71) and Sloper ('71). Not all authors, however, have recognized the intermediate component as dendritic.

The F1 profile is less common, but is found with equal frequency inside and outside of the "glomeruli" (Guillery '69a, Famiglietti and Peters '72). It takes part in symmetrical synaptic contacts with dendrites of all sizes, the F2 terminal and the soma, although axosomatic contacts are not common.

The RSD profile is found predominantly, but not exclusively, in the surrounding neuropil. It forms a single asymmetric contact, always as the presynaptic element, with a medium to small, presumably more distal dendrite or occasionally with the F2 terminal (Ralston and Herman '69, Jones and Powell '69a, Guillery and Colonnier '70). It is the most abundant profile found in thalamic nuclei (e.g., Ralston and Herman '69, Wong-Riley '72a).

The synaptic relationships of the lateral posterior-pulvinar complex of the cat and the pulvinar of the monkey are similar to those described above. Aggregations of neuronal profiles are distributed throughout the neuropil. In the cat, these synaptic zones resemble the "glomeruli" described by Szentagothai ('63) and others because of the surrounding glial lamellae (Majorossy et al. '65, Hajdu et al. '74). In the monkey, these zones resemble the "synaptic islands" of Colonnier and Guillery ('64), because of the absence of the glial sheath. Mathers ('72a) recognized that the glial capsule was absent but still names these aggregations "glomeruli". Campos-Ortega and Hayhow ('73) preferred the terminology "synaptic complexes". The authors stressed that the distinction between the synaptic complexes and interstitial neuropil is difficult and somewhat artificial. A more meaningful subdivision, according to them, divides the synaptic relationships according to proximal and distal dendritic types.

Nonsynaptic filamentous adhesions have been described in many of the thalamic nuclei (e.g., Guillery '69a, Ralston and Herman '69, Mathers '72a) between dendrites and somata, in dendrodendritic, dendrosomatic or somasomatic arragements. They resemble the "filamentous" contacts formed by the RLP profile but with the cytoplasmic densities in both profiles appearing symmetrical.

iii) Source of the Different Terminals

The source of the various terminals described above have been identified mainly through degeneration studies. Two types of anterograde degeneration of axon terminals have been observed in electron microscope studies, the "filamentous" degeneration (Gray and Hamlyn '62) and the "dense" degeneration (Colonnier '64).

The filamentous degeneration was originally described by Gray and Hamlyn ('62) in the optic tectum of the chick following eye enucleation, and has since been described in several regions of the central nervous system after interruption of the appropriate afferent fibers.

Filamentous degeneration is characterized by a dramatic neurofilamentous hypertrophy, in which the degenerating profile rapidly becomes filled with randomly oriented, interweaving bundles of neurofilaments (Colonnier and Guillery '64, Guillery '65). Occasionally, the neurofilaments form an annular configuration. The synaptic vesicles and mitochondria become crowded towards the centre~~, or~~ more frequently, are found in clusters at the periphery. Glycogen granules have sometimes been associated with these events (Szentagothai et al. '66, Lund '69). The neurofilamentous reaction has been observed by most investigators to be the initial or primary stage of degeneration (Szentagothai et al. '66, Mugnaini and Walberg '67, Wong-Riley '72b). It is followed by a second stage of degeneration in which the vesicles, mitochondria and filaments begin to break down into clumps of electron dense material. Eventually, the entire profile becomes opaque. The terminal shrinks in size and neuroglial processes begin to surround it. Finally, the degenerated profile is engulfed and phagocytized by the glial cells. The time sequence of the entire degenerative process is variable, depending on the species and system studied. The transition from the filamentous to the dense stage of degeneration has been observed as early as two or three days following the lesion (Sterling '71, Jones and Rockel '71) or as late as ten days (Wong-Riley '72b). In many cases, however, the process is complete by the seventh to ninth day (Szentagothai et al. '66, Ralston '69, Jones and Rockel '71).

In the second variety of degeneration, the affected terminals become electron-dense directly; as first described by Colonnier ('64). The cytoplasm increases markedly in density, displaying a granular appearance. The mitochondria become swollen and begin to fragment. The synaptic vesicles soon are no longer recognizable. The terminals shrink, become distorted and are engulfed by glial processes. The onset of this process is rapid, within one or two days after the lesion. It is often complete by the seventh day, although some profiles are still being phagocytized at the tenth day or later. "Dense" degeneration reaction has been described by Colonnier ('64), Walberg ('65), Ralston ('68b), Lund ('69), Jones and Powell ('69b), Sterling ('71) and Mathers ('72b).

In the specific relay nuclei of the thalamus the RLP profile of Guillery ('69a) undergoes neurofilamentous degeneration when the primary sensory afferent pathways have been interrupted. This has been observed in the lateral geniculate nucleus after enucleation of the eye (Colonnier and Guillery '64, Szentagothai et al. '66, Guillery '69b, Pecci-Saavedra et al. '70, Wong-Riley '72b), the medial geniculate nucleus after lesions of the inferior colliculus (Jones and Rockel '71) and in the ventrobasal complex after lesion of the dorsal column nuclei (Ralston '69). It has been suggested that this type of terminal has a powerful driving influence in the areas which it innervates because of its prominent position on proximal dendrites within the glomeruli (Colonnier '74).

The RSD profile of Guillery ('69a) undergoes dense degeneration in the specific relay nuclei of the thalamus after lesions of the appropriate regions of cortex. This mode of termination has been observed in the lateral geniculate nucleus (Szentagothai et al. '66, Guillery '69b, Famiglietti and Peters '72) and the medial geniculate nucleus (Majorossy and Rethelyi '68, Jones and Powell '69b). It is presumed that the RSD profile has a more diffuse influence on the cells with which it contacts because of its position on the smaller, more distal dendrites, usually outside of any synaptic glomerulus.

The F terminals have not been observed to undergo degeneration after lesions of any of the known afferents to the thalamic nuclei, and therefore have been considered to represent profiles of Golgi type II interneurons (Szentagothai et al. '66, Majorossy and Rethelyi '68, Guillery '69b, Famiglietti and Peters '72, Wong-Riley '72b).

In the context of this thesis postulating that the tectopulvinar projection is part of a pathway involved in visual orientation, it was logical to expect that the tectal fibers would end as RLPs on the large, proximal dendrites of neurons in the inferior nucleus of the pulvinar. Indeed such a function requires that the visual input has a high priority and a powerful driving influence. It has recently been reported, however, that lesions of the superior colliculus in the monkey result in dense degeneration of part of the RSD profiles (Mathers '71), whereas lesions in the visual cortex produce dense degeneration in the RSD profile as one might predict, but also causes neurofilamentous degeneration of the RLP profile (Majorossy et al. '65, in the cat; Mathers '72b, Campos-Ortega and Hayhow '73, in the monkey). This suggests that the inferior nucleus of the pulvinar is mainly driven by the visual cortex and not by the colliculus. Such an arrangement is very different from that found in specific relay nuclei. It was therefore considered essential to continue this project as planned and to reinvestigate the electron microscopy of the tectopulvinar projection.

The superior colliculus also projects to the intralaminar nuclei (Myers '63) and so it was deemed important to study this projection electron microscopically in order to compare the mode of termination of the collicular fibers in the intralaminar nuclei to those found in the inferior nucleus of the pulvinar. The intralaminar nuclei are classified as nonspecific thalamic nuclei and are functionally related to states of arousal. One might therefore expect that the fibers from the colliculus terminate as RSDs on distal dendrites where they would have a modulating rather than a driving influence. This was felt to be an especially important part of the study because of the lack of electron microscope reports on nonspecific thalamic nuclei. The paracentral nucleus which receives one of the densest collicular projections was chosen for this part of the study.

PROBLEM FORMULATION

1. Although there was considerable evidence that the lateral posterior nucleus of non-primate mammals was homologous to the inferior nucleus of the pulvinar, no evidence was available at the initiation of the present study for a tectopulvinar projection in simians. This connection is important if the homology is to be established. Therefore, the present study was undertaken to determine whether the tectopulvinar projection exists in the Old World monkey, Macaca mulatta.

2. If a tectopulvinar projection exists and is to be involved as part of a second visual pathway concerned with visual orientation, it should be topographically organized. Otherwise it is difficult to imagine that it could subserve this function. Therefore, the second aim of the study was to determine whether the tectopulvinar projection is indeed topographically arranged, and if so, to elucidate this topography.

3. The involvement of the superior colliculus in states of arousal and visual attention is supported anatomically by Myers' ('63) finding that the superior colliculus of the "monkey" projects to the intralaminar complex which is part of the ascending activating system. Myers' results, however, are presented in abstract form only and, therefore, the present study attempts both to confirm the tectointralaminar projection in the macaque, and also to specify to which intralaminar nuclei this projection occurs.

4. A description of the exact mode of termination of the tectal fibers in

the inferior nucleus of the pulvinar is required to determine whether the pattern of the projection is compatible with the postulated function of the second visual pathway. For the reasons stated in the previous chapter one might expect tectopulvinar fibers to end mainly as RLPs on large proximal dendrites. Therefore, an electron microscopic study was undertaken to reinvestigate the manner in which axons from the superior colliculus terminate in the inferior nucleus of the pulvinar.

5. A similar study was also planned for the intralaminar nuclei in order to determine whether tectal fibers terminate in the same manner as in the inferior nucleus of the pulvinar. As stated earlier one might more reasonably expect this projection to be in the form of RSDs on distal dendrites. This part of the study was felt to be particularly important because of the lack of electron microscope reports on nonspecific thalamic nuclei. Therefore an electron microscope study of the paracentral nucleus, as an example of the intralaminar nuclei, was carried out to consider its synaptic morphology and to determine the mode of termination of tectal fibers in this nucleus.

MATERIALS AND METHODS

The present research project was carried out on young adult rhesus monkeys of the species Macaca mulatta, weighing three to five kilograms. Seventeen monkeys were used for light microscopy and ten for electron microscopy.

I. Lesions

Lesions of varying size were made in the superior colliculus by means of electrocoagulation with monopolar stainless steel electrodes. In some animals, discrete lesions were made in different parts of the superior colliculus. In others, large lesions were planned to destroy as much as possible of the entire structure. The lesions were placed unilaterally in all but one of the monkeys used for light microscopy and bilaterally in most of the monkeys used for electron microscopy.

A. Electrodes

The size of the lesion was determined by the number of electrodes, the amount and duration of current applied to them and by the size of the electrode tip (see Tables 2 and 3).

The electrode consisted of a monopolar stainless steel core, insulated with epoxy resin, except at the tip. The tip of the smaller electrodes measured approximately 0.25 mm. in diameter and 0.5-1.0 mm. in length, and that of the larger electrodes, 0.5-0.75 mm. in diameter and 3-4 mm. in length.

TABLE 2

Parameters for Lesions in the Light Microscope Study

Animal	Approach	Electrode size, number	Lesion size, total number	Plane of section
CS-1	contralateral	1.0 mm tip, (1)	3 mA, 15 secs; (1)	frontal
CS-2	contralateral	1.0 mm tip, (1)	3 mA, 15 secs; (1)	frontal
CS-3	contralateral ant.-post.	1.0 mm tip, (1)	3 mA, 10 secs; (1)	frontal
CS-4	contralateral ant.-post.	1.0 mm tip, (1)	3 mA, 10 secs; (1)	frontal
CS-5	vertical	0.5 mm tip, (1)	3 mA, 10 secs; (1)	sagittal
CS-6	contralateral ant.-post.	1.0 mm tip, (1)	3 mA, 10 secs; (1)	frontal
CS-7	contralateral post.-ant.	1.0 mm tip, (2)	2 mA, 10 secs; (4)	frontal
CS-8	contralateral post.-ant.	1.0 mm tip, (2)	2 mA, 10 secs; (4)	frontal
CS-9	vertical	1.0 mm tip, (1)	2 mA, 15 secs; (2)	frontal
CS-10	vertical	1.0 mm tip, (1)	2 mA, 15 secs; (2)	frontal
CS-11	vertical	1.0 mm tip, (1)	2 mA, 15 secs; (1)	frontal
CS-12	vertical	1.0 mm tip, (1)	2 mA, 15 secs; (1)	frontal
CS-13	parasagittal	0.5 mm tip, (1)	2 mA, 10 secs; (2)	sagittal
CS-14	parasagittal	0.5 mm tip, (1)	2 mA, 10 secs; (2)	frontal
CS-15	parasagittal	1.0 mm tip, (1)	2 mA, 15 secs; (1)	sagittal
CS-16	rt. cerebellar oblique	1.0 mm tip, (1)	3 mA, 15 secs; (1)	frontal
	lt. cerebellar parasagittal	3.5 mm tip, (2)	4 mA, 20 secs; (4)	frontal
CS-17	vertical and parasagittal	1.0 mm tip, (2) 1.0 mm tip, (2)	3 mA, 30 secs; (4) 3 mA, 30 secs; (4)	frontal

TABLE 3

Parameters for Lesions in the Electron Microscope Study

Animal	Approach	Electrode size, number	Lesion size, total number	Survival
CSE-1	--	--	--	normal.
CSE-2	cerebellum oblique	4 mm tip, (1)	2 mA, 30 secs; (1) unilateral	5 days
CSE-3	--	--	--	normal
CSE-4	cerebellum oblique	4 mm tip, (2)	3 mA, 40 secs; (2) bilateral	5 days
CSE-5	cerebellum parasagittal	4 mm tip, (4)	4 mA, 40 secs; (4) bilateral	3 days
CSE-6	cerebellum parasagittal	4 mm tip, (4)	4 mA, 40 secs; (4) bilateral	7 days
CSE-7	cerebellum parasagittal	4 mm tip, (4)	4 mA, 40 secs; (4) bilateral	5 days
CSE-8	contralateral post.-ant.	1 mm tip, (6)	3 mA, 30 secs; (14) unilateral	3 days
CSE-9	contralateral post.-ant.	1 mm tip, (4)	3 mA, 30 secs; (12) unilateral	5 days
CSE-10	contralateral post.-ant.	1 mm tip, (4)	3 mA, 30 secs; (10) unilateral	1 day

B. Approaches

Several different approaches to the superior colliculus were used depending on the desired size and location of the lesion (Table 2 and 3). The medial aspect of the superior colliculus was readily approached through the contralateral hemisphere at an angle of 37-47 degrees to the horizontal. The electrode was orientated in the frontal plane or somewhat obliquely (14-18 degrees) anteroposteriorly or posteroanteriorly. In these animals, tissue damage caused by the electrode track was confined to the opposite hemisphere. To reduce the number of variables and thus the chance of error, a vertical approach was also employed through the ipsilateral hemisphere. In this situation, a control electrode was similarly placed on the contralateral side without penetrating the colliculus in order to assess extraneous damage caused by the electrode track. To place a lesion in the anterolateral aspect of the superior colliculus which is partially covered by the overhanging posterior pole of the pulvinar, the electrode was directed through the ipsilateral hemisphere, posteroanteriorly in the parasagittal plane, at an angle of sixty degrees to the horizontal. Again a control electrode was placed in a similar orientation through the contralateral hemisphere stopping before the colliculus was reached. In an attempt to avoid all damage to the cerebral hemispheres, some electrodes were introduced through the cerebellum, posteroanteriorly, either in a parasagittal plane or obliquely from a lateral position, and at an angle of 35-45 degrees below the horizontal plane.

C. Placement of the Lesion

Prior to the operation the monkey was tranquilized intramuscularly with 0.25 cc. of phencyclidine hydrochloride (Sernylan) at the concentration of 20 mg./cc. After fifteen minutes, the animal was anaesthetized intraperitoneally with sodium pentobarbital (Nembutal) at a concentration of 25 mg./kg body weight. Additional anaesthetic was administered in 0.5 cc. doses when necessary.

The animal was secured in the Horsley-Clarke apparatus with the ear bars inserted into the external auditory meatus, the eye-piece clamped down on the infraorbital ridges, and the mouth-piece raised and clamped against the roof of the mouth.

All procedures of the operation were carried out under aseptic conditions. The head was shaved, cleaned and swabbed with 1% iodine in 70% alcohol. A longitudinal incision 5-8 cm. in length was directed through the tissue to the bone, centred in a parasagittal plane at the site for the electrode penetration. The skin and muscle were then retracted. Bleeding was controlled with 1% hydrogen peroxide and direct pressure. If bleeding persisted, the severed vessels were sealed by means of electrocoagulation.

The electrode carrier was placed on the Horsley-Clarke instrument and the electrode directed towards the skull. The site of the planned penetration was marked on the bone and the electrode carrier subsequently removed. A dental drill was used to carefully remove the appropriate amount of bone, caution being taken not to overheat the dental burr which would cause transdural coagulation of the cortex. When a hole of sufficient size was complete, the debris was cleared with warm sterile saline. A very small hole was made in the dura mater with a cutting suture needle and enlarged with fine scissors, care being taken not to damage the underlying cortex. The electrode carrier was replaced on the Horsley-Clarke apparatus and the electrode carefully lowered through the opening in the dura to penetrate the brain tissue. The electrode was directed towards its target according to Horsley-Clarke coordinates obtained from Snider and Lee's Stereotaxic Atlas of the Monkey Brain ('61). From early experiments it became obvious that corrections were necessary. Measurements were made from a series of previously processed brains, marked stereotaxically, and from another perfused brain which was left in the skull and from which stereotaxic parameters were determined on the directly exposed superior colliculus. It was found that the Snider and Lee coordinates had to be adjusted 1.5-2.0 mm. anteriorly and usually 1.0-2.0 mm. vertically downwards. To help in this correction, a mild stimulus (50 c/s, square wave, 2 millisecond duration) was applied to the monopolar electrode within the range of 1-6 volts, when the predetermined surface of the colliculus was reached. The system was effectively grounded by attaching the negative pole to the flesh exposed at the site of the operation. The electrode was advanced one millimeter and the stimulus reapplied. The monkey's eyes were observed as these steps were repeated, looking for conjugate contralateral eye deviation, preferably at a stimulus threshold of less than four volts. Comparing the strength of the response to the planned target site, the lesion was made at the most appropriate site along the electrode pathway. Occasionally, when no response was obtained, it was assumed that the superior colliculus had been missed entirely and the electrode was withdrawn. One of the coordinates was varied in order to move the electrode towards the centre of the superior colliculus (as determined from the calculated parameters) and the entire procedure was then repeated. In some experiments, no eye movements could be elicited and the lesion was placed only according to the coordinates.

The lesion was made by passing 2-5 milliamps of current through the electrode for 10-30 seconds, causing coagulation at the uninsulated tip of the electrode. When more than one lesion was required, the electrode was retracted 1.5 mm. and the lesion repeated. The electrode was allowed to cool and then withdrawn. A second electrode penetration and lesion was carried out when a still larger lesion was planned. In some experiments, two penetrations were undertaken in one step, by placing both electrodes 2-3 mm. apart in the same electrode carrier.

The hole in the skull was filled with Gelfoam and the muscle and aponeurosis were sutured with cotton thread. The skin was closed and secured with Michel clips. The wound was cleaned with 1% iodine in 70% alcohol and then sealed with collodion. Following the operation, 1.5 cc. of antibiotics (Pen-Di-Strep) was injected intramuscularly as a precautionary measure.

Finally the monkey was transferred from the stereotaxic instrument to its cage to recover from the anaesthetic.

II. Preparation of Tissue for Light Microscopy

A. Perfusion

Four days following the operation, the animal was deeply anaesthetized, and the thoracic cavity and pericardial sac were opened to expose the heart. The apex of the heart was secured with a blunt hemostat, the right atrium cut, and the cannula (10-12 gauge hypodermic needle) inserted into the left ventricle. The animal was perfused by gravitational flow with 300-400 ml. of 0.9% saline solution, followed by 1000-2000 ml. of 10% formalin. After the perfusion was complete, the animal was placed in the stereotaxic instrument and the cranium removed. Two vertical electrode tracks were made at the anterior limit of the thalamus (determined from the atlas), 10 mm. on either side of the midline. These served as useful landmarks for proper orientation during frozen sectioning. The anterior and posterior regions of the brain that were not desired in the study, were sectioned away stereotaxically in the frontal plane with a flat, stainless steel, double-edged blade mounted in the electrode carrier. The cortex was removed by horizontal and vertical cuts, and the right side notched for orientation. The remaining block of tissue (mainly diencephalon and mesencephalon) was stored in 10% formalin for 1-6 months before processing.

The frozen section technique for cutting serial sections through the brain was first described by Marshall ('40) and has been adopted with various modifications. The brain was placed in a sucrose-saline solution (30 gm sucrose and 0.9 gm sodium chloride in 100 ml. distilled water) and allowed to sink (approximately four days). This step was intended to reduce freezing artifacts. The block of tissue was then blotted dry and the posterior surface placed on a moist piece of filter paper on the platform of the freezing microtome. After rapidly freezing the block with dry ice, sections were cut at a thickness of 25 microns. The brain was properly oriented in the frontal plane when the two electrode marks at the rostral limit of the thalamus were observed. From this point onwards, sections were saved and stored in plastic boxes consisting of 24 compartments each. Five sections were placed in the first compartment of a box containing 2% formalin, and five were placed in the similar compartment of a second box containing 10% formalin. The procedure was continued in consecutive compartments until the entire block of tissue was cut as far as the site of the lesion. At this point, five sections were saved as usual in 2% formalin and then a 75 micron section was cut, followed by two 25 micron sections. These were stored in 10% formalin in the same sequence as before. This procedure was repeated throughout the antero-posterior extent of the lesion. When the cutting was completed, the tissue in 2% formalin was stored in the refrigerator, and the sections in 10% formalin were stored at room temperature.

B. Photography of the Lesion Site

This procedure was adapted from that described by Guzman et al. ('58). The method was designed to rapidly determine the site and extent of the lesion, although the finer details of tissue damage were determined from Nissl stains. The steps were as follows:

1. 75 micron sections were rinsed in distilled water.
2. The sections were mounted from 5% alcohol on glass slides with a fine, sable hair brush.
3. Excess fluid was removed.
4. The sections were placed in an enlarger as if they were negative film.
5. An exposure at 4-5X magnification on high contrast photographic paper was made and developed in the usual manner.

The contrast between white matter and gray matter and the various structures of the brain resulted in prints of good quality for estimating the site of the lesion.

C. Nissl Stain

This stain was carried out with 25 micron sections in order to study nuclear relationships and to determine the precise localization of the lesion. A 0.1% buffered cresyl echt violet solution was made up as follows:

1. 2% stock solution: 2 gm cresyl echt violet in 100 ml. water one hour at 40^{o}C., filtered through double filter.
2. Buffer I: 0.1 N acetic acid: 6 ml. of glacial acetic acid in 1000 ml. distilled water.
3. Buffer II: 0.1 N sodium acetate: 1.36 gm in 100 ml. distilled water.

4. Staining solution: stock solution........50 ml.
buffer I.............920 ml.
buffer II.............80 ml.
1050 ml.

The staining procedure using this solution is summarized as follows:

Sections were

1. Transferred from 10% formalin to petri dish of distilled water.
2. Mounted from 50% alcohol onto previously albumenized slides, blotted and air dried for 1-3 hours.
3. Transferred to 70% alcohol at 40°C for at least 24 hours, preferably 3-4 days.
4. Transferred to 50% alcohol, 5 minutes.
5. Rinsed in distilled water.
6. Placed in the 0.1% buffered cresyl echt solution, 5-15 minutes.
7. Rinsed in 1-2 changes of distilled water to remove excess stain.
8. Differentiated in 70%, 70% and 95% alcohol.
9. Dehydrated in two changes of absolute alcohol, cleared in two changes of xylene and coverslipped.

D. Silver Impregnation of Degenerating Axons

Originally the first several brains were stained with the techniques of Nauta and Gygax ('54), Fink and Heimer, method II ('67) and Wiitanen ('69). The most favourable results in our hands were obtained with the Wiitanen silver stain and therefore the results reported in this thesis are essentially based on sections stained with this method. A nylon tissue holder was used to carry up to twelve sections (depending on their size) through the various solutions. The holder consisted of a nylon net placed snugly across a plexiglass ring, 145 mm. in diameter. A series of large

Petri dishes (150 x 20 mm.) contained approximately 200 ml. of the appropriate solutions.

The Wiitanen silver stain protocol is as follows:

Sections were

1. Taken from 2% formalin, placed in tissue holder in distilled water and washed in 2-3 changes of distilled water, 10-15 minutes.
2. Transferred to 0.05% potassium permanganate, 10 minutes with agitation.
3. Rinsed briefly in distilled water.
4. Placed in 1:1 solution of 1% oxalic acid and 1% hydroquinone (freshly made) 1 minute or until completely decolorized.
5. Placed in distilled water, 4 changes, 4-5 minutes each.
6. Transferred to 5% uranyl nitrate, 10 minutes with agitation.
7. Placed in distilled water, 4 changes, 4-5 minutes each.
8. Transferred individually to 0.3% silver nitrate, 9-10 minutes with agitation.
9. Washed in distilled water and the process continued to step #14 with one section at a time.
10. Placed in ammonical silver solution, 1-2 minutes with agitation. This solution was made up just prior to use with 50 ml. 1.5% silver nitrate, 30 ml. 95% alcohol, 5.0 ml. concentrated ammonium hydroxide and 4.0-4.5 ml. 2.5% sodium hydroxide.
11. Transferred to reducer solutions 1 and 2, for a total time of 1-2 minutes. Agitation was started immediately for more even staining. The solution consisted of 1712 ml. distilled water, 180 ml. absolute alcohol, 54 ml. 1% citric acid and 54 ml. 10% formalin, made up in this order. If sections were too dark, the amount of citric acid was increased up to 64 ml.

12. Rinsed briefly in distilled water.
13. Transferred to 0.5% sodium thiosulfate, 2 minutes or longer.
14. Placed in distilled water, 4 changes, 4-5 minutes each.
15. Transferred to 0.1% buffered cresyl echt violet solution, 8-10 minutes.
16. Rinsed in distilled water.
17. Mounted in 0.5% gelatin in 40% alcohol (modified from Albrecht '54). The solution was made up by adding 2.5 gm of gelatin to 250 ml. distilled water and dissolving in the oven at 40°C. When the solution cleared, 250 ml. of 80% alcohol was added.
18. Differentiated in 70%, 70% and 95% alcohol.
19. Dehydrated in two changes of absolute alcohol, cleared in two changes of xylene and coverslipped.

When other silver methods were used, the sections were taken from 10% formalin for staining.

III. Preparation of Tissue for Electron Microscopy

The survival times for electron microscopy varied from 1-7 days so that the pattern of degeneration could be studied. Two normal monkeys served as controls (Table 3).

After the animals were anaesthetized a tracheotomy was performed and the animals artificially respirated with a gas mixture of 10% carbon dioxide, 20% oxygen and 70% nitrogen. The carbon dioxide served as a vasodilator. The thoracic cavity was opened and the pericardial sac incised to expose the heart. A ligature of soft braided nylon was passed through the transverse sinus and loosely tied around the pulmonary trunk and ascending aorta. The right atrium and left ventricle were cut and a metal cannula (4 mm. in diameter) was inserted through the cut ventricle into the ascending aorta. The perfusion was started while the ligature was tightened against the shaft of the cannula. Finally the descending aorta was clamped.

The initial perfusion pressure was set at 100 mm. mercury with compressed air (Fig. 5), resulting in a flow of 300 ml./min. or greater. After 4-5 minutes, the flow was decreased to 100-150 ml./min. for 30 minutes, and thereafter the flow was maintained around 20-30 ml./min. Total perfusion time was two hours and approximately 6,000 ml. of fixative was used.

In most perfusions, the fixative contained 2% paraformaldehyde and 1% glutaraldehyde, 1.5% dextrose, 0.005% calcium chloride and phosphate buffer at a pH of 7.3 (see Table 4 for preparation of fixatives). The osmolarity of the buffer-dextrose solution was maintained at 300 milliosmoles and the osmolarity of the total fixative at approximately 1050 milliosmoles. In order to determine the osmolarities most appropriate for monkey brain, the dextrose concentration was varied from 1.5-2.5% and the paraformaldehyde concentration from 1-3% in the first three monkeys. In the first five animals, the primary fixation and sampling procedures were carried out at room temperature and in the last five at 4-5°C. The colder solutions appeared to improve the quality of fixation.

After perfusion, the animal was placed in the Horsley-Clarke apparatus and the calvarium removed. A horizontal cut above the corpus callosum removed the dorsal cerebral cortex. The anteroposterior parameters of the intralaminar nuclei, the inferior nucleus of the pulvinar and the superior colliculus were determined from the atlas of Olszewski ('52) and Snider and Lee ('61) and frontal slices were made with the stereotaxic knife at appropriate 2 mm. intervals. The remainder of the cortex and extraneous por-

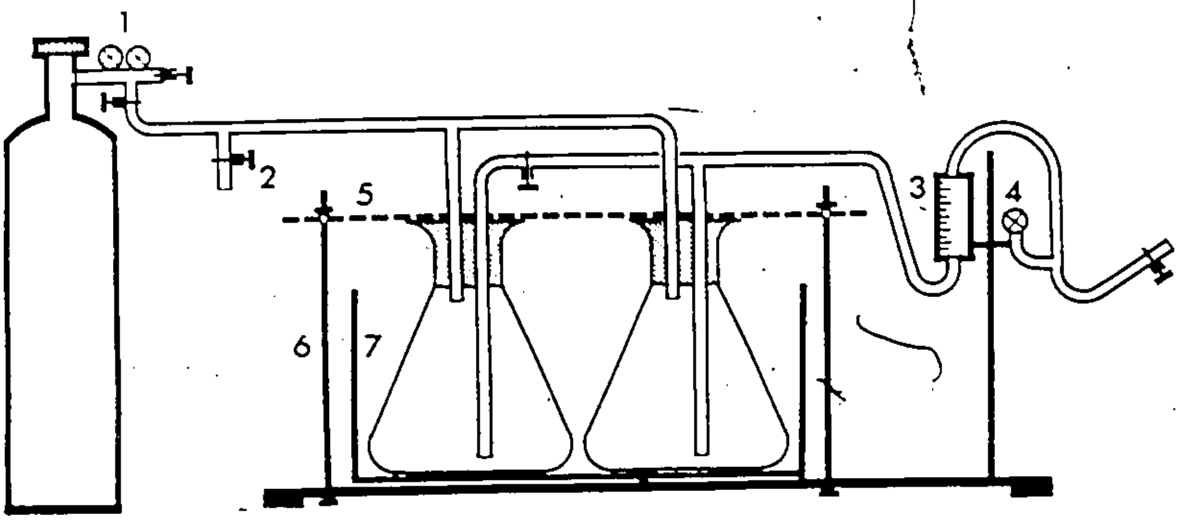


Fig. 5 1. Twin Gauge air-pressure regulator, 2. bleed valve, 3. flow-meter, Gilmont No. 13, 0.002-0.30L/min, 4. aneroid manometer, 5. retainer held down by rubber straps (6), 7. tray with ice.

TABLE 4

FIXATION OF MAMMALIAN BRAIN TISSUE FOR ELECTRON MICROSCOPY

Primary Fixation:	Paraformaldehyde concentration	2%
	Glutaraldehyde concentration	1%
	Osmolarity of buffer-dextrose solution	300 mOs
	Osmolarity of fixative	1050-1060 mOs
	pH of fixative	7.3-7.4

1. Solution A: 13.8 gm sodium phosphate, monobasic plus distilled water to make 500 ml. in volumetric flask.
2. Solution B: 56.8 gm sodium phosphate, dibasic plus distilled water to make 2000 ml. in volumetric flask.
3. $CaCl_2$: 1 gm calcium chloride in 10 ml. distilled water.
4. 80 gm paraformaldehyde dissolved in 1680 ml. of solution B by vigorous stirring to 60°C, then cool to room temperature.
5. Add 320 ml. of solution A to paraformaldehyde solution.
6. Add 160 ml. of 25% glutaraldehyde (Sigma grade IV). Before use, check for polymerization by mixing a small volume with an equal amount of water, when no cloudiness should appear.
7. Dissolve 60 gm dextrose in small amount of water and add to the above solution.
8. Add water to make a total volume of 4000 ml.
9. Add $CaCl_2$ drop by drop with continuous stirring, until a thin cloudiness persists. Between 3-4 ml. will go into solution. Filter.

Check:
1. pH
2. osmolarity of fixative.
3. osmolarity of buffer-dextrose solution. Sample is made with 16 ml. solution A, 84 ml. solution B, 100 ml. distilled water and 3 gm dextrose.

Secondary Fixation: 2% osmium tetroxide

1. 25 ml. buffer (16 ml. of solution A and 84 ml. of solution B)
2. Add 1 gm osmium tetroxide. Agitate 4-6 hours, store in refrigerator.
3. Add 25 ml. distilled water with 0.75 gm dextrose.

tions of the brain were trimmed away and discarded. The slabs of tissue were removed en masse and stored in cold fixative overnight.

Following careful observation of both surfaces of each slab of tissue, a core of tissue was removed from the appropriate nucleus with a modified 16-18 gauge hypodermic needle. The needle was driven through the tissue either perpendicularly or obliquely (as the case required), then removed and the core in turn pushed out of the needle. It was stored in primary fixative or buffer-dextrose solution while the remaining samples were taken. Several cores of tissue were removed from the ipsilateral and contralateral paracentral nucleus of the intralaminar complex and the inferior nucleus of the pulvinar. When all the samples were taken, they were carefully blotted to remove excess solution and post-fixed for two hours in cold, phosphate-buffered 2% osmium tetroxide solution containing 1.5% dextrose.

The material was then dehydrated in ethyl alcohol and embedded in standard Spurr medium (Polysciences Incorporated) according to the following schedule:

1. 50% ethyl alcohol, 2 changes, total time 10 minutes.
2. 70% ethyl alcohol, 2 changes, total time 10 minutes.
3. 95% ethyl alcohol, 2 changes, total time 10 minutes.
4. 100% ethyl alcohol, 30 minutes.
5. 100% ethyl alcohol, 30 minutes.
6. 1 part 100% alcohol and 1 part Spurr medium, 30 minutes.
7. 1 part 100% alcohol and 2 parts Spurr medium, 30 minutes.
8. 100% Spurr medium, 2-3 hours.
9. 100% Spurr medium, overnight.
10. 100% Spurr medium at $70^{\circ}C$ for 8 hours.

