AN ELECTRON MICROSCOPIC STUDY OF THE CENTRE-MEDIAN AND VENTROLATERAL NUCLEI OF THE THALAMUS IN THE MONKEY

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[Plates 1–35]

CONTENTS

An electron microscopic study has been made of the normal ventrolateral and centre-median nuclei of the thalamus of the monkey and, in experimental material, of the mode of termination in the nuclei of afferent fibres from the motor cortex, the globus pallidus and the deep cerebellar nuclei. There are striking similarities but also a few subtle differences in the ultrastructure of the centre-median and ventrolateral nuclei. Three classes of cell are present: a large multipolar cell with much cytoplasm filled with many organelles is probably the relay cell; a small fusiform cell with a thin rim of cytoplasm and light vacuolated mitochondria, which may contain discoid vesicles, gives rise to P profiles and axon initial segments; the third type is intermediate between the other two in size and other features. There are four types of vesicle-containing synaptic profiles. The most frequent are SR axon terminals, which are small, with spherical synaptic vesicles and are pre-synaptic at asymmetrical contacts with small and medium dendrites and their spines and P profiles; SR terminals are found mainly in the interglomerular neuropil. LR terminals, the largest synaptic profiles, are found in all glomeruli; they contain many round synaptic vesicles and form numerous asymmetrical synapses, being presynaptic to the main dendrite and all its spines and many of the P profiles in a glomerulus. P profiles are irregular pale processes, which occur in considerable numbers outside and within glomeruli (70 % of intra-glomerular profiles) and contain pleomorphic synaptic vesicles which are discoid. They arise from tiny unmyelinated profiles and they may have synaptic interaction in several glomeruli. Larger processes, similar in

character to proximal dendrites, but with discoid vesicles and synaptic features like those of smaller P profiles are also found, and may be in continuity with a cell soma. P profiles are post-synaptic to LR, SR and F axons, both pre- and post-synaptic to other P profiles and pre-synaptic to conventional dendrites; there are reciprocal synapses between pairs of P profiles. F axons, the least common profiles, are usually extra-glomerular and synapse with proximal dendrites and cell somata; they contain cylindrical synaptic vesicles and are pre-synaptic to P profiles and dendrites at symmetrical synapses. Cell somata in the centre-median nucleus possess spines, and in both nuclei dendrites have spines, both in glomeruli and the neuropil. Multivesicular bodies are frequently present in the parent dendrite subjacent to the spine. Spines in the neuropil are post-synaptic to SR and P profiles and, in the centre-median nucleus, also to F axons. Some spines appear to be post-synaptic only to F axons. At least half the extraglomerular spines are associated with two synapses, a dyadic arrangement with one synapse on the spine and one on the parent dendrite close to the base of the spine, while many dyads have only a single pre-synaptic profile. Some spines have a more complex synaptology including serial synapses and triads. In glomeruli, spines are always post-synaptic to the LR bouton and always dyadic as the LR terminal also contacts the dendritic shaft close to the base of the spine. Spines account for half the contacts between an LR terminal and the main dendrite in a glomerulus.

Glomeruli are found in both nuclei and serial sections have shown the multiplicity of profiles and the complexity of synaptic organization within them. Each glomerulus contains one LR bouton, one main dendrite, and a large number of P profiles, with an occasional SR or F axon terminal at the periphery of the aggregation. The dendrites are of medium calibre, often with several spines, around which the other profiles are situated. An analysis is presented of the profiles and synaptic arrangements in thirty glomeruli from the centre-median and ventrolateral nuclei, with a reconstruction of one large glomerulus. The LR bouton makes numerous synaptic contacts with the main dendrite, half the contacts being upon spines, and a considerable number with P profiles. The latter also have many synapses, being approximately equally pre-synaptic to P profiles and the main dendrites. Various specific types of synaptic array are present within the glomeruli: serial synapses; sequential arrays, where the third profile of a serial synapse is again pre-synaptic; reciprocal synapses; triads which are similar to serial synapses but with an additional contact, profile 1 also being pre-synaptic to profile 3. The complexity of the glomerular synaptology is accentuated by the overlapping of several different types of synaptic array in a given glomerulus. Afferent fibres from the motor cortex and globus pallidus terminate in both nuclei as SR boutons, and in the ventrolateral nucleus the mode of termination of both groups of fibres is very similar. In the centre-median nucleus the terminals of fibres from the cortex have a higher proportion of multisynaptic contacts, are more frequently pre-synaptic to P profiles, and the dendrites upon which they end are less often in receipt of other synapses. The termination of fibres from the globus pallidus in the centre-median nucleus differs from terminals of fibres from the cortex and globus pallidus in the ventrolateral nucleus in being pre-synaptic to fewer P profiles. When the somatic sensory cortex was destroyed as well as the motor area degenerating axon terminals were present in the ventroposterior nucleus; their mode of termination was similar to those in the ventrolateral nucleus, but they were far greater in number. Axons from the cerebellar deep nuclei end in the ventrolateral nucleus as LR boutons within glomeruli. There was no evidence of degeneration in the centre-median nucleus after damage of the cerebellum.

