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The morphology of laminae A and A_1 of the dorsal nucleus of the lateral geniculate body of the cat

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INTRODUCTION

In the cat, the lateral geniculate body is composed of a ventral nucleus and a dorsal nucleus (nucleus dorsalis) that has three distinct laminae. These laminae were first recognized by Tello (1904), who carried out a study of the nucleus in Golgi stained preparations and described the S-shaped form of the nucleus when it is viewed in parasagittal sections, but it was not until Thuma (1928) made a study with Nissl-stained preparations that the true morphology of the lateral geniculate body became apparent. Thuma (1928) designated the three distinct laminae of the dorsal nucleus of the lateral geniculate body as pars dorsalis A, A_1 and B; pars dorsalis A being the dorsal-most lamina and pars dorsalis B the ventral lamina, with A_1 sandwiched between them.

This lamination of the dorsal nucleus of the lateral geniculate body of the cat makes it a very suitable structure for experimental analysis, especially as there are a number of anatomical studies concerned with the projection of the optic tract fibres on to the different laminae. Hayhow (1958), in the most recent study of the cytoarchitecture of the lateral geniculate body of the cat, has pointed out that these studies are of three kinds and have been made after nerve section to determine the distribution of the terminals of the optic nerve fibres. First, there are those studies which have employed the Marchi methods of staining to determine the course and distribution of myelin sheaths that have degenerated (Minkowski, 1913; Overbosch, 1927; Barris, Ingram & Ranson, 1935). Secondly, studies using special silver impregnation methods to examine the sites of degeneration of axon terminals in the lateral geniculate body (Glees, 1941; Hayhow, 1959), and lastly, those showing the transneuronal degeneration of the lateral geniculate neurons (Minkowski, 1920; Barris, 1935; Cohn, 1956). For the present purpose there is little need to review this work on degeneration in detail, since that has already been done by Hayhow (1958), so suffice it to say that with the exception of a few large cells (nucleus interlaminaris centralis of Thuma (1928)) occurring at the boundaries between adjacent laminae, all of the investigations support the conclusion first arrived at by Minkowski (1913, 1920). This conclusion is that the crossed and uncrossed nerve fibres within each optic nerve terminate in separate laminae; the crossed fibres terminate in laminae A and B, while the uncrossed fibres terminate in laminae A_1.

The lateral geniculate body of the cat has also attracted the attention of a number of neurophysiologists interested in the visual process (see Bishop, 1953, 1964; Hubel & Wiesel, 1961) They have been particularly interested in the high degree of topographical representation of the retina in the lateral geniculate body and in the

ability of this nucleus to integrate the information that is projected from the retina.

Largely because of its lamination, which makes it an easily identified structure, and also because of the physiological and anatomical studies that have already been made, the lateral geniculate body was chosen for an electron microscope study. The results have been correlated with the appearance of Golgi-stained preparations of the nucleus, in particular the pattern of termination of axons that form synapses upon the geniculate neurons. By this means, it was hoped to obtain sufficient information about the finer details of its structure to enable neurophysiologists to interpret, on an anatomical basis, some of their results, since we believe that it is only at the electron microscope level that such a correlation is possible.

Soon after the study was commenced, some aspects of the structure of the lateral geniculate body of the cat, as seen with the electron microscope, were considered by Szentagothai (1962, 1963). There has also been a more recent study by Smith, O'Leary, Harris & Gay (1964). Neither of these descriptions gives any indication of which lamina they are considering, and both of them are only concerned with certain details of its morphology. These descriptions will be taken into account whenever appropriate but, as will be seen, some of their conclusions are at variance with those arrived at as a result of the present investigation. Perhaps more pertinent from the point of view of the present investigation is the electron microscope study of the lateral geniculate body of the monkey, by Colonnier & Guillery (1964).

MATERIALS AND METHODS

The material for this investigation was obtained from five normal cats varying in weight between 0·75 and 1·5 Kg. The brains of these animals were fixed by perfusion with osmic acid solutions according to the method described by Palay, McGee-Russell, Gordon & Grillo (1962).

The cats were anaesthetized with Nembutal and while artificial respiration was carried out, the heart was exposed and 0·1 ml of heparin injected into it. Immediately afterwards between 1 and 2 ml of 1 % sodium nitrite was also injected into the heart over a period of 1 min. When the heart beat returned to normal, the descending aorta was clamped at the level of the diaphragm, the tip of the heart amputated and a glass canula inserted into the common aorta. Perfusion was begun immediately and artificial respiration discontinued.

Perfusion was initiated with 25–50 ml of warm washing-out solution, the actual volume used to wash out the blood depending upon the size of the cat. This was followed, without interruption, by a warm, and then a cold, solution of 1 % osmium tetroxide buffered with veronal-acetate to a pH of 7·3–7·4. Between 300 and 400 ml of fixative were used and the perfusion was continued for 30 min.

Initially, the washing-out solution was the balanced salt solution recommended by Palay *et al.* (1962), but in the later perfusions this was replaced by a solution of veronal-acetate buffer (Palade, 1952) containing 1 g of calcium chloride and 0·3 g of sodium chloride per 200 ml.

At the end of the period of perfusion, the brain was carefully removed and bisected along the mid-sagittal plane. Each half of the brain was then cut into either

coronal or sagittal slices about 2 mm thick and the slices further fixed by immersion in an osmium tetroxide solution having the same composition as that used for perfusion. At the end of 2 h, the dehydration of the slices in methanol was commenced at room temperature, and during this time the slices were examined to select those containing parts of the lateral geniculate bodies. Such slices were taken through into Epon 812 and left to soak overnight. Later, the lateral geniculate body was removed from the slices and cut into small pieces of known orientation and location, before being embedded in capsules.

When the blocks of lateral geniculate tissue had hardened, sections of about 1 μm thick were cut for light microscopy. Since the orientation of these blocks was known, as well as their location within the lateral geniculate body, it was possible to determine which of the three laminae (A, A_1 and B) was present. Only those blocks in which the laminae could be identified with absolute certainty were used for this electron microscope examination of laminae A and A_1.

Thin sections were cut for electron microscopy with glass knives and double stained with uranyl acetate and lead citrate before examination in either an RCA EMU 3E, or an AEI, EM6, electron microscope.

Serial sections of the lateral geniculate body of the cat, stained by myelin and cytoplasmic stains, were examined by the light microscope, as was material stained by the Golgi technique after fixation by either immersion or perfusion (see Morest, 1964).

OBSERVATIONS

General description

In order to appreciate the appearance of structures in Golgi-stained and electron microscope preparations, a brief description of the structure of the dorsal nucleus of the geniculate body of the cat is necessary.

As demonstrated by Thuma (1928), the dorsal nucleus is composed of three laminae, or layers of neurons, A, A_1 and B. The relations between these laminae are rather difficult to follow in coronal sections, but in sagittal sections they appear as flat plates, piled one above the other and, as shown in Fig. 1, their over-all appearance is that of a flattened sigmoid curve. Ventrally, below lamina B, lie the fibres of the optic tract. These penetrate the nucleus in a direction approximately normal to the laminae and then ascend to their site of termination. The axons of the neurons in the laminae of the pars dorsalis give rise to the nerve fibres of the optic radiation, and these also pass through the laminae in a dorsal direction. In laminae A, where their highest concentration occurs, the optic radiation fibres form bundles in which the fibres continue in their dorsal direction, to emerge from the upper surface of the nucleus at the hilum.

The successive laminae of neurons of the dorsal nucleus of the lateral geniculate body are separated from each other by intervening layers composed of a few, somewhat larger neurons, to which Thuma (1928) gave the name of nucleus interlaminaris centralis (Fig. 1, n. interlam. cent.). The layer that these neurons make between laminae A_1 and B is readily apparent in Nissl-stained preparations and forms a clear boundary between them, but the boundary is also readily visible because the small, spindle-shaped neurons of lamina B are quite different in appearance

from the rounded and generally larger neurons of lamina A_1. Although the cells of the nucleus interlaminaris centralis serve as a useful guide, the interval between laminae A and A_1 is less clearly marked by their presence. Instead the boundary between these laminae is made readily apparent, in sections stained for myelin sheaths, by a well-defined fibre complex that is situated between them, a complex which, as pointed out by Hayhow (1958), does not appear to have an equivalent between laminae A_1 and B.

Surrounding the dorsal nucleus on its anterior and dorsal surfaces is a zone of scattered cells (Fig. 1; n. peri) making up the nucleus perigeniculatus (Thuma, 1928).

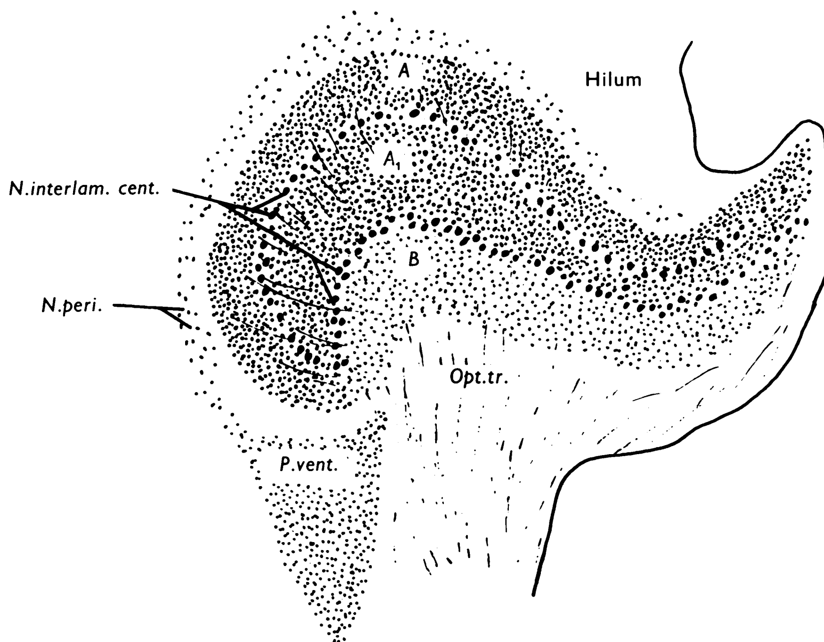

Fig. 1. Diagrammatic representation of a parasagittal section through the lateral geniculate body. *Opt. tr.*, optic tract; *N. peri.*, nucleus perigeniculatus; *P. vent.*, pars ventralis; *N. interlam. cent.*, nucleus interlaminaris centralis.

Histology of pars dorsalis A and A_1

These laminae, A and A_1, appear to be of identical composition when examined in Nissl preparations, both being composed of irregular shaped, multipolar neurons with well-dispersed Nissl substance. The distribution of neurons is fairly uniform throughout the laminae and the diameters of the perikarya vary between 10 and 40 μm, the numbers at each size being approximately proportional to the diameter of the perikarya.

The neurons of laminae A and A_1 appear to be arranged in groups or clumps of three to five cells. A similar grouping was also noticed by Toboada (1927) in the lateral geniculate body of the monkey and it was also mentioned by O'Leary (1940) in his study of the cat.

As first demonstrated by Tello (1904) and later confirmed by O'Leary (1940), the neurons of laminae A and A_1 are of two different types: (1) there are the principal cells that are defined as those cells whose axons enter the optic radiation; and (2) the neurons that have short axons not extending beyond the lamina in which the parent cell body is situated. The latter conform to Golgi type II cells.

Some examples of the dendritic trees of the principal cells of laminae A and A_1 are shown in Fig. 2. Between three and six main dendrites usually arise from the cell body and each of these branches extensively to form a relatively loose plexus

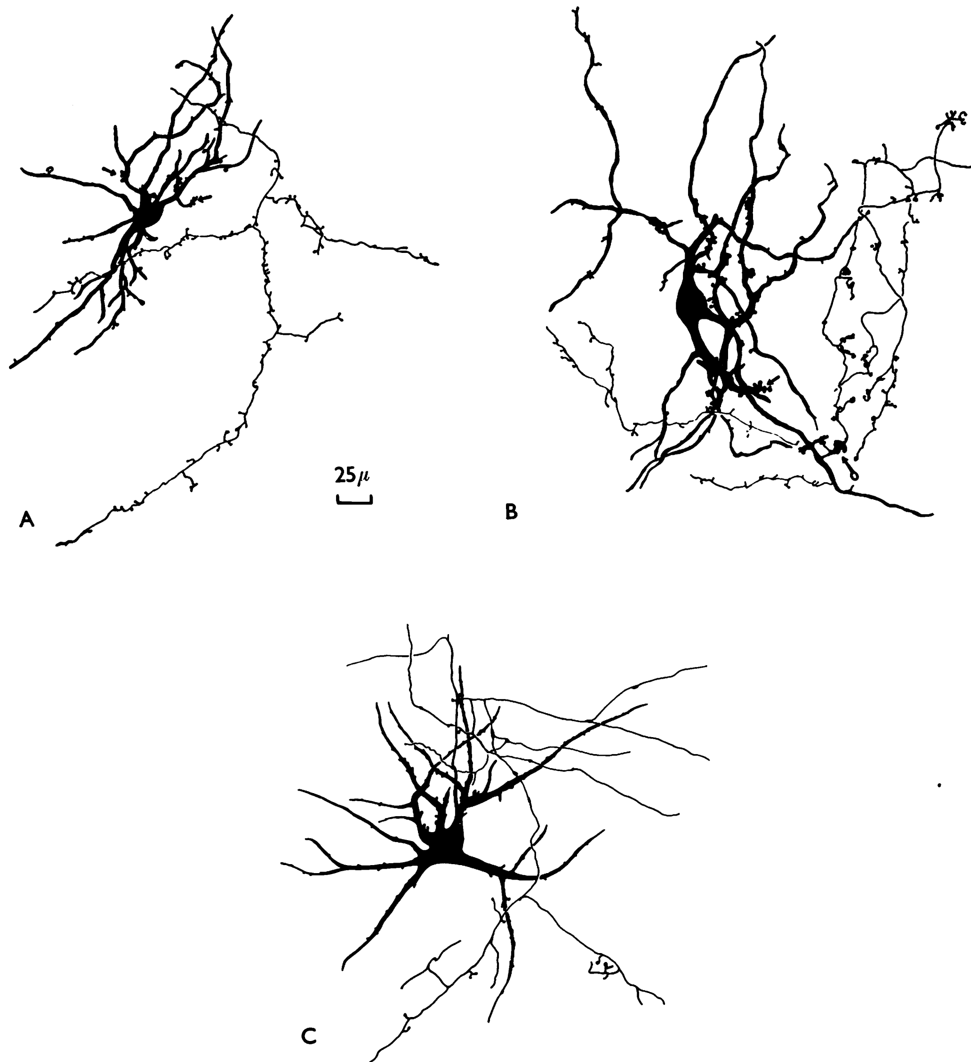

Fig. 2. Camera lucida drawings of neurons from Golgi preparations of laminae A and A_1. Grape-like protrusions of the dendrites are indicated by arrows. In A, and in the left part of B, thin axons with short side branches ending in boutons are shown. In B, on the right, is an axon forming claw-like terminals. The neuron in C has a branching axon.

radiating away from the cell. As observed by O'Leary (1940), the dendrites never seem to extend far beyond the lamina containing the parent neuron. Although definite proof of this statement is very difficult to establish from Golgi-stained preparations, it is supported by the fact that the neurons in the middle of a lamina have dendrites that pass out in all directions to form an almost spherical field, whereas those of neurons at the periphery of a lamina tend to pass towards the middle of the lamina in which the cell body lies (Taboada, 1927).