Bar grids 150-200 micron were coated with a thin film of polyvinyl plastic

(Formvar). Stock solution of Formvar, at 0.5% concentration was diluted to 0.25% concentration with 1,2-dichloroethane. An ordinary microscope slide was dipped into this solution and then allowed to drain slowly. When the film had dried, the edges of the slide were cut with a razor blade. The slide was immersed at a 45^{0} angle into a dish of distilled water, and the film floated off on the surface. The grids were placed on the film, and finally the film and the grids were picked up with a piece of absorbent paper and allowed to air dry. In order to reinforce the plastic film, the grids were then coated with a thin layer (approximately 50 A) of evaporated carbon.

Trimmed blocks of tissue were sectioned for electron microscopy using glass knives mounted in a Reichert OmU2 ultramicrotome. Sections which appeared silver by reflected light were picked up on the previously prepared grids.

They were then stained with uranyl acetate and lead citrate. The solutions were prepared as follows:

Uranyl acetate: (Watson '58) 16 gm of uranyl acetate was dissolved in 100 ml. of absolute ethyl alcohol in a clean ray-sorb flask and filtered prior to use.

Lead citrate: (according to Reynolds '63)

1. 1.33 gm of lead nitrate and 1.76 gm of sodium citrate was dissolved in 30 ml. of distilled water in a 50 ml. volumetric flask. The suspension was shaken vigorously for one minute and then intermittently for 30 minutes to ensure the complete conversion of the lead nitrate to lead citrate.
2. 8.0 ml. of 1 N sodium hydroxide (4.27 gm NaOH in 100 ml. H_2O) was added.
3. The solution was then diluted to a 50 ml. volume with distilled

water and mixed by inversion.

The staining procedure was carried out as follows:

Grids were

1. Placed in 16% uranyl acetate, 8-10 minutes.
2. Washed in 3 changes of absolute ethyl alcohol.
3. Washed in 3 changes of distilled water.
4. Drained to remove excess water.
5. Placed in Reynold's lead citrate solution, 8-10 minutes.
6. Washed in 3 changes of 0.02 N sodium hydroxide.
7. Washed in 3 changes of distilled water.
8. Drained to remove excess water and allowed to air dry before use.

The completed grids were examined with a Siemens 101 electron microscope.

In order to assess the accuracy of the site from which these samples were taken, the slabs of tissue from which the samples were taken were cut and stained. The sites of the lesions were similarly processed. Because the tissue was only 2 mm. thick, a 3-4 mm. base of gelatin (15 gm gelatin dissolved in distilled water, hardened and stored in 10% formalin) was placed on the platform of the freezing microtome and levelled prior to mounting the tissue. Frozen sections (25 microns) were cut throughout the depth of the slices and stored in 10% formalin. Nissl stains were prepared and occasionally silver stains were attempted. The latter method, however, was not entirely successful, presumably because of the glutaraldehyde used in the primary fixation.

IV. Analysis of Material Prepared for Light Microscopy

A series of Nissl stains in the frontal, sagittal and horizontal planes was carefully studied in order to appreciate the three-dimensional configuration of the inferior nucleus of the pulvinar and its surrounding relationships. A comparison of frontal sections through the anteroposterior extent of the inferior nucleus of the pulvinar was made in three typical monkeys. From these, seven levels (at approximately half millimeter intervals) were selected as representative sites to be used in summary diagrams. Nissl pictures and diagrams were prepared at three levels of the intralaminar complex (at approximately two millimeter intervals) in order to illustrate the intralaminar nuclei receiving a projection from the superior colliculus, i.e., parafascicular, central lateral and paracentral nuclei.

The pattern of degeneration observed in eleven monkeys was mapped on photographs of Nissl stains at the appropriate individual levels. The information was accumulated and transferred to the summary diagrams.

RESULTS

I. Light Microscopy

A. Limits and Boundaries of the Inferior Nucleus of the Pulvinar

Nissl stains of the inferior nucleus of the pulvinar were prepared and studied in the sagittal, horizontal and frontal planes. The nucleus is illustrated sagittally at the lateral limit of the medial geniculate nucleus (Fig. 6a), horizontally approximately halfway through the dorsoventral extent of the inferior nucleus of the pulvinar (Fig. 6b) and frontally at seven levels through the entire posteroanterior extent of the nucleus (Figs 6c, 7, 8); i.e., at the most caudal extent of the inferior nucleus of the pulvinar (Fig. 6c), at the caudal extent of the medial geniculate nucleus (Fig. 7a), at the fusion of the inferior and lateral nuclei of the pulvinar (Fig. 7b), at the division of the lateral nucleus of the pulvinar into a dorsal and ventral segment (Fig. 7c), at the caudal extent of the lateral geniculate nucleus (Fig. 8a), midway between the caudal extent of the lateral geniculate nucleus and the rostral extent of the inferior nucleus of the pulvinar (Fig. 8b) and at the most rostral limit of the inferior nucleus (Fig. 8c). These levels were selected at approximately half millimeter intervals with the aid of recognizable landmarks, to facilitate comparison from monkey to monkey. Summary diagrams of these seven levels were used to map the topography of the tectopulvinar projection. Alternate levels were also used in conjunction with more anterior views of the thalamus, in order to present the total thalamic projection of the superior colliculus.

The anterior and posterior relationships of the inferior nucleus of the pulvinar are most clearly seen in the horizontal plane (Fig. 6b) in which the inferior nucleus appears as a blunt arrowhead between the medial and lateral geniculate nuclei. The inferior nucleus of the pulvinar is bordered anteriorly by the medial and lateral geniculate nuclei, and posteriorly by the medial and lateral nuclei of the pulvinar. The medial aspect of this anteroposterior relationship is also illustrated in the sagittal view (Fig. 6a), in which the inferior nucleus is found between the medial geniculate nucleus anteriorly and the medial nucleus of the pulvinar posteriorly.

Dorsally, the inferior nucleus of the pulvinar is bordered by the medial and lateral nuclei of the pulvinar in the posterior region of the nucleus (Fig. 7), by the oral nucleus of the pulvinar (Fig. 8a), and finally, by the lateral geniculate nucleus at the most anterior extent (Figs 8b, c). Ventrally, the inferior nucleus forms the lower free border of the thalamus (Figs 7, 8).

The medial relationship of the inferior nucleus of the pulvinar is formed by the medial geniculate nucleus (Figs 7, 8). The lateral relationship is formed by the lateral nucleus of the pulvinar posteriorly (Figs 6c, 7, 8a) and the lateral geniculate nucleus anteriorly (Fig. 8). It is apparent in the horizontal plane (Fig. 6b), that the inferior and lateral nuclei of the pulvinar are clearly separate, as suggested by Friedeman ('12), Crouch ('34) and Walker ('38). However, it is easy to appreciate Olszewski ('52) and Hassler's ('59) inclusion of the ventral part of the lateral nucleus of the pulvinar with the inferior nucleus because of their apparent blending when viewed in the frontal plane (Figs 7a, b).

B. Limits and Boundaries of the Intralaminar Nuclei

The plotting of degenerating fibers after tectal lesions has also been

Legend

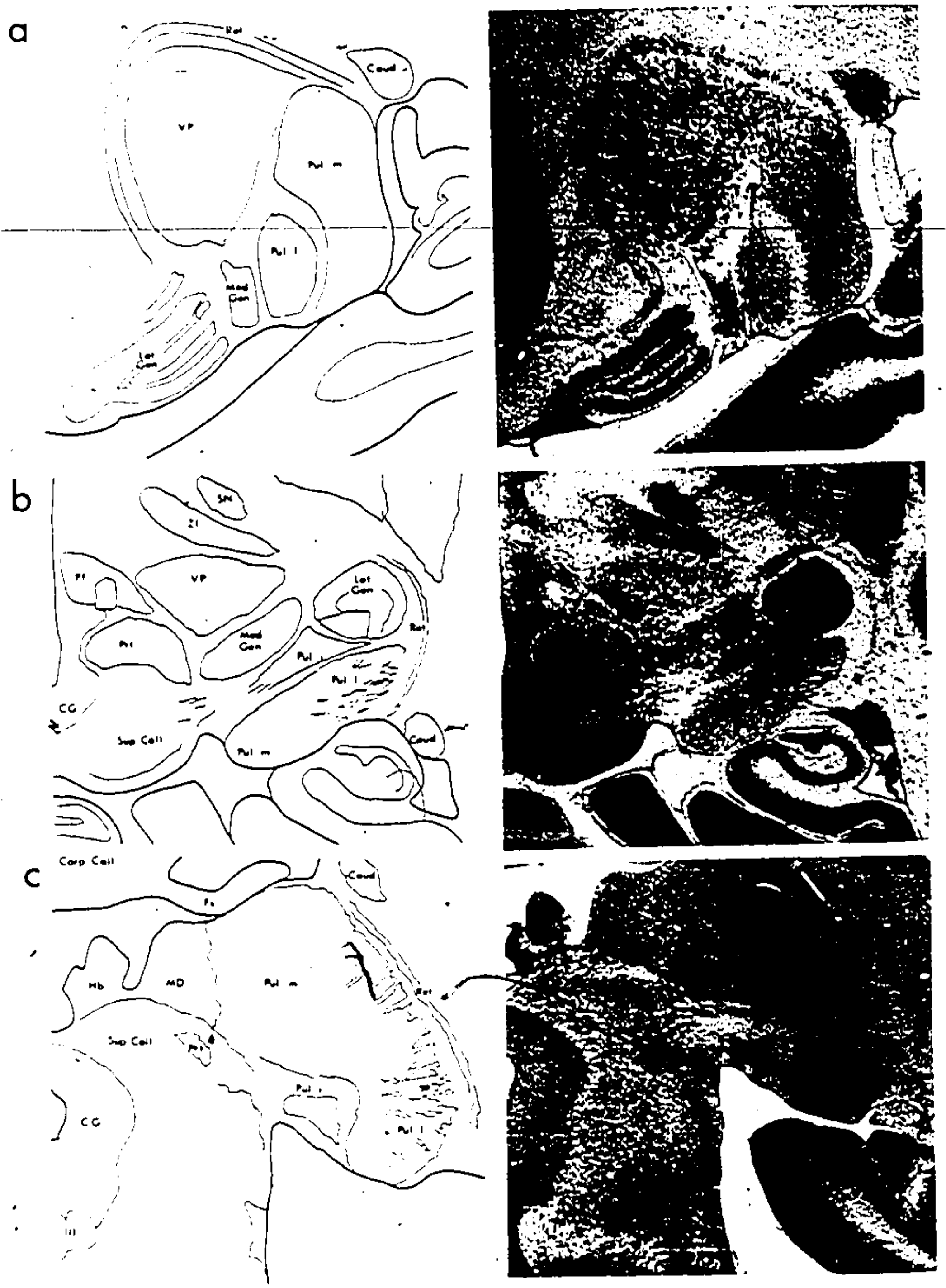
III	oculomotor nucleus
Ant	anterior nucleus
Caud	caudate nucleus
CG	central gray
CL	central lateral nucleus
CM	centromedian nucleus
~~Corp Call~~	~~corpus callosum~~
Fx	fornix
Hb	habenula
Lat Gen	dorsal lateral geniculate nucleus
LD	Lateral dorsal nucleus
LGNv	ventral lateral geniculate nucleus
LP	lateral posterior nucleus
MD	dorsomedial nucleus
Med Gen	medial geniculate nucleus
NL	nucleus limitans
OT	optic tract
Pc	paracentral nucleus
Pf - CM	parafasicular - centromedian nuclei
Prt	pretectum
Prt a.	anterior pretectal nucleus
Pul. i	inferior nucleus of pulvinar
Pul. l	lateral nucleus of pulvinar
Pul. m	medial nucleus of pulvinar
Pul. o	oral nucleus of pulvinar
Put	putamen
Ret	reticular nucleus of thalamus
Ru	red nucleus
SN	substantia nigra
Sub Th	subthalamic nucleus
Sup Coll	superior colliculus
Supr Gen	suprageniculate nucleus
VL	ventral lateral nucleus
VPL	ventral posterior nucleus
X	area X
Zl	zona incerta

Figure 6 Sagittal, horizontal and frontal views of the inferior nucleus of the pulvinar stained with cresyl echt violet. Magnification 4X.

Fig. 6a Sagittal view of the inferior nucleus of the pulvinar at the most lateral limit of the medial geniculate nucleus. Anterior is towards the left and posterior towards the right of diagram.

Fig. 6b Horizontal view of the inferior nucleus of the pulvinar approximately half-way through the dorsoventral extent of the nucleus. Note the arrowhead appearance of the inferior nucleus between the medial and lateral geniculate nuclei. Anterior is towards the top and posterior towards the bottom of the diagram.

Fig. 6c Frontal view of the inferior nucleus of the pulvinar at its most caudal limit.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Ret
Sup Coll
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Pul l
CG
III

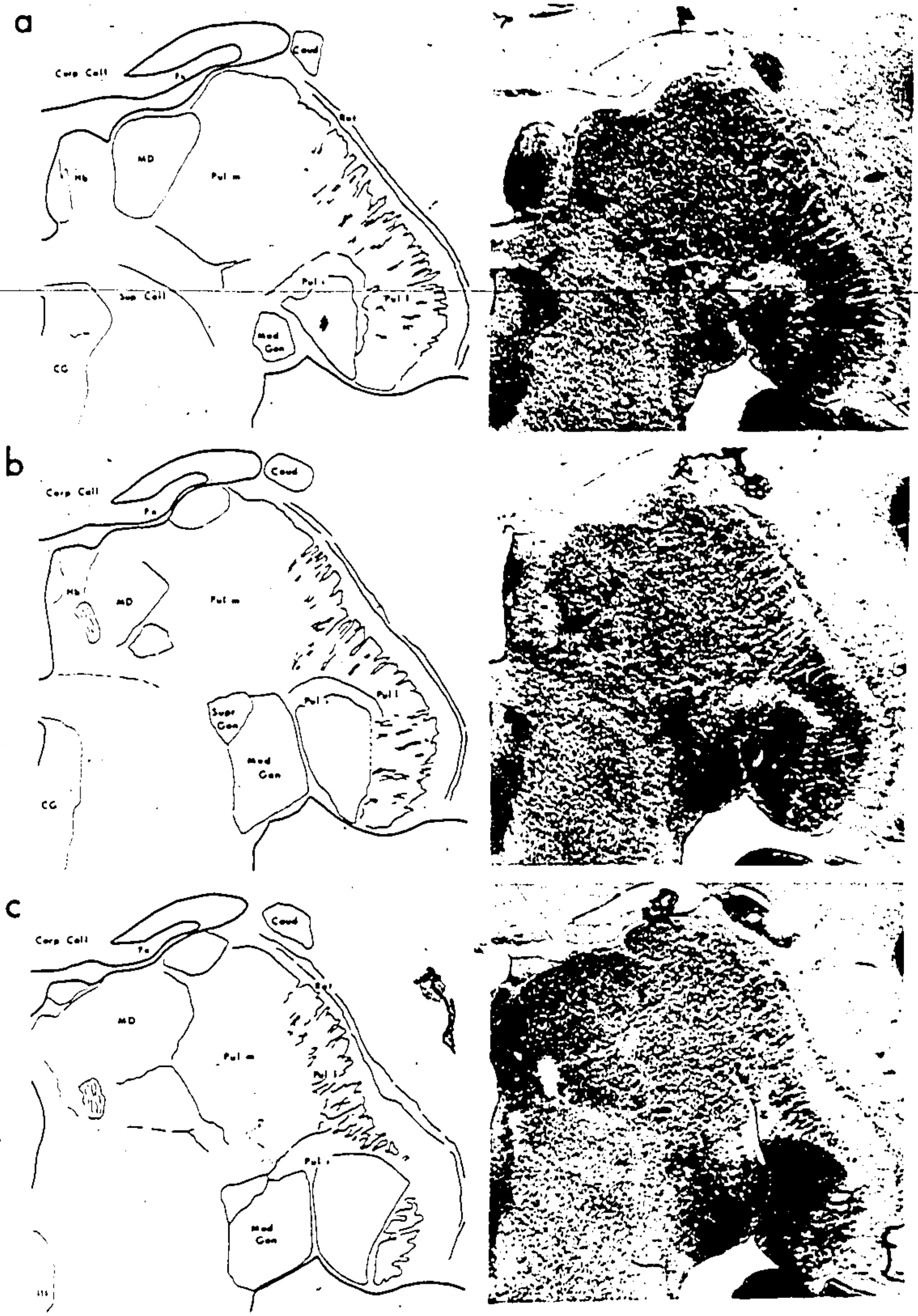
Figure 6

Figure 7 Three levels of the inferior nucleus of the pulvinar in the frontal plane, stained with cresyl echt violet. Magnification 4X.

Fig. 7a Frontal view of the inferior nucleus of the pulvinar at the caudal extent of the medial geniculate nucleus.

Fig. 7b Frontal view of the inferior nucleus of the pulvinar at the fusion of the inferior and lateral nuclei of the pulvinar.

Fig. 7c Frontal view of the inferior nucleus of the pulvinar at the division of the lateral pulvinar nucleus into a dorsal and ventral portion.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Pul i
Med Gen

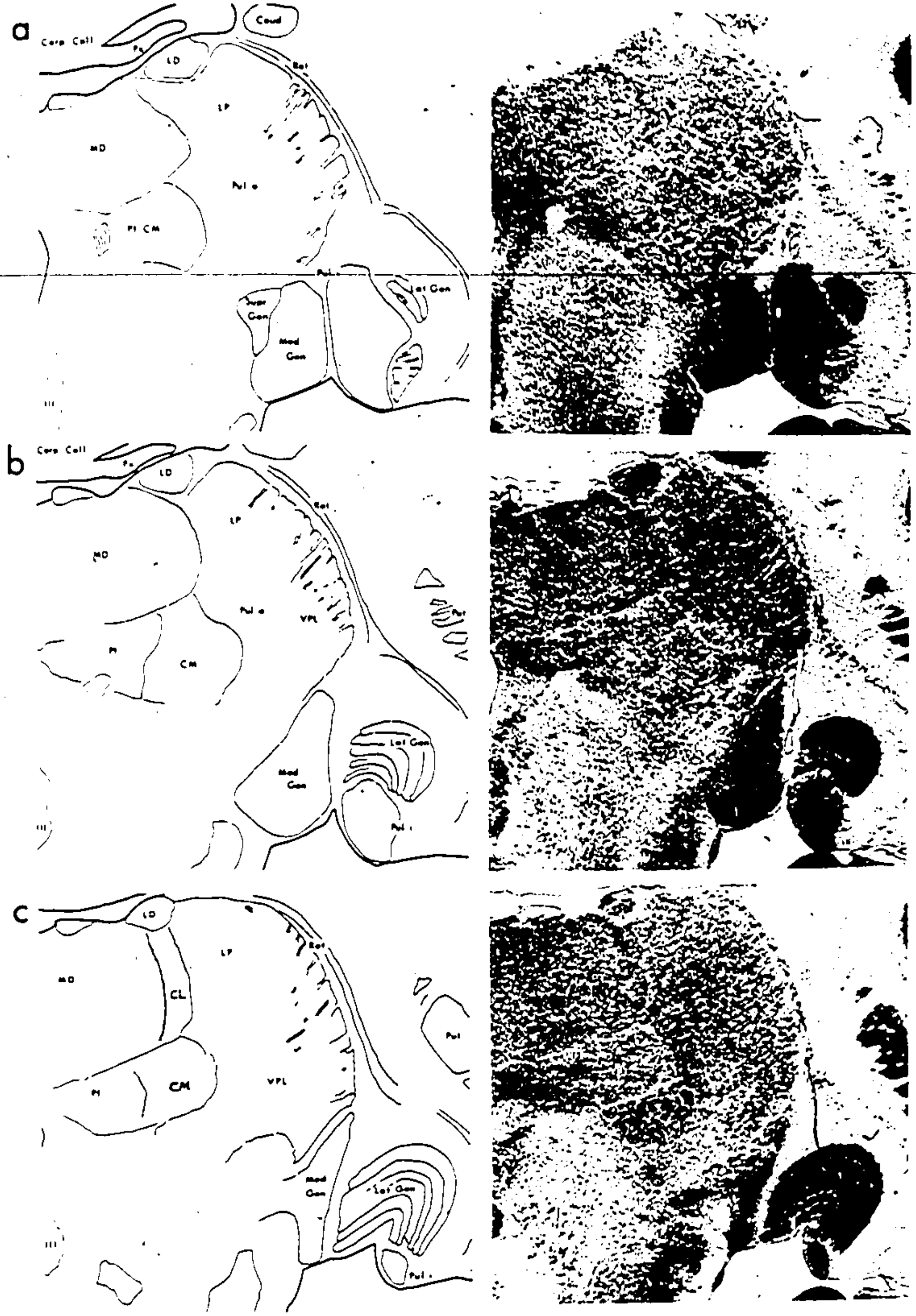
Figure 7

Figure 8 Three levels of the inferior nucleus of the pulvinar in the frontal plane, stained with cresyl echt violet. Magnification 4X.

Fig. 8a Frontal view of the inferior nucleus of the pulvinar at the caudal extent of the lateral geniculate nucleus.

Fig. 8b Frontal view of the inferior nucleus of the pulvinar midway between the caudal extent of the lateral geniculate nucleus and the rostral extent of the inferior nucleus.

Fig. 8c Frontal view of the inferior nucleus of the pulvinar at its most rostral extent.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LP
MD
Pul o
VPL
Put
Pf
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Lat Gen
Med Gen
Pul i
III
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CL
Put
Pf
CM
VPL
Med Gen
Lat Gen
Pul i
III

Figure 8

carried out at three representative levels anterior to the inferior nucleus of the pulvinar at consecutive two millimeter intervals. The first level was chosen at the rostral pole of the medial geniculate nucleus (Fig. 9a), the second, in the region where the centromedian nucleus approaches the midline in place of the parafascicular nucleus (Fig. 9b) and the third and most anterior level, at the rostral pole of the lateral geniculate nucleus, where the paracentral nucleus is found in place of the centromedian and central lateral nuclei (Fig. 9c). These levels clearly illustrate the relationships of the centromedian, parafascicular, central lateral and paracentral nuclei.

The parafascicular-centromedian complex can be observed in figures 8 and 9a, bordered dorsally by the dorsomedial nucleus and the central lateral nucleus, ventrally by the tegmentum and laterally, by the pulvinar oralis at more posterior levels, and by the lateral posterior and ventral posterior nuclei more anteriorly. The parafascicular and centromedian nuclei can be differentiated by the densely-staining cells of the former, compared to the lighter-staining cells of the latter, although the boundary between the two is somewhat ambiguous. The parafascicular nucleus is replaced anteriorly by the centromedian nucleus which now extends to the midline (Fig. 9b).

The central lateral nucleus can be seen in figures 8c and 9a, b, extending vertically between the centromedian nucleus ventrally and the lateral dorsal nucleus dorsally. It is bordered medially by the dorsomedial nucleus and laterally by the lateral posterior nucleus more posteriorly and the ventral lateral and ventral posterior nuclei anteriorly. It blends into the paracentral nucleus at the anterior extent of the centromedian nucleus.

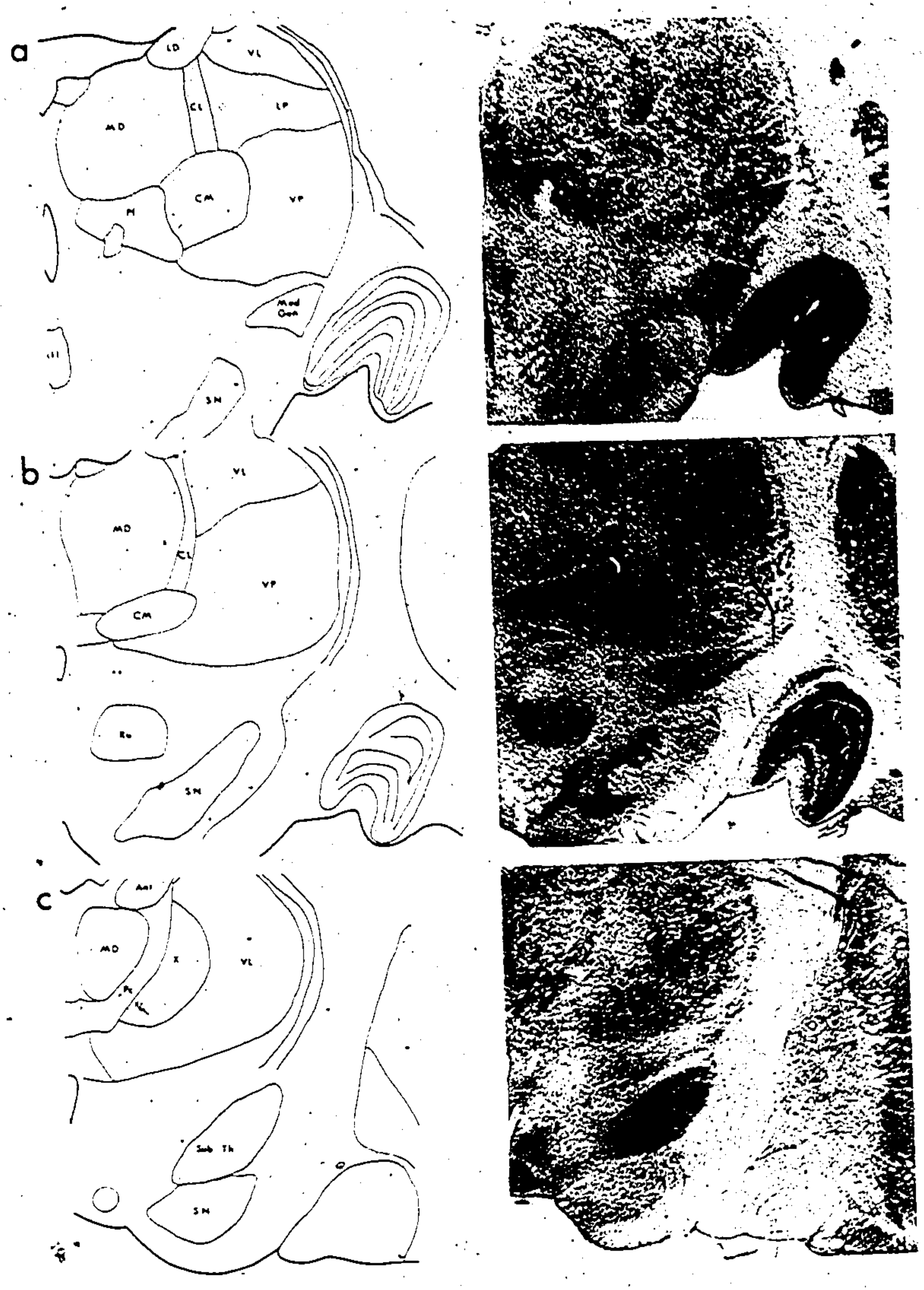
The paracentral nucleus is represented at the anterior limit of the

Figure 9 Three levels of the intralaminar nuclei in the frontal plane, stained with cresyl echt violet. Magnification 4X.

Fig. 9a Frontal view of the parafascicular-centromedian complex and central lateral nucleus at the rostral pole of the medial geniculate nucleus.

Fig. 9b Frontal view of the centromedian and central lateral nuclei at the site where the centromedian nucleus extends towards the midline.

Fig. 9c Frontal view of the paracentral nucleus at the region just rostral to the anterior pole of the lateral geniculate nucleus.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III
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c
Ant
MD
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Pc
Sub Th
SN

Figure 9

centromedian and central lateral nuclei (Fig. 9c). At this same level, the dorsal boundary of the intralaminar complex changes from the lateral dorsal nucleus to the anterior nucleus. The paracentral nucleus continues anteriorly, gradually curving medially around the dorsomedial nucleus to eventually approach the paracentral nucleus of the opposite side. They meet ventrally but remain separated dorsally by the midline nuclei. The paracentral nucleus is bordered ventrolaterally by area X of Olszewski ('52) and also by the ventrolateral nucleus.

The site of the lesion was not always located exactly as planned because of the variability in size and shape of the individual brains. The results of the lesion placement, however, were usually satisfactory, but with occasional damage to surrounding structures. Two penetrations missed the superior colliculus completely (Table 5).

The results from larger lesions (Figs 10a, b, c) were helpful in tracing the total thalamic projection of the superior colliculus. The more discrete lesions in different parts of the superior colliculus (Figs 10d, e, f) were particularly useful in determining the topography of the projection to the inferior nucleus of the pulvinar. Even the larger lesions, however, yielded some information with regard to topography.

In addition to the complete misplacement of the lesion in two animals, the site of two other lesions proved unsatisfactory (Table 5). In one, only the electrode track damaged the superior colliculus, and the lesion was located in the inferior colliculus. The number of degenerating fibers in the material was too few to be properly studied. In another animal, the lesion damaged only layer 7 of the colliculus. Consequently, only descending degenerating fibers were observed.

Ten of the remaining thirteen experimental animals provided useful results for the analysis of the projections of the superior colliculus to

TABLE 5

Results of Operation and Staining for Light Microscopy

Animal	Lesion Size	Location of Lesion: Superior Colliculus	Location of Lesion: Other Structures	Stain	Tectopulvinar Topography
CS-12	*	missed	corpus callosum	---	-----
CS-13	*	missed	cerebellum	---	-----
CS-6	**	medial, layer 7	central gray	--	descending fibers only
CS-5	*	electrode track	inferior colliculus	--	too few fibers
CS-2	*	posterolateral	-----	X	-----
CS-9	***	medial	-----	X	-----
CS-4	*	anteromedial	-----	--	useful
CS-11	*	extreme medial	-----	--	useful
CS-16	*	anterolateral	inferior colliculus central gray	--	useful
CS-1	**	posterior	central gray visual cortex	--	useful
CS-3	**	medial	-----	---	useful
CS-7	**	posteromedial	inferior colliculus	-	odd nuclear configuration
CS-14	**	middle, lateral	hippocampus	---	useful
CS-15	**	posterolateral	-----	--	useful
CS-10	***	lateral	-----	---	useful
CS-8	****	medial & anterior	pretectum ?	---	useful
CS-17	****	anterolateral, posteromedial	fornix corpus callosum central gray inferior colliculus	---	useful

Lesion Size: * small, ** medium-small, *** medium-large, **** large (in superior colliculus)

Staining Properties: - poor, -- average, --- excellent, X failure

Figure 10 Frontal view of the right superior colliculus to show the site of various large (10a, b, c) and small (10d, e, f) lesions. Cresyl echt violet stain. Magnification 12X.

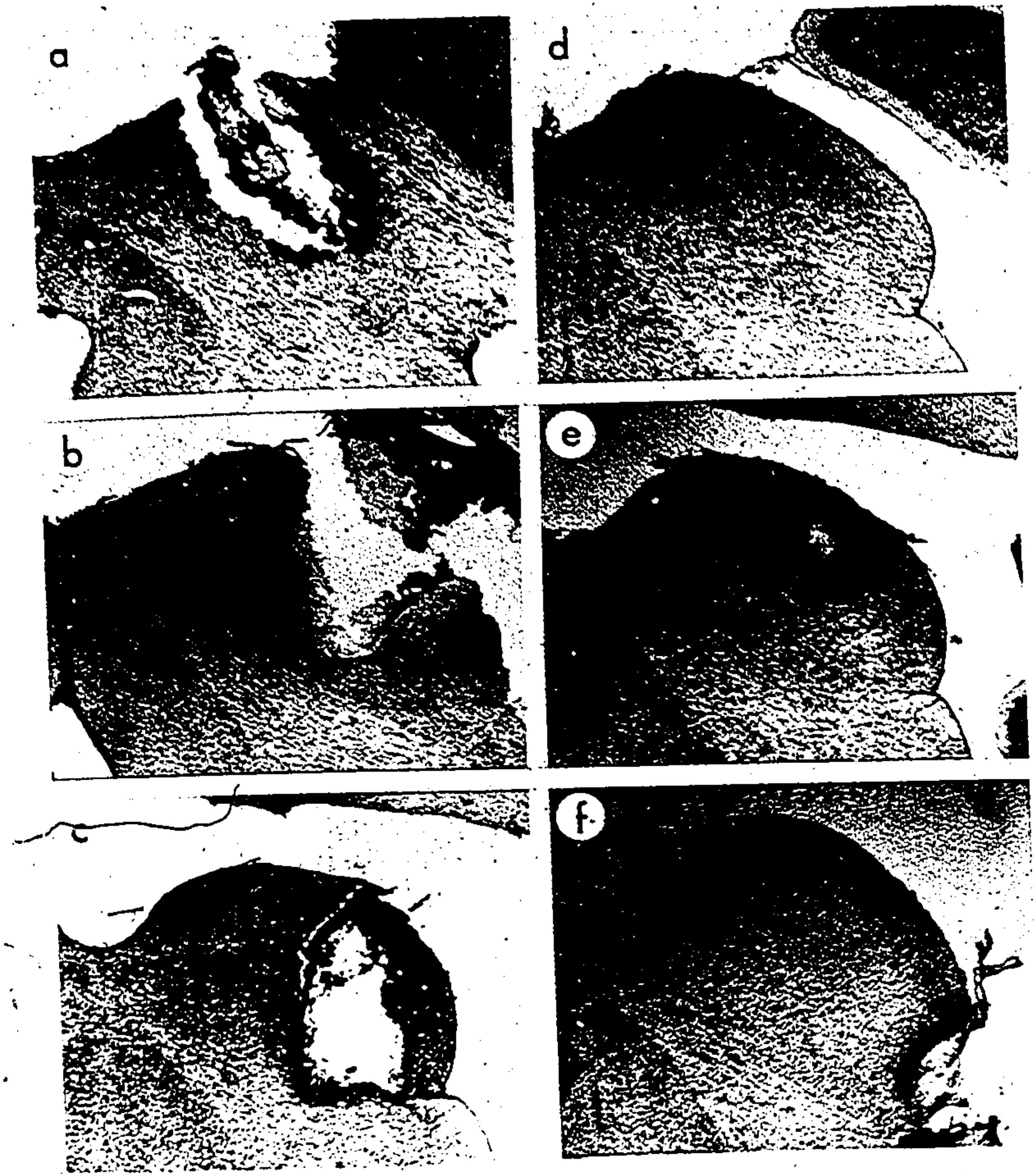

Figure 10

the thalamus.