Introduction

There is extensive anatomical and physiological evidence for the division of the nuclei of the thalamus into two main groups, the principal nuclei and those of the intralaminar group. The principal nuclei project in a well organized manner upon the neocortex, most nuclei being related to well defined cytoarchitectural or functional areas. Removal of a cortical area results in severe retrograde cellular degeneration in the relevant nucleus (Walker 1938) and after a stereotaxically placed lesion in a nucleus orthograde fibre degeneration can be traced into the cortex, the majority of the fibres terminating in layer IV (see, for example, Wilson & Cragg 1967; Jones & Powell 1969*a*; Hubel & Wiesel 1972). Electrical stimulation within a principal nucleus causes a well defined evoked response in a localized region or regions of the cortex, the site being in accord with the anatomical evidence (Guillery, Adrian, Woolsey & Rose 1966). The intralaminar nuclei, on the other hand, show less marked cellular changes after removal of the cortex and although there is evidence for a projection from them upon the cortex from experiments using retrograde cellular degeneration (see, for example, Murray 1966; Macchi *et al.* 1975) and axoplasmic flow methods (Ralston & Sharp 1973; Jones & Leavitt 1974; Kuypers, Kievit & Groen-Klevant 1974) it would appear that their major projection is to the caudate nucleus and putamen (Powell & Cowan 1956; Kemp & Powell 1971; Jones & Leavitt 1974; Nauta, Pritz & Lasek 1974). The termination in the cortex of the axons from the cells of the intralaminar nuclei is probably to the superficial layers (Jones 1975) and repetitive electrical stimulation of this group results in widespread recruiting responses in the cortex (Morison & Dempsey 1942; Jasper 1960). To some extent the principal and intralaminar nuclei also differ in their afferent connections, particularly as the latter receive more connections from the nuclei of the brain stem reticular formation (Nauta & Kuypers 1957) but there is also evidence for certain components at least of each group receiving fibres from the same ascending pathways (Jones & Powell 1971). Whether the functional differences between the principal and intralaminar nuclei are due to these differences in their connections or to differences in their intrinsic structure and synaptic organization is not known. The ultrastructure of several of the principal nuclei, particularly those of the sensory relay group which have been the most thoroughly studied (see, for example, Szentágothai, Hámori & Tömböl 1966; Guillery 1969; Ralston & Herman 1969; Morest 1971; Le Vay 1971; Famiglietti & Peters 1972) has been shown to be surprisingly similar, but little is known of the intralaminar group.

For these reasons it was decided to study the intrinsic structure of one component of the intralaminar group and to compare it with that of a principal nucleus. The centre-median nucleus of the monkey was chosen, mainly because it is sufficiently large to allow the small blocks necessary for electron microscopy to be obtained with a reasonable degree of confidence, whereas the other intralaminar nuclei are so narrow and interspersed between the principal nuclei that it would be difficult to be certain that the blocks had been taken from them and not from the immediately adjoining principal nuclei. In addition, the connections of the centre-median nucleus in the monkey have been investigated with light microscopical methods (Mehler 1966) and it is known that it receives afferent fibres from area 4 of the motor cortex (Auer 1956; Niimi, Kishi, Miki & Fujita 1963; Petras 1964) and from the globus pallidus (Nauta & Mehler 1966; Carpenter & Strominger 1967). The pattern of these connections suggested that the ventrolateral nucleus should be the principal nucleus with which to compare the centre-median as it also receives fibres from the same two sites in the cerebral hemisphere as well as