While little information is available in the literature about the shapes and forms of the dendrites of the principal neurons of the dorsal nucleus of the lateral geniculate body, in the Golgi-stained preparations that we examined, there is no doubt that the smaller dendrites are rough-surfaced (Fig. 2), having a number of thorns or spines, whereas the main dendrites have relatively smooth surfaces. Furthermore, some of the larger dendrites have characteristic protrusions arising from them (arrows, Fig. 2A and B) which are up to 5 μm in length and consist of a short stem which expands into a terminal ball. These protrusions have been described as 'grape-like' by Szentagothai (1963), and this term will be retained here, since as far as can be ascertained the structures that he describes here are the same as those marked by arrows in Fig. 2. Such grape-like protrusions are usually found along the primary divisions of the main dendrites and, indeed, are frequently present at the actual site of division. It should perhaps be pointed out though, that with the exception of these grape-like protrusions, Szentagothai (1963) states that the dendrites are smooth, and have no spines or thorns, a statement which is not substantiated either by the present study, or by the illustrations of Tello (1904), Cajal (1911) and O'Leary (1940).

In most preparations of the lateral geniculate body stained by the Golgi method, the axons of the neurons failed to stain, a feature which is common in preparations of adult material. In the preparations of Dr Morest, axons of the principal cells were stained and one such cell is shown in Fig. 2C, where it will be seen that the axon branches. Branching has also been described by Tello (1904) and Cajal (1911), but O'Leary (1940) found that collateral arborizations of the axons of the principal cell were unusual. In common with other workers, O'Leary observed that the axons of the Golgi type II cells branch quite frequently within their own lamina, in the immediate vicinity of the cell body.

To turn now to the other types of axons that have been observed within the Golgi-stained preparations of laminae A and A_1.

According to Tello (1904), once an optic nerve fibre has penetrated the ventral surface of the nucleus, it runs to its lamina of termination, where it bifurcates repeatedly, until an extensive brush-like arborization is produced. The arborization Tello (1904) likens to that of a cypress tree and, according to him and to O'Leary (1940), this arborization is predominantly directed towards the upper surface of the lamina, although where the lamina is thickest, it may not extend over its entire width. Szentagothai (1963) states that these brush-like terminations are probably preterminal, the true terminations of the axons being in the form of short, claw-like endings. Such claw-like terminals have also been observed in the present Golgi preparations, and as shown in both Fig. 3C and on the right-hand side of Fig. 2B, each claw is composed of a group of four or five terminal knobs, each of which has

a diameter of 1–1·5 μm. The true form of branching of the axon giving rise to these knobs is very difficult to follow in detail, because it is so prolific; but it is apparent that each of these arborizations is localized in extent and related to a small group of neurons. The claw-like terminals sometimes appear to come into contact with the grape-like protrusions of the principal neurons (Fig. 2B, ringed arrow) in the manner indicated by Szentagothai (1963).

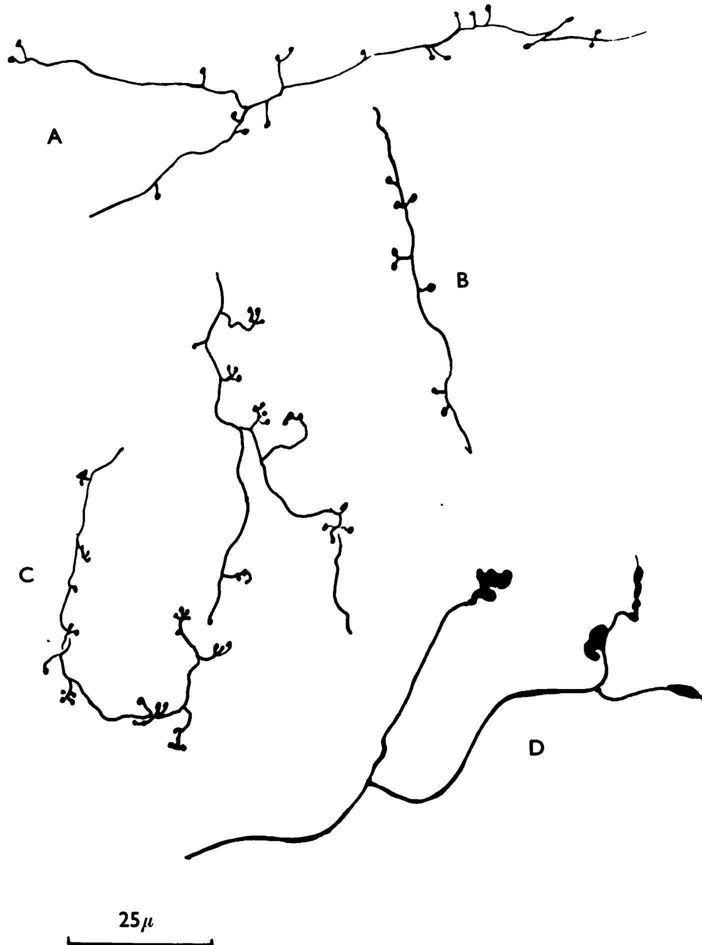

Fig. 3. Camera lucida drawings of different types of axons present in Golgi preparations. A, a thin axon with short side-branches ending in boutons; B, a thicker axon with short side-branches; C, an axon forming claw-like terminals; D, an axon forming expansions.

In addition to the claw-like terminals of the cypress tree arborizations, three other types of axon have been identified in the Golgi preparations of laminae A and A_1.

(1) The most common of these is a thin type of axon that runs for long distances within the laminae (Figs. 2A and 3A). At irregular intervals, such axons give off short side branches, each of which terminates in a knob. Because it is so slender,

the thickness of the parent axon is difficult to measure accurately, but the knob-like terminals have a diameter of 0·5–1·0 μm. The impression has been gained that these thin axons are derived from the optic tract.

(2) The third type of axon identified in the Golgi preparations is shown in Fig. 3B. It is similar in appearance to the thin axon described above, although it is obviously thicker (about 1 μm) and the short side branches come off the main trunk at wider spaced intervals; the terminal knobs of these have a diameter of 1–2 μm. The origin of these axons could not be determined, but it is clear that they are quite distinct from the thinner variety and that there is no graduation in size between the two extremes.

(3) The last type of axon to be identified is a relatively thick one with a diameter of about 1 μm. This type of axon is characterized by having expansions, or blobs, at intervals along its length (Fig. 3D). In a 41-day-old cat, these expansions varied in diameter between 2·0 and 3·5 μm, the mean value of fifteen measurements being 2·6 μm. The expansions are irregular in shape (Fig. 3D), occur at variable intervals along the length of the axon, and are sometimes terminal expansions of short side branches. The origin of these axons has not been determined, but in relation to the morphology of the lateral geniculate body as seen with the electron microscope, it is pertinent to mention that in one instance, what appeared to be expansion, was surrounded by a claw-like axon terminal of the type shown in Figs. 2B (ringed arrow), and 3C.

Electron microscope observations

In agreement with the results obtained by a light microscope examination of the structure of pars dorsalis A and A_1, the appearance of these two laminae is almost identical in electron microscope sections. The only apparent difference between them is in the number of nerve fibres that are passing dorsally to form the optic radiation. As the nerve fibres pass towards the optic radiation proper, they come together as the bundles that are a prominent feature of lamina A (Fig. 4). These bundles are composed of both myelinated and unmyelinated nerve fibres. The myelinated nerve fibres have diameters varying between 0·6 and 2·0 μm, the majority being about 1·0 μm (Fig. 4), while the unmyelinated nerve fibres have diameters of 0·2–0·3 μm.

The neurons of laminae A and A_1 are multipolar and as the main dendrites leave the cell body they branch, giving rise to primary, and eventually secondary dendrites, that penetrate into the surrounding neuropil. Some of the axons within the neuropil form boutons of various sizes (Figs. 9, 11) that synapse with the surfaces of the dendrites. Other axon terminals enter into junction with relatively large projections of the dendrites to form synaptic complexes that Szentagothai (1963) has referred to as glomeruli (Figs. 14–17). These are usually partially encapsulated by sheet-like astrocyte processes that isolate them from the components of the surrounding neuropil (Figs. 14, 17, *X.*), and it is because of this capsule that it is generally easy to identify them in low-power electron micrographs.

One of the features of the neuropil is that the components fit together, so leaving

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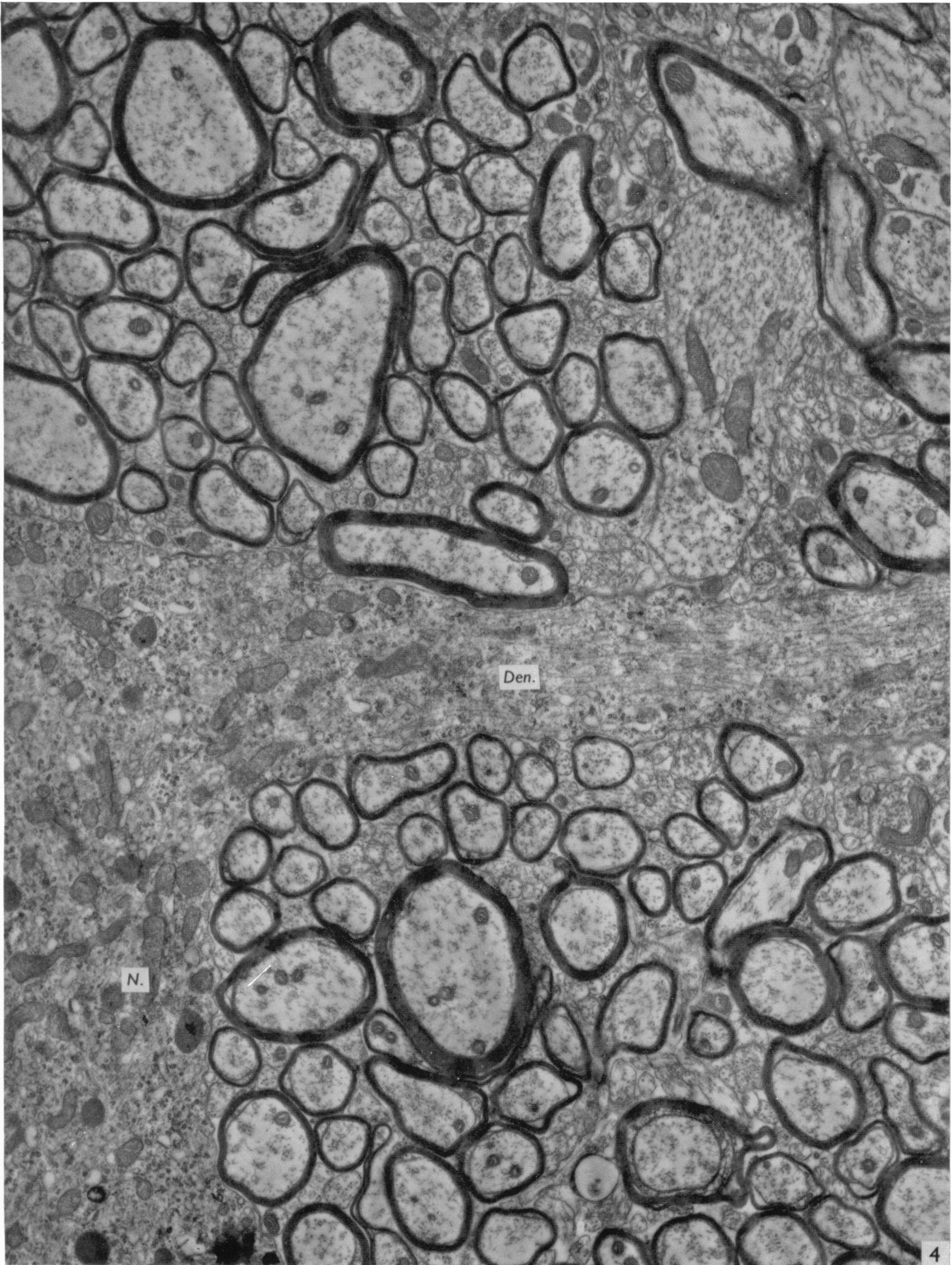
Fig. 4. The dorsal part of lamina A, showing two bundles containing myelinated and unmyelinated fibres that enter the optic radiation. In the bottom left is the cell body of a neuron (*N.*) with a dendrite (*Den.*) emerging to pass between the nerve fibres. ×11 000.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little free space beyond the 150 Å or so gap between the outsides of the plasma membranes of adjacent components (Fig. 5). Many of the irregular spaces between the various components are filled by sheet-like processes of astrocytes (see Fig. 11, *X.*). Both the cell bodies and the processes of the astrocytes have very irregular contours that are difficult to follow in low-power electron micrographs, contours that give the impression of being imposed upon them by the components of the surrounding neuropil. The nuclei of the astrocytes have a relatively homogeneous appearance (Palay *et al.* 1962) and their cytoplasm is characterized by bundles of fibrils that run throughout the processes and the cell body. The thin, sheet-like processes, to which these cells give rise, are derived directly from both the cell body and the main processes, and they pass into the surrounding neuropil either to isolate individual components, e.g. axon terminals (Fig. 11), or to isolate groups of components (e.g. glomeruli (Figs. 14–17, *X.*)). Other processes of astrocytes are encountered around capillaries, where they form end-feet resting upon the surface of a basement lamina. In the cat, collagen fibres are sometimes found around capillaries, in the interval between this basement lamina and that surrounding the endothelial cells of the capillary wall.