C. Projections of the Superior Colliculus

Degenerating axons were observed descending from the superior colliculus to lower levels and also crossing in the commissure of the superior colliculus to the opposite site. Only the ascending degenerating fibers to the thalamus were studied in detail. Particular attention was directed to the collicular projections to the inferior pulvinar nucleus and to the intralaminar complex.

The total projection of the superior colliculus to the ipsilateral thalamus was determined by accumulating the results from all lesions (Fig. 11). Moderate to dense degeneration was observed in the inferior nucleus of the pulvinar and somewhat less in the pretectum. Degenerating fibers were also observed travelling through the nucleus limitans to end diffusely in the parafascicular nucleus, not at all in the centromedian nucleus, in small clusters in the central lateral nucleus and densely throughout the paracentral nucleus. An inconstant projection was found in the suprageniculate nucleus and magnocellular part of the medial geniculate nucleus (labelled together as the suprageniculate nucleus in the diagrams, because of the difficulty to differentiate these nuclei). Very sparse degenerating fibers were occasionally observed in the dorsal and ventral divisions of the lateral geniculate nucleus.

Thus, one of the main projections of the superior colliculus terminates throughout the inferior nucleus of the pulvinar. Although degeneration was not observed in the most ventrolateral region of the nucleus, the ~~lesions~~ did not destroy all parts of the colliculus. It seemed reasonable, however, to extrapolate the data to conclude that the colliculus projects to the entire nucleus. Typical examples of degeneration in the inferior nucleus of

Figure 11 Tectothalamic projections in the monkey.

the pulvinar are illustrated in figure 12. Fibers of passage were often observed streaming towards their site of termination (Fig. 12a). The fibers displayed the broken appearance and varicosities typical of anterograde degeneration, and were interpreted as preterminals and terminals when a random pattern of intertwining fibers was observed (Fig. 12b). The presence of silver granules in regions of profuse preterminals was also interpreted to be degenerative debris (Fig. 12c). However, these granules in the absence of preterminal fibers were not considered convincing evidence of degeneration, particularly with the Wiitanen technique. Although the granules may represent terminals, they sometimes apparently occur as random precipitation and therefore were not a reliable criterion for sites of degeneration.

In many of the animals, degenerating fibers travelled across the inferior nucleus of the pulvinar to accumulate at the border of the lateral geniculate nucleus near its posterior pole (Fig. 13a). Although a few fibers entered the lateral geniculate nucleus at this point (Figs 13b, c), this small number of fibers did not appear to be sufficient to account for the rather dense projection seen at the border of the pulvinar. It is possible, however, these degenerating fibers had funnelled together as they crossed the pulvinar before spreading throughout the anteroposterior extent of the lateral geniculate nucleus. This would conceivably account for the large number of fibers seen at the posterior pole of this nucleus. Indeed, sparse degeneration has been observed in both the magnocellular and parvocellular layers throughout the dorsal division of the lateral geniculate nucleus (Figs 13d, e). Unfortunately, the number of fibers was insufficient to determine whether they were fibers of passage or preterminals. However, their general orientation towards the ventral division of the lateral geniculate nucleus, and the slightly greater amount of degeneration occasionally found in this latter nucleus (Fig. 13f), would perhaps suggest

Figure 12 Degeneration in the inferior nucleus of the pulvinar. Wiitanen silver impregnation, counterstained with cresyl echt violet.

Fig. 12a Degenerating fibers of passage travelling across the medial part of the nucleus and arborizing in a terminal field more laterally. Magnification 120X.

Fig. 12b Random arborizing fibers indicative of preterminal field. Magnification 260X.

Fig. 12c Preterminal field with fine silver granules. The granules may or may not represent terminals. Magnification 350X.

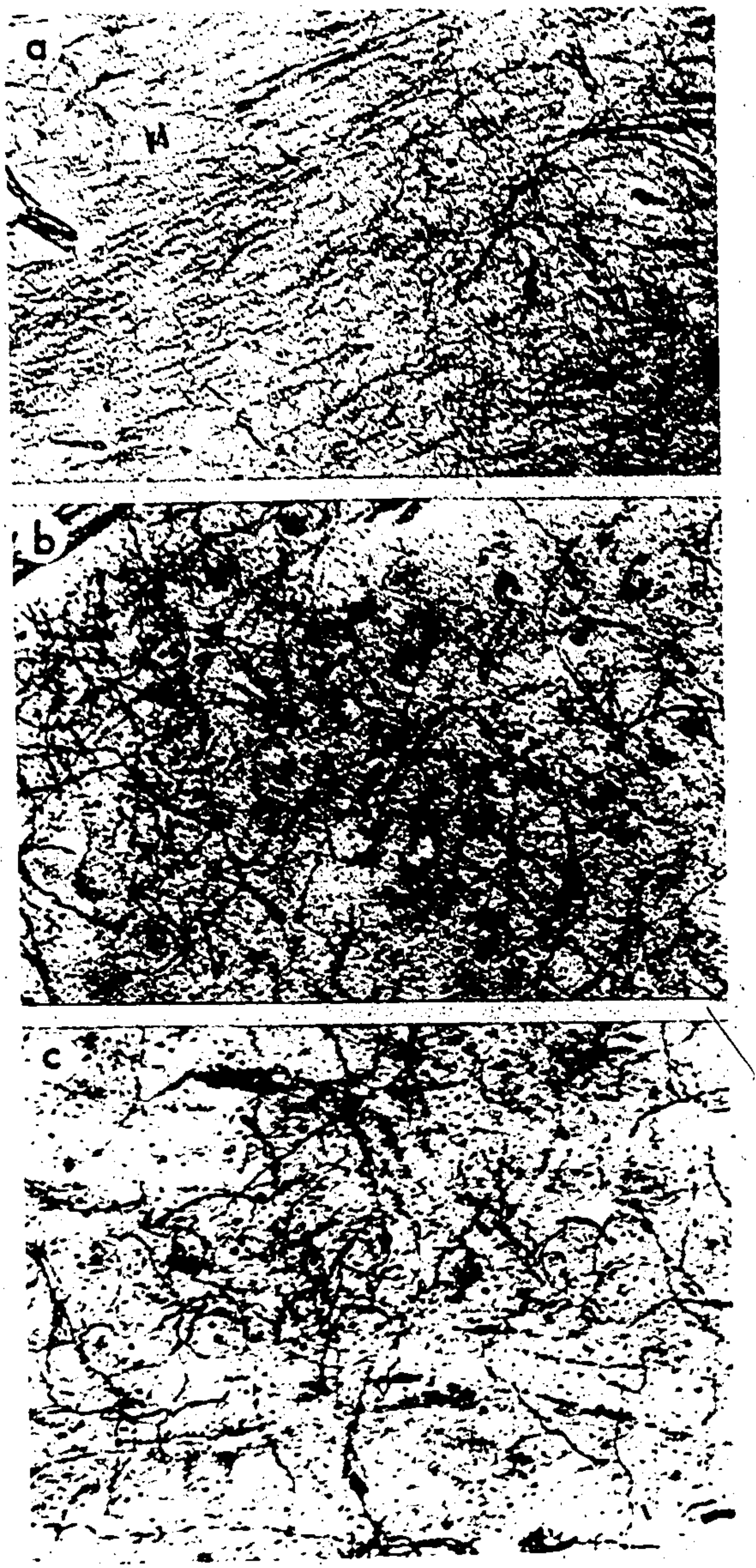

Figure 12

Figure 13a	Cluster of degenerating fibers in the inferior nucleus of the pulvinar at the border of the lateral geniculate nucleus. The arrow indicates the same blood vessel in figure 13b. Magnification 75X.
Figure 13b	Higher magnification of figure 13a. A few degenerating terminals can be observed in the magnocellular layer of the lateral geniculate nucleus. Magnification 200X.
Figure 13c	Another example of degenerating fibers in the inferior nucleus of the pulvinar at the border of the lateral geniculate nucleus. Magnification 200X.
Figure 13d	Sparse degeneration in parvocellular layer of the dorsal lateral geniculate nucleus. Magnification 300X.
Figure 13e	Degenerating fibers in magnocellular layer of the dorsal lateral geniculate nucleus. Magnification 300X.
Figure 13f	Degenerating preterminals in the ventral lateral geniculate nucleus. Magnification 300X.

- Wiitanen technique, counterstained with cresyl echt violet.

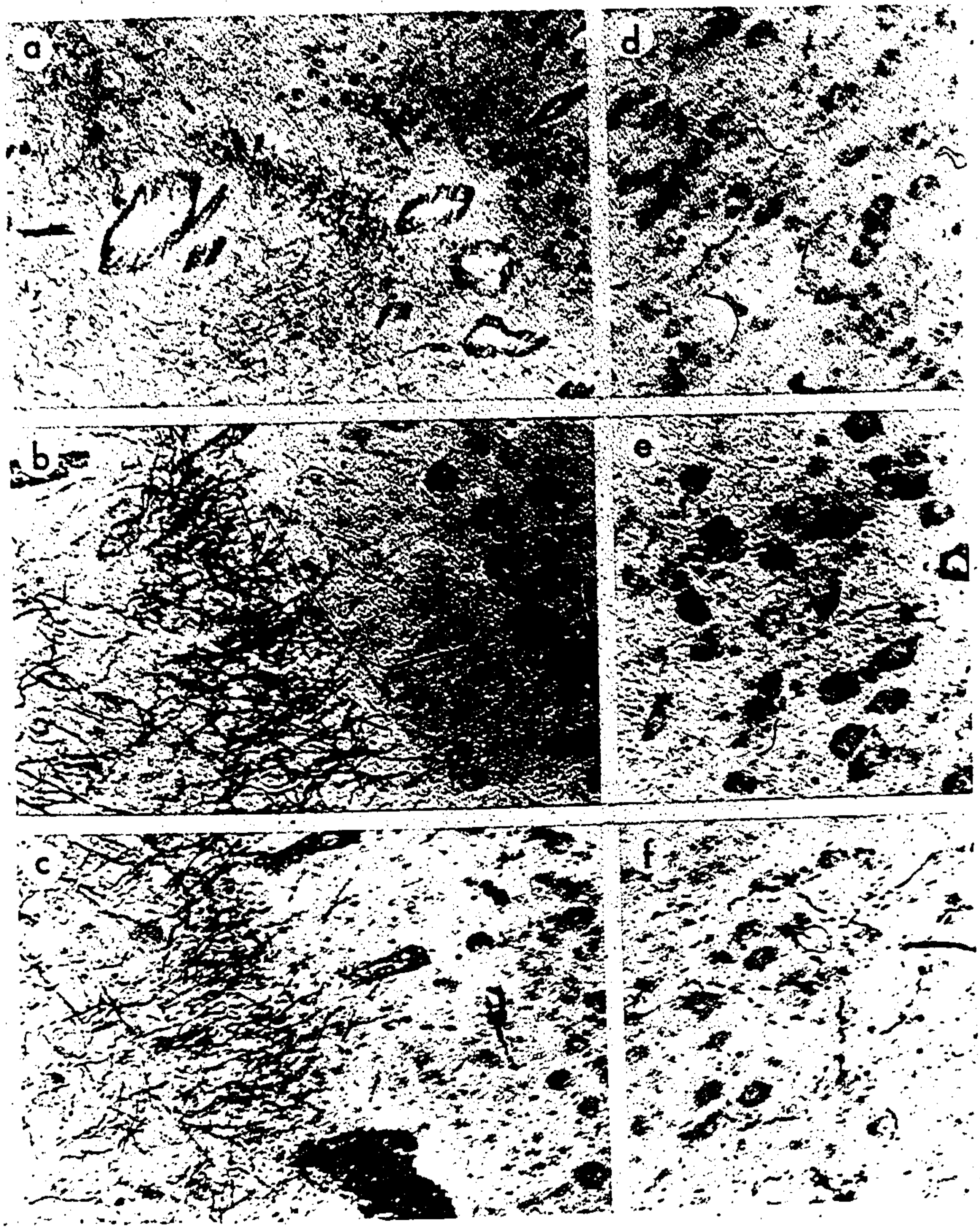

Figure 13

that the ventral division of the lateral geniculate nucleus is the final terminal site of many of these fibers.

The superior colliculus sends a moderate projection to the pretectum. The degeneration was seen typically as short, scattered fibers in various parts of the nucleus, and no obvious pattern of distribution was found (Fig. 14a).

The degenerating preterminals found in the suprageniculate nucleus and magnocellular division of the medial geniculate nucleus were generally sparse in all but one animal (Fig. 14b). The lesion in this animal was located rather anteriorly and may have involved part of the pretectal region. The boundary between the superior colliculus and pretectum is vague, deeper layers of the colliculus blending anteriorly into the pretectal region (Kappers et al. '36). Hence, it is possible that the degeneration observed may result from damaged fibers projecting from the pretectum and not from the superior colliculus.

Degenerating fibers to the intralaminar complex passed through the nucleus limitans (Figs 14c, d). Although some fibers may terminate in this nucleus, many appeared to be fibers of passage. Note that the cell bodies are argyrophilic, accumulating several granules of silver. This characteristic was independent of the lesion, since it was also present on the contralateral side, without the degenerating fibers.

The projection of the superior colliculus to the parafascicular nucleus was sparse to moderate in density (Fig. 15). Some fibers may be interpreted as fibers of passage (Fig. 15a). Others were clearly preterminal fibers (Fig. 15b). The cell bodies of this nucleus are also argyrophilic (Fig. 15c), a characteristic independent of the site or size of the lesion. Due to the affinity of the neurons to silver, the nucleus was readily identifiable on silver preparations, even without counterstaining.

Figure 14a Degenerating fibers in the pretectum. Magnification 190X.

Figure 14b Degeneration in the suprageniculate nucleus. Magnification 180X.

Figure 14c Degeneration in the nucleus limitans, predominately fibers of passage and only sparse preterminals. Magnification 190X.

Figure 14d Degeneration in the nucleus limitans, presumably fibers of passage. Magnification 190X.

- Wiitanen technique, counterstained with cresyl echt violet.

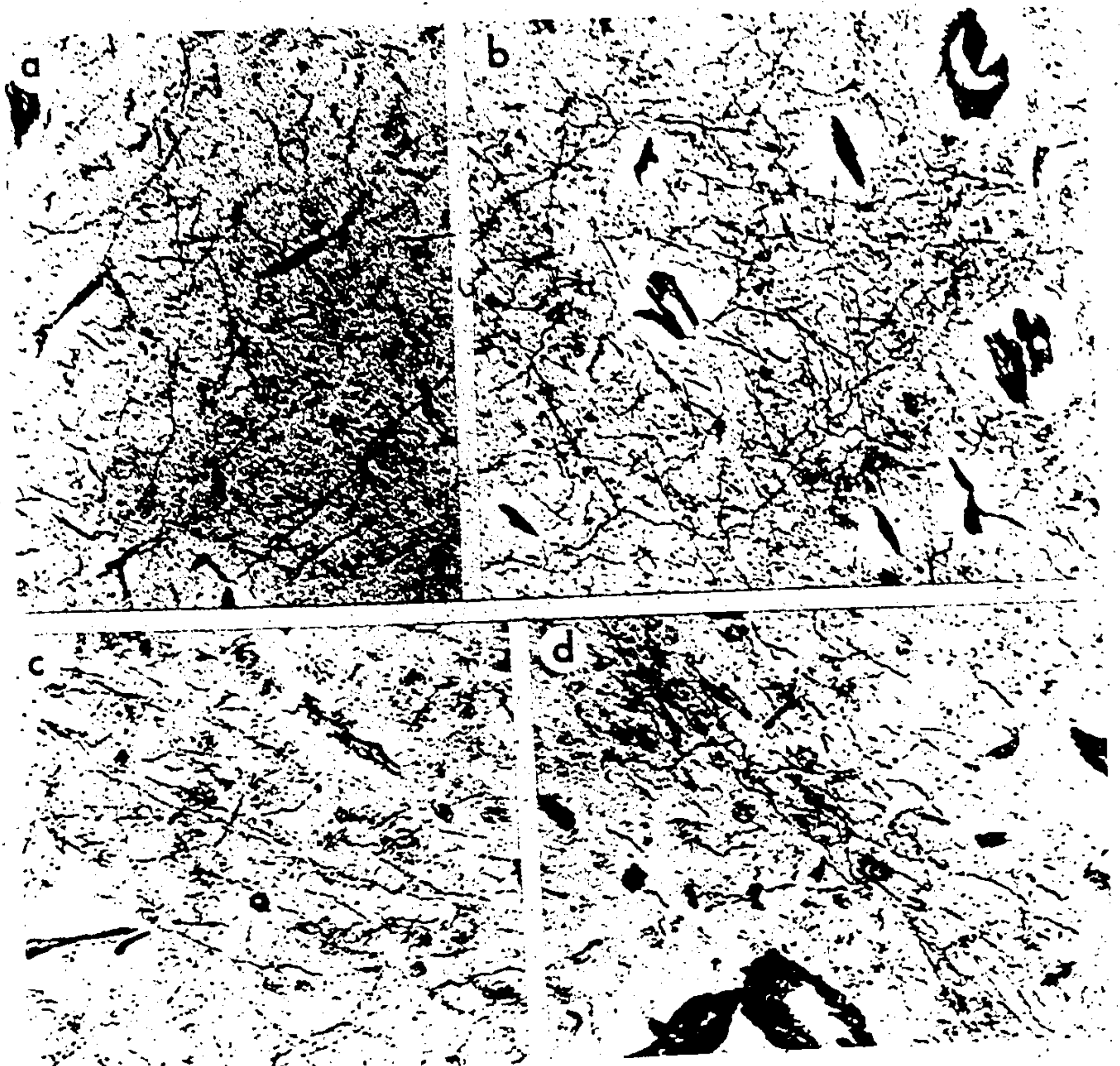

Figure 14

Figure 15a Degenerating fibers of passage in parafascicular nucleus. Magnification 220X.

Figure 15b Degenerating preterminals in parafascicular nucleus. Magnification 280X.

Figure 15c Argyrophilic cells in parafascicular nucleus. Magnification 350X.

- Wiitanen technique, counterstained with cresyl echt violet.

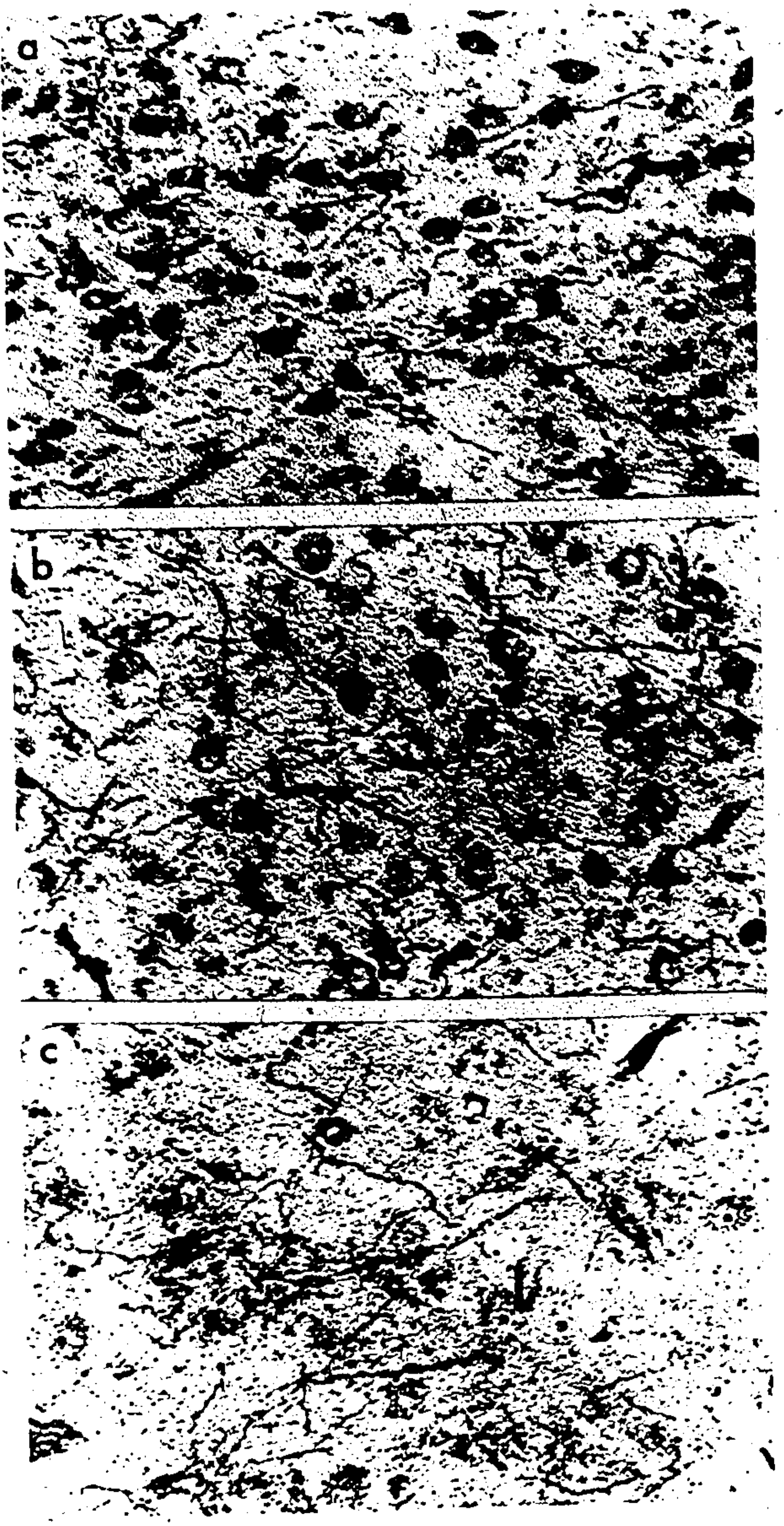

Figure 15

The projection of the superior colliculus to the central lateral nucleus terminated in small clusters in the vicinity of small groups of large cells (Fig. 16). A few clusters were scattered throughout the nucleus in no apparent pattern. Only rarely were two clusters seen in the same section. Small degenerating fibers were present individually in other parts of the nucleus. The soma of the large cells were only slightly argyrophilic.

The projection of the superior colliculus to the paracentral nucleus was denser than to other intralaminar nuclei (Figs 17, 18). The density of this projection seemed to depend on the size of the lesion. The degenerating fibers and preterminals resulting from large lesions were more numerous (Fig. 17a) than those seen after small to medium-sized lesions (Fig. 17b). The fibers were usually found in all parts of the nucleus and there were no density patterns sufficiently obvious to permit a topographic mapping of the projection. The cell bodies of the paracentral nucleus were also argyrophilic in nature (Fig. 17b) in the same manner as the cells of the nucleus limitans and of the parafascicular nucleus. In the more posterior aspect of the paracentral nucleus, the degeneration was confined within the relatively narrow margins of the nucleus (Fig. 18a), as compared to the somewhat wider spread of degenerating fibers in its more anterior regions (Fig. 18b). The fibers appeared to stream more profusely towards the most rostral extent of the nucleus (Fig. 18c), but ended abruptly at this point. In this region, the lateral border is very distinct whereas medially, degenerating fibers tend to taper off towards the dorsomedial nucleus (Fig. 18d).

The superior colliculus also projects contralaterally to the corresponding intralaminar nuclei, i.e., the parafascicular, central lateral and paracentral. The degenerating fibers are very sparse in the parafascicular (Fig. 19a) and central lateral nuclei (Fig. 19b).

Figure 16 Degenerating fibers around clusters of rather large cells in the central lateral nucleus. Wiitanen technique, counterstained with cresyl echt violet.

Fig. 16a Magnification 220X.

Fig. 16b Magnification 285X.

Fig. 16c Magnification 285X.

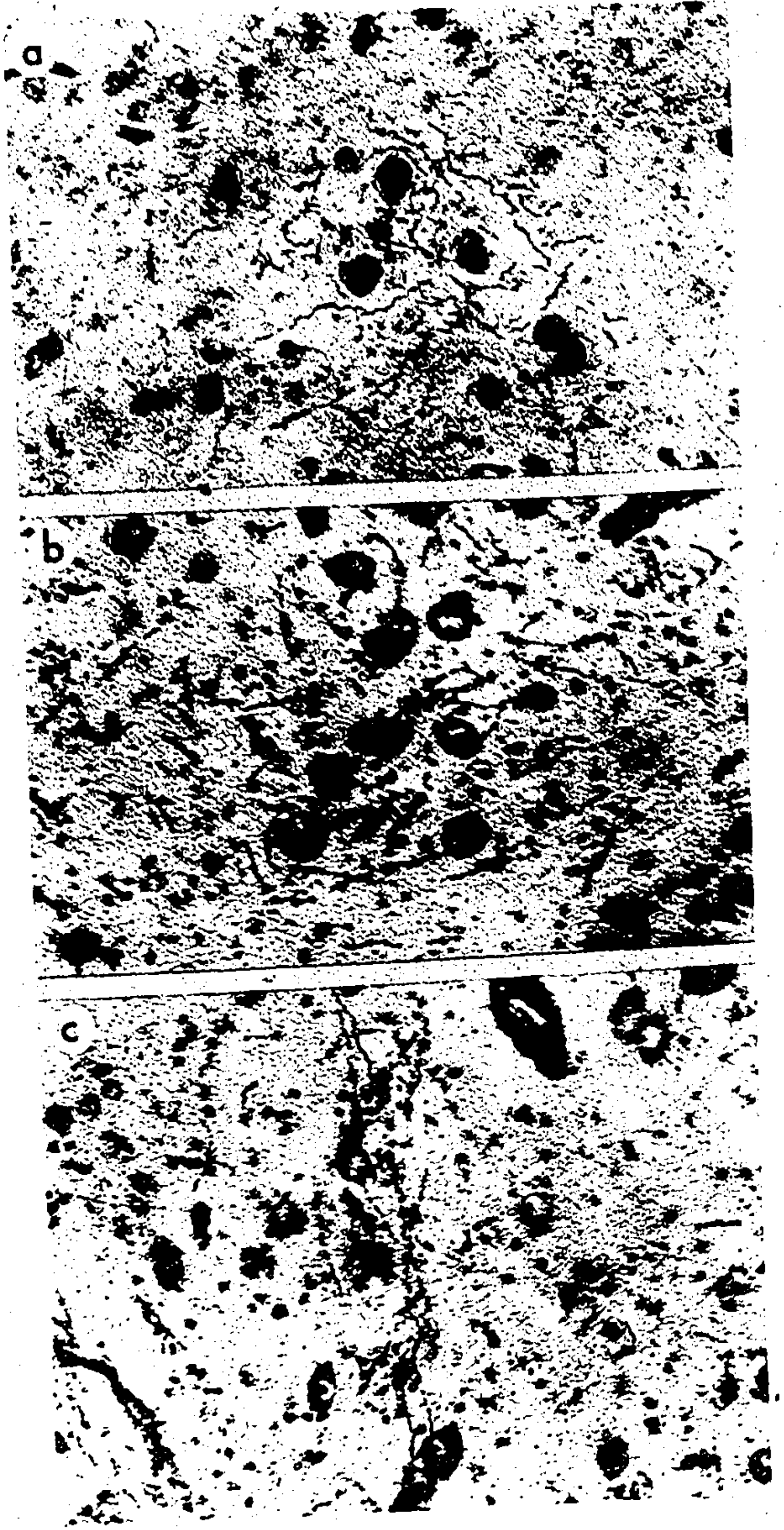

Figure 16

Figure 17a Dense degeneration in the paracentral nucleus following a large lesion. Magnification 200X.

Figure 17b Small amount of degeneration in the paracentral nucleus following a small lesion. Magnification 200X.

- Wiitanen technique, counterstained with cresyl echt violet

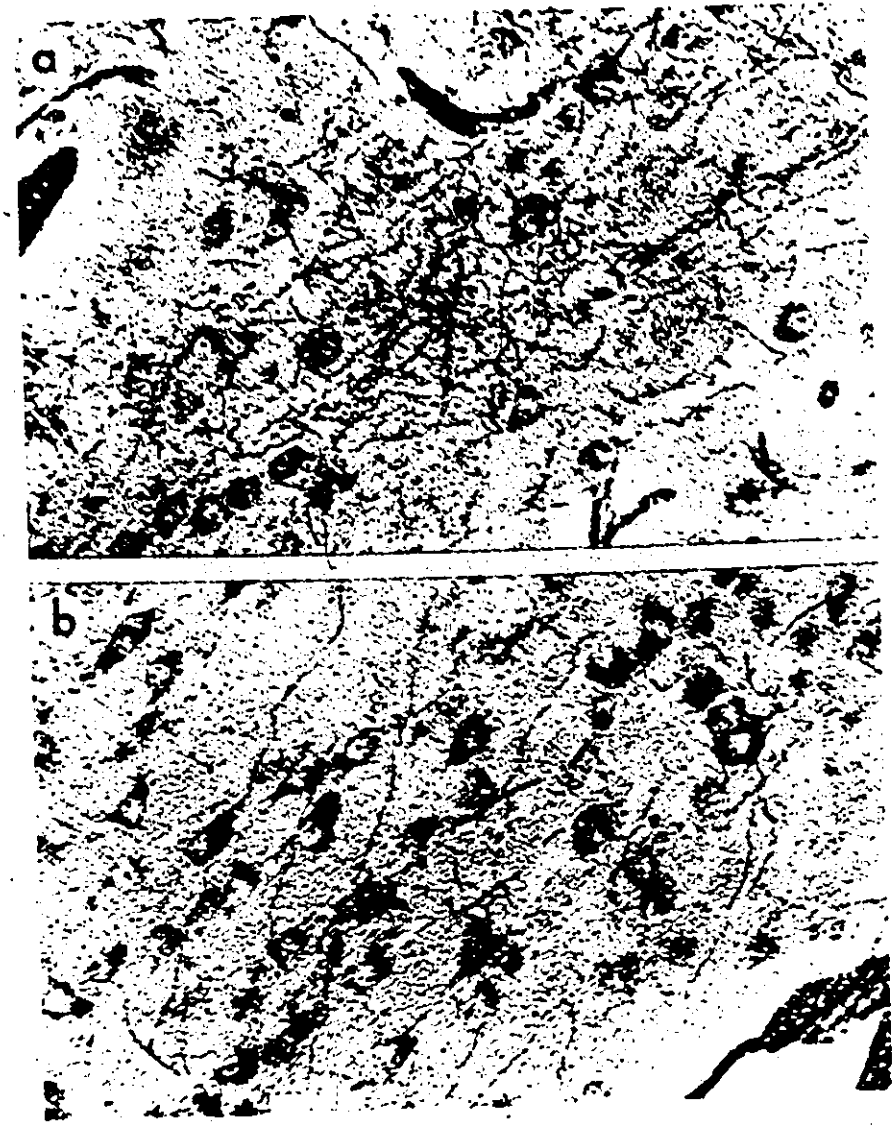

Figure 17

Figure 18 Degeneration in the paracentral nucleus. Wiitanen technique, counterstained with cresyl echt violet.

Fig. 18a Narrow limits of degeneration found at the more posterior levels of this nucleus. Magnification 155X.

Fig. 18b Wider spread of degeneration found at the more anterior levels. Magnification 155X.

Fig. 18c Degenerating fibers in the more anterior region of the nucleus. Magnification 320X.

Fig. 18d The degeneration outlines the distinct lateral border of the nucleus and the more vague medial border. Magnification 130X.

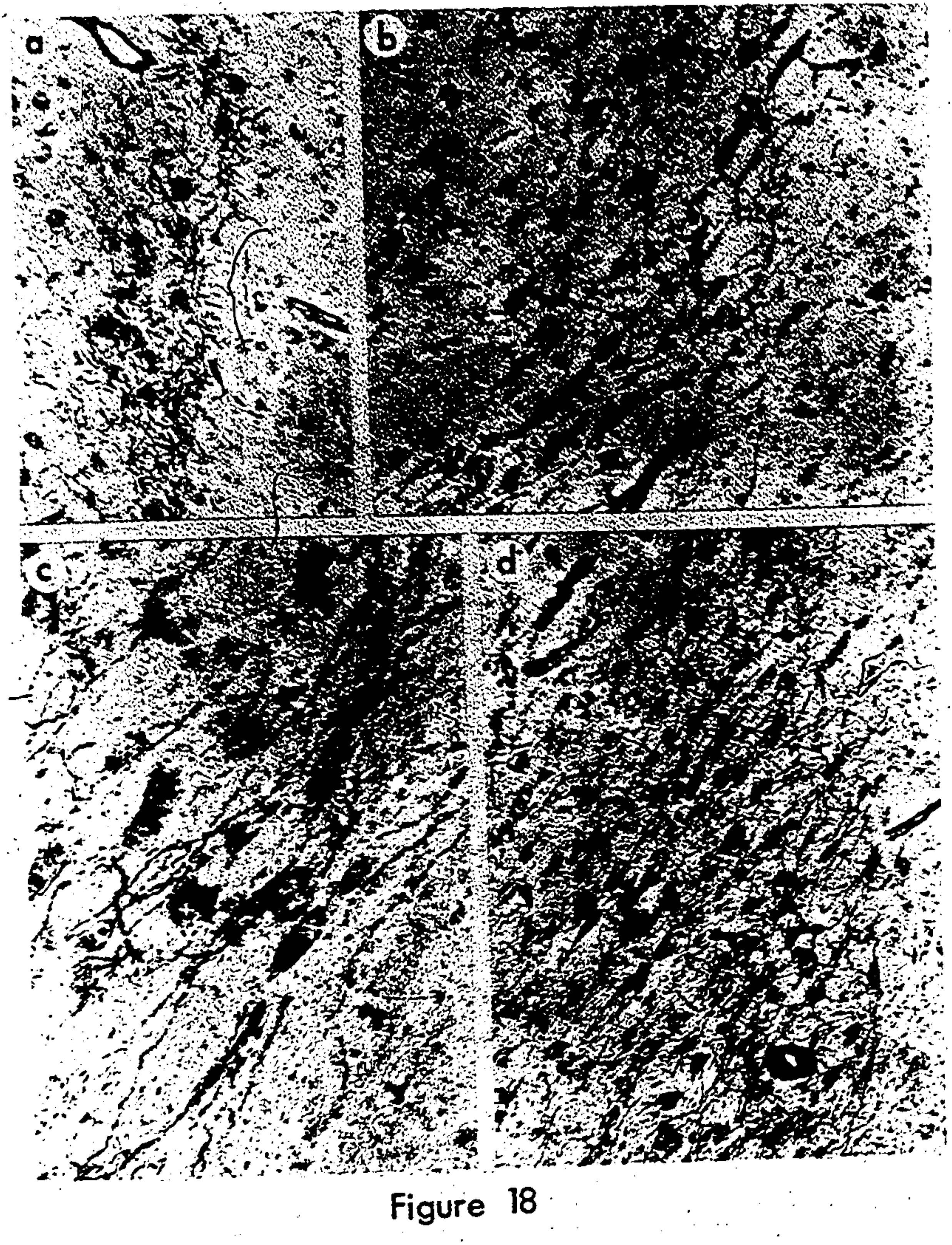

Figure 18

Figure 19 Degeneration in the contralateral intralaminar nuclei. Wiitanen technique, counterstained with cresyl echt violet.