from the deep nuclei of the cerebellum. In some respects the centre-median nucleus is not a typical representative of the intralaminar group (Powell & Cowan 1967), however, in that it does not show any cellular degeneration after removal of the cortex, it is relatively large in primates whereas the intralaminar nuclei as a group are relatively smaller and it is the only element of the group which receives a fibre pathway from the globus pallidus. The morphology and synaptic organization of the two nuclei have been studied in normal brains and the mode of termination of the afferent fibres from the motor cortex, globus pallidus and cerebellum determined in experimental material after selective damage of these pathways. As in previous studies on the other principal nuclei, the glomerulus has been found to be a major feature of the intrinsic structure of the two nuclei, and the complexity of the interrelations between its constituent processes has been investigated by the use of serial sections. Preliminary reports of certain of the findings have already been published (Harding 1971, 1973*a*, *b*) and in the meantime a brief description of the ultrastructure of the centre-median parafascicular nuclei in the cat has appeared (Westman & Bowsher 1971).

Material and methods

The brains of 34 young adult monkeys were used. The ultrastructure of the normal centre-median and ventro-lateral nuclei was studied in material taken from normal unoperated animals and from the normal hemisphere of the operated animals. The mode of termination of the afferent fibres to these nuclei from the motor cortex, the globus pallidus and the deep nuclei of the cerebellum was determined in experiments in which these structures had been damaged. The operations were done under Nembutal anaesthesia and with aseptic precautions.

For the study of the projection of the cortex upon these nuclei the pre- and postcentral gyri of one hemisphere were exposed in 16 animals, and the motor cortex was removed either alone or together with that of the somatic sensory area. In eight monkeys an electrolytic lesion was made in the globus pallidus of one hemisphere stereotaxically by a vertical approach and was large enough to interrupt all efferent fibres from the globus pallidus to the thalamus. In three monkeys one half of the cerebellum was exposed by removal of the squamous part of the occipital bone, and most of it was removed by suction. These animals were allowed to survive for periods between 3 and 8 days. One group of three animals was allowed to survive for 3–6 months after removal of the motor cortex and were then operated upon again, when an electrolytic lesion was placed stereotaxically in the globus pallidus of the operated hemisphere; after the second operation, a survival period of 3–6 days was allowed. This procedure was

Description of plate 1

Figure 1. A large neuron in the centre-median nucleus. The abundant cytoplasm contains numerous organelles with considerable stacks of rough endoplasmic reticulum (er). Go, Golgi apparatus. The nucleus (N) has a marked indentation. (Magn. × 7000.)

Description of plate 2

Figure 2. High power of initial segment (IS) of cell in figure 3. The axon is post-synaptic to an F bouton (F) and there is a subsynaptic cistern (large arrowhead). The initial segment has the characteristic features of ribosomes (r), neurotubules and dense material lying beneath the limiting membrane. (Magn. × 52000.)

Figure 3. A montage illustrating a small neuron, with an axon hillock (A) and initial segment (IS). Ringed arrow points to an F bouton pre-synaptic to the initial segment (see figure 2). (Magn. × 13000.)