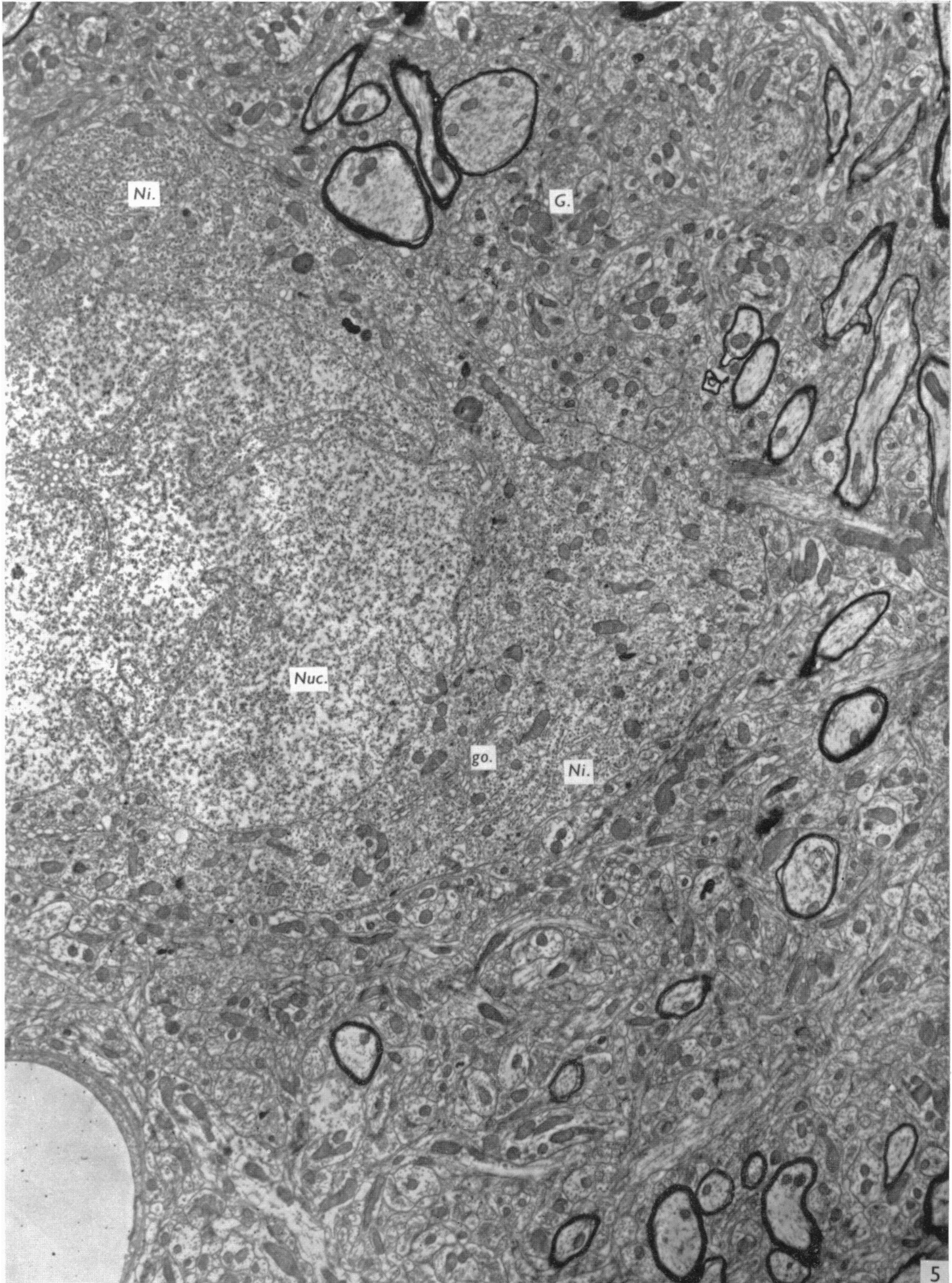
Another type of cell encountered in the lateral geniculate body is the oligodendrocyte. This glial cell is smaller than the astrocyte. Its electron-dense cytoplasm is rich in ribosomes and usually forms only a thin rim around the rounded nucleus. Oligodendrocytes are scattered throughout the neuropil, but are most commonly found in relation to the bundles of optic radiation fibres within laminae A and A_1. When processes are found to arise from the cell body, they have dark cytoplasm, like that of the parent cell, and contain a number of tubules, very similar in appearance to those within dendrites. Other oligodendrocytes form satellite cells to neurons and in this location have only rarely been observed to give rise to processes.

Cell bodies and dendrites of neurons

The nuclei of the neurons of laminae A and A_1 frequently have an irregular shape, the nuclear membrane being indented into a series of deep folds that may extend half-way across the diameter of the nucleus (Fig. 5, *Nuc.*). The particles of the nucleoplasm are disposed in random manner, so that the nucleus has a homogeneous appearance. Sometimes nucleoli are apparent.

In the cytoplasm surrounding the nucleus there are numerous ribosomes. Many of these are associated with membranes of the endoplasmic reticulum (Figs. 6, 13, *er.*), which are obvious at the periphery of the neuron. In the zone between the nuclear membrane and the subsurface Nissl bodies lie the majority of the randomly oriented mitochondria. In the same zone most of the Golgi apparatus occurs (Fig. 5, *go.*). This is not to suggest that the agranular reticulum is confined to this zone, but it is here that the largest groups of smooth cisternae are found. A prominent feature of the neurons of laminae A and A_1 is the presence of structures within the cytoplasm that Morales, Duncan & Rehmet (1964) have termed laminated

Fig. 5. Most of the field is occupied with a neuron that has an irregular nucleus (*Nuc.*). The cytoplasm of the neuron contains Nissl substance (*Ni.*) and Golgi apparatus (*go.*). The remainder of the field is occupied by neuropil. Note the glomerulus (*G.*). × 8 000.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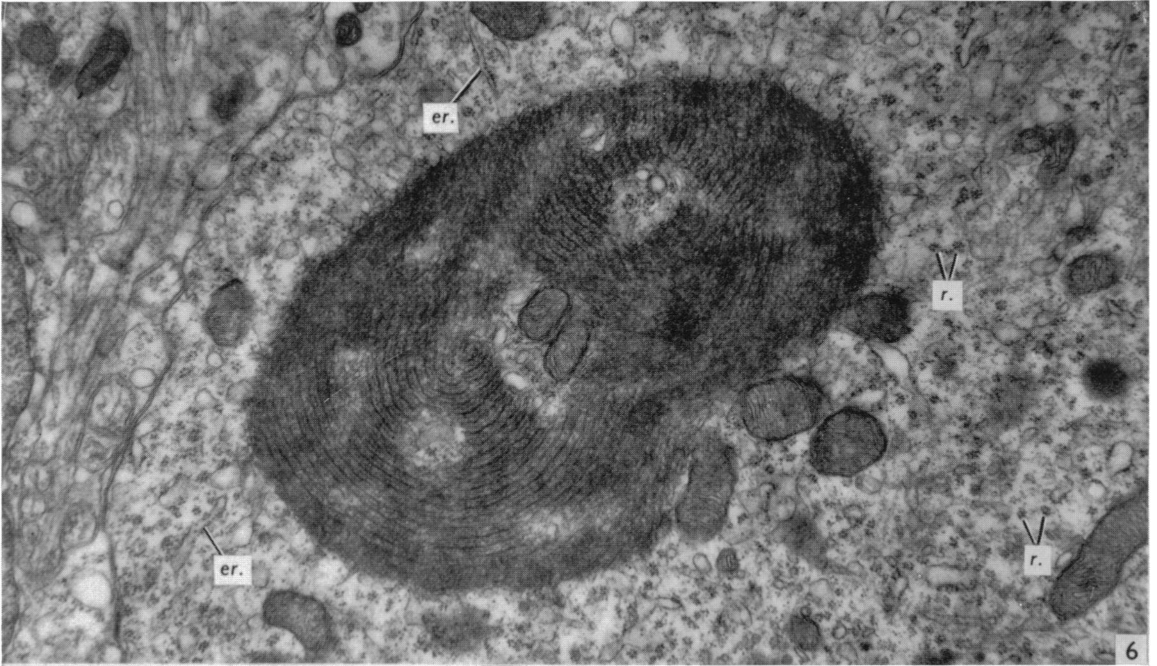
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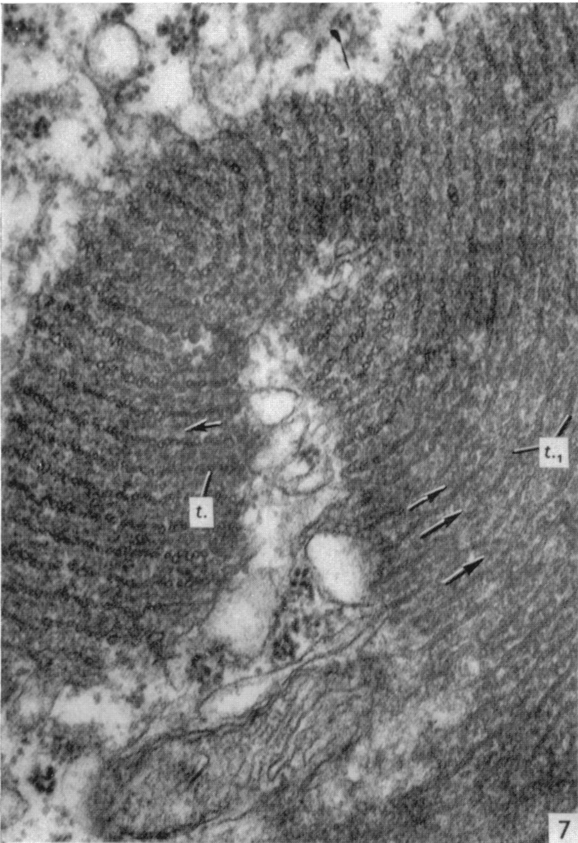
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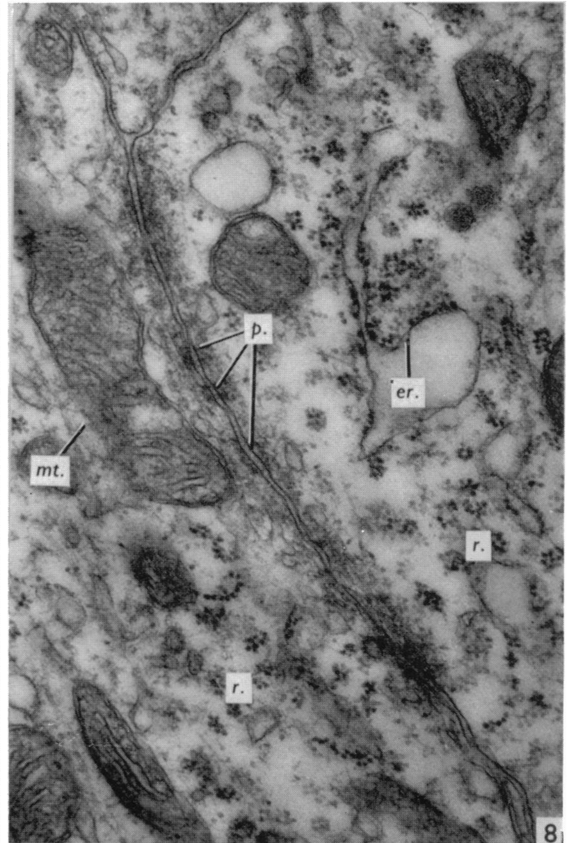
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bodies. These bodies (Figs. 6, 7) are up to 5 μm in diameter and may occur anywhere within the cytoplasm of the soma, probably not more than one or two per cell. At low magnifications, the laminated bodies are striking in appearance because they are composed of regularly repeating dark and lighter lines, often arranged in whorls, the minimum separation between adjacent dark lines being about 700 Å. At higher magnifications, it is evident that every one of the dark lines is composed of a sheet of tubules, each about 200 Å in diameter (Fig. 7), the sheets sometimes being sectioned so that the tubules are seen in transverse sections (Fig. 17, *t.*), as shown by Morales *et al.* (1964) and in other places along their length, as on the right-hand side of Figure 7 ($t._1$). It is presumably this latter appearance of the tubules that led Smith *et al.* (1964) to consider that the laminated bodies are composed of layers of membranes.