Fig. 19a Sparse degeneration in the contralateral parafascicular nucleus. Magnification 300X.

Fig. 19b Sparse degeneration in the contralateral central lateral nucleus. Magnification 300X.

Fig. 19c Moderate degeneration in the contralateral paracentral nucleus at the more anterior levels. Magnification 300X.

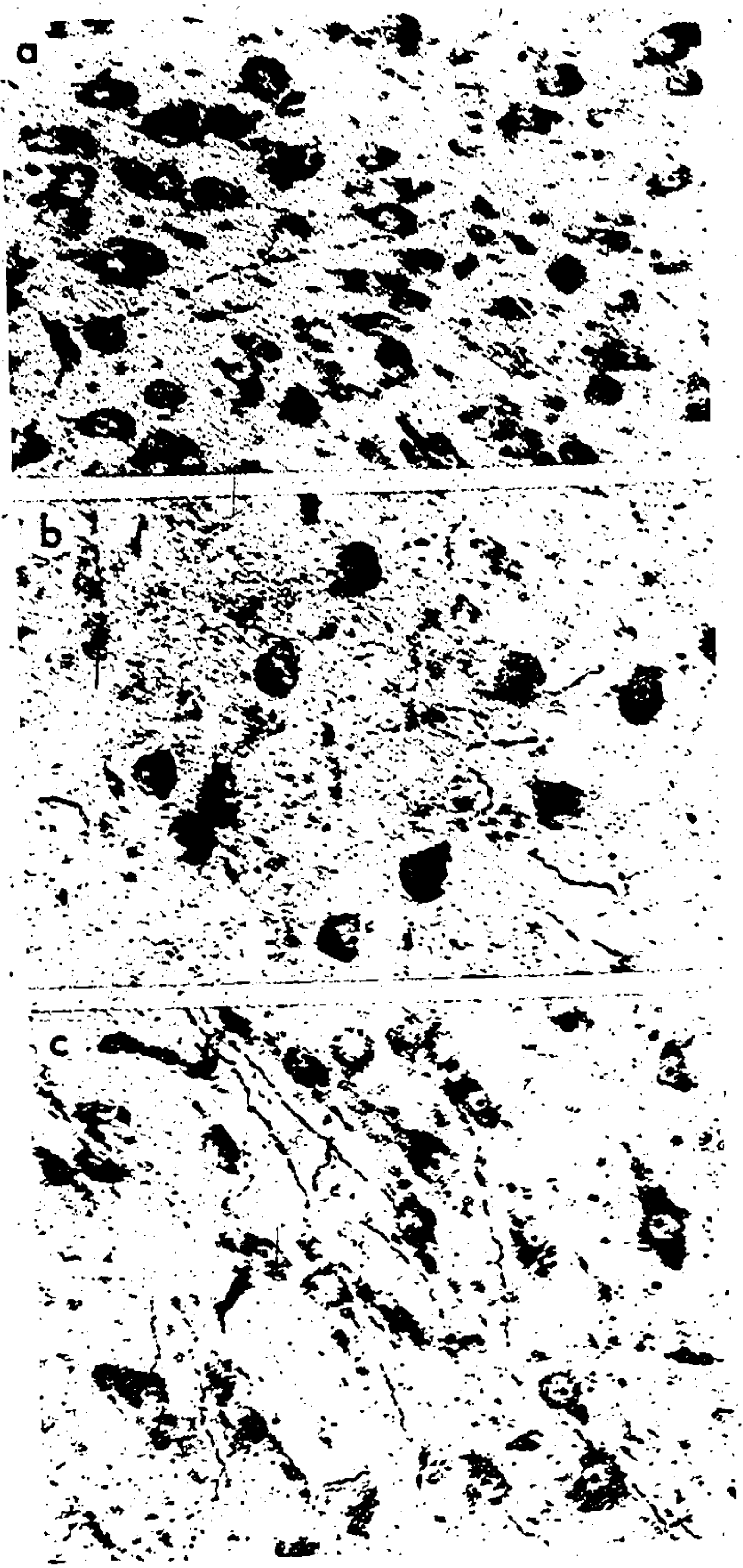

Figure 19

Degeneration in the paracentral nucleus is more obvious (Fig. 19c) and shows similar characteristics, posteriorly and anteriorly, to the ipsilateral side (compare Fig. 18c).

The present study did not specifically address itself to the question of whether superficial layers of the superior colliculus project to the inferior nucleus of the pulvinar and the deeper layers to the intralaminar complex. It was noted, however, that small lesions confined to the superficial layers resulted in definite degeneration in the pulvinar but little indication of degeneration in the intralaminar complex. On the other hand, large lesions including both superficial and deep layers of the superior colliculus resulted in degeneration in both the inferior nucleus of the pulvinar and the intralaminar nuclei (except the centromedian nucleus). It was difficult to assess, however, whether the smallness of the lesion in the superficial layers or the actual absence of a projection, was responsible ~~for~~ the lack of degeneration in the intralaminar nuclei.

D. Topography of the Tectopulvinar Projection

The projection of the superior colliculus to the inferior nucleus of the pulvinar is topographical. If no topography existed, a small lesion would cause diffuse degeneration throughout the nucleus, whereas a larger lesion would result in more dense degeneration throughout the nucleus. This did not occur, however. A small discrete lesion in the superior colliculus resulted in a discrete region of degeneration in the inferior nucleus of the pulvinar (Figs 20a, b). A large lesion in a particular part of the colliculus caused degeneration over a wide area of the inferior nucleus (Fig. 20c) but with definite boundaries. Fibers of passage often travelled across the medial aspect of the nucleus to terminate at their appropriate site, leaving the most lateral part free of degeneration (Fig. 20c). Lesions of different

Figure 20 Degeneration in the right inferior nucleus of the pulvinar. Wiitanen technique, counterstained with cresyl echt violet.

Fig. 20a Degeneration resulting from a small lesion in superior colliculus. Magnification 150X.

Fig. 20b A discrete region of degeneration resulting from a small lesion in the superior colliculus. Magnification 100X.

Fig. 20c Degeneration resulting from a large lesions in superior colliculus. Fibers of passage, a terminal field and an area free of degeneration (laterally) can be observed. Magnification 100X.

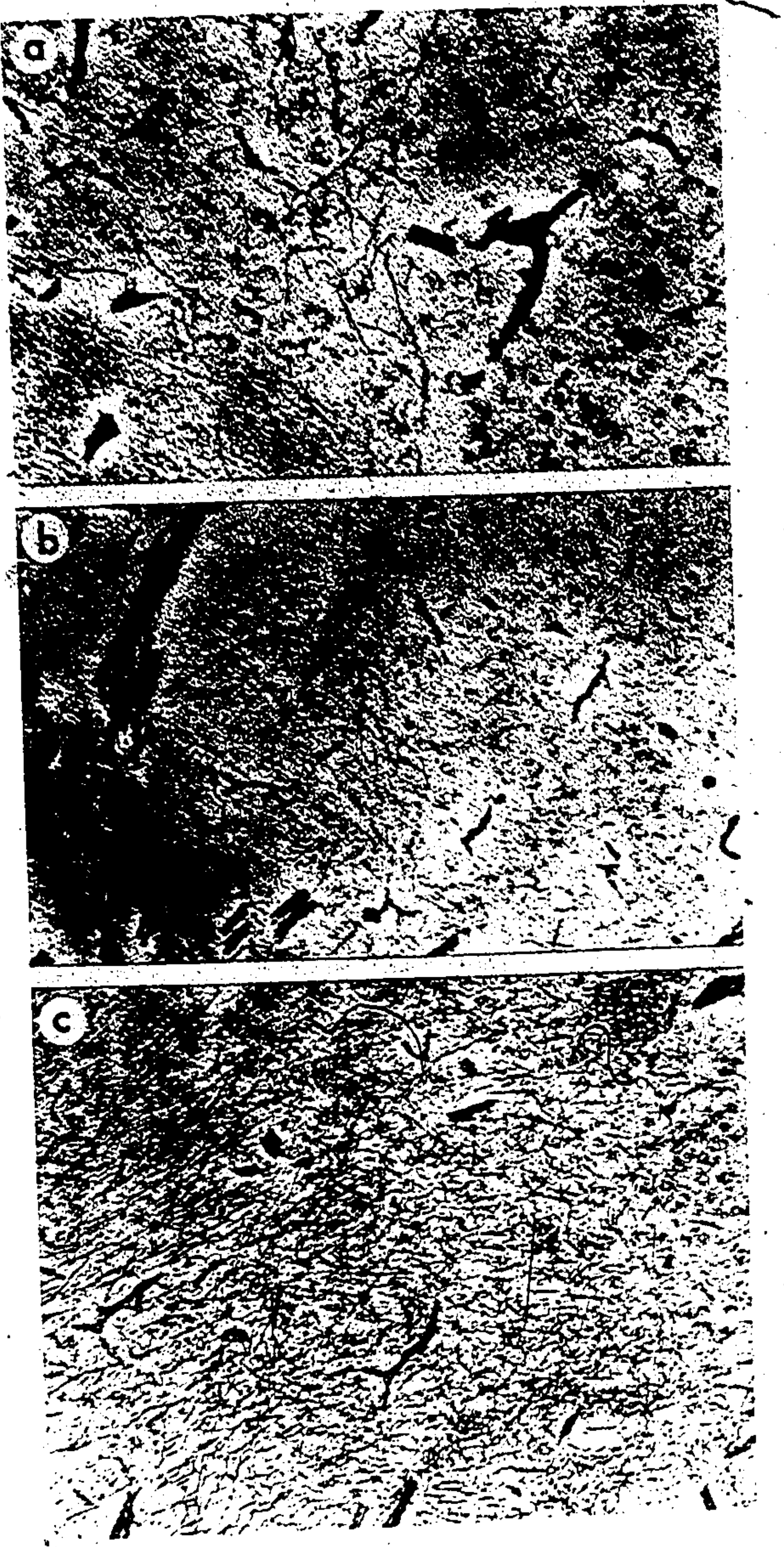

Figure 20

size and location resulted in different patterns of degeneration in the inferior nucleus of the pulvinar. For example, in figure 21, a large zone of degeneration can be observed dorsally whereas the more ventral portion of the nucleus is free of degenerating fibers.

In order to analyze the topography of this projection, it was essential to relate the sites of the lesions to the degeneration found in the inferior nucleus of the pulvinar. The most meaningful way to present the results of the study was to relate the lesioned areas to their known visual field representation, and to transpose this representation to the area of degeneration in the pulvinar.

The representation of the visual field on the surface of the superior colliculus was obtained from the work of Wilson and Toyne ('70), Cynader and Berman ('72) and Robinson ('72) in the macaque (Fig. 22a). The upper visual field is located medially and the lower field laterally. The peripheral limit of the upper and lower vertical meridians was not precisely indicated in these works and therefore it remains slightly vague in the diagram. Similarly, the obliquity of the horizontal meridian from the sagittal plane varied somewhat according to the different authors, although the general orientation was the same. Therefore, with the above limitations in view, the resulting representation of the visual field in the colliculus was used as a basis for the descriptions of the tectopulvinar projections.

The location of the lesions in the superior colliculus were carefully mapped on this diagram to show the extent of damage to the superficial layers (Fig. 22b). However, damage to the underlying layers was sometimes rather extensive and not always located under the superficial site of the lesion (indicated whenever possible by a broken line in the diagram). This variation in the location of the lesion depended on the angle of the electrode penetration relative to the surface of the superior colliculus. For

Figure 21 Degeneration in the inferior nucleus of the pulvinar. The same section is illustrated at three increasing magnifications (i.e., 18X, 45X and 150X) to demonstrate a specific region of degeneration within the nucleus. The arrow indicates the same blood vessel in each photagraph. Wiitanen technique, counterstained with cresyl echt violet.

Figure 21

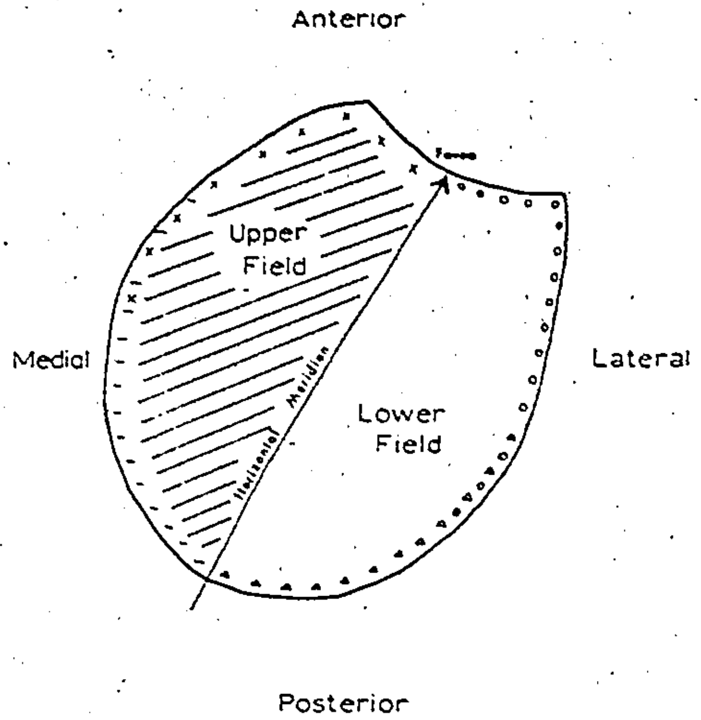

Figure 22a Topographical representation of the visual field on the surface of the right superior colliculus. The data for this map was obtained from the literature (see text). The upper vertical meridian is indicated with x's, the lower with o's. The periphery is indicated by means of bars and triangles.

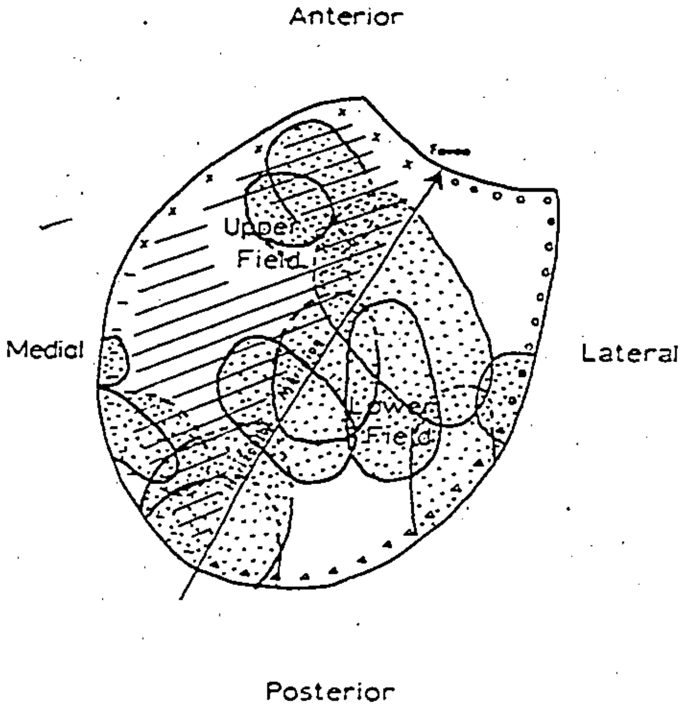

Figure 22b Surface representation of the right superior colliculus to illustrate the site of each lesion. Solid lines indicate damage in superficial layers, broken lines indicate damage deep to the superficial layers.

example, a contralateral approach caused damage to the superficial layers medially and damage to the deeper layers more laterally; therefore, it was difficult to assess the exact area of visual representation in these situations.

In many animals a cluster of degeneration was observed at the lateral border of the inferior pulvinar, adjacent to the dorsal lateral geniculate nucleus. As stated previously this degeneration was considered to be mainly fibers of passage destined for either the dorsal or ventral lateral geniculate nucleus. It was therefore discounted in the following analysis as unrelated to the topographical representation.

The first detail of the map to be considered is the location of the horizontal meridian. In CS-14 (Fig. 23), the lesion damaged the area of the superior colliculus representing the horizontal meridian, including mainly the lower visual field. The site of degeneration was found dorsomedially at the most posterior levels (1, 2) and then shifted slightly ventrally and laterally away from the dorsomedial border, at the adjacent anterior levels (3, 4). The results obtained from CS-1 (Fig. 24), help to determine where the periphery is located along this meridian since the lesion in this animal destroyed the region of the colliculus representing the periphery of the horizontal meridian. Unfortunately it also encroached upon the overlying visual cortex (upper visual field according to Zeki '69). A small field of degeneration (typical of tectopulvinar projections in other animals) was found along the medial border of the inferior nucleus, shifting ventrally at successively more anterior levels (1-4). It corresponds to the medial edge of degeneration seen in the previous animal, CS-14. A rather coarse type of degenerating fibers was also found in the ventrolateral aspect at levels 5 and 6. This latter field of rather atypical appearance was attributed to the extraneous damage to the visual cortex. Therefore, it appears that the horizontal meridian is represented obliquely across the nucleus from a medioventral to a laterodorsal position, with the periphery represented medially and fovea dorsolaterally. The meridian shifts ventrally at more anterior levels.

It is now necessary to determine the location of the upper and lower visual fields, i.e., dorsomedial or ventrolateral to the horizontal meridian. The data obtained from CS-16 and CS-4 clarify this issue. In CS-16 (Fig. 25), the lesion was confined to the region of the colliculus representing the lower visual field. The degeneration was found in the dorsal part of the nucleus at levels 2 to 6. The lower visual field is therefore represented dorsomedially in the inferior nucleus of the pulvinar, and consequently, the upper field should be represented ventrolaterally. Confirming this assumption, the lesion in CS-14, which was located in the area representing the upper visual field, indeed caused degeneration ventrally and somewhat laterally.

The results from several other lesions correspond to this arrangement (e.g., Figs 27, 28, 29). In figure 29, however, two sites of degeneration were observed, one dorsomedially and the other ventromedially. The more ventral area of degeneration corresponds to the postulated representation of the upper field periphery, i.e., at the ventromedial border of the nucleus, but the degeneration located dorsally cannot be readily explained. On careful examination of the Nissl preparations, however, it was found that a group of cells in the dorsomedial corner of the inferior nucleus was partially separated from the remainder of the nucleus by inconstant fiber bundles. Perhaps this area corresponds to the suprabrachial nucleus of Hassler ('59) or the posterior nucleus of Mathers ('71). This subnucleus was not a common feature in the present study (see Table 5, CS-7).

In an attempt to destroy the entire superior colliculus, large lesions were placed anteriorly and posteriorly in each of two animals. Unfortunately only part of the colliculus was damaged and yet the lesions were too large to provide useful data for determining the topography. The pattern of degeneration, however, was consistent with the postulated visual representation (e.g., Fig. 30, CS-8).

Degeneration was not observed in the most ventrolateral border of the inferior nucleus of the pulvinar from lesions in the superior colliculus. However, comparison of the surface representation of all lesions (Fig. 22b) indicates that a considerable portion of the anteromedial part of the superior colliculus had not been damaged in this series of experiments. It was concluded, therefore, that this region of the colliculus would project to the most ventrolateral part of the inferior nucleus, according to the postulated map.

At this point in the investigation, two visual maps for the inferior nucleus of the pulvinar appeared in the literature based on electrophysiological recordings (Allman et al. '72) and corticopulvinar projections (Campos-Ortega and Hayhow '72). These maps confirmed the developing topography in this study and hence, to proceed further was considered not useful.

The proposed topographical representation of the tectopulvinar projection can thus be summarized (Fig. 31) at three frontal levels. The horizontal meridian divides the inferior nucleus of the pulvinar obliquely, into a dorsomedial lower visual field that increases in size anteriorly, and a ventrolateral upper visual field that increases in size posteriorly. The foveal area is represented dorsolaterally, with the lower vertical meridian forming the dorsal border and the upper vertical meridian forming the lateral border. The periphery of the visual field is represented along the medial border of the nucleus.

Figures 23-30 Schematic diagram of the seven levels of the inferior nucleus of the pulvinar in the frontal plane, numbered from the posterior pole. The terminal fields of degeneration are represented by dots, the fibers of passage by dashes and the areas of degeneration that could be interpreted as either, are indicated by short wavy lines. A surface view of the superior colliculus is represented in the upper left corner to illustrate the site of the lesion.

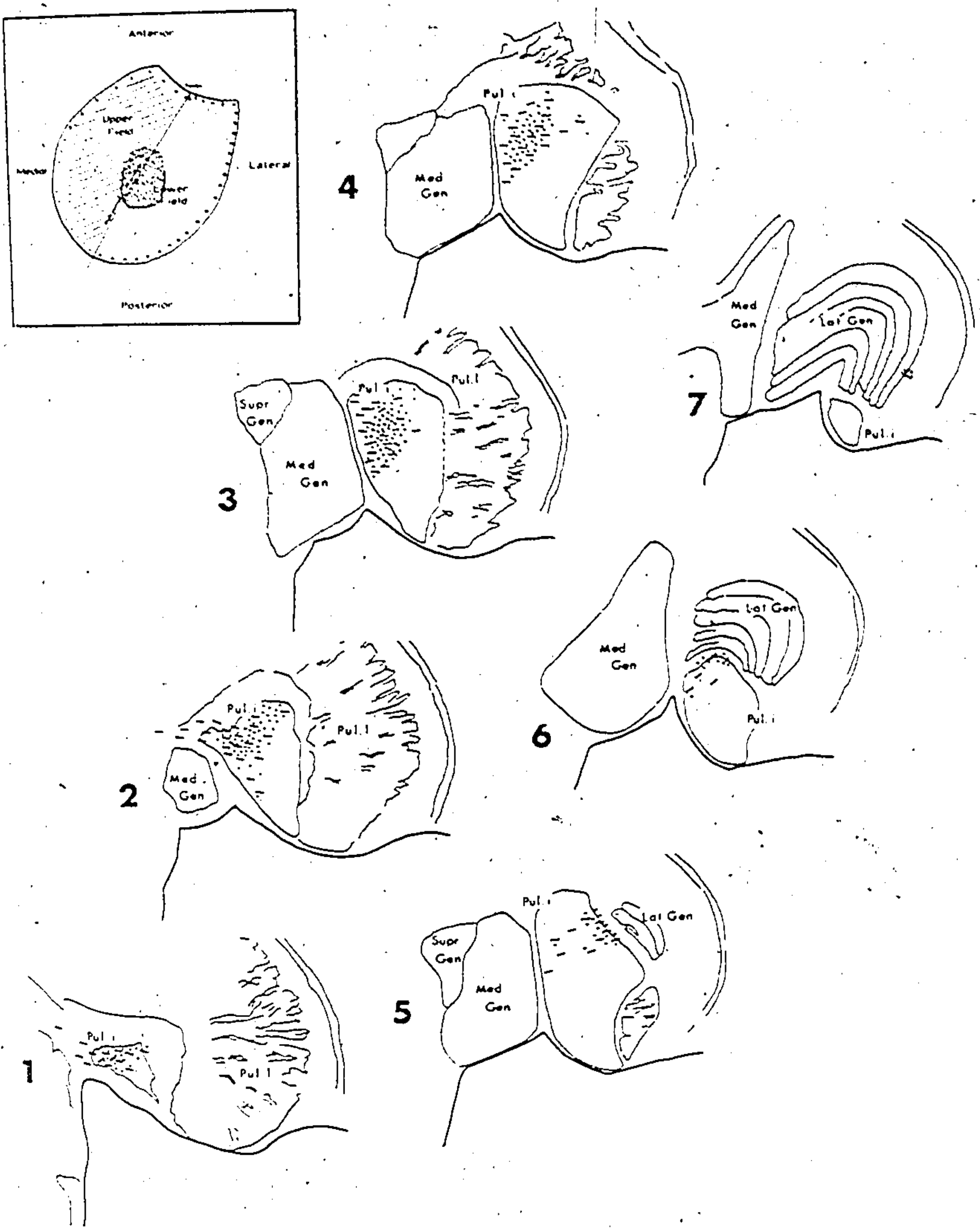
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Figure 23

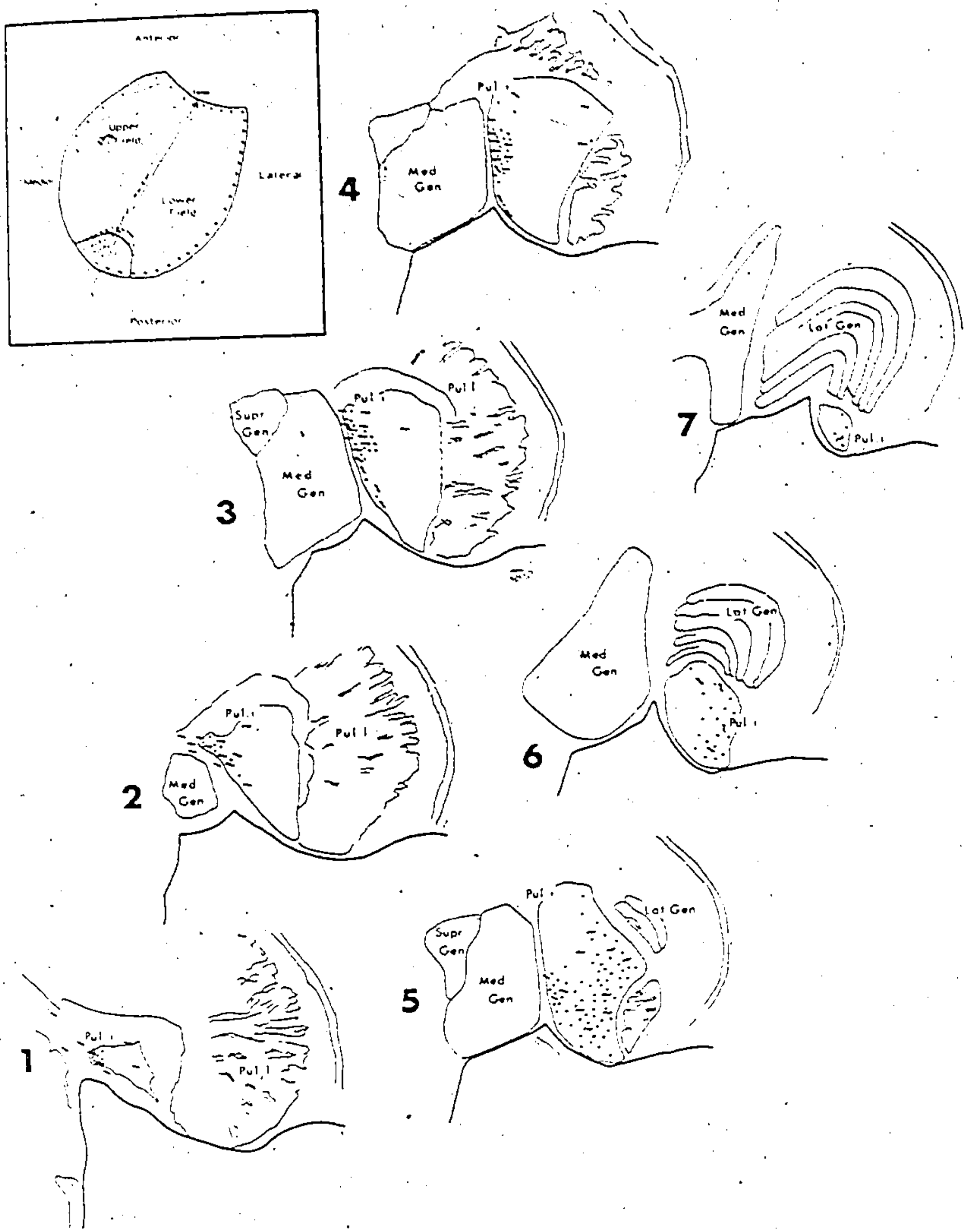
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Figure 24

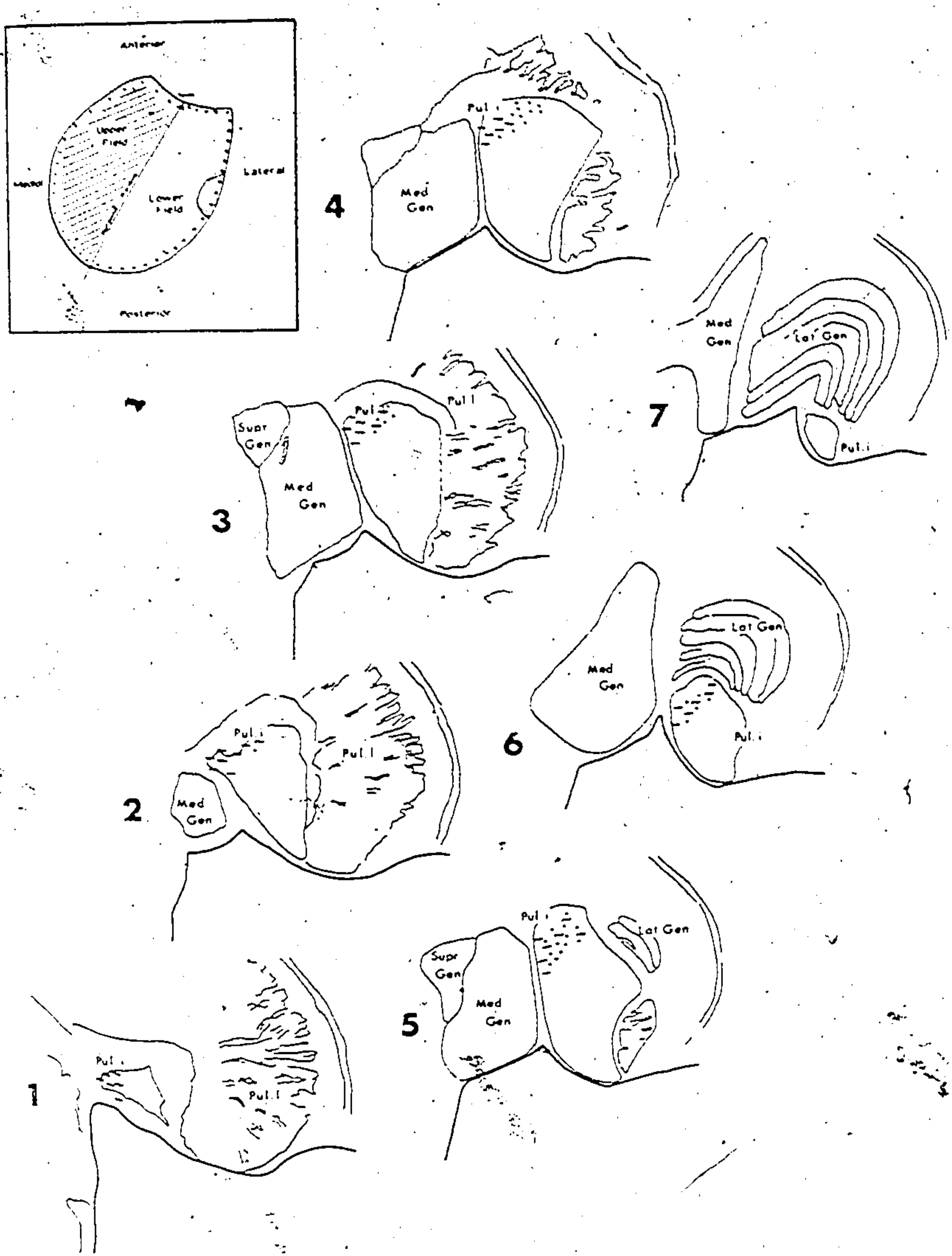
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Figure 25