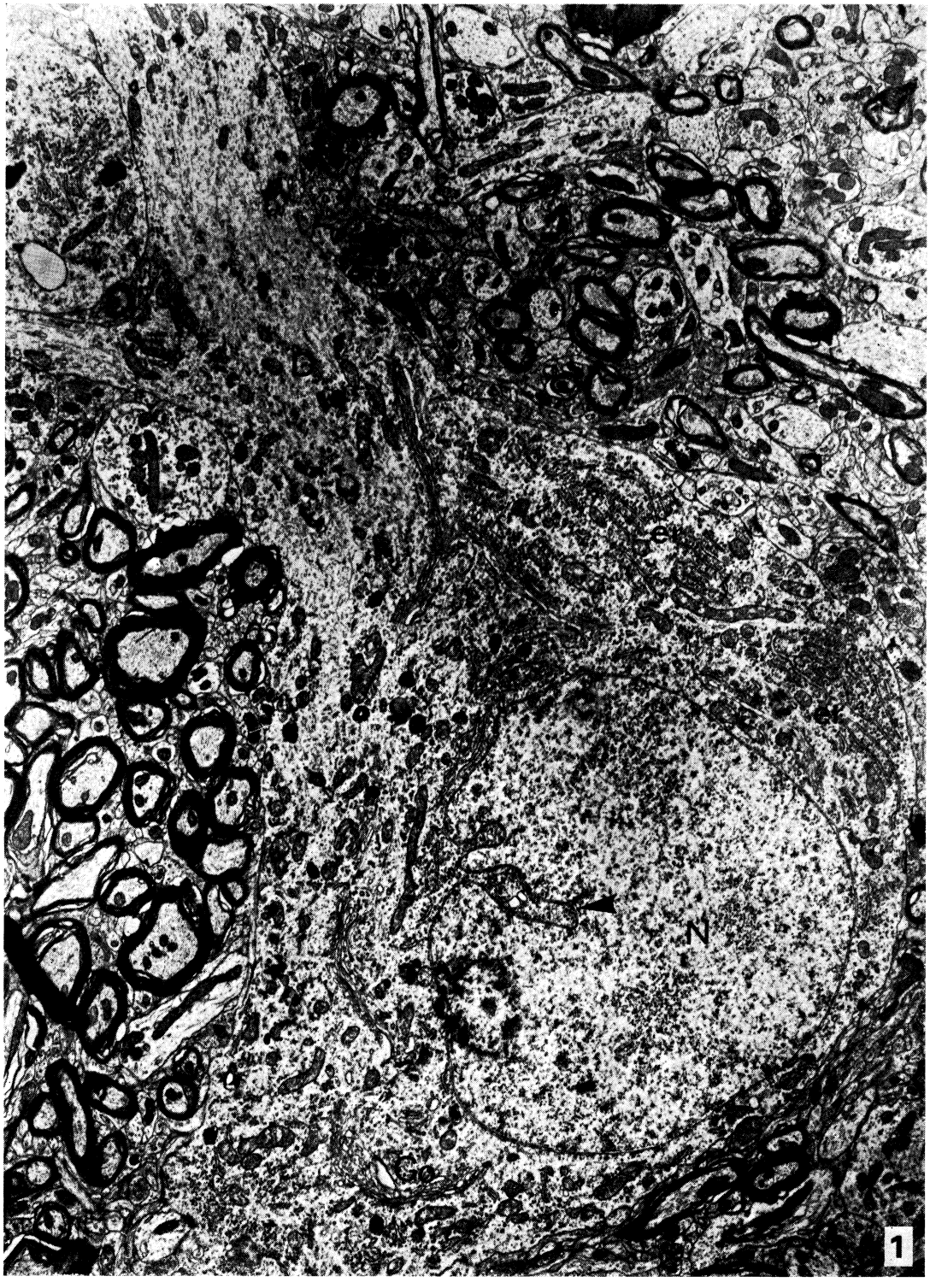

FIGURE 1. For description see opposite.