Between the sheets of tubules is an electron-dense substance; half-way between the sheets of tubules, this is concentrated to give the appearance of an intermediate, dark line (Fig. 7, arrows). This material appears to be composed of filaments oriented parallel to the tubules.

Neither the form, nor the situation of these bodies gives any indication of their function, but it is interesting that small islands of ordinary cytoplasm are usually present within them (Fig. 6), and the bodies frequently have a number of mitochondria in their vicinity, often situated very close to their outer surface (Fig. 6).

Contrary to the findings of Smith *et al.* (1964), these laminated bodies have only been observed within the cytoplasm of the soma and not the dendrites, which otherwise, since they arise from the neurons directly, contain the same cytoplasmic components. The appearance of the dendritic cytoplasm is somewhat different from that of the soma because at the base of a dendrite there is a decrease in the amount of ribosomal material, so that the dendrites are generally lighter in appearance than the cell body itself. This loss of ribosomal material applies in particular to that associated with the endoplasmic reticulum, most of the ribosomal material within the dendrites being in the form of free particles, generally lying towards the periphery of the dendrites (Figs. 8, 11). The other change is that at the base of a dendrite, the microtubules become oriented in such a way that they funnel into the dendrite and enter it in a parallel array (Fig. 4). This orientation of the microtubules, parallel to the length of the dendrite, continues even into the smaller branches (Figs. 8, 9 and 11, *mt.*).

Fig. 6. Laminated body from the cytoplasm of a neuron of lamina *A*. Mitochondria are closely associated with the body and the profiles of two of them are included in an island of cytoplasm in the centre of the body. In the surrounding cytoplasm are ribosomes (*r.*) and endoplasmic reticulum (*er.*). × 19 000.

Fig. 7. Part of a laminated body at higher power. The dark lines seen in Fig. 6 may be observed to be formed by sheets of tubules, those on the left are sectioned transversely (*t.*) and on the right, longitudinally ($t._1$). Midway between the sheets of tubules, the electron-dense material is concentrated to form intermediate dark layers (arrows). × 83 000.

Fig. 8. Part of two large dendrites, the left one sectioned longitudinally and the right one transversely, contain microtubules (*mt.*), ribosomes (*r.*) and endoplasmic reticulum (*er.*). The plasma membranes of the dendrites come together to form a series of adhesion plaques (*p.*). These are marked by an accumulation of electron-dense material in the adjacent cytoplasm. × 31 000.

Like the cell body of the neuron, the main stem dendrites have relatively smooth outlines, and although they are intimately surrounded by the components of the neuropil, it is not common to find axon terminals synapsing upon their surface (see Fig. 4). Only occasionally are synapses present, and these are formed by the large axon terminals, as will be described later.

A feature of dendrites of the lateral geniculate neurons is that they are not surrounded by sheet-like processes of astrocytes, as are some neurons in other parts of the central nervous system (see Palay & Peters, 1965). Thus, adjacent dendrites often come to lie side by side, when adhesion plaques may occur between their plasma membranes (Fig. 8, *p.*). At these adhesions, the distance between the outsides of the two plasma membranes increases from the usual gap of 120–150 Å, to one of about 250 Å, or about 300 Å from centre to centre of adjacent membranes. The plasma membranes also come to lie parallel to each other and appear to be more clearly defined then elsewhere (Fig. 8). Part of this increase in definition of the plasma membranes is due to an increase in the amount of darkly staining material in the cytoplasm adjacent to the vicinity of the adhesion area. The darkly staining material appears to be mainly amorphous (Fig. 8).

These adhesion points may either occur individually or, as is more common, in a series (Fig. 8). From their appearance it is clear that they have much in common with the desmosomes, or maculae adherentes, that have been described elsewhere in the literature (see Farquhar & Palade, 1963). The main difference appears to be that, so far, no central line has been observed in these adhesions in the interval between the plasma membranes. Until more is known about these adhesions, they will not be given any special name, but be referred to merely as adhesions.

At the places where the primary dendrites are formed by bifurcation of the main stem dendrites, it is sometimes possible to find very short, thick side branches of dendrites that enter into union with axon terminals to form glomeruli (see Fig. 14). This is not to suggest that glomeruli are formed exclusively in this region, though they appear to be more common where the surface of the dendrite loses its smooth outline and gives rise to surface irregularities in the form of spines and thorns.

As the dendrites become smaller in diameter and are further distant from the parent cell body, their character changes somewhat. Ribosomal particles become fewer within the cytoplasm and tend to lie immediately adjacent to the plasma membrane in small groups, although occasional ribosomes may also be present between the microtubules forming the central core of the dendrite (Fig. 11). It is indeed fortunate that ribosomal particles are always present within the cytoplasm of dendrites, for it is possible, by their presence, to identify the smaller dendritic branches which cannot be related to a neuronal cell body in a section, and to differentiate them from the smaller unmyelinated axons that pervade the neuropil. Like the dendrites, small axons have microtubules within their cytoplasm as may be seen in Fig. 13 (*mt.*) which shows the preterminal part of an axon. Differences that are useful in identification of neuronal processes are that small dendrites usually have irregular contours and tend to course through the neuropil as individuals that often bear thorns and spines (Figs. 9, 14, *t.*), whereas axons generally have a regular outline and often run in bundles in which they are arrayed parallel to each other. As pointed out by Wolfe (1961), perhaps the most critical test that can be applied

to differentiate axons and dendrites is whether or not the cytoplasm contains synaptic vesicles (Figs. 10, 11, *v.*), 300–600 Å in diameter. Unfortunately, this means of identification is only relevant when an axon is near a terminal, but it is important since, as far as can be determined, groups of vesicles having the features of those associated with synapses are only rarely found in processes that display features, such as their content of ribosomal particles, that would identify them as dendrites.

On the basis of the criteria outlined above, it would be wrong to suggest that every neuronal process within an electron micrograph can be identified as either an axon or a dendrite with absolute certainty. Nevertheless, the above criteria have been found to form a useful working basis, particularly in the early phases of this investigation. Later, the identity of many of the isolated neuronal processes became more certain as they were found to be in continuity with the larger processes whose identification was more readily apparent.

Axon terminals and synapses

Since the present state of our knowledge of the fine structure of the central nervous system demands that many assumptions be made, it is necessary to state how the terms 'axon terminal' and 'synapse' are used in the following account.

An axon terminal is considered to be any enlargement of a process that contains synaptic vesicles (see Figs. 10, 12, *v.*), 300–600 Å in diameter and, when it is sufficiently large, an accumulation of mitochondria. Such terminals may occur either at the tips of axons, when they will be called end-boutons, or they may occur along the length of an axon, when they will be referred to as boutons *en passant*. When the plasma membrane of an axon terminal comes into apposition with the plasma membrane of either a second neuronal process or a cell body, in such a way that the two plasma membranes lie parallel to each other, and are accentuated by an accumulation of electron-dense material in the adjacent cytoplasm (Palay, 1956, 1958), it is assumed that the presence of a synaptic contact, or junction, is indicated (Figs, 10, 12). Such contacts are regarded as definitely synaptic only if in the majority of contacts made between the two types of structure there is an accumulation of vesicles in their immediate vicinity, intermixed with the electron-dense material associated with the contact zone. Consequently, if there is an accumulation of electron-dense material in the cytoplasm immediately adjacent to the apposed plasma membranes, but no synaptic vesicles associated with it, the contact is regarded as adhesive, and not synaptic in function, even though some vesicles may be present within the cytoplasm of one of the components (see Fig. 12). The accumulation of electron dense material in the cytoplasm immediately adjacent to the plasma membrane at a synapse is sometimes asymmetric in its distribution (Gray, 1959).

As to the direction of conduction of a synapse; the presence of vesicles within the cytoplasm of only one of the processes taking part in the formation of a synaptic junction has led to the assumption that this structure is pre-synaptic. When, however, vesicles are present in the cytoplasm of both processes, neither of which contain ribosomes, it is assumed that we are dealing with an axo-axonic synapse, and that the pre-synaptic element is one in which the vesicles are accumulated close to the area of contact (see Fig. 20).

For the purposes of description, the synapses of the lateral geniculate body will

be considered in two groups, non-glomerular synaptic contacts and glomerular synaptic contacts. The non-glomerular synaptic contacts are those synaptic contacts that are formed between a single pre-synaptic axon terminal, and a single post-synaptic element, which may be either the soma or the dendrite of a neuron. The glomerular synaptic contacts are those between the members of groups of neuronal processes giving rise to glomeruli. In glomeruli, the neuronal processes form a relatively compact group and are partially isolated from the components of the surrounding neuropil by the processes of astrocytes.

It is important to note that the three types of non-glomerular synapses to be described below appear to be formed almost exclusively by the end-boutons of axons and that each bouton may form synapses upon more than one dendrite or cell body. Only a very few instances have been found of axons forming boutons *en passant* in laminae A and A_1. This finding is contrary to that of Smith *et al.* (1964) who, on the basis of methylene blue stained preparations consider that chains of boutons *en passant* extend along the dendrites of the neurons of the cat lateral geniculate body, as far as their base at the soma of a neuron. In their electron microscope studies, however, these authors found no evidence to substantiate this claim.

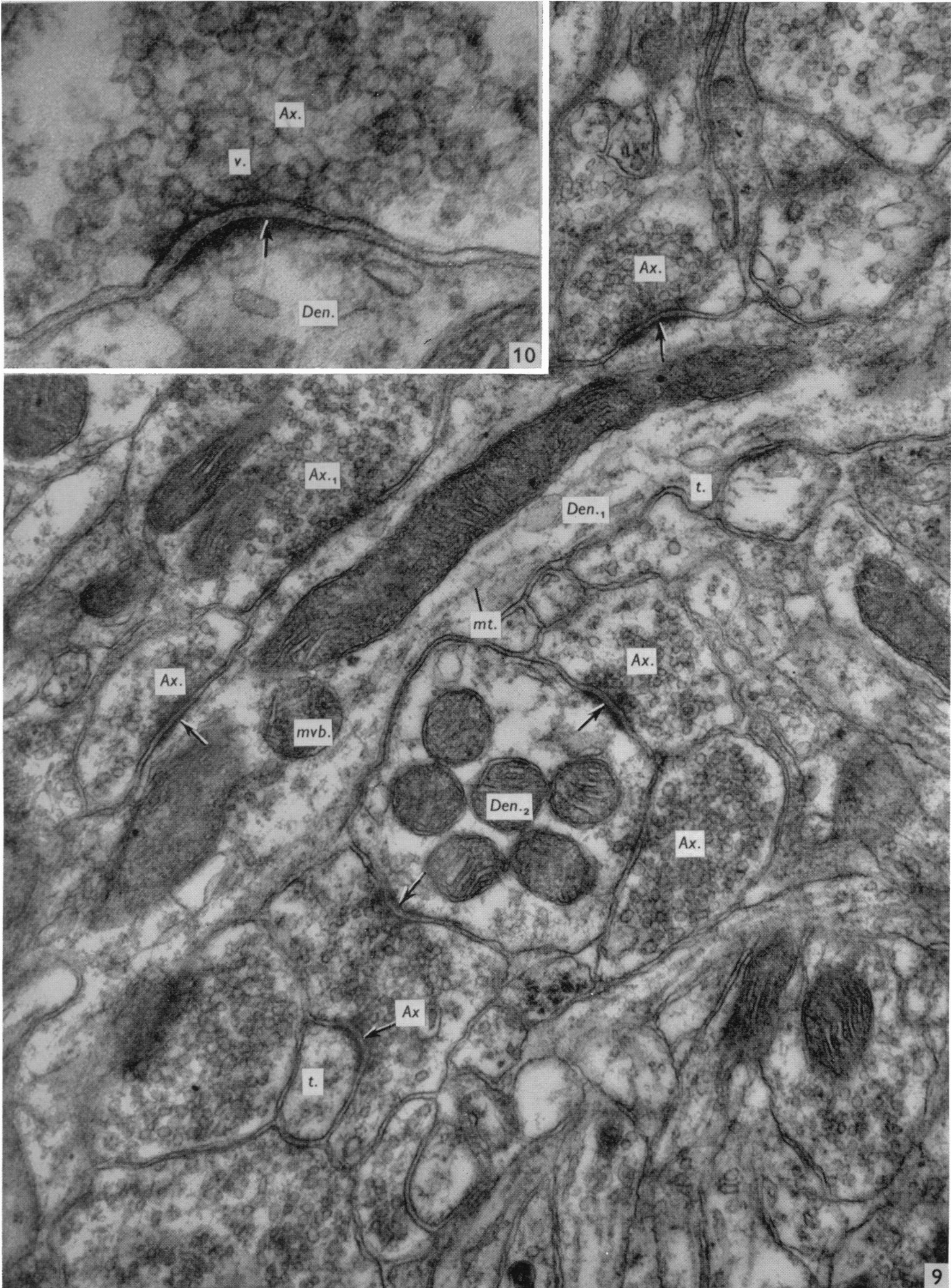
Non-glomerular synaptic contacts upon dendrites

(*a*) The synapses most commonly found in laminae A and A_1 are depicted in Fig. 9 and 10 (arrows). Such synapses are most common upon the smaller dendrites, sometimes upon the sides and bases of thorns (Fig. 9, *t.*) and are made very conspicuous by the dense osmiophilic material that is particularly obvious on the post-synaptic side of the single junctional zone between the apposed plasma membranes of the axon terminal and dendrite.

At the junctional zone, which commonly extends for a distance of 0·3 μm, the outsides of the adjacent plasma membranes are separated by an interval of between 250–300 Å (see Loos, 1963). Within the cytoplasm of both sides of the synapse, the osmiophilic material comes right up to the cytoplasmic surface of the plasma membrane forming the junction, and the junction is often curved in such a way that the concavity indents the axon terminal (Fig. 10, *Ax.*). In the less conspicuous electron-dense material of the presynaptic side of the synapse, some synaptic vesicles are embedded (Fig. 10, *v.*). Vesicles often pack the terminals, which are only about 1 μm in diameter, so that it is rare to find the profile of more than one or two mitochondria in a given section of the terminal (Figs. 9, 10).