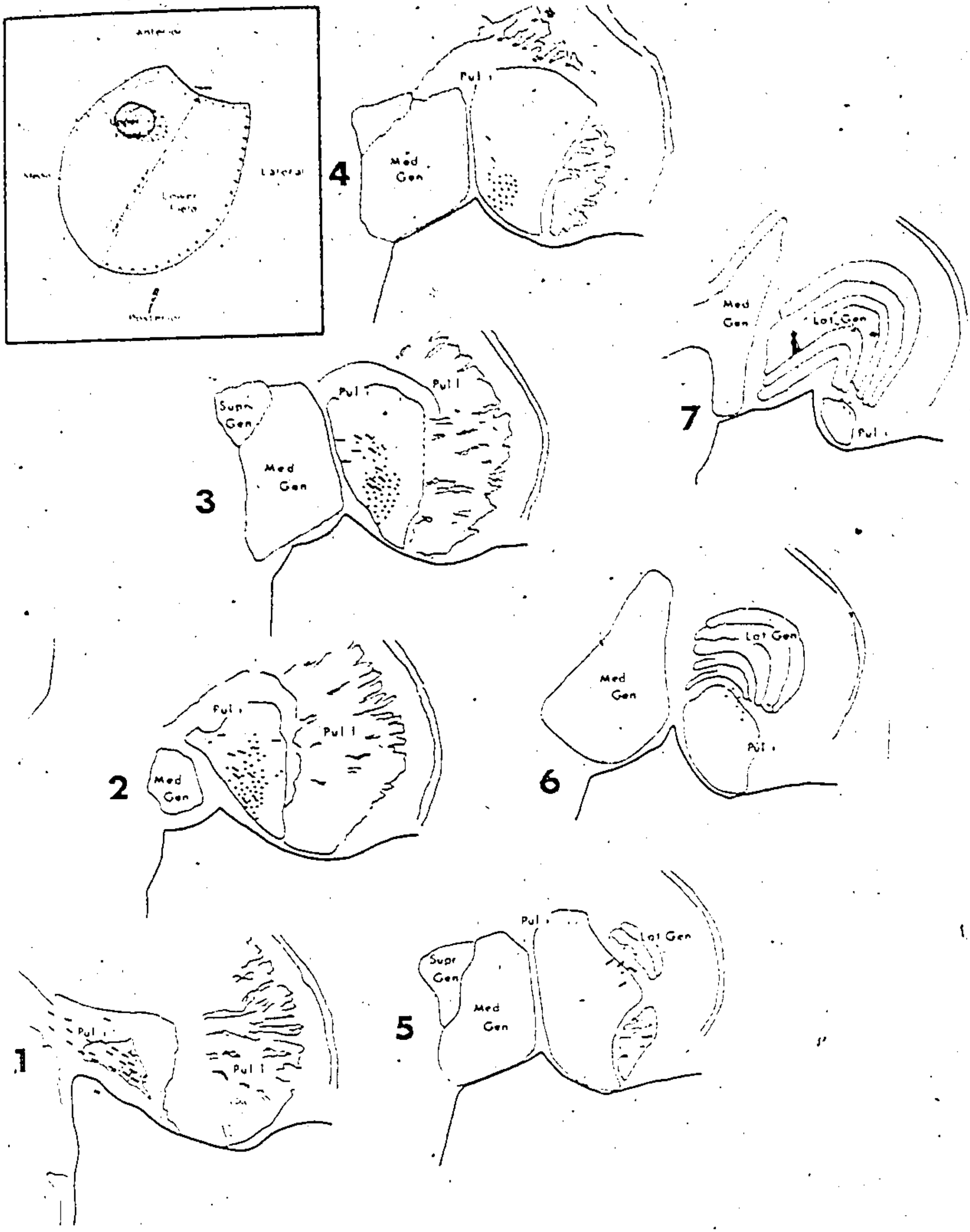
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Figure 26

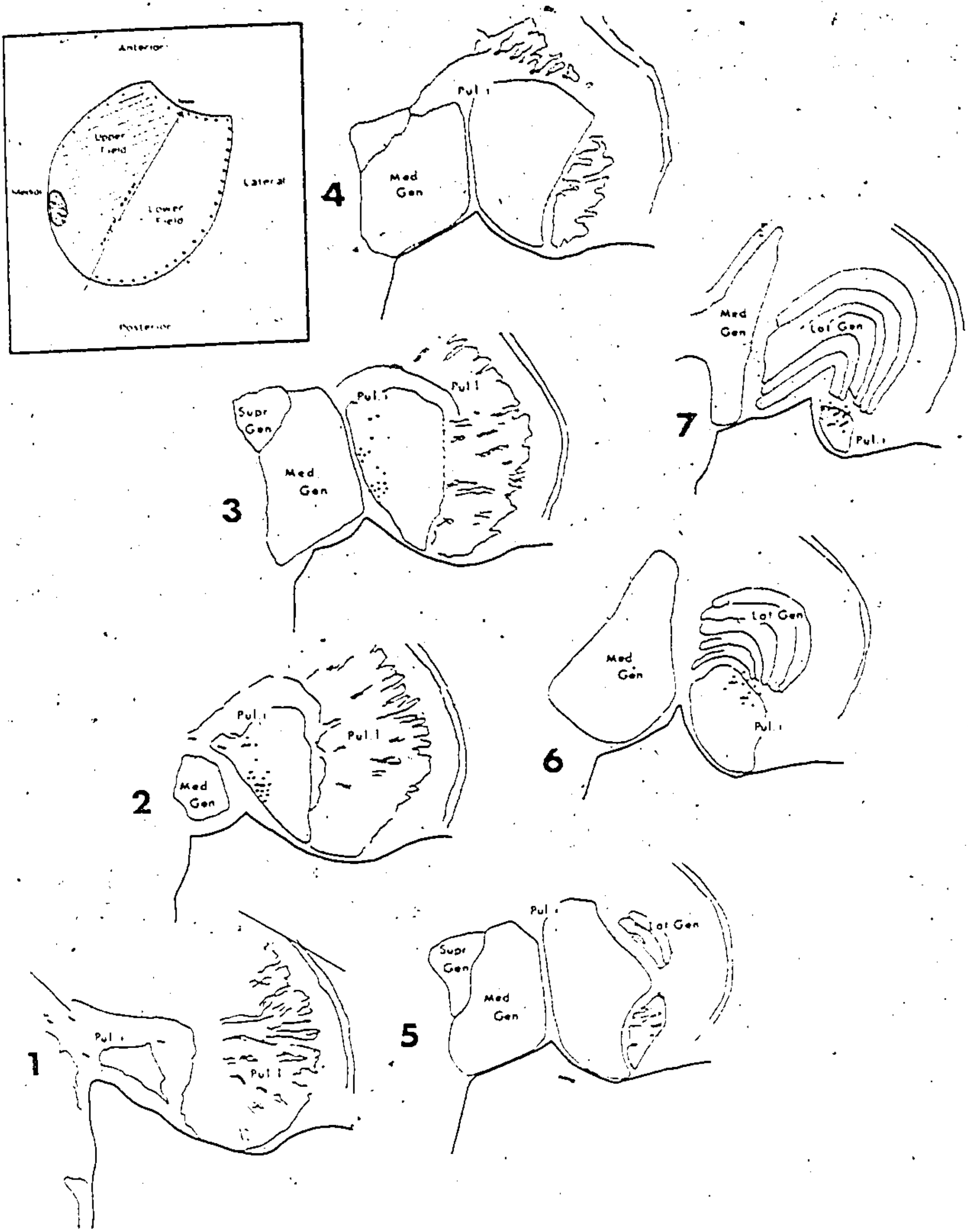
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Figure 27

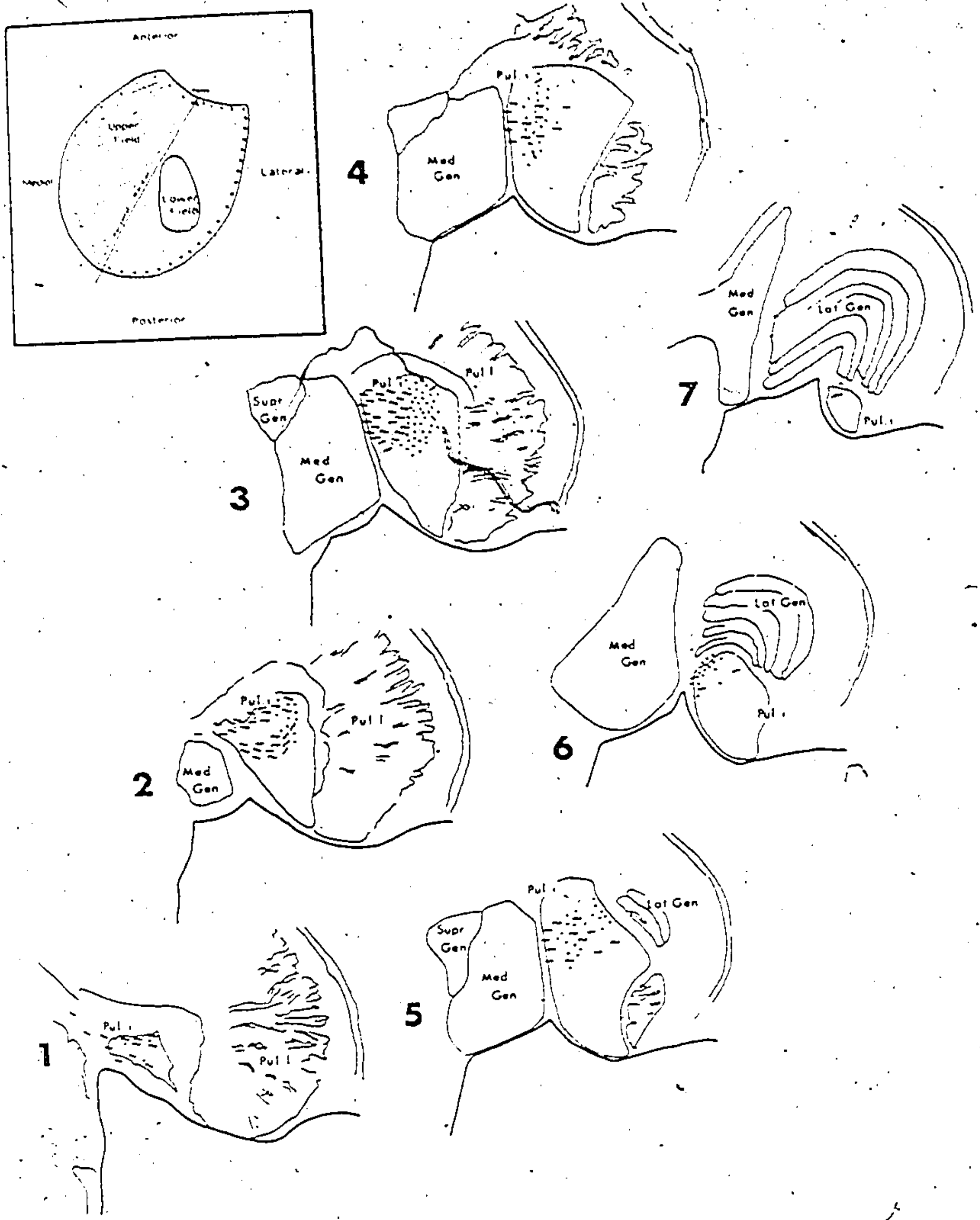
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Figure 28

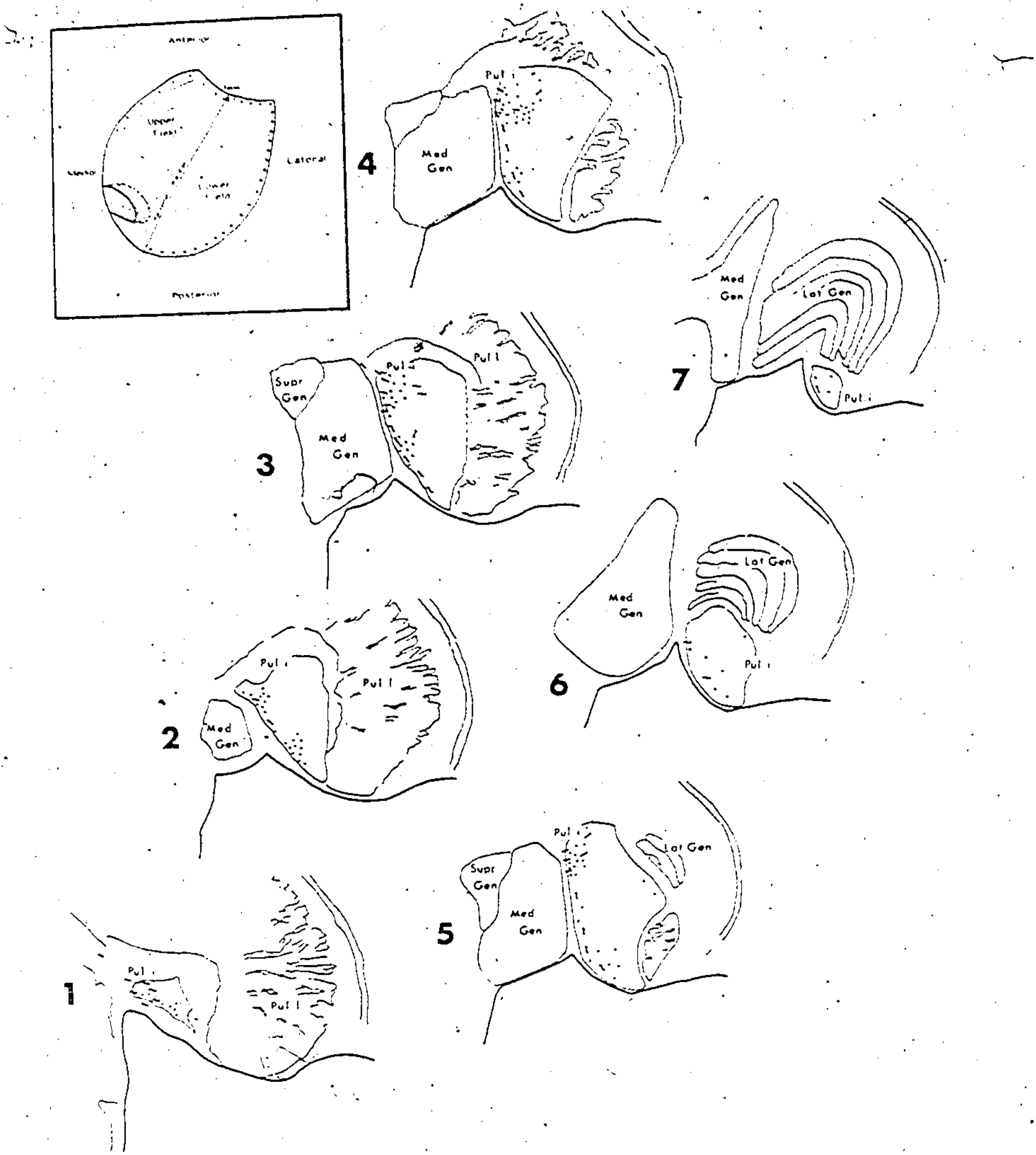
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Figure 29

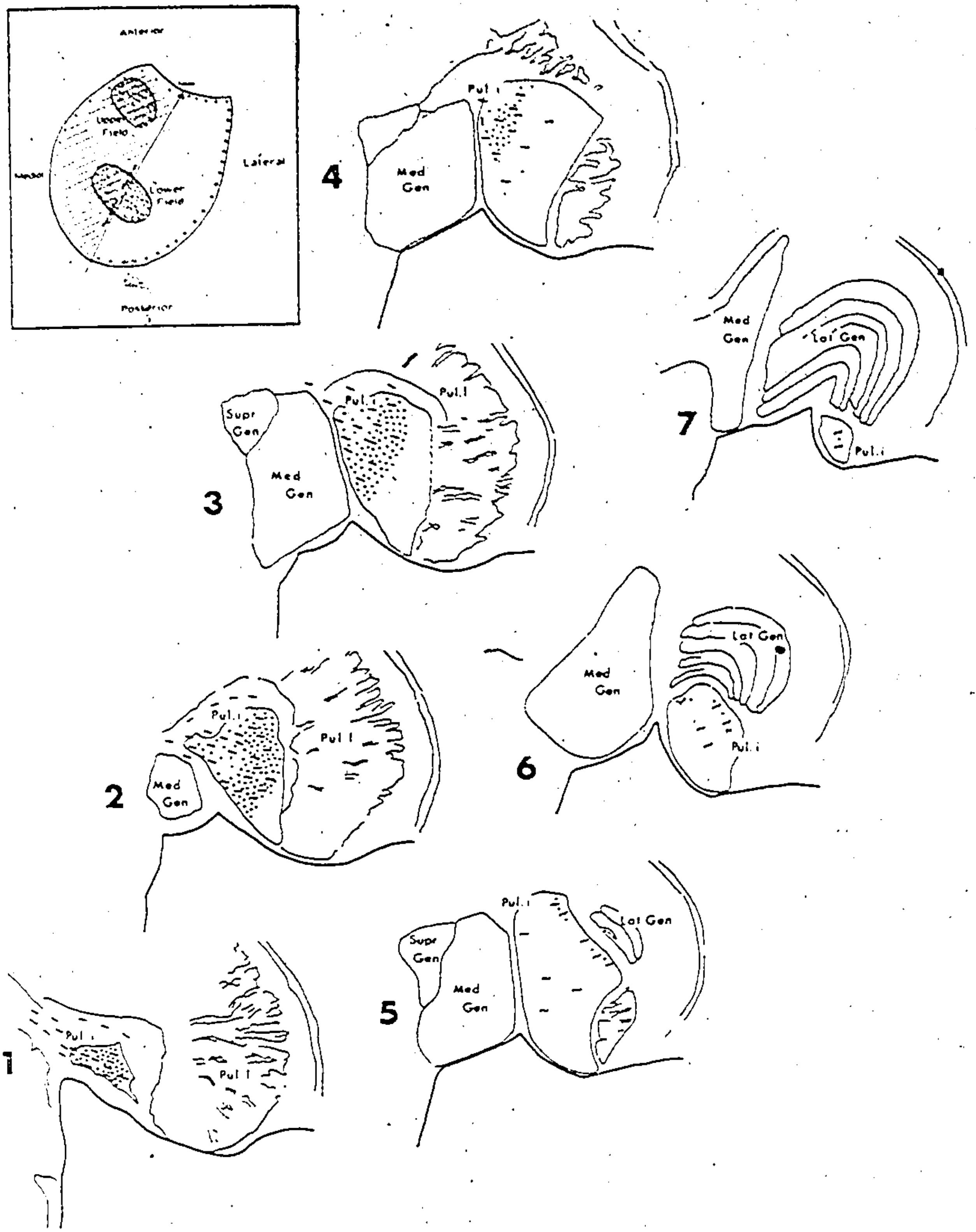
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Figure 30

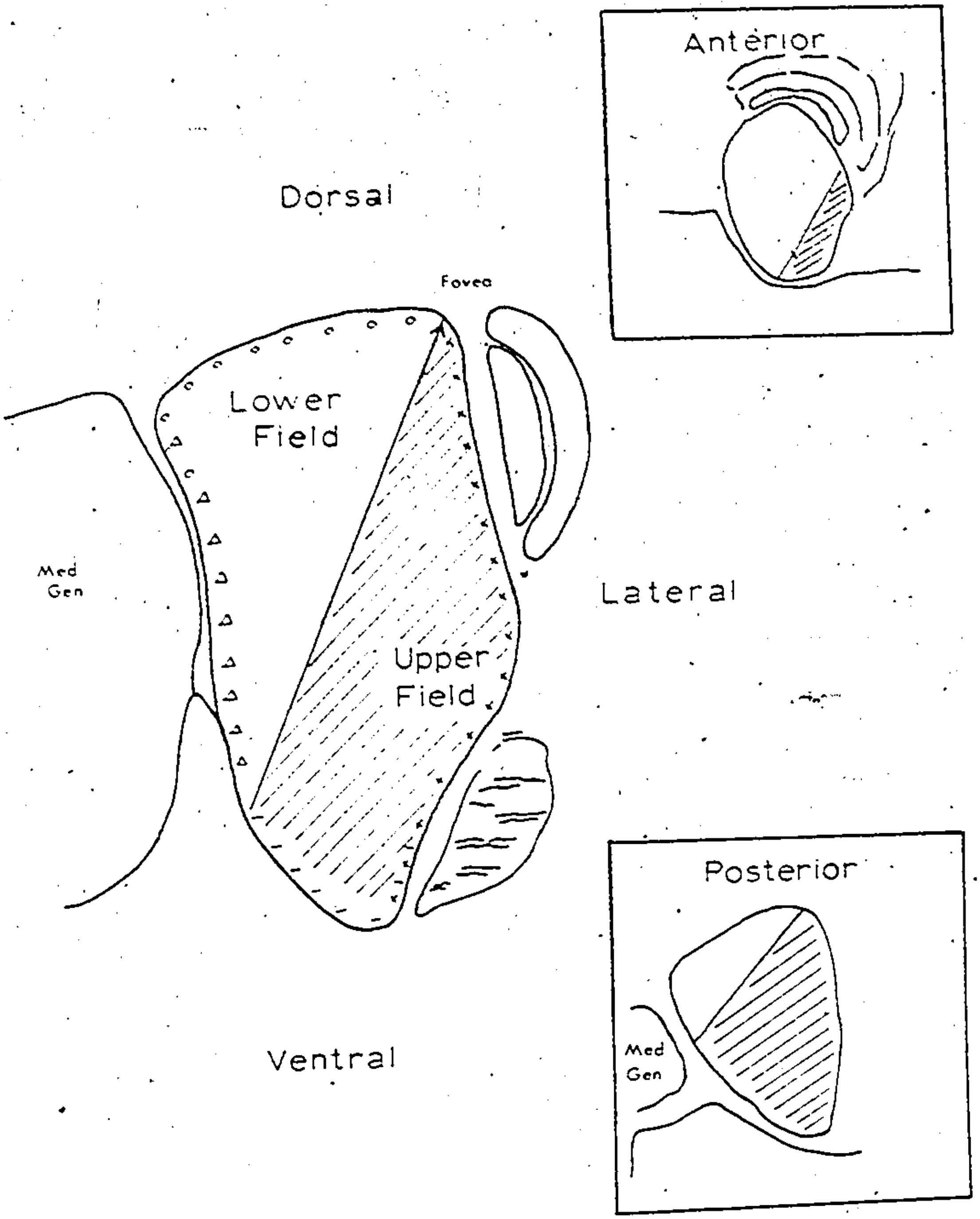


Figure 31 Representation of the visual field in the inferior nucleus of the pulvinar.

II. Electron Microscope Study

An electron microscope study of the inferior nucleus of the pulvinar and the paracentral nucleus of the intralaminar complex was carried out in two normal monkeys and eight experimental animals, sacrificed 1 to 7 days following lesions of the superior colliculus. Extensive lesions were placed in the superior colliculus through a variety of electrode approaches in an attempt to destroy as much of this structure as possible. Because of the large size of the lesions and normal variations in the size and shape of the monkey's brain, damage was often found in the neighboring structures, particularly the central gray, inferior colliculus and corpus callosum (Table 6). The preparation of the material for electron microscopic examination was generally satisfactory although occasional difficulties in the perfusion procedure resulted in limited use of some material.

The sampling technique was carried out as described in the methods section. Several samples of tissue were taken from the paracentral nucleus and the inferior nucleus of the pulvinar. The accuracy of the sampling was verified (Fig. 32) with the photographic technique of Guzman et al. ('58) and on Nissl preparations. Errors were sometimes encountered in the sampling because of the limited contrast in the tissue slabs. The narrowness and oblique anteroposterior orientation of the paracentral nucleus also contributed to these difficulties. Blocks that were not located in the correct nuclei were discarded.

A. Identification of the Various Synaptic Types

The criteria used to identify synapses are similar to those given in previous electron microscopic studies of the central nervous system and reviewed in the introduction. These criteria are the presence of differen-

TABLE 6

Results of Operation and Sampling for Electron Microscopy

Animal	Survival	Lesion in Sup. Coll.	Extraneous Damage	Perfusion	Sampling
CSE-1	---	---	---	acceptable	*** IP, Pc
CSE-2 right	5 days	small	---	acceptable	*** IP ** Pc
CSE-3	---	---	---	good	*** IP * Pc
CSE-4 right	5 days	small	---	good	** IP * Pc
CSE-4 left	5 days	medium	---	good	*** IP ** Pc
CSE-5 right	3 days	small	inferior colliculus central gray pretectum	good	* IP ** Pc
CSE-5 left	3 days	small	inferior colliculus central gray pretectum	good	* IP ** Pc
CSE-6 right	7 days	large	corpus callosum central gray	excellent	*** IP *** Pc
CSE-6 left	7 days	---	corpus callosum	excellent	** IP ** Pc
CSE-7 right	5 days	medium	inferior colliculus central gray	poor	*** IP *** Pc
CSE-7 left	5 days	small	inferior colliculus central gray	poor	** IP *** Pc
CSE-8 right	3 days	large	corpus callosum central gray	acceptable	** IP ** Pc
CSE-9 right	5 days	large	inferior colliculus central gray pretectum	good	*** IP ** Pc
CSE-10 right	1 day	medium	corpus callosum medial pulvinar ?	good	*** IP ** Pc

Sampling: * poor, ** average, *** good

Figure 32a Photographic enlargement of an unstained section to show the site of samples from the inferior nucleus of the pulvinar (arrows) for electron microscopy. Magnification 5X.

Figure 32b Photographic enlargement of an unstained section to show the site of samples from the paracentral nucleus for electron microscopy. Magnification 5X.

Figure 32

tiated membranes of two opposed profiles, at least one of which contains a group of vesicles agglomerated towards the membrane differentiation. The differentiated membranes have an increased density and appear relatively straight. The extracellular space between them is slightly widened as a rule and is often filled with an electron-dense substance.

Three types of synaptic profiles were distinguished on the basis of the shape and size of their synaptic vesicles in the inferior nucleus of the pulvinar and in the paracentral nucleus. These different synaptic vesicle populations will be referred to as round, flattened or polymetric.

A <u>round vesicle population</u> is one in which most vesicles are circular in shape and relatively uniform in size. Terminals containing these round vesicles can be further subdivided into two groups. The first is a small terminal with a smooth, non-jagged outline. It has darkish cytoplasm crowded with vesicles and only occasionally contains one or two mitochondria (Figs 33a, c). It corresponds to the RSD profile described by Guillery ('69a), where R signified round vesicles, S, the smallness of the terminal and D, the darkened mitochondria. In the present material, however, the mitochondria in these profiles are not significantly darker than in the other types of terminals. The label RSD will nevertheless be retained, the D now referring to the high density of vesicles usually found in the profile, and not to the denser mitochondria.

The second terminal containing round vesicles is much larger and has an irregular, jagged outline. The vesicles are less closely packed than in the RSD terminal, and a large number of mitochondria are present (Fig. 33b). It has been seen to arise from a myelinated axon (Fig. 34a). The terminal is similar to the RLP profile of Guillery ('69), where R signifies the round vesicles, L, the largeness of the terminal and P now refers to the overall paleness of the profile due to the relative diminution in the packing density of vesicles, rather than to the pale mitochondria. The relative density of vesicles in RSD and RLP profiles is perhaps best described by noting that in the former, most vesicles touch or overlap other vesicles, while in the latter, many vesicles are isolated from the others. Although the RLP profile appears pale in comparison to the RSD terminal, both types are darker than other neuronal profiles, such as dendrites.

A <u>flattened vesicle population</u> is one in which the vesicles are smaller in size than those of the round population, and many are flattened or irregular in shape (Figs 33b, d). It is the smallness of these vesicles, as much as their flattened appearance, that distinguishes this population of vesicles. The terminals vary in size, some being as small as RSDs and others are quite large, even as large as RLPs. The cytoplasm is similar in density to that of the RLP and many contain several mitochondria (Fig. 33b). They will be referred to as F terminals.

A <u>polymetric vesicle population</u> is one in which the vesicles range in size from small to large, and vary in shape, being round, oval or flattened (Fig. 33c). The vesicles are sparse. The cytoplasm of the terminal is characteristically very pale and often contains irregular membranous sacs. In addition to these vacuoles, other more definite dendritic characteristics are sometimes present, i.e., rosettes of free ribosomes and numerous microtubules (Fig. 35). This particular profile could be traced back to the cell body in a rare but fortunate plane of section (Fig. 35). The vesicle population appears to correspond closely to those referred to as F_2 by Guillery ('69a), polymorphic by Famiglietti and Peters ('72), or discoid by Lieberman and Webster ('72) and Colonnier ('74). Note that the shape of the vesicles is intermediate in appearance between rounds and flats. In some profiles nearly all vesicles are round, while in others many are quite flat. It is really the considerable variation in size of the vesicles which most typically distinguishes them as a separate group. For this reason, this vesicle population will be called "polymetric", (P); <u>poly</u> is

Figure 33a	Electron micrograph of three RSD terminals contacting dendrites. Magnification 35,000. Inferior Pulvinar.
Figure 33b	Electron micrograph of an RLP terminal (top) and F terminal (bottom). Magnification 35,000. Inferior Pulvinar.
Figure 33c	Electron micrograph of a P profile (bottom) being contacted by an RLP terminal. Magnification 35,000. Inferior Pulvinar.
Figure 33d	Electron micrograph comparing an F terminal (left) and an RSD terminal (right). Magnification 35,000. Inferior Pulvinar.

Figure 33

Figure 34a Electron micrograph of a myelinated RLP terminal contacting a dendrite. Magnification 21,000. Paracentral Nucleus.

Figure 34b Electron micrograph of a longitudinal section of dendrite studded with RSD terminals. Magnification 21,000. Inferior pulvinar.

Figure 34

Figure 35 Electron micrograph of a presynaptic dendrite (P profile, see inset), in continuity with the cell soma. Magnification 7,200 and 28,000. Inferior Pulvinar.

Figure 35

Greek for "many", and is the root most often used by the Greeks for compound words (Treggiari '74), and metron is Greek for "measurement". Thus, a P type profile is characterized by polymetric vesicles, pale cytoplasm and membranous sacs.

Therefore, four types of terminals can be identified in the inferior nucleus of the pulvinar and paracentralis nucleus, the RSD, RLP, F and P profiles, all of which can be seen and compared in a single field in figure 36.

Although four types of synaptic profiles are readily identified, some individual profiles are difficult or impossible to classify. Indeed, the vesicle characteristics occasionally varied considerably even within one element. Nevertheless most profiles containing an adequate number of vesicles were readily identified as belonging to one or the other type.

B. Membrane Specialization

The membrane differentiations towards which the vesicles agglomerate are of two types. In the first, the postsynaptic membrane is bordered by a cytoplasmic opacity giving the contact an asymmetric appearance, as described by Colonnier ('68). This type of contact is formed by both the RSD and RLP terminals (Figs 33a, c),. In contacts formed by the other types of profiles, i.e., the F and the P types, the specialized cytoplasmic postsynaptic opacity is absent, and hence the contacts are more symmetric in appearance (Figs 33[illegible] 36). It is essential to observe this characteristic in sections cut exactly perpendicular to the plane of the membrane specializations. Otherwise, membrane differentiations seen in the oblique plane may appear indistinct or blurred giving the impression of a cytoplasmic opacity regardless of whether it is present or not. In this situation, the membrane differentiation may wrongly be interpreted as asymmetric.

Figure 36a Electron micrographs of an RLP, RSD, F and P profile in one field. Magnification 42,000. Inferior Pulvinar.

Figure 36b Electron micrographs of an RLP, RSD, F and P profile in one field. Magnification 42,000. Paracentral Nucleus.

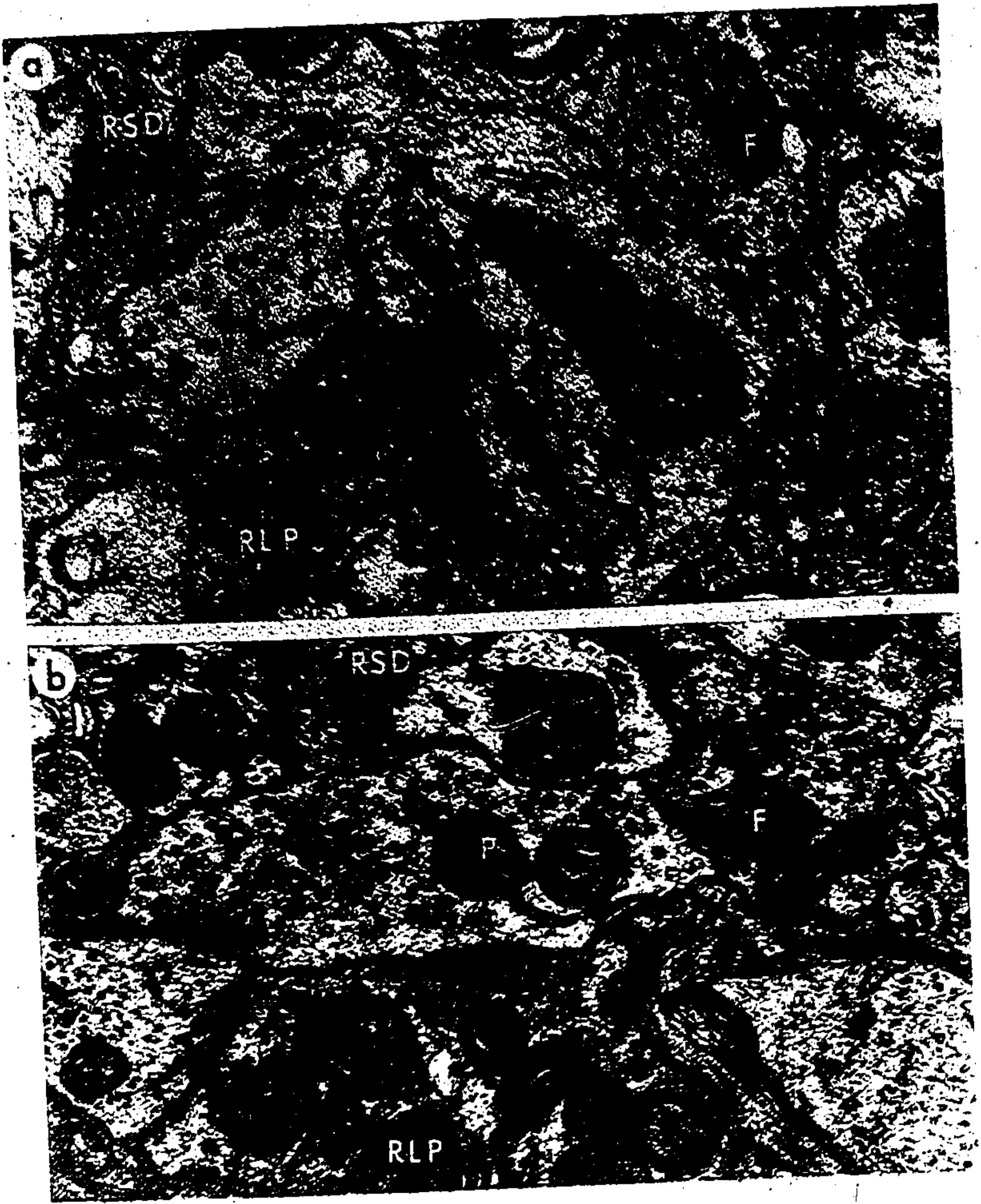


Figure 36

Membrane differentiations also exist between axon terminals and opposed profiles in regions where vesicles do not agglomerate. The membranes are thickened and the interstitial space widens and narrows along the length of the contact. They are usually arranged as an irregular, discontinuous series of up to ten individual specializations forming one large contact (Figs 36a, 37). The length of each zone is much less than a regular synaptic differentiation but the overall length of contact is usually 2-4 times longer than those towards which vesicles agglomerate. Some very long contacts have been observed, up to 4-5 u in length. In the widened gaps between these differentiated membranes, the extracellular material has increased markedly in density. The cytoplasm to each side of these punctate specializations contains an indistinct opacity, usually more apparent on the dendritic side. This results in an uneven patchy appearance along the length of the attachment (Fig. 37a). A suggestion of neurofilaments extending from these opacities can often be observed in the dendrite (Fig. 37b). These are the filamentous contacts described in the introduction. The vesicle-containing element involved in the filamentous contact with a dendrite or soma is commonly the RLP terminal (Fig. 37a), less frequently the P profile (Fig. 37b) and rarely even an F profile (Fig. 41c).