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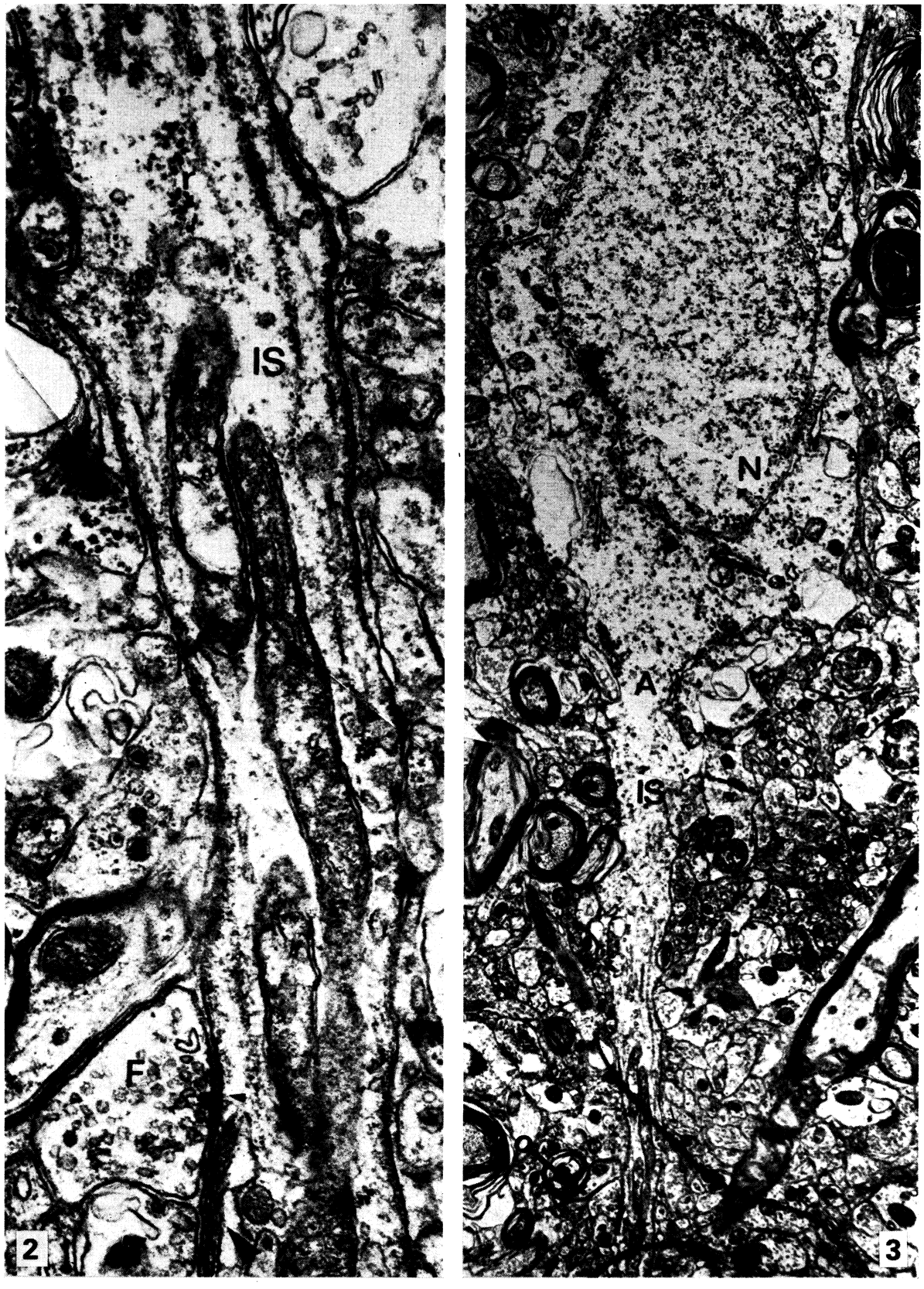