Fig. 9. The slender dendrite (*Den.*$_1$) crossing the field diagonally contains a long mitochondrion, microtubules (*mt.*) and a multivesicular body (*mvb.*). Both this dendrite and a second one sectioned transversely (*Den.*$_2$) have axon terminals (*Ax.*) forming simple synaptic contacts with their surfaces (arrows). Two thorns (*t.*) are present, one of which forms a synapse. A larger axon terminal (*Ax.*$_1$) also appears to form a synapse with the longitudinally sectioned dendrite. ×34 000.

Fig. 10. A simple synaptic contact (arrow) formed between a dendrite (*Den.*) and a small axon terminal (*Ax.*). Note the concavity of the synaptic junction and the electron-dense material on the postsynaptic side. Within the axon the electron-dense material is less apparent and is intermingled with vesicles (*v.*) near the junctional region. ×80 000.


Ax.
v.
Den.
10
Ax.
Ax.₁
t.
Den.₁
mt.
Ax.
Ax.
mvb.
Den.₂
Ax.
Ax
t.
9

This type of synapse (Figs. 9, 10) has been called a type 1 synapse by Gray (1959), but here it will be referred to as a 'simple synaptic contact', because a constant feature of such a synaptic contact is that there is only one, long synaptic or junctional zone present between the plasma membranes of the axon terminal and the dendrite. Such simple synaptic contacts are not entirely restricted to the surfaces of small dendrites. They have also been found upon the surfaces of the larger dendrites of the lateral geniculate neurons, although they never appear to occur upon either the main stem dendrites or the somata. Thus, as far as the neurons of laminae A and A_1 are concerned, the impression has been gained that the frequency of occurrence of simple synaptic contacts upon the dendrites increases with the distance from the parent cell body.

(*b*) The other type of axon terminal, commonly forming synapses with the dendrites, is larger than the one described above. It usually has the appearance of being flattened against the surface of the dendrite, so that although the diameter of the terminal is between 2·0 and 4·0 μm in the direction of the long axis of the dendrite, when it is measured in the plane at right angles to this, it is only 1·5 to 2·5 μm wide (Fig. 11, $Ax._1$).

This type of axon terminal synapses most frequently upon the primary dendrites and is only rarely found upon the surface of a main stem or small dendrite. Consequently, the majority of them are found in the region beyond, or at the first division of the main stem dendrites. Farther distant from the neuronal cell body is a region where these large terminals are interspersed with the smaller axon terminals and finally a region of small dendrites with only small axon terminals forming simple synaptic junctions upon their surface.

With the large axon terminals, the synaptic junction is not localized and single, as in the case of the simple synaptic junctions, but is discontinuous. Consequently, in individual sections it appears to be formed from a series of junctional zones of various lengths (see Fig. 11), at which there is an accumulation of electron-dense material within the adjoining cytoplasm of both sides (Fig. 11). At these zones the separation of the outsides of the pre- and postsynaptic plasma membranes is about 250 Å and appears to be somewhat less than the separation between membranes at the simple synaptic junctions. Further, the electron-dense material within the adjoining cytoplasm is less evident and the junctional zones rarely exhibit much curvature. Interestingly enough, the distribution of electron-dense material at the junctional zones appears to follow one of two patterns. At some sites, where synaptic vesicles are accumulated against the junction, the electron-dense material is small in amount and distributed relatively evenly in the cytoplasm of both sides,

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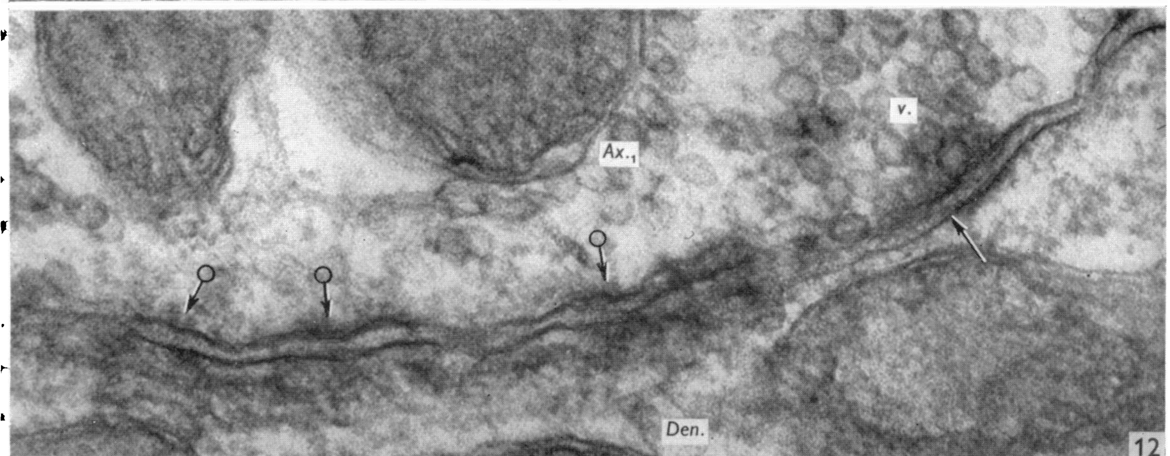
Fig. 11. A medium-sized dendrite (*Den.*) with large axon terminals ($Ax._1$) forming mixed synaptic contacts upon its surface. At these mixed contacts, some of the zones have synaptic vesicles (*v.*) associated with them (arrows), others (ringed arrows) do not. The dendrite contains microtubules (*mt.*), ribosomes (*r.*) and a multivesicular body (*mvb.*). The axon terminals contain synaptic vesicles (*v.*), mitochondria, neurofilaments (*nf.*) and agranular reticulum (*ar.*). × 14 000

Fig. 12. A mixed synaptic junction between a large axon terminal ($Ax._1$) and a large dendrite (*Den.*). Note that of the junctional zones, only one (arrow) has associated synaptic vesicles (*v.*). The other junctions (ringed arrows) are characterized by an accumulation of electron-dense material within the dendrite (*Den.*). × 80 000.

v.
nf.
Ax.₁
Den.
x.
x.
ar.
mt.
v.
mvb.
Ax.₁
Ax.₁
x.
r.
11


v.
Ax.₁
Den.
12

sometimes being more apparent in the presynaptic cytoplasm (Figs. 11, 12, arrows). At other sites, synaptic vesicles are not usually concentrated against the presynaptic membrane and most of the electron-dense material is accumulated on the dendritic side of the junctional zone (Figs. 11, 12, ringed arrows). Since synaptic vesicles are absent from the immediate vicinity of this latter type of zone, by definition, they are considered to be adhesive.

Because both synaptic and adhesive junctional zones are present between the same plasma membranes in the case of the contacts made between these large axon terminals and the dendrites of the geniculate neurons, this type of synapse will be referred to as a 'mixed synaptic contact'.

In contrast to the smaller axon terminals, these larger ones giving rise to mixed synaptic contacts, contain a number of mitochondria, interspersed with synaptic vesicles that are distributed throughout the entire terminal (Figs. 11, 12), although overall, the vesicles are less concentrated than those within the smaller terminals. In addition, a few microtubules and filaments (Fig. 11, *nf.*) may be present within the terminal, as well as irregular profiles of agranular reticulum (Fig. 11, *ar.*).

Synaptic contacts with the cell body.

Axo-somatic synapses appear to be relatively rare upon the neurons of laminae A and A_1, although it is impossible to estimate their actual number from electron microscope studies. When synapses are found, the axon terminals have a diameter of between 1·5 and 2·0 μm and as seen in Fig. 13, they have an appearance similar to that of the larger axon terminals synapsing upon the dendrites. These synapses also exhibit a number of contact zones, only a few of which have synaptic vesicles in immediate association with them, so that the synaptic contact is of the mixed variety. Like the larger axon terminals synapsing with the dendrites, those synapsing with the somata of the neurons are frequently separated from the elements of the surrounding neuropil, usually in an incomplete manner, by thin processes of astrocytes (Fig. 13, *X.*).

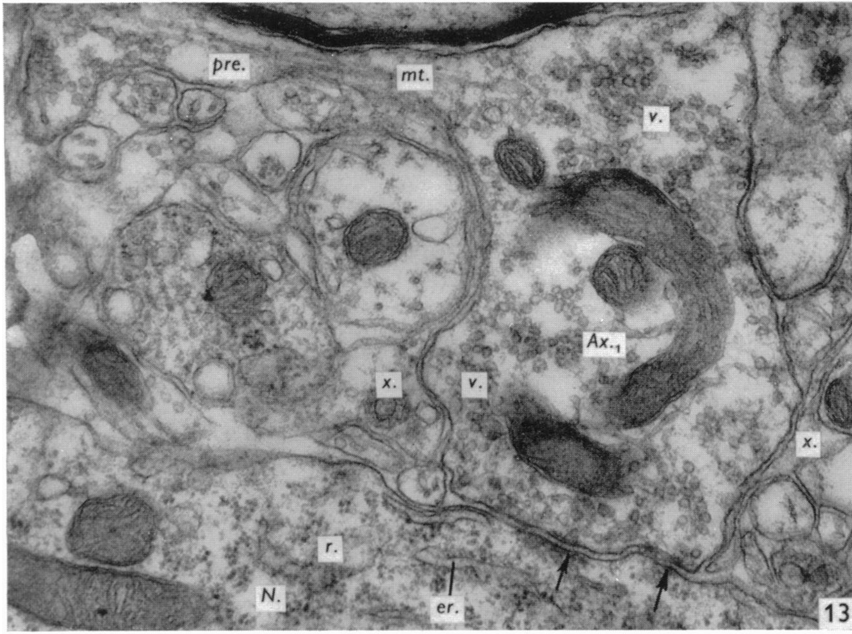
Geniculate glomeruli

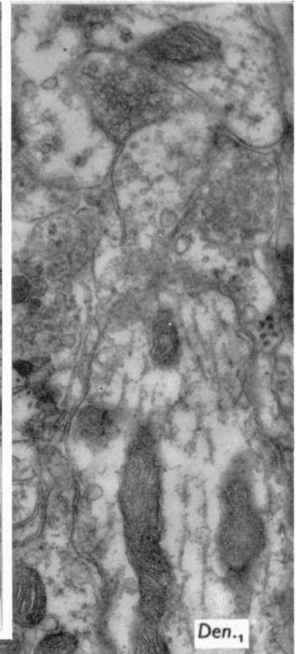
The term geniculate glomeruli, to describe the closely packed groups of neuronal processes that occur throughout the neuropil, was first used by Szentagothai (1962, 1963), because of the similarity between these groups of processes and those forming the glomeruli within the granular layer of the cerebellar cortex (Gray, 1961). Since it seems appropriate the term has been retained here.

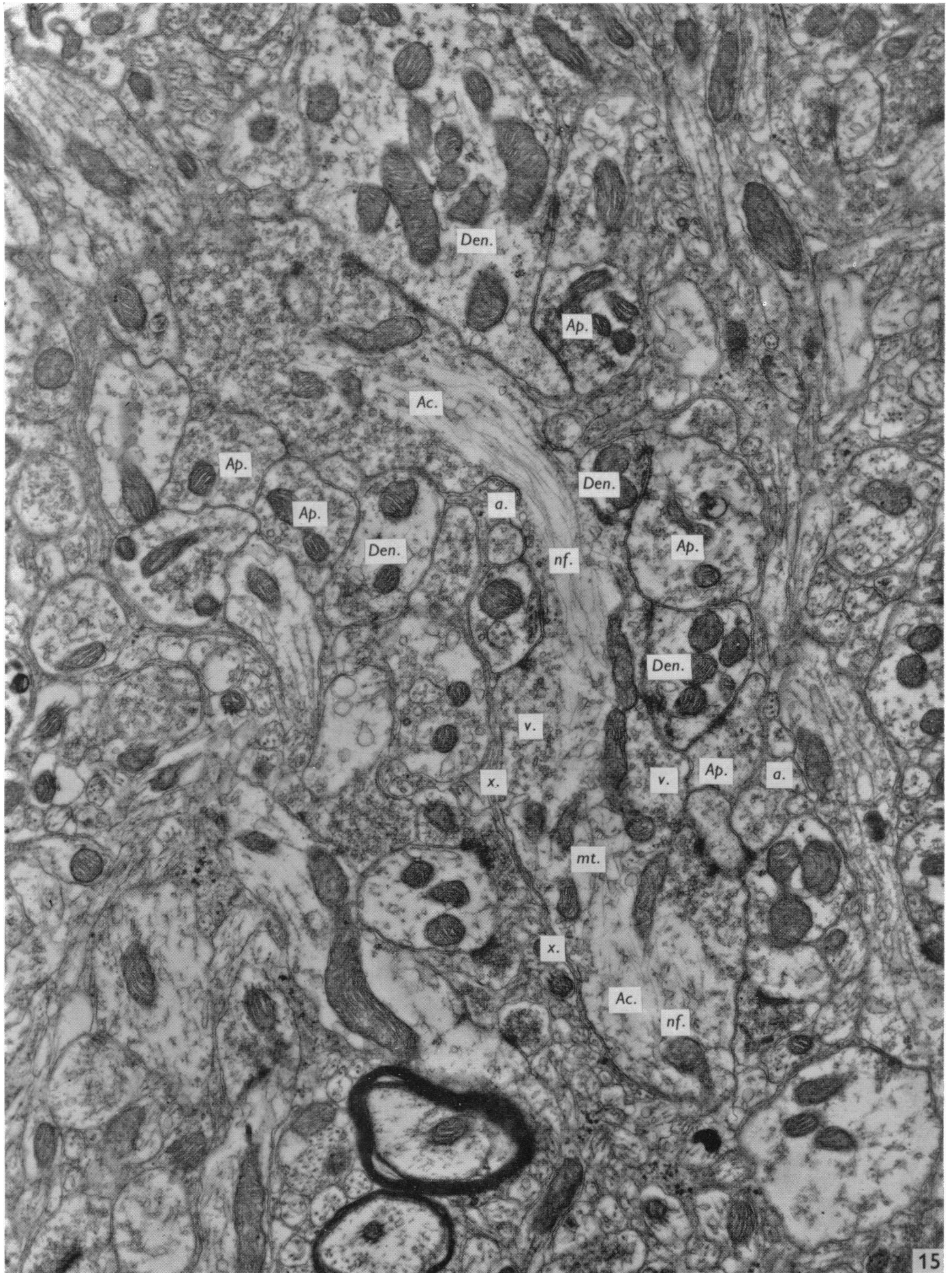
The geniculate glomeruli occur throughout laminae A and A_1 and are easily

Fig. 13. An axon terminal (*Ax_1*) containing mitochondria and vesicles (*v.*), forming a mixed synaptic junction (arrows) with the surface of a neuron (*N.*). The axon terminal, arises as an expansion of a pre-terminal axon (*pre.*) containing microtubules (*mt.*). The axon terminal is partially surrounded by sheet-like astrocyte processes (*x*). Note the ribosomes (*r.*) and endoplasmic reticulum (*er.*) within the neuronal cytoplasm (*N.*). × 30 000.