The filamentous contact is often seen between two dendrites, a dendrite and soma or between two somata. In these situations, the region of contact is more symmetrical in appearance because the adjacent cytoplasmic opacities are similar in both components (Fig. 38). The neurofilaments associated with these specializations are especially obvious in oblique cuts (Fig. 38c), but their cut ends can also occasionally be seen as small dark dots in sections perpendicular to the membrane differentiations (Fig. 38a). Transverse sections of neurotubules were sometimes associated with these filaments (Fig. 38a).

Figure 37a Electron micrograph of an RLP terminal forming a filamentous contact (arrows) with a dendrite. Magnification 42,000. Paracentral Nucleus.

Figure 37b Electron micrograph of a P profile (left) forming a filamentous contact with a dendrite. An RLP terminal can also be seen contacting the same dendrite over a substantial distance as well as contacting a small P profile (lower right). Magnification 26,000. Inferior Pulvinar.

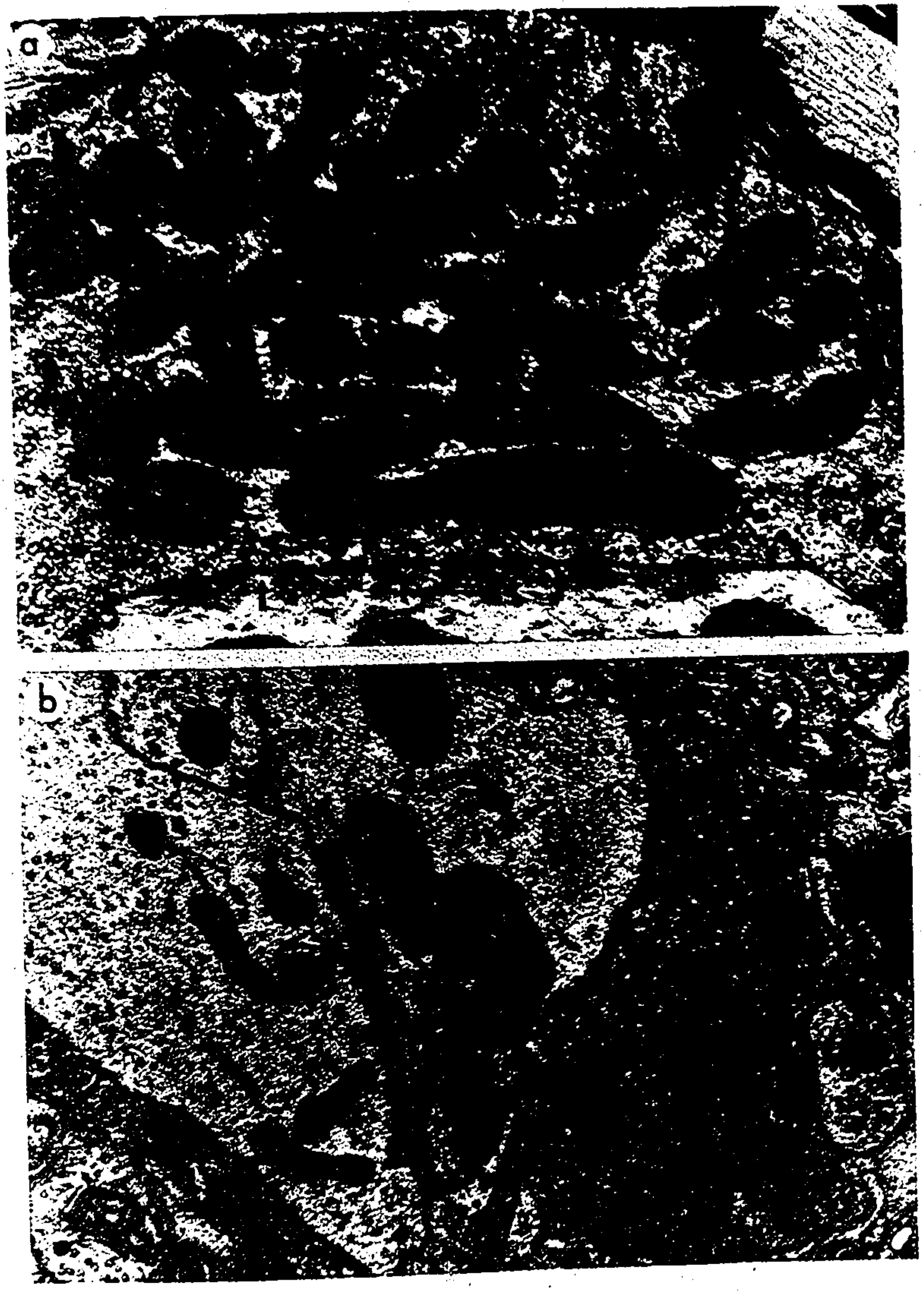


Figure 37

Figure 38a Electron micrograph of a dendrodendritic filamentous contact. The microtubules have been sectioned longitudinally in the one profile and transversely in the other. Magnification 36,500. Inferior Pulvinar.

Figure 38b Electron micrograph of a somatodendritic filamentous contact. Magnification 41,500. Inferior Pulvinar.

Figure 38c Electron micrograph of a dendrodendritic contact sectioned obliquely in which the neurofilaments associated with the contact are clearly shown. An RLP terminal packed with vesicles can be seen forming a lengthy synaptic contact with one of the dendrites. Magnification 36,000. Inferior Pulvinar.

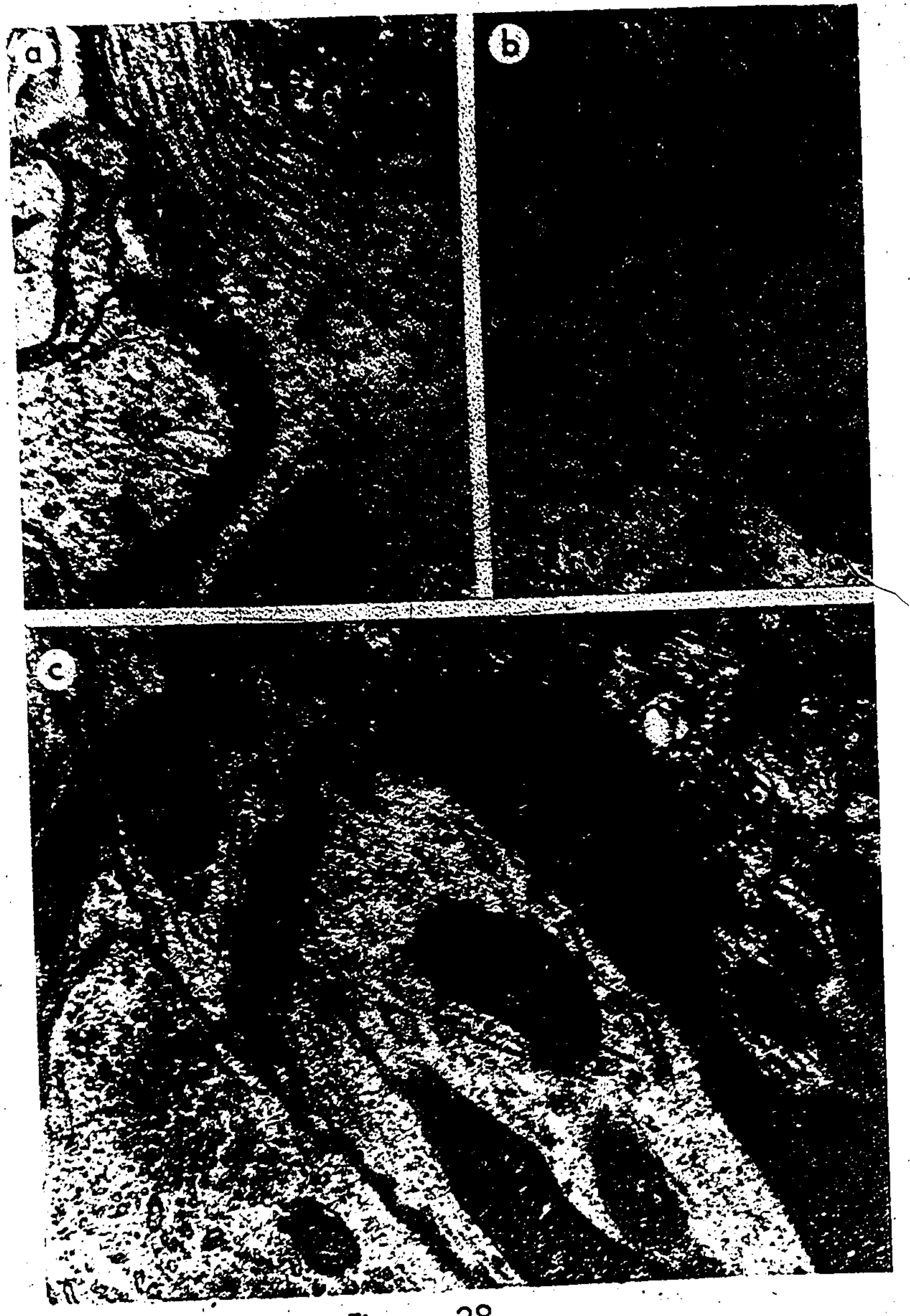


Figure 38

C. Synaptic Organization

The synaptic organization of the inferior nucleus of the pulvinar and the paracentral nucleus are essentially similar, and will be described together. It was felt, however, that certain quantitative differences existed and these will be noted in the text. A quantitative analysis would be necessary to confirm the exactness of these differences.

The majority of contacts in the inferior nucleus of the pulvinar and paracentral nucleus consist of the RSD type, which by far outnumber all the others. They sometimes cluster in large groups giving the impression of "synaptic islands" consisting almost exclusively of RSDs (Fig. 39a). They form asymmetric contacts with both small and large dendrites (Figs 33a, 39c). Several RSD contacts were often found along a dendrite sectioned longitudinally (Fig. 34b), or surrounding a dendrite cut transversely. Dendrites studded with RSDs seemed more characteristic of the pulvinar than of the paracentral nucleus where the RSD profiles are more scattered. Some RSD terminals also contact the P profiles (Fig. 39b). This is seen rather regularly in the inferior nucleus of the pulvinar but is rare in the paracentral nucleus.

The RLP terminals usually contact large dendrites, some of which contain numerous polyribosomes, indicating that they are proximal dendrites close to the cell body (Fig. 40a). These RLPs are themselves often very large and appear to dominate the large dendrite by partially surrounding it (Fig. 40b). Others synapse on smaller, more distal dendrites (Fig. 40c). In rare instances they have been also seen on cell bodies. They form both filamentous and asymmetric contacts (Fig. 40a). These are usually separate one from the other along the membranes, but are sometimes in continuity (Fig. 40a). They are often seen forming asymmetric contacts with P profiles, but always as the presynaptic component (Figs 33c, 36b, 40a). In

Figure 39a Electron micrograph of a field of mainly RSD terminals. Magnification 25,000. Inferior Pulvinar.

Figure 39b Electron micrograph of an RSD terminal contacting a P profile. Magnification 48,000. Paracentral Nucleus.

Figure 39c Electron micrograph to show two RSD terminals contacting a large dendrite (arrows). Magnification 32,000. Inferior Pulvinar.

Figure 39

Figure 40a Electron micrograph of an RLP terminal contacting a small P profile (right) and a large proximal dendrite with ribosomes. A synaptic contact in continuity with a filamentous contact can be seen (arrow). Magnification 27,500. Inferior Pulvinar.

Figure 40b Electron micrograph of an RLP terminal partially surrounding a dendrite. Magnification 21,000. Inferior Pulvinar.

Figure 40c Electron micrograph of an RLP terminal contacting two small dendrites. Magnification 44,000. Paracentral Nucleus.

Figure 40d Electron micrograph of an RLP terminal forming a rather long synaptic contact with a dendrite. Magnification 38,500. Inferior Pulvinar.

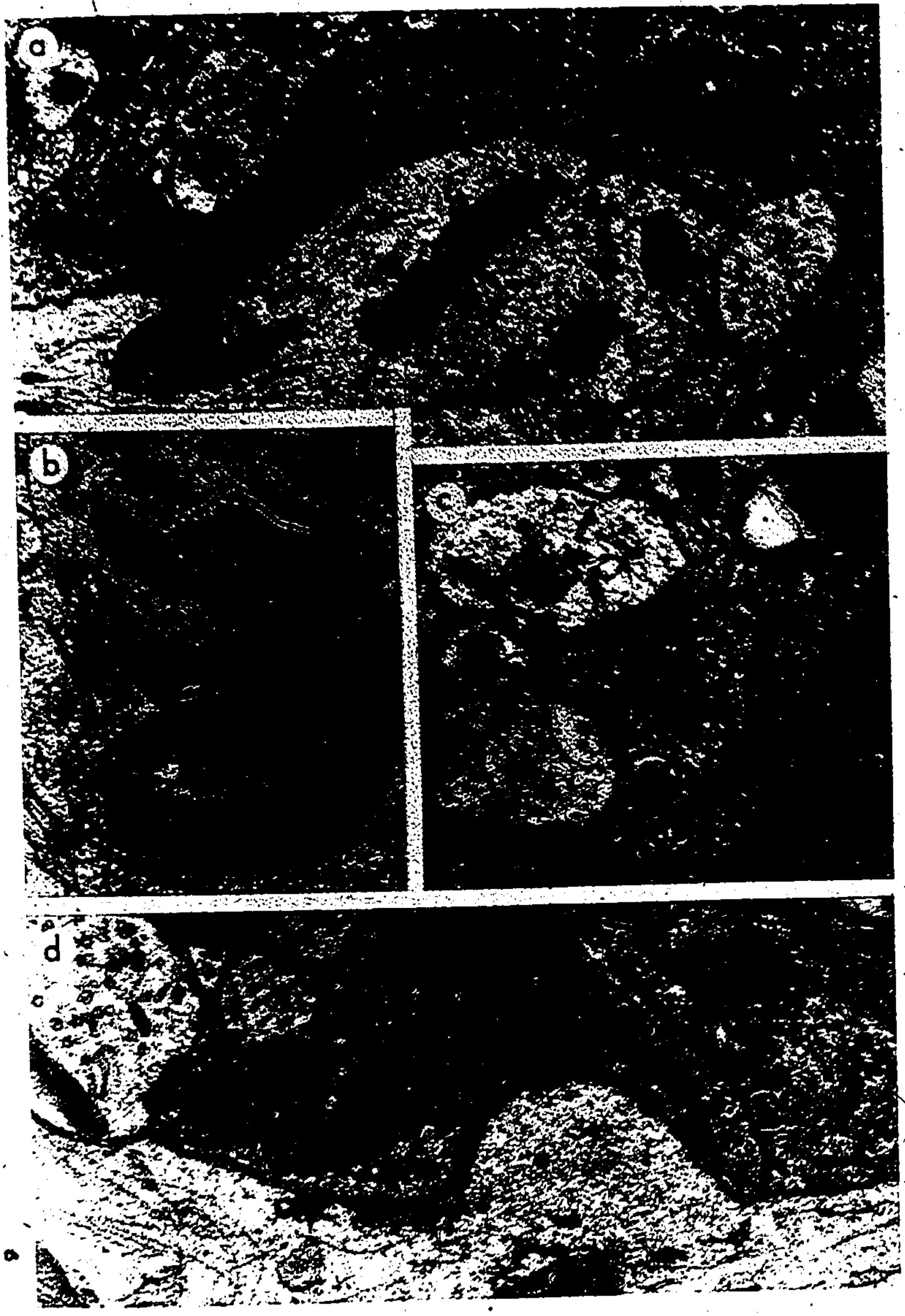


Figure 40

some profiles where the vesicle population is relatively dense, the region of synaptic membrane differentiation is markedly increased in length (Figs 37b, 38c, 40d).

Most F terminals form symmetric synaptic contacts with both large and small dendrites (Figs 41a, b), neuronal soma (Fig. 41c) and less frequently with P profiles (Fig. 41d). A single profile often takes part in several contacts (Fig. 41a). The F profile has been observed in filamentous contact with the soma of cells in the paracentral nucleus (Fig. 41c), but this has not been observed with certainty in the inferior nucleus of the pulvinar. F terminals are not as common as RSDs or RLPs in either the pulvinar or paracentral nucleus, but seem to be more frequent in the paracentral nucleus than in the inferior nucleus of the pulvinar.

The P profile forms symmetric types of contact usually with medium to large-sized dendrites (Fig. 42a) and seldom with the finer, presumably more distal dendrites. Occasionally, they are also involved in filamentous contacts with dendrites (Fig. 37b). It is surprising to see how infrequently these often-occurring profiles are actually forming the presynaptic element of a synaptic contact. The P profile is most often seen as a postsynaptic element, commonly in relation to the RLP terminal (Figs 33c, 36b, 40a), and less frequently with the F (Fig. 41d), RSD (Fig. 39b) and other P profiles (Fig. 43a). No record of a P profile postsynaptic to the F profile is available for the inferior nucleus of the pulvinar, but this may have been a sampling problem since Fs, as stated earlier, are relatively rare in this nucleus. Serial relationships could be seen in a single plane of section, in which the postsynaptic P profile was also presynaptic to a dendrite (Fig. 43). In figure 43c, a serial synapse consisting of an RLP-P-dendrite series, as well as a F-P-dendrite relationship is illustrated, in which the same P profile is involved in both serial arrangements.

Figure 41a Electron micrograph of an F terminal forming three synaptic contacts with dendrites. Magnification 30,000. Inferior Pulvinar.

Figure 41b Electron micrograph of an F terminal contacting a large dendrite (arrow). Magnification 31,000. Inferior Pulvinar.

Figure 41c Electron micrograph of an F terminal contacting the cell soma. Magnification 36,000. Paracentral Nucleus.

Figure 41d Electron micrograph of a large F terminal contacting a P profile (arrow). Magnification 30,000. Paracentral Nucleus.

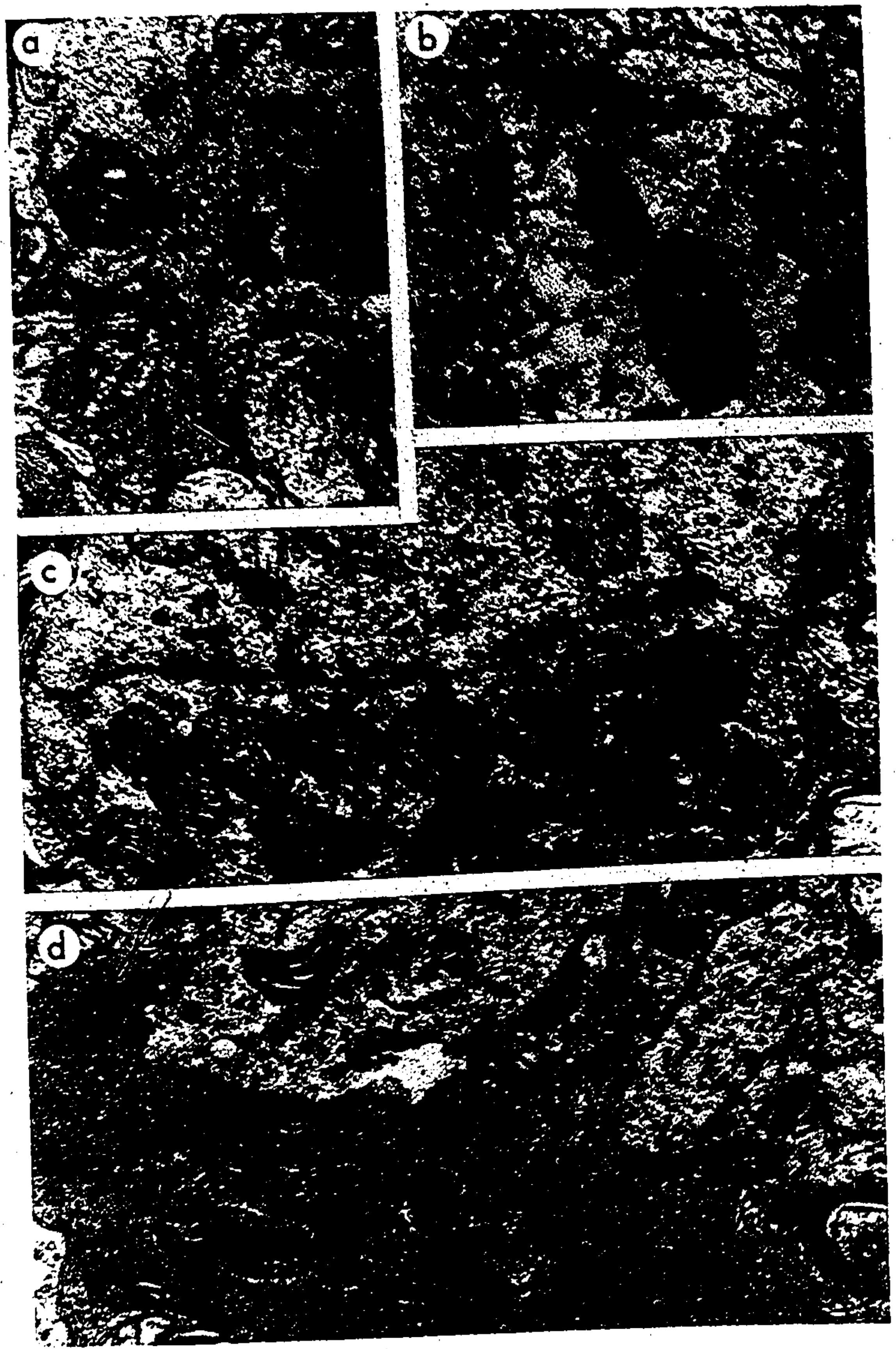


Figure 41

Figure 42a Electron micrograph of a P profile contacting a dendrite. Note the membranous whorls in this profile apparently in continuity with an adjacent vesicle-containing profile. Magnification 33,500. Inferior Pulvinar.

Figure 42b Electron micrograph of several P profiles surrounding a dendrite in the paracentral nucleus. Magnification 35,000. Paracentral Nucleus.

Figure 43a Electron micrograph of a serial synaptic arrangement P-P-dendrite (arrows). Magnification 39,000. Inferior Pulvinar.

Figure 43b Electron micrograph of a serial synaptic arrangement, RSD-P-dendrite (arrows). Magnification 28,000. Inferior Pulvinar.

Figure 43c Electron micrograph of two serial synaptic arrangements with the same intermediate P profile (bottom), RLP (upper left)-P-dendrite and F (upper right)-P-dendrite. Magnification 28,000. Paracentral Nucleus.

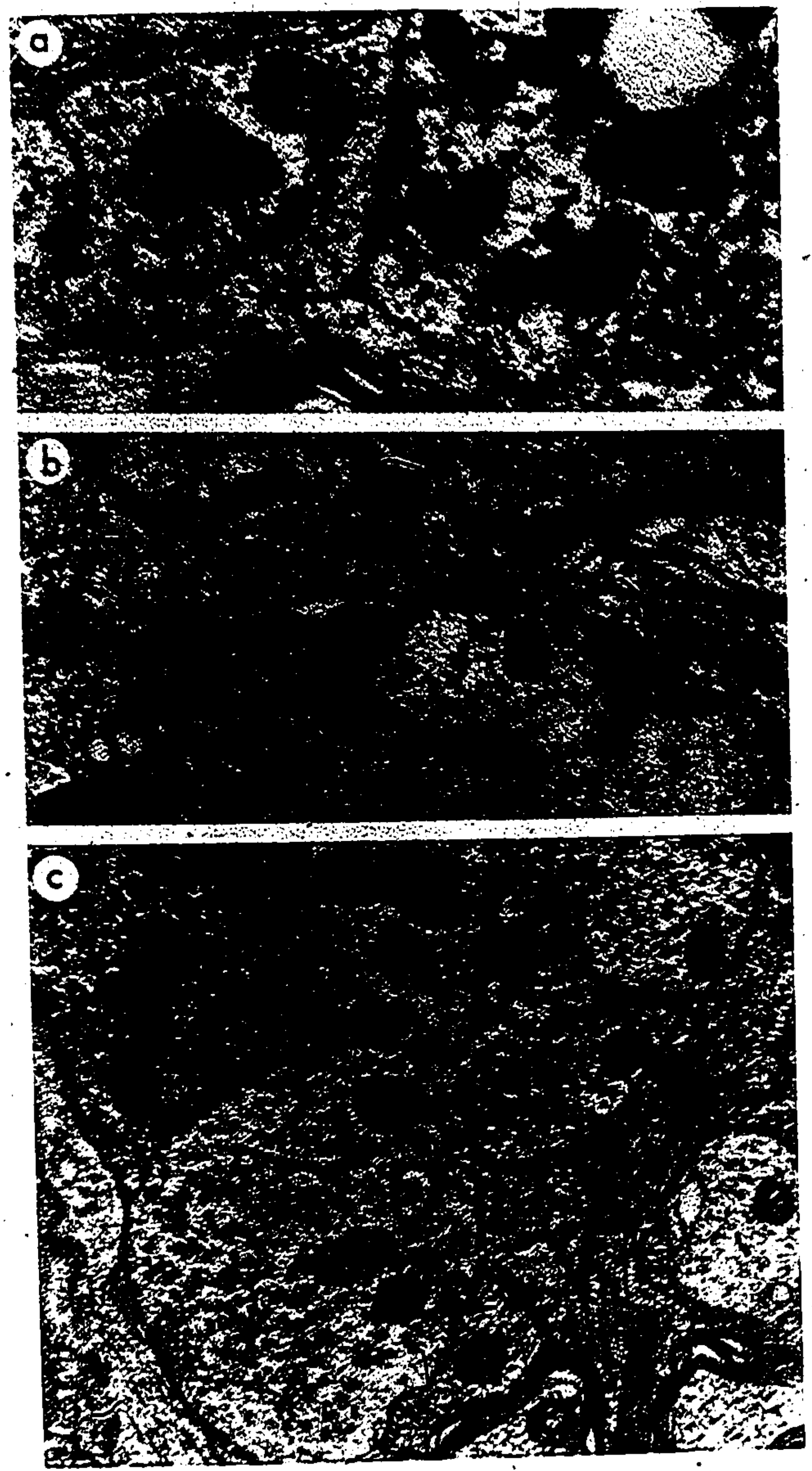


Figure 43

In the paracentral nucleus, the P profile seemed to be more abundant than in the inferior nucleus of the pulvinar. Clusters of these profiles were often found presynaptic to a dendrite (Fig. 42b), similar to the clusters of RSDs contacting a dendrite in the inferior nucleus of the pulvinar (compare Fig. 34b).

The triadic synaptic relationship was only occasionally observed in the paracentral nucleus and the inferior nucleus of the pulvinar. In this situation, a first vesicle-containing profile was presynaptic to both a P profile and dendrite, and the P profile was presynaptic to the same dendrite (Figs 44a, c). In most instances, the first vesicle-containing profile was clearly an RLP. In at least one recorded example (Fig. 44b), it was not an RLP, but either an F or a P. Some might even be interpreted as RSDs as in figure 44d.

Neither the inferior nucleus of the pulvinar, nor the paracentral nucleus was organized in such a manner that clusters of neuronal elements, i.e., synaptic islands or glomeruli, could be distinguished from the surrounding neuropil. Rather, the individual contacts of the four types of terminals on dendrites or serial and triadic arrangements were found scattered throughout. Figure 45 shows a typical example of the neuropil. Only when individual dendrites were densely studded with RSDs or Ps, did it seem appropriate to speak of synaptic agglomerations. This arrangement, however, does not correspond to the synaptic islands or glomeruli of the literature.

A rather unusual arrangement of the smooth endoplasmic reticulum was often observed in various neuronal profiles. Complex membranous whorls were often found within neuronal profiles, i.e., axon terminals (Fig. 46a) and dendrites (Fig. 46b). They seemed to consist of an invagination of the cytoplasmic membrane, together with that of an adjoining neuronal profile (Figs 42a, 46c).

Figure 44a Electron micrograph of a triadic synaptic arrangement with an RLP (upper right) as the first component. Magnification 35,000. Inferior Pulvinar.

Figure 44b Electron micrograph of a triadic arrangement with an F or P (centre) as the first component. Magnification 35,000. Inferior Pulvinar.

Figure 44c Electron micrograph of a triadic arrangement with an RLP (top) as the first component. Magnification 30,000. Inferior Pulvinar.

Figure 44d Electron micrograph of a triadic arrangement with an RSD (lower centre) as the first component. Magnification 30,000. Paracentral Nucleus.

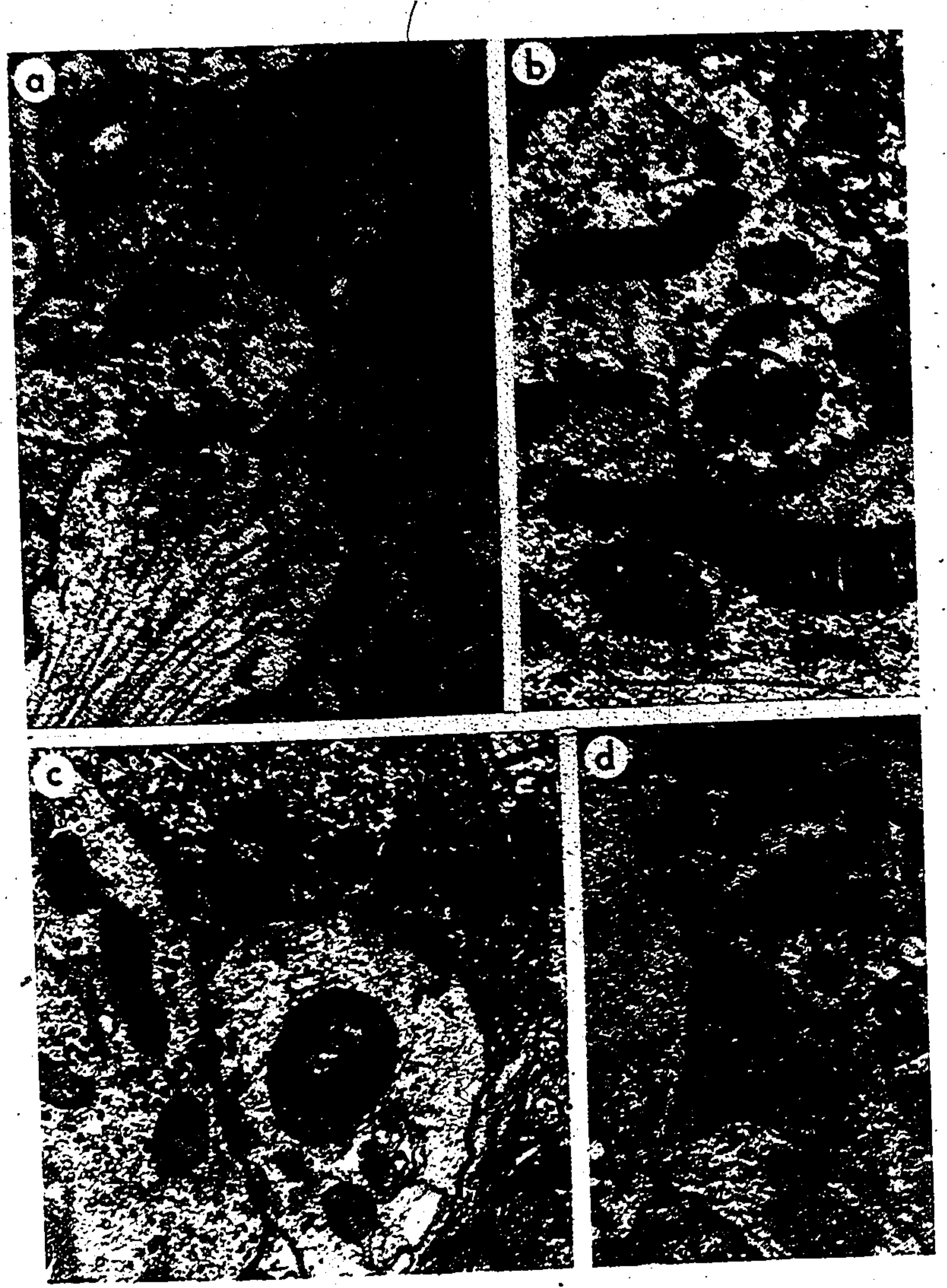


Figure 44

Figure 45 Electron micrograph of a typical field in the inferior nucleus of the pulvinar or the paracentral nucleus. Magnification 19,000. Inferior Pulvinar.

Figure 45

Figure 46a Electron micrograph of whorls of membranous material in a vesicle-containing profile apparently in continuity with a second vesicle-containing profile. Magnification 48,000. Inferior Pulvinar.

Figure 46b Electron micrograph of whorls of membranous material in a dendrite. Magnification 42,000. Paracentral Nucleus.

Figure 46c Electron micrograph of whorls of membranous material between an axon and dendrite. Magnification 42,000. Paracentral Nucleus.