Fig. 14. A geniculate glomerulus. The dendrite on the right (*$Den._1$*) gives off two processes (*$D._1$* and *$D._2$*) that enter (arrows) a glomerulus partially bounded by astrocyte processes (*x.*). One of the dendrite processes (*$D._1$*) has a thorn (*t.*) that invaginates the central axon terminal (*Ac.*) and has a synapse (small arrow) upon its surface. Other profiles within the glomerulus are of peripheral axon terminals (*Ap.*) and one other dendritic process (*$Den._2$*). × 15 000


pre.
mt.
v.
Ax.-1
x.
v.
x.
r.
N.
er.
13


Den.-1
x.
Ap.
D.-2
Ap.
Ac.
t.
x.
Ap.
Den.-2
D.-1
Ap.
14


Den.
Ap.
Ac.
Ap.
Ap.
Den.
a.
Den.
nf.
Ap.
Den.
v.
x.
v.
Ap.
a.
mt.
x.
Ac.
nf.
15

identified because each one consists of a closely packed group of neuronal processes circumscribed by a capsule of narrow, sheet-like processes of astrocytes (Figs. 14–17, *X.*). Sometimes this outer capsule is incomplete, so that it only effects a partial separation between the processes in the glomeruli and those of the surrounding neuropil, but the capsule is always complete on any side of a glomerulus that comes up against either a neuronal cell body or another glomerulus.

In sections, the glomeruli show considerable variation in size. Some consist of the profiles of only four to five neuronal processes (see Fig. 17), while others contain twenty or more profiles (see Fig. 16), but in all cases the processes that they contain are always of three types. There is one type of dendritic component and two types of axonal components, the latter being in the form of axon terminals.

The dendritic component of a glomerulus is formed from short side branches that arise from relatively large dendrites. The branches (Fig. 14, D_1 and D_2) frequently originate in the vicinity of the division of the main stem dendrites into primary dendrites (Fig. 14, $Den._1$) and within a glomerulus they give rise to profiles that are readily recognizable, because they contain larger mitochondria than either of the two axonal components (Figs. 14–17). The dendrites also contain ribosomes and in addition have microtubules, but no vesicles in the concentration present within the axon terminals (see Figs. 14–17). Further, as established in sections where the connexions with the parent dendrite are visible (Fig. 14), the profiles of these dendritic branches are usually characterized by a large number of adhesion plaques that their plasma membranes make with those of the adjacent processes within the glomeruli, both axons and dendrites.

Like the adhesion plaques that are formed between the plasma membranes of adjacent dendrites within the surrounding neuropil (Fig. 8) these adhesions within the glomeruli have an accumulation of electron-dense material within the cytoplasm on each side (see Fig. 16, ringed arrows), and never have synaptic vesicles either in close association with them, or intermixed with the electron-dense material (Fig. 14). The actual form of the adhesion varies to some extent, depending upon whether the second plasma membrane taking part in the formation of the adhesion plaque belongs to another dendrite, or to an axon. In situations where there is a second dendrite, the adhesion has a symmetrical appearance (Fig. 16, ringed arrows), similar to those adhesions between non-glomerular dendrites (Fig. 8), because the cytoplasm on each side of the two parallel plasma membranes, which are separated by about 250 Å, contains an equal amount of osmiophilic material and thin fibrils. It is this accumulation of osmiophilic material, rather more extensive than between the non-glomerular dendrites, that makes these adhesions within the glomerulus such prominent structures (Figs. 14–17).

Where the second plasma membrane contributing to the formation of an adhesion plaque belongs to an axon, then the adhesion has a somewhat different appearance,

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Fig. 15. A geniculate glomerulus in which the central axon terminal (*Ac.*) is sectioned along its length and shows the core of neurofilaments (*nf.*) with an occasional microtubule (*mt.*). The vesicles (*v.*) are located more peripherally within the terminal. Surrounding the central terminal are the profiles of dendrites (*Den.*) and peripheral axon terminals (*Ap.*), that appear to arise as a result of expansions of small groups of axons of the type indicated (*a.*). Note the astrocyte processes (*X.*). × 17 000.

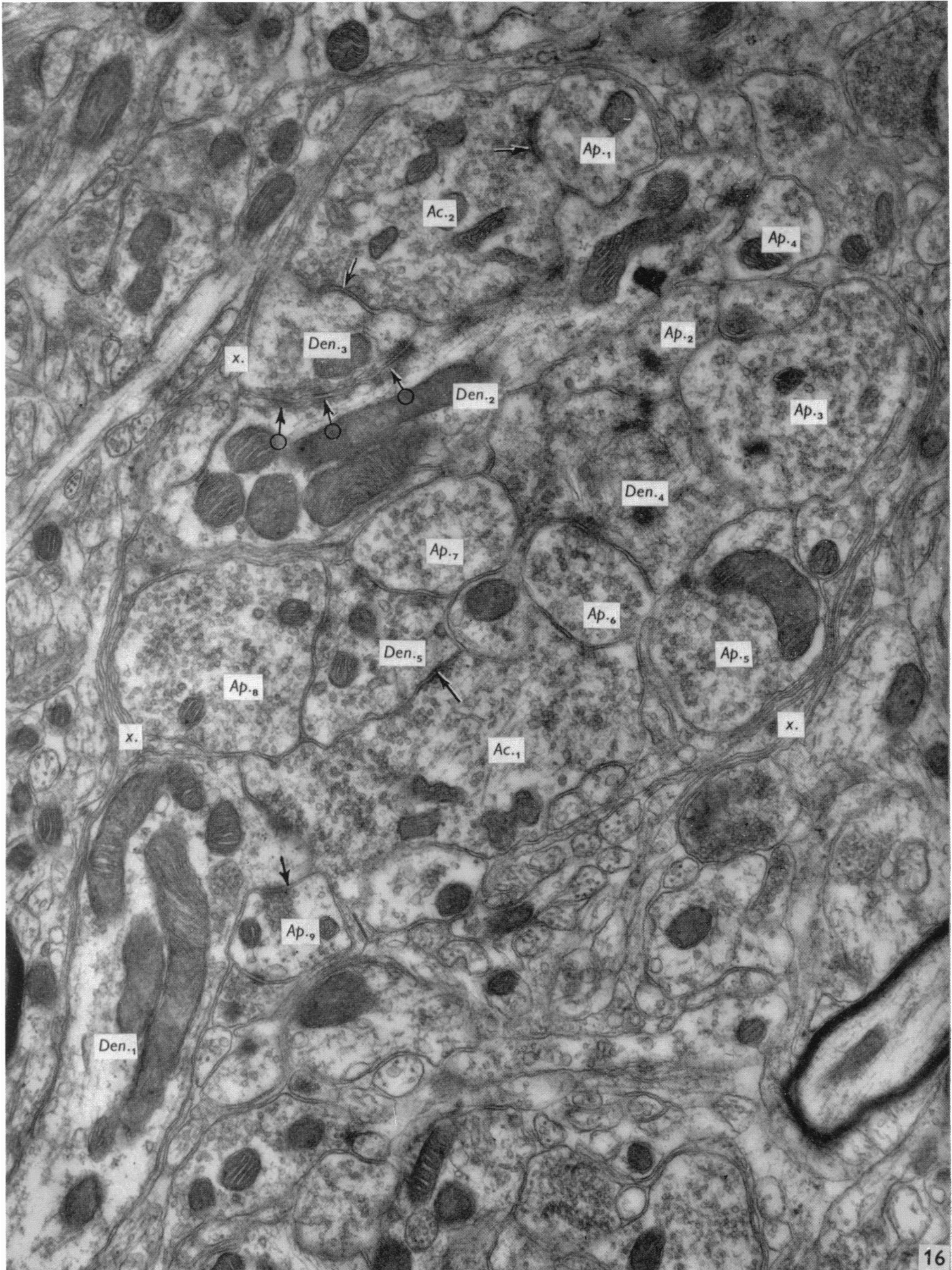
for it is asymmetrical. The asymmetry occurs because the amount of osmiophilic material associated with the adhesion is much less within the cytoplasm of the axon (Figs. 18, 19, ringed arrows), although it is unchanged in amount in the dendrite. It is important to make clear that these structures formed between the plasma membranes of dendrites and axons within the glomeruli, are regarded as adhesion plaques because they never have synaptic vesicles associated with them, either closely applied to the membrane or intermixed with the electron-dense material. Synaptic vesicles may be present within the axon terminal taking part in the formation of the adhesions but they are always at some distance from these areas. Nevertheless, synaptic vesicles may be present in association with other junctional areas between the same pair of membranes, and these latter (Figs. 18, 19, arrows) are regarded as being synaptic.

Although the average length of the adhesion plaques is 0·15 μm, they vary between 0·05 and 0·2 μm. The effect of the electron-dense and fibrillar material which is associated with these adhesions, is to make the periphery of a dendrite dark in appearance (Figs. 14, 16). More than one dendritic profile is usually present within a glomerulus and, while it is clear that the profiles are sometimes formed either by more than one branch arising from the same parent dendrite (Fig. 14), or by the sections passing through different parts of the same dendritic branch, in other glomeruli there is no doubt from the position and orientation of the dendritic components that they are derived from different parent stems. This has also been observed in serial sections.

The two types of axonal terminals within the geniculate glomeruli will be referred to as 'central axon terminals' and 'peripheral axon terminals'.

As the name suggests, central axon terminals usually lie towards the middle of the glomeruli and they have the largest axonal profiles (Figs. 14–17, *Ac.*). As far as can be determined, there is usually only one central axon involved in the formation of each glomerulus, although this may have short side-branches and be sectioned in more than one place, so that it is represented by more than one profile (Fig. 16, $Ac._1$ and $Ac._2$). The central axon terminals are derived from axons that are between 0·4 and 0·6 μm in diameter. These enter the glomeruli and expand into sac-like terminals of irregular shape, which may have a diameter of between 1·8 and 3·5 μm; the average diameter of twenty-seven central axon terminals was 2·4 μm. In some examples the axon has been found to approach the glomerulus, expand into a sac-like terminal, and then pass out of the other side of the glomerulus again as a thin axon, which may even expand again a little further on to form a terminal within the middle of another glomerulus. Two expansions along the course of a central axon are shown in Figure 15 (*Ac.*). In other examples in which the structure of a glomerulus has been followed in serial sections, the impression has been gained that some of the sac-like expansions are true terminals of an axon, because the axon has not been observed to continue by passing out of the glomerulus again. This point will be referred to again later.

Fig. 16. A large geniculate glomerulus in which it is possible to identify the profiles of two central axon terminals ($Ac._1$ and $Ac._2$), nine peripheral axon terminals ($Ap._1$–$Ap._9$) and five dendritic processes ($Den._1$–$Den._5$). Between two of the dendrites ($Den._2$ and $Den._3$) are symmetrical adhesion plaques (ringed arrows). Some of the synaptic junctions are indicated by arrows. Note the capsule of astrocyte processes (*x.*). ×18 000.


Ap.1
Ac.2
Ap.4
Ap.2
Den.3
x.
Den.2
Ap.3
Den.4
Ap.7
Ap.6
Den.5
Ap.5
Ap.8
x.
x.
Ac.1
Ap.9
Den.1
16

As already mentioned, one feature of the central axon terminals is that they give rise to the largest profiles within the glomeruli (Figs. 14–17, *Ac.*). Another is that the terminals are irregular in shape and when they are sectioned along their long axis, it is seen that they have a central core of neurofilaments (Fig. 15, *nf.*) and microtubules (Fig. 15, *mt.*); between these lie the mitochondria. The synaptic vesicles are mainly confined to the periphery of the terminals (Fig. 15, *v.*) and more are concentrated in the vicinity of the synaptic junctions (Figs. 16, 17, arrows). These same features are also apparent in transverse sections of the central axon terminals (Figs. 16, 17, *Ac.*).

The other type of axon terminal within a glomerulus is the peripheral axon terminal. These terminals are more numerous than those of the central axons and generally give rise to smaller, more rounded profiles, with an average diameter of about 1 μm (Figs. 14–17, *Ap.*). The peripheral axon terminals often contain large numbers of synaptic vesicles that are concentrated at synaptic junctions. They also contain mitochondria but, as far as can be determined, they rarely contain microtubules or neurofilaments, which is a useful guide in distinguishing them from the central axon terminals.

The preterminal axons giving rise to the peripheral axon terminals usually enter the glomeruli in groups, such as those shown in Fig. 15 (*a*), the number of such groups depending upon the size of the glomerulus. Each of the axons within a group is about 0·1 μm in diameter, and from serial sections it appears likely that such groups are formed as a result of branching of one or two parent axons. As each member of a group enters a glomerulus it expands into a peripheral axon terminal, which may be elongated in shape, so that two apparently separate profiles may belong to the same terminal, the terminal having curved around the central axon and so been sectioned in different places.

So much for the form and characteristics of these axon terminals within the geniculate glomeruli. The point to be considered now is how they are related both to each other and to the dendritic component. In the first place, it should be emphasized that these three different components are intermingled within a glomerulus, the central axon terminal lying towards the middle and the peripheral axon terminals and the dendritic components towards the outside; the majority of profiles within a glomerulus belong to the peripheral axon terminals (see Fig. 16). These components are bound together by the adhesion plaques that have been

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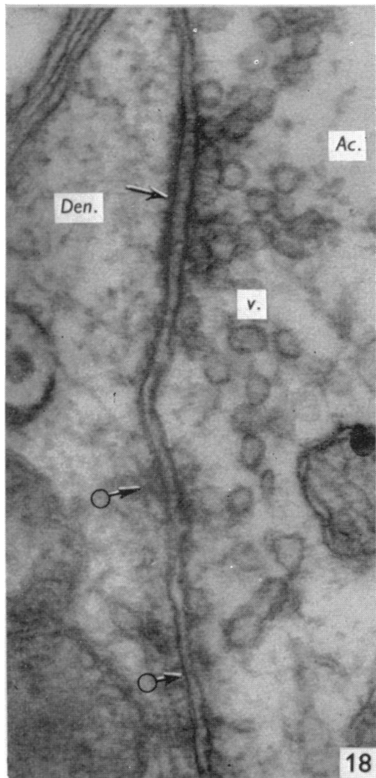
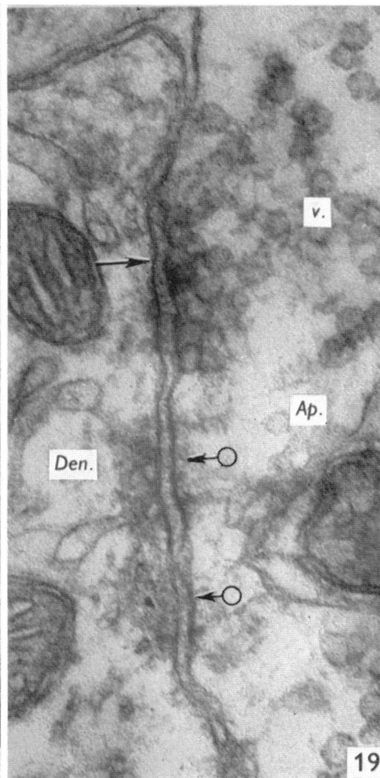
Fig. 17. A small geniculate glomerulus composed of one central axon terminal (*Ac.*), two dendrites (*Den.*$_1$ and *Den.*$_2$) are two peripheral axon terminals (*Ap.*$_1$ and *Ap.*$_2$). The central axon terminal synapses (arrows) upon each of the dendrites and upon one peripheral axon terminal (*Ap.*$_1$), which in turn also synapses with a dendrite (*Den.*$_1$). The glomerulus is surrounded by astrocyte processes (*X.*). ×33 000.

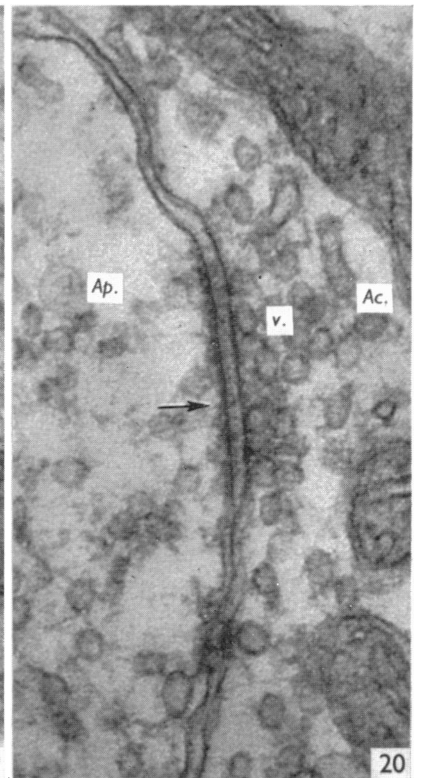
Fig. 18. A synaptic junction (arrow) between a central axon terminal (*Ac.*) and a dendrite (*Den.*) within a glomerulus. Note that at two other junctional zones (ringed arrows) there are no associated synaptic vesicles (*v.*) and the osmiophilic material is most prominent within the dendritic cytoplasm. ×60 000.

Fig. 19. A synaptic junction (arrow), within a glomerulus, between a peripheral axon terminal (*Ap.*) and a dendritic process (*Den.*). Note the two junctional zones (ringed arrows) that have no associated vesicles (*v.*). ×60 000.

Fig. 20. An axo-axonic synapse (arrow) between a central axon terminal (*Ac.*) and a peripheral axon terminal (*Ap.*). The synaptic vesicles (*v.*) are concentrated close to the junctional region on the central axon side of the synapse. ×60 000.


Ac.
Den.
v.
18


v.
Ap.
Den.
19


Ap.
v.
Ac.
20

described above although, so far, adhesions of this type have not been found to occur between the plasma membranes of adjacent axon terminals. In addition to these adhesion plaques, however, there are structures that have the characteristics of synapses, that is areas where adjacent plasma membranes run parallel to each other and where there is an accumulation of both osmiophilic material and synaptic vesicles within the cytoplasm immediately adjacent. Such synaptic unions occur between each of the two forms of axon terminal and the dendritic component, as well as between the axon terminals themselves, so that there are three types of synapse within a glomerulus, two axo-dendritic and one axo-axonic.

The synaptic junctions that occur between either a central axon terminal or a peripheral axon terminal and a dendrite are similar (Figs. 18, 19). As measured by the extent of the accumulation of osmiophilic material within the cytoplasm on each side of the junction, they are between 0·2 and 0·4 μm in length, the average being 0·3 μm. Such synaptic junctions are sometimes curved in shape (Fig. 17) with the concave side of the curve towards the cytoplasm of the dendritic component, but they do not show the same dense accumulation of osmiophilic material that is present on the postsynaptic side of the simple synaptic junctions formed by axon terminals upon the non-glomerular dendrites (Figs. 9, 10). Instead, as shown in Figs. 18 and 19, the synapses resemble the mixed synaptic junctions formed by the larger axon terminals outside the glomeruli (Figs. 11, 12), in which the accumulation of the osmiophilic material tends to be symmetrical or perhaps somewhat more obvious on the presynaptic side of the junction. This similarity is reinforced by the fact that the asymmetric adhesions, formed within the glomeruli between the same axonic and dendritic membranes (Figs. 18, 19, ringed arrows), closely resemble those junctional zones of the mixed synaptic junctions which also have no synaptic vesicles associated with them (Fig. 12, ringed arrows).

It is not uncommon to find spines or thorns that arise from the dendritic component and invaginate the central axon terminals (Fig. 14, *t.*). Such thorns usually form a synapse with the central terminal. No thorns that invaginate a central terminal have been found to arise from other axons, in the manner suggested by Szentagothai (1962).

Synaptic junctions are also present between the central axon terminals and the peripheral axon terminals (Figs. 17, 20). Their appearance does not differ greatly from those between the axon terminals and the dendritic component of the glomerulus (cf. Figs. 18, 20). At these junctions, the adjacent plasma membranes are separated by a distance of about 250 Å and the electron-dense material between the two membranes has little organized structure, although it seems to form an intermediate line in some cases (see Fig. 19). Osmiophilic material lies within the cytoplasm of both sides of the junction and sometimes this may be more apparent within the cytoplasm of the central axon terminals (Figs. 17, 20), which always exhibits an accumulation of synaptic vesicles close to the junction (Fig. 20, *v.*). These junctions are between 0·2 and 0·6 μm long in sections, and their average length is 0·4 μm. Such synaptic junctions may or may not be curved, but when they do exhibit curvature, the concave side always faces the cytoplasm of the peripheral axon terminal. As already pointed out, the synaptic vesicles occur within the cytoplasm of both sides of the junctional zone, but usually they are accumulated close to the

junction only within the cytoplasm of the central axon terminals. Within the peripheral axon terminals, synaptic vesicles occur in the immediate vicinity of this type of synaptic junction only when that terminal is itself packed with vesicles throughout. Thus, on the basis of the definitions given earlier, it is assumed that in these axo-axonal synaptic junctions the central axon terminal is the presynaptic element.

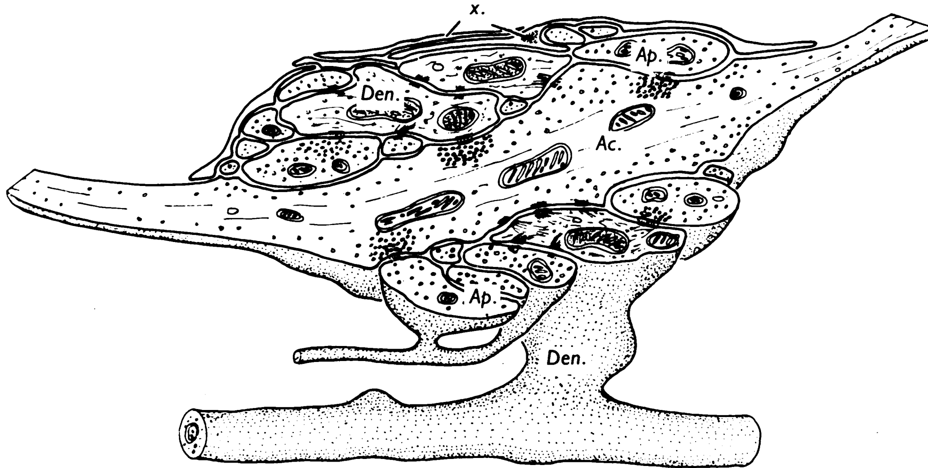


Fig. 21. A diagrammatic representation of the structure of a geniculate glomerulus. The central axon terminal (*Ac.*) forms the axis of the structure, and is surrounded by processes of dendrites (*Den.*) and peripheral axon terminals (Ap.). The whole is enclosed by astrocyte processes (*x.*). For further explanation see text.

To summarize: on the basis of the criteria laid down for structures defined as synapses, the central axon terminals within the geniculate glomeruli form synapses both with the dendritic components and with the peripheral axon terminals; in each case the central axon terminal is the presynaptic element. The peripheral axon terminals also synapse upon the dendritic components, and in respect of these synapses they are presynaptic. The form and structure of the geniculate glomerulus and the relation between its components is given in Fig. 21.

DISCUSSION

A summary of the results obtained in the present investigation of the structure and synaptology of laminae A and A_1 of the lateral geniculate body of the cat is given in Fig 22, in which an attempt has been made to correlate the findings derived from both Golgi-stained preparations and the electron microscope preparations. In this diagram it will be seen that there are at least four, and possibly five, different types of axonal terminations in relation to the principal cells. First the simple axon terminals related to the surfaces of the dendrites and soma will be considered, and afterwards those involved in the formation of the glomeruli.

By far the most common type of axon terminal forming synapses upon the surface of the dendrite is the one with a diameter of about 1 μm that forms simple synaptic contacts, or the type 1 axo-dendritic junction of Gray (1959). Such

terminals have also been described on the non-glomerular parts of the dendrites of the lateral geniculate body of the cat by Szentagothai (1963) and of the monkey by Colonnier & Guillery (1964). As pointed out, these terminals occur with greatest frequency upon the thinner dendritic branches and appear to increase in concentration the more distant the surface of the dendrite is from the cell body. There is

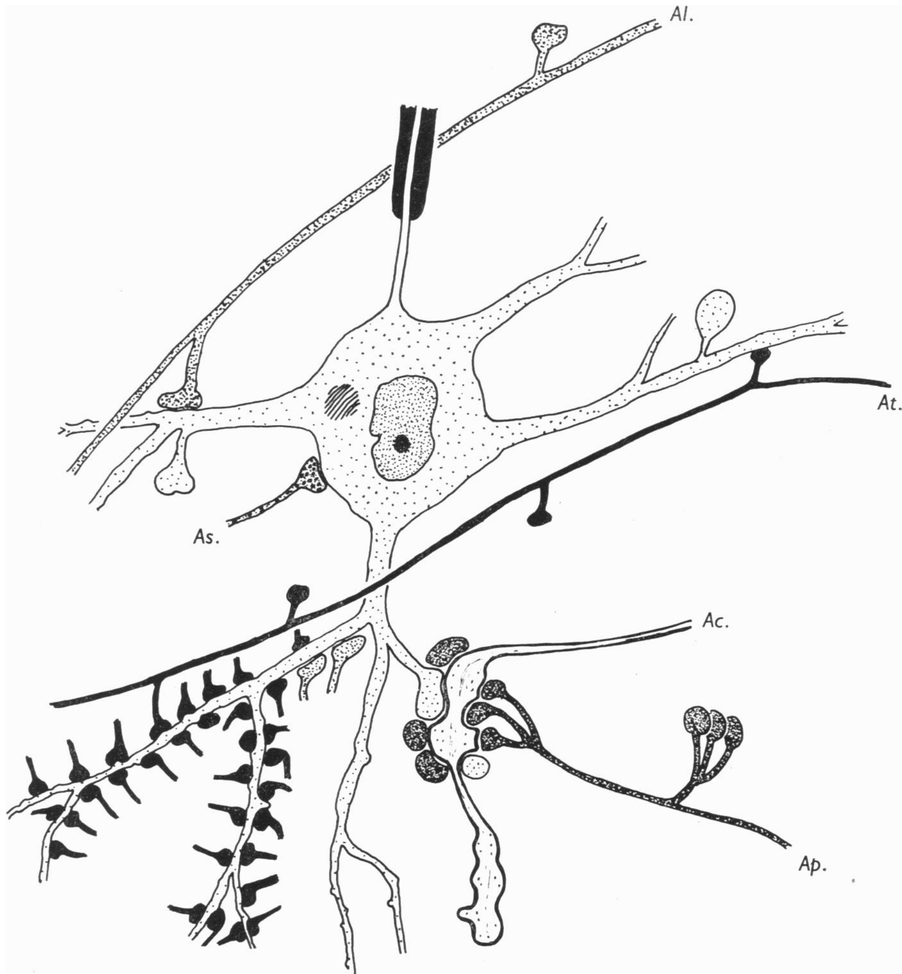


Fig. 22. A diagrammatic representation of the suggested correlation between the results obtained by the Golgi and electron microscope studies. Five different types of axon are represented (*Al.*, *At.*, *Ac.*, *Ap. and As.*) as forming synapses upon the principal neurons of laminae A and A_1. For further explanation see Discussion.

little doubt from their size and frequency of occurrence that these terminals are derived from the thin axons that are seen in Golgi preparations (Fig. 3A) to give off short side branches that terminate in expansions of about 1 μm in diameter (Fig. 22, *At.*). A similar conclusion is also arrived at by Szentagothai (1963).