Figure 46

D. Degeneration Study

i) Synaptic Types Undergoing Degeneration

The pattern of degeneration in the inferior nucleus of the pulvinar, and the paracentral nucleus, was the same at one, three, five and seven days, following lesions of the superior colliculus. The majority of degenerating terminals were of the RLP type, while a lesser number resembled the RSD. All affected profiles underwent dense degeneration directly, with no indication of neurofilamentous hyperplasia. The onset of degeneration was rapid, with characteristics of dense degeneration present as early as one day after the lesion. Occasionally fields were observed with large amounts of degenerating debris (Fig. 47), but this was exceptional. Usually, only scattered, isolated fragments were found.

Most degenerating terminals could be identified by their size and membrane specialization. The large RLP profile was the type most frequently seen to undergo degeneration. It was clearly identifiable by its large size and abundant synaptic vesicles (Fig. 48a). The membrane differentiation could often be identified as asymmetric (Fig. 48b) or filamentous (Fig. 48c). In some cases, both types of contacts were observed as part of one degenerating profile (Fig. 48d). A lesser number of degenerating terminals could be interpreted as RSDs because of their small size, their densely packed vesicles and their asymmetric contacts (Fig. 49). These criteria, however, are not reliable, as will become clear when the stages of degeneration have been fully described.

ii) Stages of Degeneration

In all preparations some profiles were only slightly changed from the normal, whereas others were greatly altered. It was the amount of change in a profile from its normal configuration that was used to interpret the

Figure 47 Electron micrograph of a field with several degenerating profiles after a large lesion in the superior colliculus. Magnification 17,000. Inferior Pulvinar. 7 day survival.

Figure 47

Figure 48a Electron micrograph of a degenerating RLP terminal. Magnification 28,000. Inferior Pulvinar. 1 day survival.

Figure 48b Electron micrograph of two degenerating RLP terminals forming asymmetric contacts with a dendrite. Magnification 28,000. Inferior Pulvinar. 3 day survival.

Figure 48c Electron micrograph of a degenerating RLP profile forming a filamentous contact with a dendrite. Magnification 28,000. Inferior Pulvinar. 7 day survival.

Figure 48d Electron micrograph of a degenerating RLP profile forming both a synaptic and filamentous contact with a dendrite. Magnification 28,000. Paracentral Nucleus. 7 day survival.

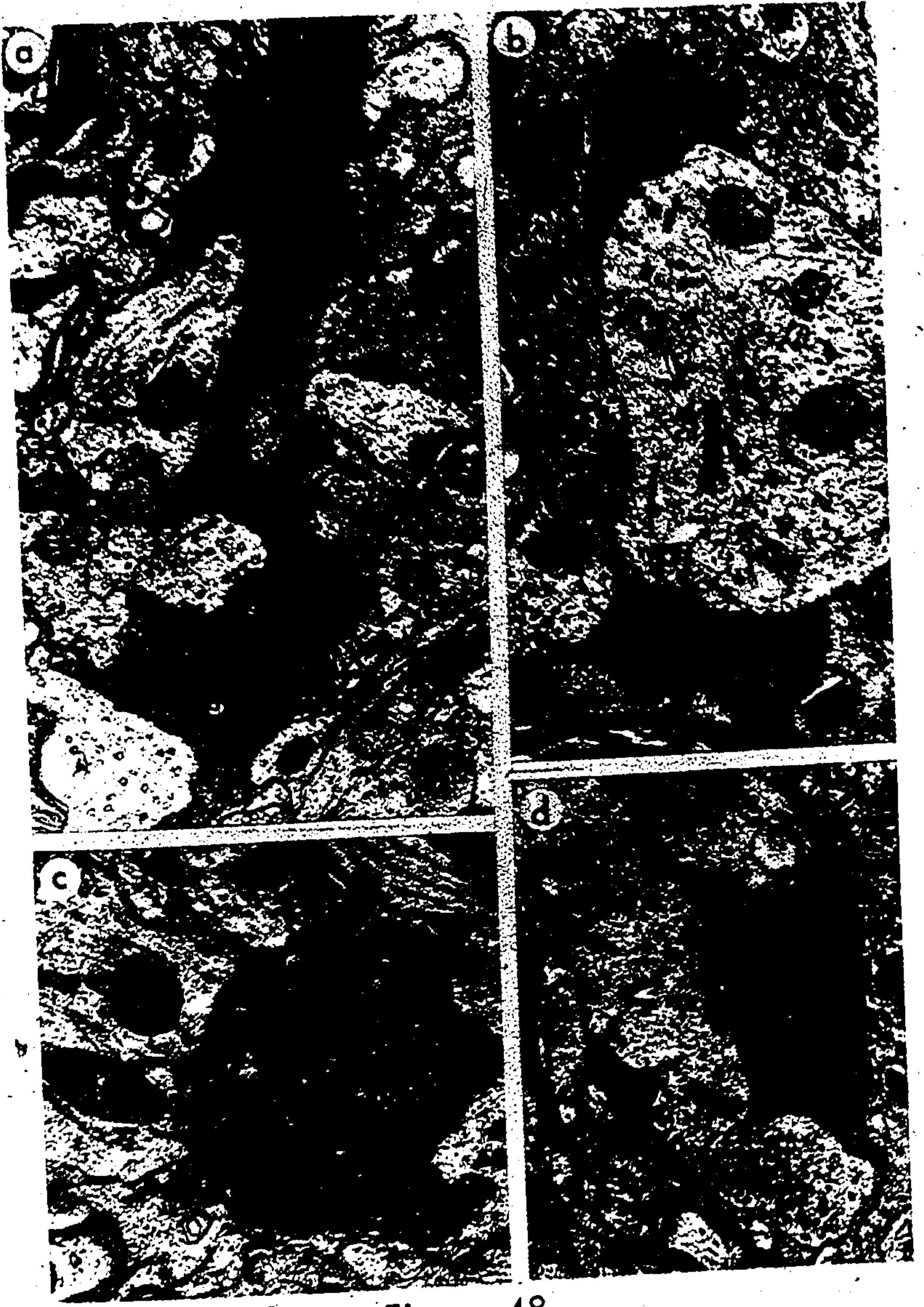


Figure 48

Figure 49a Electron micrograph of a small degenerating profile resembling an RSD. Magnification 35,000. Inferior Pulvinar. 3 day survival.

Figure 49b Electron micrograph of a small degenerating profile contacting a large dendrite. Magnification 40,000. Inferior Pulvinar. 7 day survival.

Figure 49c Electron micrograph of a small degenerating profile resembling an RSD. Magnification 40,000. Paracentral Nucleus. 7 day survival.

Figure 49d Electron micrograph of a degenerating RSD terminal contacting the same dendrite with several normal RSDs. Magnification 40,000. Inferior Pulvinar. 5 day survival.

Figure 49e Electron micrograph of a small degenerating terminal contacting a normal P profile. Magnification 35,000. Inferior Pulvinar. 5 day survival.

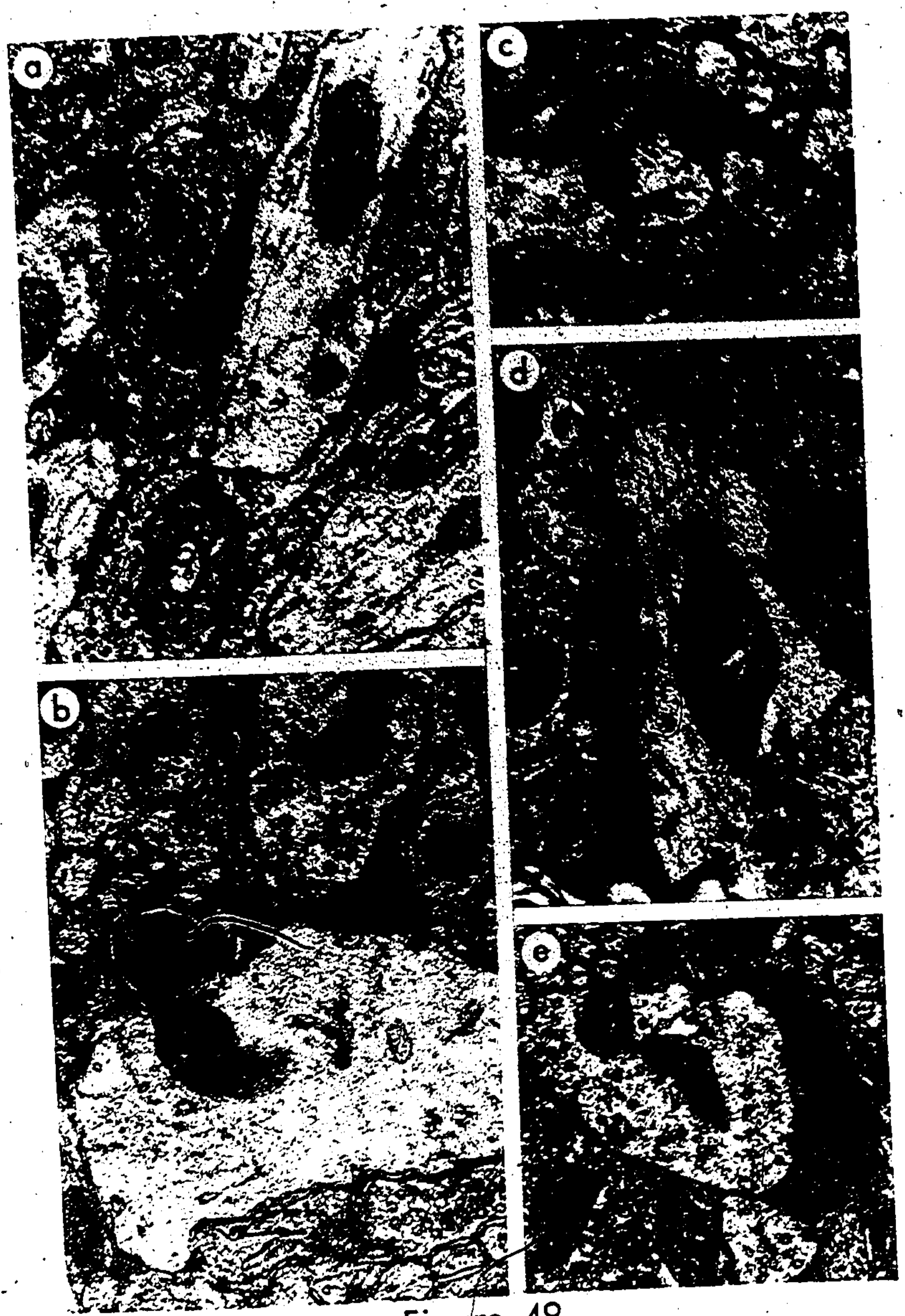


Figure 49

various stages of degeneration, i.e., the lesser changes were considered to be the earlier events, whereas the more marked changes were interpreted as later stages. The degenerating profiles were often seen at the different survival times to be in many different stages of degeneration, the earlier stages being found mainly in the shorter survival days, and the later ones at longer survivals. There was, however, a considerable amount of overlap. What would be interpreted as late degeneration could be seen even at one day, while "early changes" were still present later. Degeneration seems to proceed according to the following sequence of events.

At the earliest stages, profiles are dark gray in appearance, but the contents of these profiles are fairly normal (Fig. 50a). These terminals were darker than the surrounding vesicle-containing profiles, but not as dark as in later stages of degeneration when the cytoplasm is very densely electron-opaque (Figs 48b, 50b, c). At this stage, some degenerating terminals are found crowded with vesicles, presumably due to shrinkage of the profile (Figs 48c, 50d). In others, the swollen and sometimes clear synaptic vesicles are found scattered throughout the profile (Fig. 50c), or in clumps, often independent of the membrane differentiations (Fig. 50b). The structure of the mitochondria appears to break down. At later stages, the degenerating profiles become more shrunken and distorted, and some change their relationship to glial profiles which now become opposed to them over widespread areas, as if to engulf them (Fig. 51a). These glial profiles often contain glycogen-like particles (Fig. 51b). The distortion at this stage gives rise in the neuropil to long, finger-like extensions of the remaining parts of degenerating profiles (Figs 51a, b). At this stage, many membrane differentiations between axons and dendrites remain well-preserved (Figs 51a, b). In the final stage, the degenerating component is completely surrounded by a single glial profile (Fig. 51c). Sometimes the postsy-

Figure 50a Electron micrograph of an RLP terminal in an early stage of degeneration. Magnification 28,000. Paracentral Nucleus. 1 day survival.

Figure 50b Electron micrograph of an RLP terminal in a later stage of degeneration, with clumping of synaptic vesicles and mitochondria partially broken down. Magnification 24,000. Paracentral Nucleus. 5 day survival.

Figure 50c Electron micrograph of a degenerating RLP terminal with scattered synaptic vesicles. Magnification 32,000. Inferior Pulvinar. 5 day survival.

Figure 50d Electron micrograph of a degenerating RLP terminal packed with synaptic vesicles. Magnification 28,000. Inferior Pulvinar. 3 day survival.

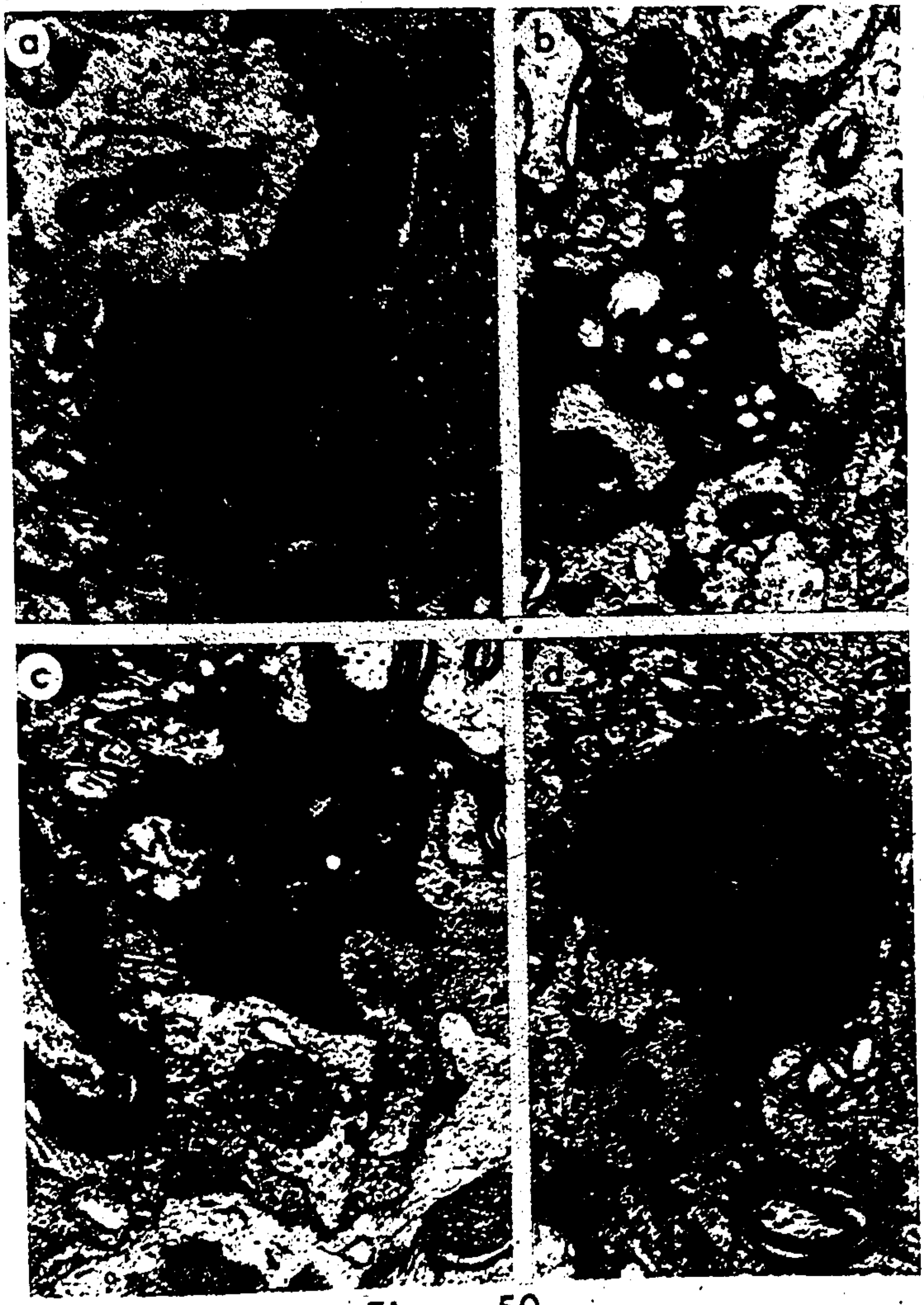


Figure 50

Figure 51a Electron micrograph of a degenerating RLP terminal partially surrounded by glia. Note the shrunken appearance of the profile with its finger-like extensions. Magnification 24,000. Inferior Pulvinar. 7 day survival.

Figure 51b Electron micrograph of a degenerating RLP terminal almost entirely surrounded by glia. Note the long finger-like extension of this shrunken profile. Magnification 28,000. Inferior Pulvinar. 5 day survival.

Figure 51c Electron micrograph of a degenerating RLP terminal completely surrounded by glia. Note the numerous glycogen-like granules in the glial element. Magnification 32,000. Inferior Pulvinar. 5 day survival.

Figure 51d Electron micrograph of a degenerating RLP terminal with its postsynaptic element completely surrounded by glia. Note the absence of glycogen granules in the glial profile. Magnification 28,000. Inferior Pulvinar. 5 day survival.

Figure 51

naptic element is also incorporated (Fig. 51d).

It is evident from the preceding description that the characteristics of profile size and vesicle packing, are no longer reliable criteria for differentiating the degenerating RLP terminal from the degenerating RSD. For example, the degenerating profile seen in figure 52a, though quite small, could easily be interpreted as a section through an RLP.

iii) Synaptic Relations of Degenerating Terminals

The distribution of those degenerating terminals which are obvious RLPs in experimental material, is similar to the distribution of RLPs in normal material. The profiles are observed to contact dendrites of all sizes (Figs 48b, 51a, 52b) and very rarely the cell soma. They often form the presynaptic element of contacts with P profiles (Figs 52c, d), and are infrequently seen as the initial component of a triadic synaptic arrangement (Fig. 52e).

The distribution of the degenerating terminals which could be interpreted as RSDs, is similar to that found in normal material, being located on dendrites of all sizes (Figs 49a, b, c), and also occasionally presynaptic to P terminals (Fig. 49e). Some of these terminals were occasionally seen on dendrites studded with normal RSDs (Fig. 49d).

iv) Unusual Degenerating Terminals

In one case, in which the lesion was very large and may have even encroached on the medial nucleus of the pulvinar, degenerating profiles were observed in the inferior nucleus of the pulvinar that resembled the P profile; i.e., darkened vesicle-containing profiles were found postsynaptic to normal RLP terminals (Fig. 53a).

Rarely, degenerating profiles that resembled dendrites were observed.

Figure 52a Electron micrograph of a shrunken degenerating profile that is difficult to classify. Magnification 31,000. Inferior Pulvinar. 7 day survival.

Figure 52b Electron micrograph of a degenerating RLP profile contacting a small dendrite. Magnification 31,000. Paracentral Nucleus. 5 day survival.

Figure 52c Electron micrograph of a degenerating RLP terminal contacting a normal P profile. Magnification 31,000. Inferior Pulvinar. 5 day survival.

Figure 52d Electron micrograph of a degenerating RLP terminal contacting two normal P profiles. Magnification 32,000. Paracentral Nucleus. 5 day survival.

Figure 52e Electron micrograph of a degenerating RLP terminal forming a triadic relationship with a P profile and dendrite. Magnification 31,000. Inferior Pulvinar. 5 day survival.

Figure 52

in experimental material (Fig. 53c). In this case, a profile containing many neurotubules is postsynaptic to several boutons. In one instance, an opaque, large dendrite was seen forming a filamentous contact with another large dendrite (Fig. 53b).

A rather unusual type of profile, apparently undergoing some type of degeneration, was sometimes observed in either the paracentral nucleus or the inferior nucleus of the pulvinar. The p~~rofile~~s are large, and contain several rounded, electron-opaque structures not seen in normal material. These electron-opaque structures are sometimes found interspersed in the cytoplasm with normal-looking mitochondria (Fig. 54a). They appear to contain membranous whorls and some dense amorphous material. They are also found in profiles with darker cytoplasm in which normal mitochondria are not present (Fig. 54b). In other instances, they seem to occupy most of the profile whose cytoplasm becomes intensely opaque (Figs 54c, d).

Figure 53a Electron micrograph of a degenerating vesicle-containing profile postsynaptic to a normal RLP terminal. Magnification 35,000. Inferior Pulvinar. 1 day survival.

Figure 53b Electron micrograph of a degenerating dendrite forming a filamentous contact with a normal dendrite. Magnification 35,000. Inferior Pulvinar. 1 day survival.

Figure 53c Electron micrograph of a degenerating dendrite being contacted by several vesicle-containing profiles. Magnification 35,000. Inferior Pulvinar. 7 day survival.

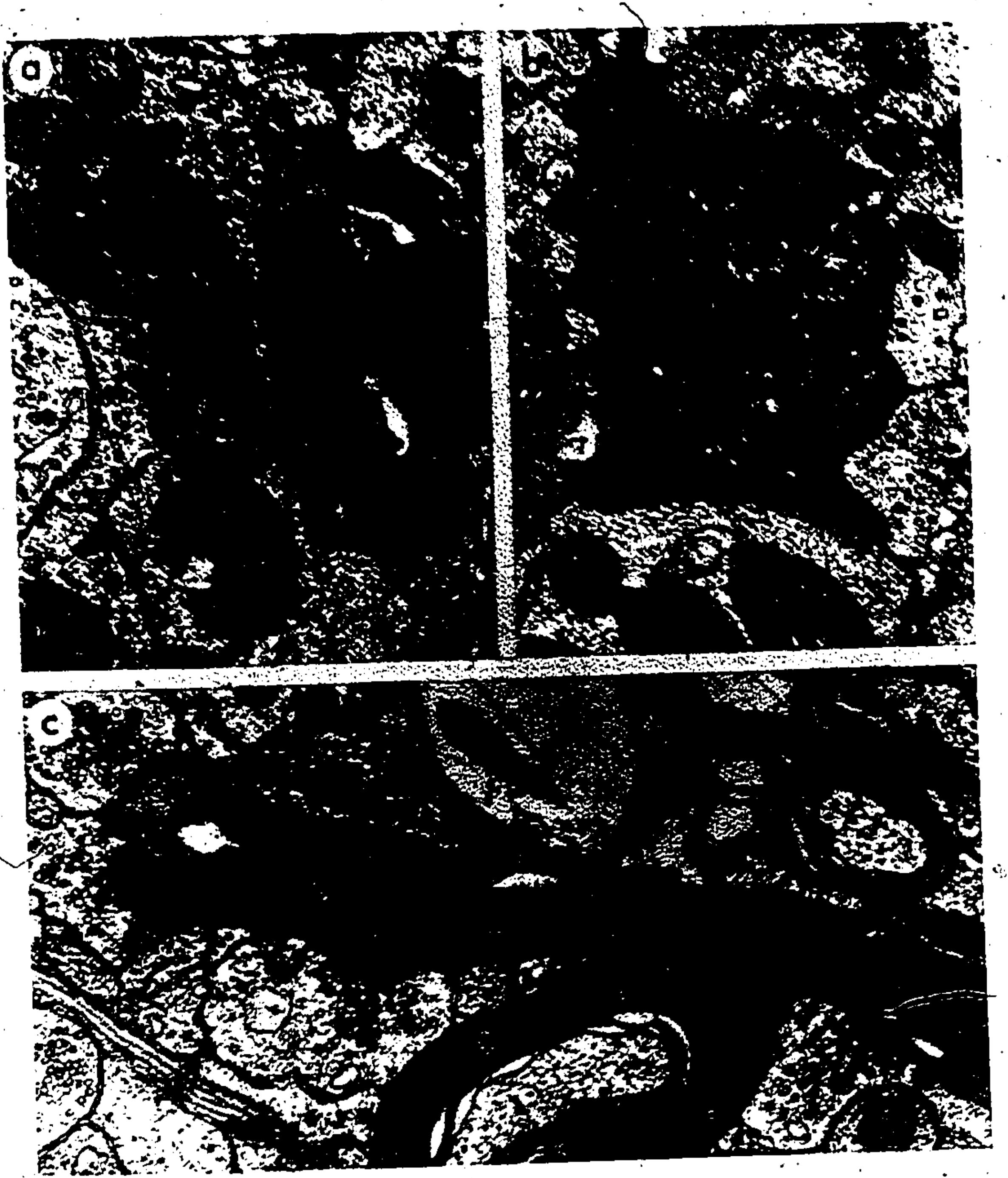


Figure 53

Figure 54 Electron micrographs of four rather atypical profiles in various stages of degeneration. Magnification 28,000.

Figure 54a Paracentral Nucleus. 3 day survival.

Figure 54b Inferior Pulvinar. 5 day survival.

Figure 54c Inferior Pulvinar. 5 day survival.

Figure 54d Inferior Pulvinar. 3 day survival.

Figure 54

DISCUSSION

I. Light Microscopy

The present study has demonstrated that the superior colliculus sends a major projection to the inferior nucleus of the pulvinar in the rhesus monkey, Macaca mulatta. This confirms the recent reports of a tectopulvinar projection in higher primates (Mathers '71, in the squirrel monkey; Benevento and Fallon '74, in the macaque). Degeneration was not observed throughout the entire inferior nucleus of the pulvinar but the largest lesions of the superior colliculus were not sufficiently large to destroy the entire structure. Nevertheless, accumulation of the results from all lesions indicates that this projection extends to all parts of the inferior nucleus of the pulvinar as defined cytoarchitechtonically by Friedeman ('12), Crouch ('34) and Walker ('38). This area corresponds to Hasslers' ('59) intergeniculate nucleus, pars griseum but excludes the more laterally placed pars fasciculosus. In earlier studies, this latter area was considered part of the lateral nucleus of the pulvinar, pars inferior (Crouch '34) or pn (Vogt '09, Friedeman '12). The present results support this early view, that the inferior nucleus does not continue laterally to the external medullary lamina (as indicated by Olszewski '52), but rather the lateral nucleus of the pulvinar extends ventrally, at levels posterior to the lateral geniculate nucleus, to form the lateral border of the inferior nucleus. The possibility still exists that this part of the lateral nucleus is functionally distinct from its superior portion adjacent to the medial nucleus of the pulvinar. The present results do not permit comment on this point.

It has been suggested that the superior colliculus of the monkey projects to only part of the inferior nucleus of the pulvinar (as now defined). Mathers ('71) found on the basis of four experimental animals, that the superior colliculus projects only to the ventromedial aspect of the inferior nucleus. Another report (unpublished observations of Snyder, Johnson and Mishkin, as cited by Diamond et al. '70) indicated that the colliculus projects only to that part of the inferior nucleus adjacent to the lateral geniculate nucleus. It is now evident from this more complete study that these authors were only partly correct. The results demonstrate that the superior colliculus projects at least dorsally as well as to these other sites. Although degeneration was not observed ventrolaterally, the most reasonable interpretation of the data would be that the colliculus does indeed project to the entire nucleus.

An important criterion for establishing homologies of the central nervous system in different species is the connectional patterns of a particular nucleus. Therefore, as one of the major recipients of tectal fibers, the inferior nucleus of the pulvinar appears homologous to the nucleus rotundus in reptiles (Hall and Ebner '70) and in birds (Revzin and Karten '66), to the lateral posterior nucleus in nonprimate mammals (e.g., Altman and Carpenter '61, Abplanalp '70, Harting et al. '72) and to the pulvinar of lower primates (Casagrande et al. '72, Harting et al. '73).

The present study has demonstrated that the tectopulvinar projection in the macaque is topographically organized. This fulfils the spatial requirements of a system involved in visual localization and provides further evidence for a spatially-organized pathway that can function independent of the geniculostriate system.

The topographical representation that has been established in this study is consistent with the reports of Campos-Ortega and Hayhow ('72) in the macaque, and Allman et al. ('72) in the owl monkey. Although the exact location of the horizontal and vertical meridian varies somewhat, these minor differences probably depend on the differences in species, as well as on variations in the visual maps on which these studies were based. Campos-Ortega and Hayhow ('72) determined the pattern of anterograde degeneration in the inferior nucleus of the pulvinar following discrete lesions in the primary visual cortex. This pattern was interpreted in terms of visual field parameters using the cortical visual maps of Talbot and Marshall ('41) and Daniel and Whitteridge ('61). Allman et al. ('72) carried out neurophysiological recordings in the inferior nucleus of the pulvinar placing small slits of light in various parts of the visual field, and hence determined directly the representation of the visual field in this nucleus.

In the present results, the interpretation of the pattern of degeneration in the inferior nucleus of the pulvinar was based on the data available for the representation of the visual field in the superior colliculus. Three reports have described the visual map in the superior colliculus of the macaque, i.e., anterograde degeneration studies of the retinotectal projection (Wilson and Toyne '70), neurophysiological recordings of the visual sensory input (Cynader and Berman '72) and observations of eye movements evoked by collicular stimulation (Robinson '72). These maps are very similar although some differences exist, mostly at the periphery. The variations can likely be attributed to the difficulties in presenting a two-dimensional surface view of the superior colliculus that accurately represents the steep curvature of the posterior and lateral aspects of this structure.

Nevertheless, it has been established that the visual field is precisely represented in the inferior nucleus of the pulvinar and its general topography has been established in three distinct studies, i.e., an electrophysiological study of visual input (Allman et al. '72), an anterograde degeneration study of the input from striate cortex (Campos-Ortega and Hayhow '72) and the present anterograde degeneration study of the tectal input.

Difficulties were encountered in the present study in determining the amount and the site of the visual field destroyed by the lesion. Serial sections of the superior colliculus successively represent more of the surface as one progresses posteriorly in the frontal plane, or laterally in the sagittal plane. Therefore, a vertically placed lesion at the posterior or lateral margin of the colliculus destroys much more of the surface area than a lesion of similar size placed in the centre of this structure. Also because of the surface curvature, a lesion extending to deeper layers involves a greater area of the visual field than the damage observed at the surface. This fact may account for the continuous field of degeneration in the animals with two distinctly separate lesions at the surface.

Certain areas of the superior colliculus were untouched by any of the lesions made in this study, e.g., the most anterolateral border and part of the anteromedial aspect. However, once the general topography has been determined it is easy to extrapolate the probable site of termination of these areas. Therefore it was not considered essential to carry out further experiments to obtain this data.

More discrete lesions confined to the superficial layers and distributed in all parts of the superior colliculus (especially its periphery) would no doubt yield a still more precise and complete representation of the visual field in the inferior nucleus of the pulvinar. The chances of missing the superior colliculus completely when attempting such lesions, however, would be greatly increased. This difficulty is further emphasized by the necessity to adjust the measurements obtained from the stereotaxic atlas. Until the general state of knowledge of the visual structure and function in the central nervous system demands greater detail, it is questionable whether the cost and time required in such a project would be warranted.

The present study has confirmed that another important thalamic projection of the superior colliculus terminates in part of the ipsilateral intralaminar complex, i.e., parafascicular, central lateral and paracentral nuclei. The density of this projection to the intralaminar nuclei was not uniform. Relatively dense degeneration was observed in the paracentral nucleus, a moderate amount in the parafascicular nucleus and small isolated clusters in the central lateral nucleus. Degenerating tectal fibers were not observed in the centromedian nucleus. Benevento and Fallon ('74), however, have recently described a tectal projection to the centromedian nucleus of the macaque, as well as to the other intralaminar nuclei. No definite explanation can be offered for this discrepancy although a suggestion will be given below when discussing fibers to the suprageniculate and magnocellular medial geniculate nuclei.

The superior colliculus also sends a sparse but definite projection to the corresponding contralateral intralaminar nuclei. Although this projection has not been mentioned in other studies, its existence was established without question in this report. Degenerating fibers were observed in all three nuclei from a large lesion in the colliculus placed with an ipsilateral electrode approach so that no contamination of the contralateral side was possible.

Altman and Carpenter ('61) have raised the possibility that degeneration in the intralaminar nuclei may not arise from superior colliculus but rather has resulted from extraneous damage to the periaqueductal gray. This can be refuted by the present results, however, because certain lesions restricted entirely to the superior colliculus caused degeneration in the intralaminar nuclei. No damage to surrounding structures was evident, and therefore it seems rather certain that the superior colliculus does project to the intralaminar nuclei.

It is interesting to note that the same intralaminar nuclei receiving tectal fibers, also receive fibers from Brodman's area 8 of cortex (Astruc '71, in the macaque), the region responsible for voluntary eye movements. Hence, it appears that areas concerned with voluntary and reflex eye movements both send projections to the intralaminar nuclei, i.e., to areas controlling the state of arousal. During ~~foveal~~ acquisitions when the eyes are directed towards an object of interest either through voluntary or reflex mechanisms, the appropriate centre (cortex, area 8 or superior colliculus) can independently bring about an increase in visual arousal via its intralaminar connections. Presumably this prepares the animal to "see" what it is about to look at, although admittedly other centres can probably suppress this visual attention.

The projection of the superior colliculus to the suprageniculate nucleus and the magnocellular portion of the medial geniculate nucleus has been described in many species (e.g., hedgehog, Hall and Ebner '70; rabbit, Tarlov and Moore '66; cat, Altman and Carpenter '61; tree shrew, Abplanalp '70; monkey, Myers '63, Benevento and Fallon '74). It was not a consistent finding in the present study. Degeneration at these sites was only observed with certainty in animals with very large lesions of the colliculus where the possibility existed of damage to the pretectum. The pretectum lies immediately ventral and anterior to the colliculus and the boundary between these two structures is rather indistinct (Kappers et al. '36). Therefore, extraneous damage to the pretectum that has not been recognized, may be present in this and other studies. For example, in reports where superficial and deep lesions were placed in the superior colliculus, degeneration in the suprageniculate and magnocellular medial geniculate nuclei was found only after the larger lesions that destroyed the deeper layers (Casagrande et al. '72, Harting et al. '73, in the tree shrew; Benevento and Fallon '74, in the macaque). These lesions could easily have encroached on the pretectum. Still larger lesions involving larger pretectal areas might show degeneration in even more thalamic areas. This may explain the wide distribution of tectothalamic fibers reported by Benevento and Fallon ('74).