The second type of axon forming synapses upon the non-glomerular regions of the dendrites is the one giving rise to terminals about 2–4 μm in diameter that synapse with the larger dendrites. These terminals form mixed synaptic contacts. The type 2 axo-dendrite synapses of Gray (1959) may be similar, although Gray makes no mention of adhesion zones mixed with the synaptic zones. From the diameter of these terminals, it would seem that they are derived from the type of axon which in Golgi preparation has a diameter of about 1 μm and gives rise to short side branches at irregular intervals (see Figs. 3B and 22, *Al.*). These larger axon terminals end upon the large dendrites in somewhat closer proximity to the cell body than the smaller and more common axon terminals.

The large diameter axon terminals have not been described either by Szentagothai (1962, 1963) in the lateral geniculate body of the cat, or by Colonnier & Guillery (1964) in the monkey. Similar types of terminals forming mixed synaptic contacts have been described by Gray (1959) in the cerebral cortex and by Hamlyn (1963) in Ammon's horn of the rabbit. Interestingly enough, Hamlyn (1963) also observed that the large axon terminals giving rise to synaptic contacts in which the thickenings are intermittent, are present only upon the surfaces of the main stem apical dendrites of the pyramidal neurons and upon their perikaryal surface. Neither Gray (1959) nor Hamlyn (1963) mention that at this type of synapse only a proportion of the junctional zones have synaptic vesicles associated with them.

The axon terminals forming synapses upon the perikarya of the neurons (Fig. 22, *As.*) are relatively few in number and this observation is in agreement with that of Szentagothai (1963) in the cat, and of Colonnier & Guillery (1964) in the monkey. Szenthagothai (1963) gives no description of the form of the synaptic contact, but Colonnier & Guillery (1964) state that in their organization they do not differ from the axo-dendritic contacts. In the present preparations, all axo-somatic axon terminals, like the large axon terminals upon the dendrites, have been found to form mixed synaptic contacts in which only some of the junctional zones have synaptic vesicles associated with them. Consequently, the two are very similar, but whether they are derived from the same type of axon is unknown.

Smith *et al.* (1964) claim to have found type 1, or simple synaptic contacts, upon the somata of the neurons within the cat lateral geniculate body. Such synapses upon the somata have never been observed in the present study and as far as we are aware, there is no other record of such synapses in this position, since they appear to be exclusively dendritic in type (see Gray, 1959).

There is perhaps little reason to consider the functions of these two types of synapses on the non-glomerular parts of the dendrites and soma of the neurons of the lateral geniculate body in any detail. Suffice it to say that Anderson, Eccles & Løyning (1963) have recently presented evidence, amplified somewhat by Eccles (1964), to suggest that the type 2 contact of Gray (1959) is inhibitory in function.

To turn now to the geniculate glomeruli. From the present investigations it is clear that three different components are involved in the formation of these glomeruli, one dendritic and two axonal. There is little doubt that the dendritic component is derived from the grape-like protrusions of the dendrites, as first suggested by Szentagothai (1963), although in his preparations it appears that these protrusions generally arise from the peripheral parts of the dendrites and not from the

primary dendrites as suggested here. As to the number of the grape-like protrusions partaking in the formation of each glomerulus, it is evident that at least two protrusions from the same parent dendrite may be involved, and there is some evidence to suggest that even protrusions from different parent dendrites may be entering the same glomerulus.

The central axon of the glomerulus that expands into a terminal is no doubt the equivalent of the axon which gives rise to a series of expansions in Golgi preparations (Fig. 22, *Ac.* and Fig. 3D). Sometimes, as seen quite clearly in both Golgi and electron microscope preparations, the expansions occur along the length of the parent axon, while other expansions are the terminations of side branches of the main axon. This suggests that each central axon may be involved in the formation of a number of different geniculate glomeruli. The number is by no means clear, but in one Golgi preparation such an axon has been observed to give rise to at least twelve separate and distinct expansions. Despite the fact that one central axon may contribute to a series of different glomeruli, no evidence has been obtained to suggest that more than one central axon takes part in the formation of each glomerulus.

All the examples in which a number of different profiles of central axon terminals have been seen within a glomerulus can be accounted for on the basis of protrusions arising from a single expansion. Indeed in serial sections of glomeruli it has often been observed that apparently separate central axon terminal profiles connect up with each other.

These central axon terminals appear to be the same structures that Szentagothai (1962) refers to as large presynaptic bags within the glomeruli, although he does not recognize this component of the glomerulus in a later communication (1963). They also appear to be the equivalent of the structures that Colonnier & Guillery (1964) refer to as large LP terminals within the lateral geniculate body of the monkey. The similarity between the two is emphasized by the type of synaptic junctions that these terminals form, and by the fact that Colonnier & Guillery mention that these terminals may be as long as 23 μm.

The other form of axon terminal within the glomerulus, the peripheral axon terminal (Fig. 22, *Ap.*) appears to be derived from the claw-like terminals that have been observed in the Golgi preparations (Fig. 3C). The diameters of the terminals are compatible with this interpretation, as is the observation that in Golgi preparations each set of terminals remains close together, as do the peripheral axon terminals within the glomeruli, and arise as expansions of a cluster of short, preterminal branches from a parent stem. Further, as observed by Szentagothai (1963) in Golgi preparations, the claw-like terminals sometimes appear to be related to the grape-like protrusions of the dendrites.

On the basis of the appearance of the axons that are observed in Golgi preparations to give rise to the claw-like axon terminals, every parent axon gives off a large number of sets of 'claws', each related to a different glomerulus. From the distribution pattern of these claw-like terminals, it would also appear that a parent axon is involved in the formation of glomeruli of a relatively small group of neurons, perhaps the groups of neurons mentioned by Taboada (1927) and O'Leary (1940). As suggested by Szentagothai (1963), these claw-like terminals appear to be the terminals of the cypress-tree arborizations described by Tello (1904) and O'Leary

(1940). Since there are only about three to five terminal expansions in each group, it is apparent that more then one set of 'claws' may contribute to the formation of a glomerulus, particularly in the larger glomeruli. This is also suggested by the observation that in serial sections of glomeruli, the small axonal branches giving rise to the peripheral axon terminals may enter a glomerulus from diametrically opposite sides.

The manner in which the geniculate glomeruli are considered to function depends a great deal upon the interpretation that is put upon the types of junction present between the plasma membranes of adjacent components. On the basis of the criteria outlined earlier in this presentation, both the central and peripheral axon terminals of a glomerulus form synapses with the dendritic protrusions, while the central axon terminals also synapse upon the peripheral axon terminals.

Unfortunately, there is no clear morphological distinction that can be made between the form of contact of the pairs of plasma membranes involved in the formation of these three different types of synapse (Figs. 18–20), but it would seem likely that the axo-axonal synapse between the central and peripheral terminals is inhibitory in function (see Eccles, 1964). Such axo-axonal synapses have also been described by Gray (1962) in the spinal cord, while they have been described previously in the cat lateral geniculate body by Szentagothai (1962) and in the monkey by Colonnier & Guillery (1964). For the present, it is interesting that this same axon terminal, the central one, forms synapses on both an axon and a dendrite, and if each axon terminal is capable of forming only one functional type of synapse this could mean that the same terminal is capable of both presynaptic inhibition in respect of the peripheral axon terminal and postsynaptic inhibition in respect of the dendritic protrusions.

As to the origin of these different types of axons, an attempt has been made to determine their origins by carrying out unilateral removal of the eye and then examining the lateral geniculate bodies with the electron microscope after periods of degeneration between 6 days and 2 weeks (Peters & Palay, 1965), It was expected that the axon terminals of optic origin would degenerate in the contralateral lamina *A*, but so far the results have been very unsatisfactory, for while changes have been observed in the optic tract fibres, degenerating axon terminals are not really apparent. One reason for this unsatisfactory result may be, as Smith *et al.* (1964) suggest, that the best time to observe degenerative changes in the terminals is within 2–4½ days after operation. In the monkey, Colonnier & Guillery (1964) found that the best time interval is 5–7 days, when the LP terminals, which appear to be the equivalent of the central axon terminals of the cat glomerulus, start to degenerate; at this time none of the SD terminals, the smaller axon terminals, showed signs of degeneration. This would suggest that the large terminals within the glomerulus are optic nerve terminals, and the same conclusion is also arrived at by Szentagothai (1962), although his evidence for arriving at this conclusion is not clear. In the same publication, Szentagothai considers that the smaller axon terminals within the geniculate glomeruli are derived from non-optic neurons (see his figure 3). There appears to be no real basis for this assumption and in another publication (1963) he suggests, as is considered here, that the claw-like endings observed in Golgi preparations are the optic nerve terminals, since they are derived from the

cypress-tree arborizations of the optic nerve that are described by Tello (1904) and O'Leary (1940). Against this suggestion is the observation of Colonnier & Guillery (1964), that when the lateral geniculate body of the cat is examined within 5–7 days after removal of an eye, the small axon terminals, which they refer to as SD terminals, show no degeneration. However, they do remark that their material does not demonstrate that all of the small terminals have an extra-retinal origin, since their size and number appear to be reduced in the monkey 54 days after operation.

Unfortunately, none of the workers who have dealt with the subject of degeneration of axon terminals as observed in the electron microscope preparations, give any real indication of the proportions of terminals that exhibit degeneration at any one time. Consequently, it is not possible to assess the value of the degeneration technique as applied to electron microscope studies in the central nervous system.

In relation to the termination of optic nerve fibres within the lateral geniculate body of the cat, Glees (1941) has also recorded that the entering nerve fibres break up into numerous ramifications.

From the foregoing it is apparent that a great deal more information is required about the source of the axons terminating within the lateral geniculate body of the cat. Until that is available no satisfactory interpretation can be placed upon the anatomical results that are presented here. Certainly the retina is not the only source of axons terminating within the lateral geniculate body, since there is evidence that some are derived from the visual cortex and others from the reticular formation of the brain stem (see Meikle & Sprague, 1964), while the Golgi type II cells that are present (O'Leary, 1940) presumably form terminals within their own laminae. Clearly, as pointed out by Hubel & Wiesel (1961), the lateral geniculate body is not a simple way-station in the pathway from the retina to the visual cortex. They have shown that receptive fields within the lateral geniculate body resemble those of the retinal ganglion cells in having an excitatory ('on') centre and inhibitory ('off') periphery or vice versa. It may well be that the source of this kind of activity is the geniculate glomerulus, which, being situated in relation to the large diameter dendrites, may exert a greater influence over the functioning of the geniculate neurons than the more numerous, yet more peripherally situated, small axon terminals that synapse with the non-glomerular parts of the dendrites.

SUMMARY

1. Laminae A and A_1 of the dorsal nucleus of the lateral geniculate body of the cat were studied by the Golgi method and by electron microscopy.

2. The neurons of these laminae are multipolar and their perikarya are characterized by laminated inclusion bodies composed of sheets of tubules. The dendrites of the neurons radiate in all directions and while the main stem dendrites are relatively smooth, where they divide into primary dendrites grape-like protrusions occur. Farther distally the smaller dendrites have thorns and spines arising from their surfaces.

3. The majority of axon terminals synapsing with the dendrites are about 1 μm in diameter. These are most commonly associated with the smaller dendrites and form synapses that are characterized by a single junctional region.

4. Nearer the cell body, larger axon terminals, about 2 μm in diameter, occur. They synapse almost exclusively with the primary dendrites and have a number of junctional zones, only some of which have synaptic vesicles associated with them.

5. The main stem dendrites are generally free of synapses and only a few synapses are present upon the perikaryon of a neuron.

6. The grape-like protrusions of the dendrites enter into the formation of glomeruli, which also contain the terminals of two types of axon. The sizes of the glomeruli vary, but they are always partially encapsulated by thin, sheet-like processes of astrocytes. One of the axonal types, the central axon, is about 1 μm in diameter, but within the glomeruli forms terminals up to 3 μm in diameter. The majority of profiles within a glomerulus are formed by the other axonal type, the peripheral axon, which gives rise to claw-like terminals. It appears that both types of axon synapse with the dendritic protrusions, and that the central axon terminals also synapse upon the peripheral axon terminals.

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