The constant focus of degeneration at the lateral border of the inferior nucleus of the pulvinar close to the lateral geniculate nucleus remains problematical and is subject to various interpretations. Perhaps the fibers terminate at this point. They may be destined for either the dorsal division or ventral division of the lateral geniculate nucleus, or possibly both. The suggestion that the fibers terminate in the pulvinar seems the least plausible since this area has not been described as either cytoarchitectonically or functionally different from other parts of the nucleus. It seems more reasonable to suggest that tectal fibers travel across the inferior nucleus of the pulvinar to funnel at the posterior pole of the dorsal lateral geniculate nucleus. From this point, they spread out through the lateral geniculate nucleus. The termination of tectal fibers in the dorsal lateral geniculate nucleus is a point of contention in the literature. In the present material, the sparse degenerating fibers seen in the magnocellular and parvocellular layers of the nucleus might easily be considered fibers of passage, but they are too few in number to be certain of this interpretation. In many situations, however, the fibers were directed towards the overlying ventral division of the lateral geniculate nucleus. Preterminal fibers were clearly observed in this region and the literature indicates that the ventral division receives fibers from the superior colliculus in all species studied. Therefore, it is postulated that the degenerating fibers found at the lateral border of the inferior nucleus of the pulvinar and in the dorsal lateral geniculate nucleus are mainly fibers of passage destined for the ventral division of the lateral geniculate nucleus.

II. Electron Microscopy

In the present study, four types of vesicle-containing profiles have been identified in the inferior nucleus of the pulvinar and the paracentral nucleus in the rhesus monkey, Macaca mulatta, the RLP, RSD, F and P types. This classification has been based upon the individual morphological characteristics of the profile and the membrane differentiation of the postsynaptic element at the point of contact. The general appearance of the profile and the size and shape of its synaptic vesicles were of prime importance in differentiating these types. Similar criteria have been used in many other studies (e.g., Colonnier and Guillery '64, Uchizono '65, Ralston and Herman '69, Guillery '69a).

The RLP profile is a large, irregular profile containing loosely-packed round synaptic vesicles of uniform size and several mitochondria. Its overall appearance is paler than the RSD type but darker than the F, P and dendritic elements. Therefore the term RLP signifies the "round" vesicles, "large" profile and "pale" appearance relative to the RSD type. It resembles the RLP type of Guillery ('69a) observed in the lateral geniculate nucleus of the cat, except that "p" stood for the pale mitochondria according to Guillery. The terminal is similar to synaptic types described in many other thalamic nuclei, i.e., the LP of Colonnier and Guillery ('64), type

1 of Szentagothai et al. ('66) and Campos-Ortega and Hayhow ('73), central axon of Peters and Palay ('66) and Pecci-Saavedra et al. ('68), large dark axon of Jones and Powell ('69a) and the RL of Wong-Riley ('72a), Mathers ('72a) and Hajdu et al. ('74).

The RSD profile is a small, dark profile, densely packed with round synaptic vesicles of uniform size and occasionally containing one, rarely two, mitochondria. The term RSD refers to the "round" vesicles, "small" size of the terminal and its "dark" appearance. It is similar to the RSD profile of Guillery ('69a) with the exception that "D" referred to the darkish mitochondria in Guillery's material. The differentiation of pale versus dark mitochondria in these two types was not obvious in the present study, but the terms were retained because of the paler and darker appearance of the profiles relative to each other. The RSD profile resembles the following types described in other studies of the thalamus, i.e., the SD axon of Colonnier and Guillery ('64), the "simple synaptic contact" of Peters and Palay ('66), the "small dark terminal" of Jones and Powell ('69a), the RS of Wong-Riley ('72a), Mathers ('72a) and Hajdu et al. ('74) and the type III of Campos-Ortega and Hayhow ('73).

The F profile varies in size, and contains synaptic vesicles that are both round and flattened in shape, and a few mitochondria. However, it was not until the introduction of aldehyde fixation (at the appropriate osmolarity) prior to osmium tetroxide, that this vesicle population was differentiated from the round vesicle population (e.g., Uchizono '65, Bodian '65, Walberg '65, '66). Once this distinction was made, it became clear that the two populations could be differentiated on the basis of vesicle size alone, the vesicles of the "flattened" population being smaller in diameter than vesicles of the "round" population (Lenn and Reese '66, Larramendi et al. '67). This point has recently been reemphasized by Ebner and Colonnier

('75). The small size of these "flat" vesicles is often the critical factor used in their identification. The F terminal is similar to the Fl of Guillery ('69a), Wong-Riley ('72a) and Hajdu et al. ('74), the IA of Famiglietti and Peters ('72) and part of the type III profiles of Szentagothai et al. ('66).

The P profile is very pale in appearance and contains only a few mitochondria and relatively sparse synaptic vesicles. In some large profiles the number of vesicles is often rather abundant but the density is usually less than that observed in the other types of vesicle-containing profiles. The vesicles vary in size from small to large and may be round, flattened or irregular in shape. Similar vesicle populations have been described as polymorphic by Famiglietti and Peters ('72), pleomorphic by Harding ('71) and Wong-Riley ('72a) or discoid by Dennison ('71), Lieberman and Webster ('72) and Colonnier ('74). It is difficult to decide which of these names is most appropriate. Polymorphic and pleomorphic suggest that the shape of the vesicles is different from that of the flat population. Yet stereoscopic studies have shown that the vesicles of a flat population have very many shapes, some having the form of cylinders, spheres, erythrocytes or tubules (Gray '69, personnal communication). They cannot be seen as "discoid" on a two-dimensional micrograph. The most critical criterion in identifying this vesicle population is the great variability in their size, some being as small as those in the F population, and some being larger than in the RLP or RSD populations. The expression polymetric, signifying "of many measurements", i.e., of many sizes, has thus been introduced. This P profile corresponds to the F2 of Guillery ('69a) and Hajdu et al. ('74), class 2b of Lund ('69), "pale terminal" of Jones and Powell ('69a), P-boutons of Lieberman and Webster ('72), ID of Famiglietti and Peters ('72) and Fd of Wong-Riley ('72a).

Many investigators have observed that this pale vesicle-containing profile occasionally contains polyribosomes and microtubules, i.e., characteristics normally associated with dendrites (Peters and Palay '66, Ralston and Herman '69, Famiglietti and Peters '72). Such dendritic structures were also sometimes seen in the P profile of the present study. It was also noted that the electron-lucent cytoplasm of this type resembled that of dendrites, so that the general appearance of dendrites and P profiles appeared remarkably similar, especially at very low magnification. The classification of these profiles as axons or dendrites, however, remains problematical. Originally, many authors considered that any profile containing vesicles agglomerated towards a membrane specialization, was an axon on the basis of this criteria (e.g., Gray '62, Guillery '69a, Jones and Powell '69a, Jones and Rockel '71). However, as early as 1965, Majorossy and his colleagues recognized in the pulvinar of the cat, a group of unusual profiles in which the synaptic vesicles are very sparse and "strangely irregular" in size, and "even the granula resemble ribosomes". Although the authors were "tempted to interpret some of these profiles as dendrites", nevertheless, on the basis of their synaptic vesicles, they were considered to be axon terminals. More recently, many authors have referred to the vesicle-containing profiles displaying dendritic characteristics such as polyribosomes and neurotubules, as "presynaptic dendrites" (Lund '69, Ralston and Herman '69, LeVay '71, Famiglietti and Peters '72, Wong-Riley '72, Lieberman and Webster '72). In the present study the P profile is also considered to be dendritic and this seems to be the most reasonable interpretation in the rare examples in which a P profile was traced back to the cell soma (see Fig. 35). The definitive characteristics of the axon initial segment, such as the dense agranular material undercoating the plasma membrane (Palay et al. '68), did not appear to be present in this example.

Many profiles were found that resembled the "presynaptic dendrite" by their pale cytoplasm, and sparse polymetric vesicles, but ribosomes and microtubules were absent. Wong-Riley ('72a) classified these as a separate group of F2 axons, as opposed to her Fd presynaptic dendrites in which ribosomes were present. LeVay ('71), however, found in his study of extensive serial sections of the presynaptic dendrite that the ribosomes thin out as one proceeds distally along the dendrite, so that most ribosomes are absent in areas where synaptic contacts are formed. The possibility also exists that certain planes of section would not always show the ribosomes that are present in a particular vesicle-containing profile. For the above reasons, it seems reasonable to classify the P vesicle-containing profiles as presynaptic dendrites even when ribosomes are lacking. Lieberman and Webster ('72) came to the same conclusion, and classified all of their P-boutons as presynaptic dendrites, regardless of whether the ribosomes were always present or not. Wong-Riley ('72a) did admit to the possibility that her F2 and Fd profiles were the same population of presynaptic dendrites and this seems the most reasonable interpretation, although definite proof is not available.

In the lateral posterior-pulvinar complex of the cat, Hajdu et al. ('74) described four types of vesicle-containing profiles, the RL, RS, F1 and F2, corresponding to the RLP, RSD, F and P of the present study. The F2 profile was interpreted to be dendritic, belonging to Golgi type II interneurons (Hajdu et al. '74). In the monkey pulvinar, however, only three types of profiles were recognized, i.e., the RL, RS and F of Mathers ('72a), corresponding to the type I, type III and type II of Campos-Ortega and Hayhow ('73). The controversial "presynaptic dendrite" was considered questionable by Mathers ('72a), and its existence in the pulvinar was denied by Campos-Ortega and Hayhow ('73). This view is not supported by the present findings and its appears from the descriptions and illustrations in these reports, that their F or type II categories included the P profile described in this investigation.

Hence, four types of vesicle-containing profiles can be differentiated in the pulvinar of both the cat, and the monkey, as well as in the intralaminar nucleus.

Transitional types of vesicle-containing profiles are frequent, and cannot easily be classified as one of the above four types. However, this does not justify making further classifications. The profiles with intermediate characteristics may result from variations in the preparation of the material such as different rates of tissue-fixative interaction or other fluctuations in embedding and staining that are difficult to assess. On the other hand, the normal range of variations in the size and shape of any one category of vesicles may result in characteristics which overlap with another category at the limits of the range.

Two types of membrane differentiations associated with synaptic vesicles were observed in the present material, the asymmetric and symmetric specializations which have been described in many other studies (see Colonnier '68). The RLP and RSD terminals take part in asymmetric contacts, whereas the F and P profiles form symmetric contacts.

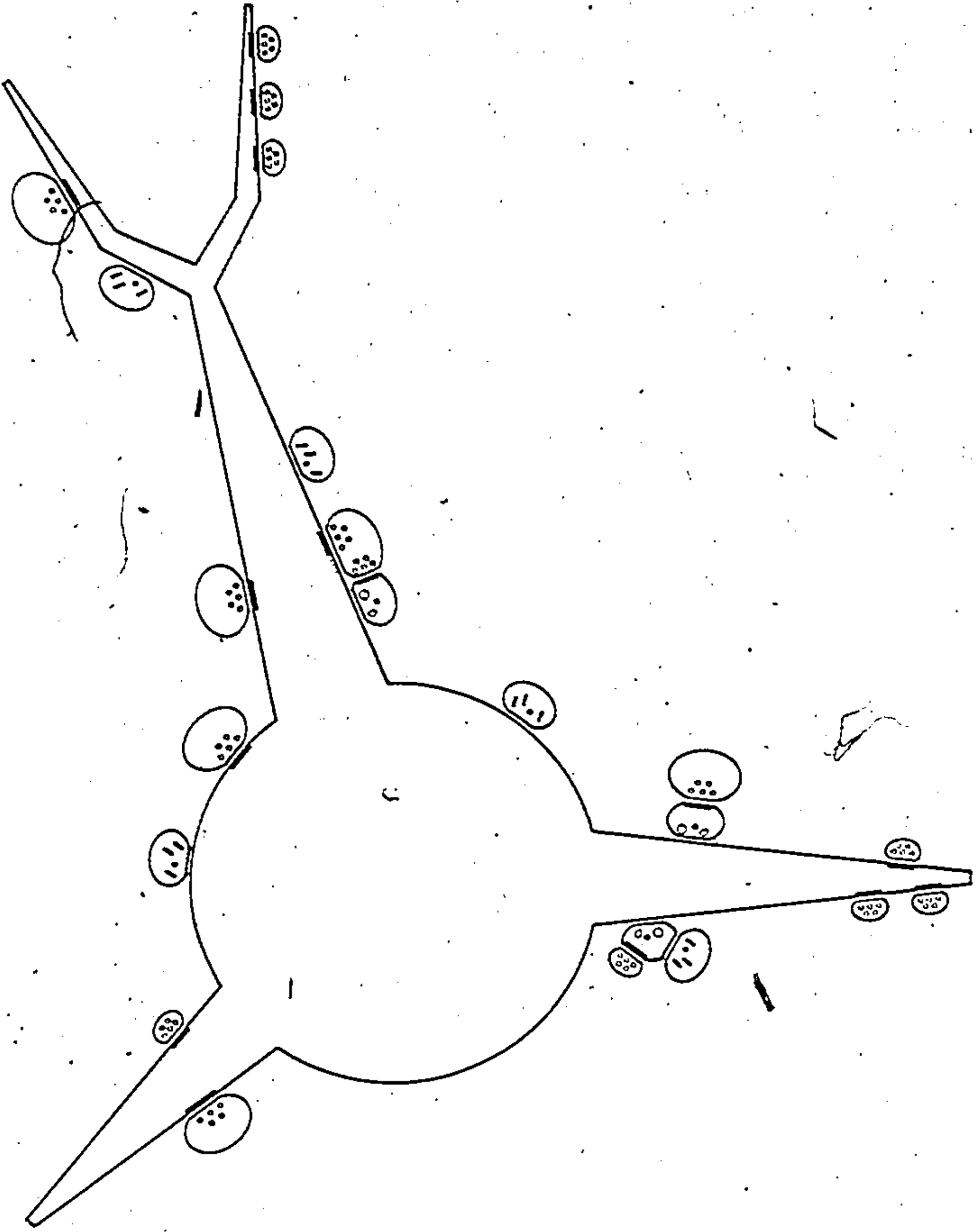
It has become evident through careful examination of these two types of membrane differentiations, that the asymmetric appearance is mainly due to electron-dense cytoplasm adjacent to the site of contact in the postsynaptic profile (Westrum and Lund '66, Colonnier '68, Ralston and Herman '69). Although the membrane specializations are slightly thicker in the post-synaptic element in both types of contacts, this appears insignificant compared to the presence or absence of the cytoplasmic opacity.

The distinction between the two types is most obvious only when the plane of section is exactly perpendicular to the differentiated membranes, such that both membranes are clearly identifiable. In sections cut slightly oblique to this plane, the postsynaptic membrane may become blurred, giving the appearance of a cytoplasmic opacity that in fact, does not exist. This possibility may account for the occasional reports in which profiles containing flattened vesicles are associated with asymmetric membrane specializations. It must be emphasized that both membranes at the site of contact be distinctly observed before being classified as one or the other type. However, the suggested relationship of round vesicles with asymmetric contacts, and flat vesicles with symmetric contacts, is not intended to be exclusive (Colonnier '74), but the probability of finding other types in the thalamus is not high. Transitional types have been observed (Colonnier '68), and indeed, in the present study, some P profiles were found with a suggestion of increased cytoplasmic opacity associated with the postsynaptic membrane specialization.

Because of the considerable evidence indicating that profiles containing round vesicles and forming asymmetric contacts are excitatory (e.g., Uchizono '65, Atwood et al. '72), it is reasonable to suggest that the RLP and RSD types are also excitatory. Furthermore, profiles with flattened vesicles forming symmetric contacts are thought to be inhibitory, and hence, the F and P types described in this study are also presumably inhibitory.

The distribution of different synaptic types with respect to the cells of the paracentral nucleus and the inferior nucleus of the pulvinar can be summarized in the following diagram. Cell bodies receive one or two contacts per plane of section and these are nearly all Fs with very few RLPs. The large proximal dendrites receive all types of contacts. Small distal dendrites receive mainly RSD contacts with some Fs and RLPs.

In many studies of the thalamus, the RLP or its equivalent is usually



Schematic diagram of the synaptic relationships found making synaptic contact with the large to moderate-sized, presumably more proximal dendrites, often in "glomeruli" (Szentagothai et al. '66, Peters and Palay '66, Guillery '69a, Jones and Powell '69a, Ralston and Herman '69, LeVay '71, Campos-Ortega and Hayhow '73, Hajdu et al. '74), but seldom, if ever with the smaller more distal dendrites in the general neuropil. However, some authors have described the RLP contacting the smaller dendrites (Guillery '69a, Wong-Riley '72a), and this has often been observed in the present material for both the inferior nucleus of the pulvinar and the paracentral nucleus. The RLP was also commonly found contacting other vesicle-containing profiles, always as the presynaptic component (e.g., Guillery '69a, Ralston and Herman '69, LeVay '71, Wong-Riley '72a, Hajdu et al. '74).

The RSD terminal usually contacts the small, peripheral dendrites (Szentagothai et al. '66, Campos-Ortega et al. '68, Jones and Powell '69a, Guillery '69a, Guillery and Colonnier '70, Wong-Riley '72a, Mathers '72a) and has not been described contacting the soma, and only infrequently the large proximal dendrites. Similarly in the present study, the RSD was frequently found contacting the smaller dendrites and never the cell soma. However, it was often seen on larger dendrites as well. The RSD also formed contacts with the P profile, but less frequently than the RLP. It has never been observed as the postsynaptic element (Guillery '69a, Ralston and Herman '69, Famiglietti and Peters '72, Wong-Riley '72a). The frequency of the RSD contacting a vesicle-containing profile, apparently varies according to the nucleus studied. Famiglietti and Peters ('72) found it to occur only rarely in the lateral geniculate nucleus of the monkey, whereas Ralston and Herman ('69) found it frequently in the ventrobasal complex of the cat. In the present study, it was rather uncommon in the paracentral nucleus but somewhat more general in the inferior nucleus of the pulvinar.

The F profile can be observed contacting all parts of the neuron, i.e., the proximal and distal dendrites and soma. Most authors agree that when contacts are found on the cell soma they are usually the F type (Guillery '69a, Guillery and Colonnier '70, Wong-Riley '72a, Famiglietti and Peters '72). In some cases, these have even been considered a separate category from F profiles found on dendrites (e.g., Ralston and Herman '69) but this distinction is only on the basis of the nature of the postsynaptic element and hence, does not warrant a separate classification of the terminal. In the inferior nucleus of the pulvinar it has been suggested that the cell soma receives no synaptic contacts (Mathers '72a, Campos-Ortega and Hayhow '73). This view is not tenable in the present study and their apparent absence in these previous works can only be attributed to sampling errors. Often one, and sometimes two axonal profiles were observed contacting a cell soma in a particular plane of section. The F profile also forms the presynaptic elements in contacts with the P profile. In previous studies, where the distinction was made between the two types of flattened vesicle-containing profiles, the F1 (e.g., Guillery '69a, Wong-Riley '72a) or 1A (Famiglietti and Peters '72) invariably formed the presynaptic component when contacting another vesicle-containing component, i.e., the F2 or 1D profile, respectively.

The P profile contacts mostly the medium to large-size dendrites. It has not been observed contacting the cell soma, and only rarely forms a synapse with small dendrites. Occasionally it may contact another P profile. Similar relationships have been described in other studies where this type of profile is recognized (e.g., Guillery '69a, Harding '71, Wong-Riley '72a, Lieberman and Webster '72).

Although P profiles were abundant in this material they were only occasionally observed as the presynaptic component. This striking lack of of presynaptic contacts has also been noted by Lieberman and Webster ('72). It is possible that this lack of contacts is related to the usual sparsity of vesicles compared to the relatively large size of the profile. It would not be unreasonable to suggest that a critical number of synaptic vesicles is required for each synaptic contact and hence, only very few contacts would be formed by this type. Therefore, in a relatively large profile forming one or few synaptic contacts, only occasionally would the plane of section pass through the region of membrane specialization. This possibility should be kept in mind when studying the two-dimensional fields of electron micrographs.

The P profile was observed as the postsynaptic element much more frequently than as the presynaptic component in the various synaptic relationships. It was most often postsynaptic to RLPs and less frequently to the RSD, F and other P profiles.

The P profile forms the intermediate component of serial synaptic arrangements, similar to those described in the superior colliculus (Lund '69), in specific relay nuclei of the thalamus (Ralston and Herman '69, Guillery '69a, Famiglietti '70, Harding '71, Morest '71, Wong-Riley '72a, Lieberman and Webster '72) and in motor cortex (Sloper '71). In most studies, the intermediate element contained flattened vesicles and was considered a presynaptic dendrite (e.g., Lund '69, LeVay '71, Famiglietti and Peters '72, Wong-Riley '72a, Lieberman and Webster '72). In the present material, examples of single synaptic contacts with P as the postsynaptic element were often observed, but it was assumed that these would also appear as serial arrangements, if the appropriate plane of section were available. The lack of presynaptic contacts formed by the P profiles would account for the relative infrequency of seeing the complete serial arrangement. It has been postulated that in the serial dendrodendritic synapse, each presynaptic dendritic segment could act as a semi-independent interneuron, presumably having an inhibitory effect in a small localized area (Colonnier '74).

Another possible role of the P profile should at least be considered at this point. In any particular field, the number of P profiles found as postsynaptic elements is much greater than those forming the presynaptic component. Therefore, it is logical to suggest that several terminals converge on each P profile which in turn forms only one or few presynaptic contacts. In this respect, the presynaptic dendrite appears to act as some type of integrative interneuronal unit.

All serial arrangements form the basis for the triadic synaptic relationship and the argument can be extended that the former may normally be part of triads if the entire relationship could be seen (Colonnier '74). This is not intended to suggest, however, that all synaptic arrangements between two vesicle-containing profiles are involved in a triadic relationship (although this possibility does exist). In the triadic dendro-dendritic synapse, the initial element could excite both the target dendrite and the intermediate presynaptic dendrite which would then inhibit the target dendrite at a time interval of one synaptic delay. In this way, the triad would act as a strictly controlled timing device to automatically switch-off the target dendrite after its initial excitation (Colonnier '74). It is more difficult to interpret the role of the triad when the initial element is an F or P profile and presumably inhibitory, and therefore, such speculation will not be attempted here.

Aggregations of neuronal elements with many P profiles resembling glomeruli or synaptic islands, were not observed in either the inferior nucleus of the pulvinar or the paracentral nucleus of the macaque. In the cat, glomeruli are usually well-defined, and so it is not surprising that they have been described in the lateral posterior-pulvinar complex (Majorossy et al. '65, Hajdu et al. '74). In the monkey, however, the aggregations are usually less clearly defined, and little or no glial capsule is present (e.g., Colonnier and Guillery '64). Despite this, Mathers ('72a) refers to aggregations of neuronal elements in the pulvinar of the squirrel monkey as "glomeruli". In the macaque, Campos-Ortega and Hayhow ('73) found the distinction between "synaptic complexes" and interstitial neuropil somewhat artificial, and preferred to differentiate the synaptic relationships according to proximal and distal dendrites. This is indeed the case in both the inferior nucleus of the pulvinar and the paracentral nucleus where the glomerular arrangement is apparently absent.

Until very recently the origin of the various synaptic profiles in the thalamus had appeared well-defined from degeneration studies of the specific relay nuclei (e.g., Colonnier and Guillery '64, Gray and Guillery '66, Szentagothai et al. '66, Ralston '69, Jones and Rockel '71, Wong-Riley '72b, Famiglietti and Peters '72). These reports had indicated that the RLP is derived from the primary sensory afferents and terminates on large proximal dendrites close to the cell body; that the RSD originates in the appropriate cortical region and ends on the small distal dendrites; and, that the F and P profiles are intrinsic to the thalamus since they have not been shown to undergo degeneration after interruption of all known afferents to a nucleus. It would be appropriate, in a specific relay nucleus, that the primary input have a powerful influence on the cortex and that the cortex have only a modulating influence; and indeed because of decremental conduction in dendrites, RLP terminals close to the cell soma would have a high priority with respect to their capacity to fire the neuron, whereas the more distally located RSD terminal would have only a modulating influence on the firing pattern of the cell.

Mathers ('71, '72b) has recently reported that fibers from the superior colliculus terminate as RSDs in the inferior nucleus of the pulvinar whereas many of the RLPs in the nucleus arise from the secondary visual cortex. This and other reports that visual cortex projects to the inferior pulvinar via RLPs (Majorossy et al. '65, Campos-Ortega and Hayhow '73), suggests that the nucleus is mainly under cortical control. The superior colliculus would then not be able to drive the inferior nucleus of the pulvinar but rather would only have a modulating influence. One might have expected the colliculus to have a more powerful influence on the pulvinar because of the suggestion that the second visual system can act independently of the first system.

In the present study, large lesions of the superior colliculus resulted in electron-opaque degeneration of large numbers of RLP terminals in both the inferior nucleus of the pulvinar and the paracentral nucleus. It is possible that all of the degenerating profiles were RLPs and the smaller terminals resembling RSDs were only the cut ends of the larger type. However, the possibility of some RSDs from superior colliculus cannot be ruled out entirely. On the other hand, it seems as if Mathers ('71) interpretation of degenerating RSDs was derived simply from the observation of electron-dense terminals in the pulvinar at short survival times. From the literature it is easy to assume that all dense degeneration is of the RSD type, that all RLPs must initially undergo neurofilamentous degeneration, and thus to conclude that the superior colliculus projects to the pulvinar via RSD terminals.

The present findings do not contradict the reports that many RLPs as well as RSDs originate in the visual cortex (Majorossy et al. '65, Mathers '72b, Campos-Ortega and Hayhow '73). These RLP and RSD terminals undergo the usual neurofilamentous and dense patterns of degeneration respectively, as described in the introduction.

Thus, there are two types of RLP terminals reacting differently when separated from their cell soma, i.e., one type undergoing neurofilamentous hyperplasia prior to dense degeneration and the other type becoming electron-opaque directly. At present, however, no morphological characteristics appear to be available to differentiate the two types in normal material.

One might reasonably expect the projection from the inferior colliculus to the medial geniculate nucleus to display characteristics similar to that of the superior colliculus projection. Majorossy and Rethelyi ('68) described dense degeneration of RLP types at day three survival, but Jones and Rockel ('71), found a few neurofilamentous RLPs along with the more abundant dense RLPs at shorter survival times (day 1-2) following lesions of the inferior colliculus. The neurofilamentous characteristics, however, were absent by the third postoperative day. The possibility exists that in the work of Majorossy and Rethelyi ('68) and in the present study, the neurofilamentous RLP was missed. However, they were carefully searched for in this study, and it seems unlikely that they were overlooked unless perhaps they were extremely rare and very transitory. Nor do the characteristics of dense degeneration, i.e., the transition from grey to very dense cytoplasm and the large accumulation of synaptic vesicles, resemble the small dense clusters of amorphous material found following the early stages of neurofilamentous hyperplasia. In any case, it appears that the majority of RLPs from either the superior or inferior colliculus undergo dense degeneration directly, with no intermediate hyperplasia.

In the inferior nucleus of the pulvinar, a large number of RLP and RSD terminals remain unaffected after relatively large lesions of the superior colliculus, and similarly, many such profiles were unaffected by large lesions of the cortex (Campos-Ortega and Hayhow '73). Whether combined lesions in the colliculus and appropriate regions of cortex would cause degeneration of nearly all RLP and RSD profiles is difficult to assess but their numbers seem so small after a tectal lesion that it seems safe to assume that there may still be other inputs to the pulvinar.

In the paracentral nucleus, it was originally suggested that the superior colliculus might only have a modulating influence and thereby its fibers would terminate as RSDs at this site. The tectal fibers, however, terminate as RLP profiles and follow the same dense pattern of degeneration as those ending in the pulvinar. A large proportion of the RLPs remain normal after extensive lesions of the superior colliculus. Although it has been demonstrated that the colliculus provides an important input to this region, it is also apparent that other important sources of fibers are present.

The occasional finding in the present study of degenerating postsynaptic vesicle-containing profiles was most unexpected in view of the many reports that seem to argue against this possibility. Neither the F nor the P profile (or its equivalent) have ever been reported to undergo degeneration, and therefore, it has logically been interpreted that they are intrinsic to the nucleus (e.g., Szentagothai et al. '66, Majorossy and Rethelyi '68, Guillery '69b, Wong-Riley '72b), or perhaps, to a specific region such as the pulvinar. Nevertheless, P profiles apparently in the process of degeneration have been found in this study, in the inferior nucleus of the pulvinar although not in the paracentral nucleus. The lesions in this case were very large and may have encroached on the medial nucleus of the pulvinar. The degenerating dendrites may be those of cells in the medial nucleus extending into the inferior nucleus, or else they may be those of cells in the inferior nucleus whose axons or dendrites extend into the medial nucleus. Acute retrograde degeneration has indeed been described in cell bodies and dendrites in very young kittens at rather short survival times following transection of the axon (Grant and Aldskogus '67, Grant and Westman '68). The degenerating dendrites were impregnated with the Nauta silver stain, and also were observed with electron microscopy, but it was stressed that the young age of the animals was a critical factor. On the other hand, Campos-Ortega and Hayhow ('73) found abundant degenerating dendrites in adult rhesus monkeys only six days following lesions of cortex.

The rather bizarre profiles containing large electron-opaque structures are certainly products of degeneration. Their frequency and relationship to other neuronal components, however, is not clear and their significance remains uncertain.

Whorls of membranous material were often found in the various neuronal elements. Membranous whorls, more regular in structure, have also been described in the cortex of reptiles and their resemblance to growth cones was noted (Ebner and Colonnier '75). Although the vacuolar structures were always observed invaginating dendrites in the reptile, a somewhat similar structure was also found extending from an RLP terminal to a P profile. In at least one situation, it appeared that the vacuoles were being emptied from the dendrite into a vesicle-containing profile. At the risk of stretching the significance of this somewhat ambiguous evidence too far, perhaps the dendrite is providing membranous material to the profile to be incorporated into synaptic vesicles. A similar function for the uptake of glial membranes by neurons has been made by Birks ('74). This suggestion must be viewed with caution, however, and the whorls of membranous material may only be artifact.

One might also speculate on the significance of the numbers of synaptic vesicles in various profiles and their relationship to membrane specializations. Although no attempt was made in the present study to correlate the number and density of synaptic vesicles to the number and length of synaptic contacts in a single profile, the relative sparseness of vesicles in P profiles and their infrequent involvement as the presynaptic component, compared to the high density of synaptic vesicles and the apparent increase in the length of the zone of contact in certain RLP terminals, lends credibility to the suggestion that these characteristics are directly related. It would also be logical to assume that they are indicative of the activity and consequently the influence of the profile on the surrounding neuronal elements. In a dynamic living situation, it might be speculated that the region of membrane differentiation is not necessarily an absolute fixed zone, but rather increases and regresses according to the activity required at that site at a particular moment. No attempt is made in most electron microscope studies of the thalamus (or central nervous system) to control the activity in the area studied.

SUMMARY AND CONCLUSIONS

The present study has shown that the superior colliculus does project to the inferior nucleus of the pulvinar in the monkey, Macaca mulatta, and that this projection is topographically organized. The horizontal meridian of the visual field divides the inferior nucleus obliquely into a dorsomedial segment which becomes more extensive anteriorly, and a dorsolateral segment which becomes more extensive posteriorly. The upper visual field is represented in the lower segment and the lower visual field in the upper segment. The periphery is represented along the medial border adjacent to the lateral geniculate nucleus. The lower vertical meridian forms the dorsomedial border and the upper vertical meridian forms the ventrolateral border. This spatially organized projection then satisfies the requirements for a system involved in visual orientation.

The superior colliculus also sends an important projection to the ipsilateral intralaminar complex, i.e., the parafascicular, central lateral and paracentral nuclei, and a lesser projection to the corresponding contralateral intralaminar nuclei. The paracentral nucleus is the main site of termination of these fibers.

The superior colliculus may also project to the dorsal and ventral divisions of the lateral geniculate nucleus, the suprageniculate nucleus and the magnocellular part of the medial geniculate nucleus. It can only be stated with certainty, however, that the ventral lateral geniculate nucleus does indeed receive tectal fibers. The degeneration observed in the other nuclei is subject to other interpretations as discussed previously.

The normal electron microscopic study of the inferior nucleus of the pulvinar and paracentral nucleus has demonstrated four types of vesicle-containing profiles, the RLP, RSD, F and P. The RLP is a large terminal containing round, loosely-packed vesicles of uniform size and several mitochondria. The RSD is a small terminal densely packed with round vesicles of uniform size and only occasionally containing one, rarely two mitochondria. The F terminal varies in size and contains numerous mitochondria and a population of smaller-sized vesicles a variable number of which are flattened. The P profile is very pale, containing a relatively sparse population of "polymetric" vesicles and occasionally ribosomes and microtubules. It has been interpreted as a presynaptic dendrite.

The RSD terminal is the most frequently observed vesicle-containing profile in either nucleus. It is always found as the presynaptic component forming asymmetric contacts mainly with the smaller more distal dendrites and occasionally with the large dendrites or P profiles, the latter especially in the inferior nucleus of the pulvinar. The RLP forms asymmetric contacts, always as the presynaptic element, predominantly with the large proximal dendrites, infrequently with smaller dendrites and rarely with the cell soma. It is the most frequent type found contacting the P profile. The F terminal forms symmetric contacts with the cell soma, dendrites of all sizes and occasionally the P profile. The P profile forms symmetric contacts with medium and large-sized dendrites and occasionally with another P profile. It is often found postsynaptic to the other types. This P profile is the intermediate element in serial and triadic arrangements. Glomeruli are virtually absent.

The experimental electron microscopic study of the inferior nucleus of the pulvinar has shown that the fibers from the superior colliculus terminate mainly as RLPs on large proximal dendrites. They undergo direct dense degeneration. A smaller number of RSD terminals probably also arise in the colliculus. Thus, the superior colliculus input terminates in a way which is compatible with its presumed controlling influence on the inferior nucleus of the pulvinar.

The tectal projection to the intralaminar nucleus is also in the form of RLPs which undergo dense degeneration and hence, the superior colliculus may also have a controlling effect, especially on the cells of the paracentral nucleus.

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