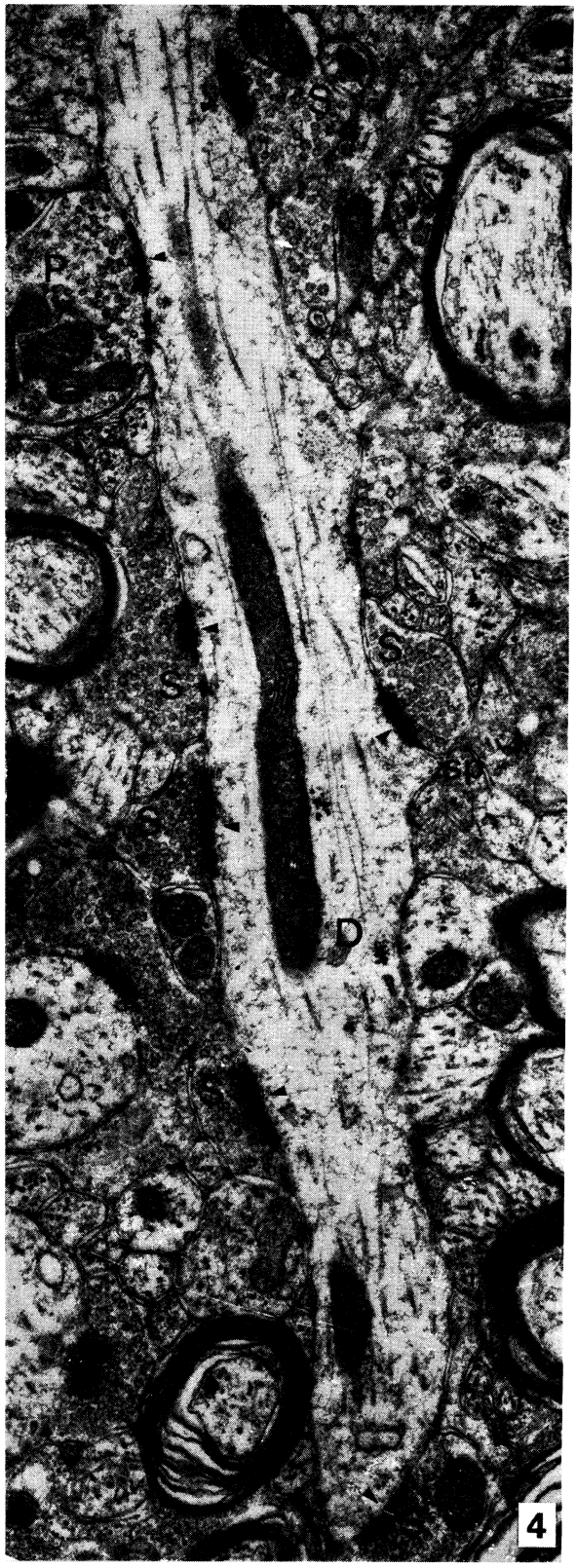
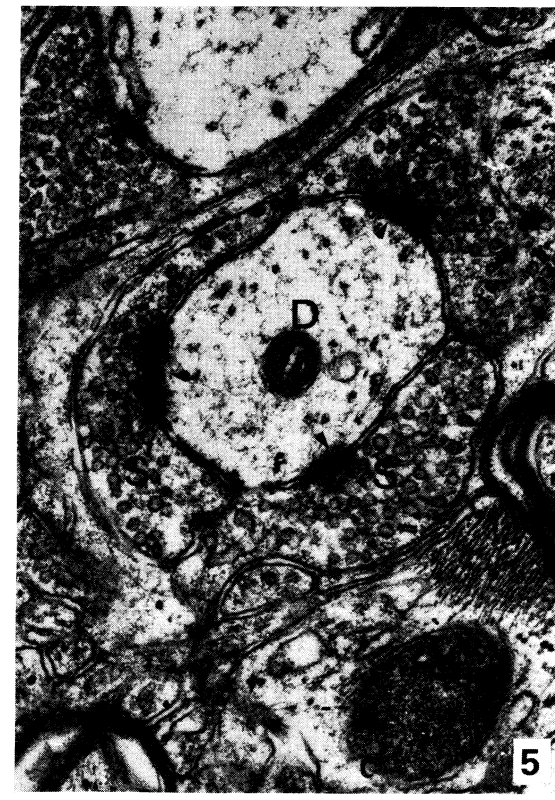
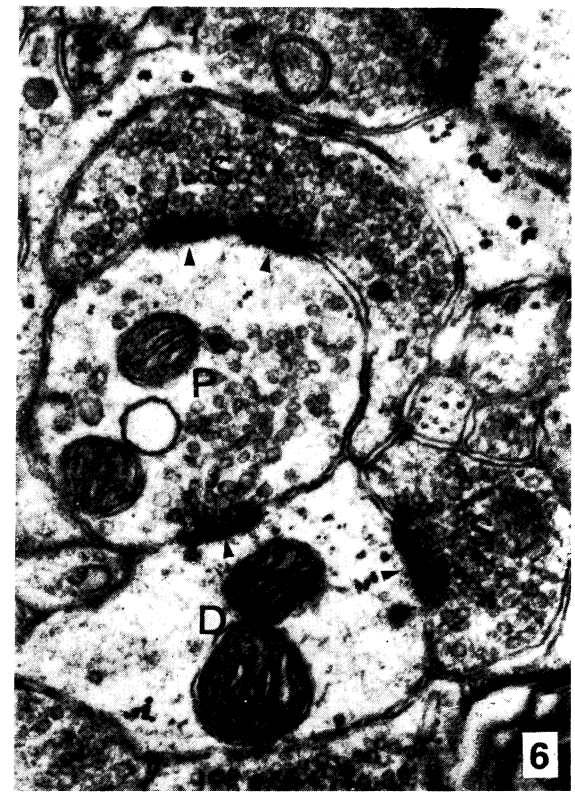


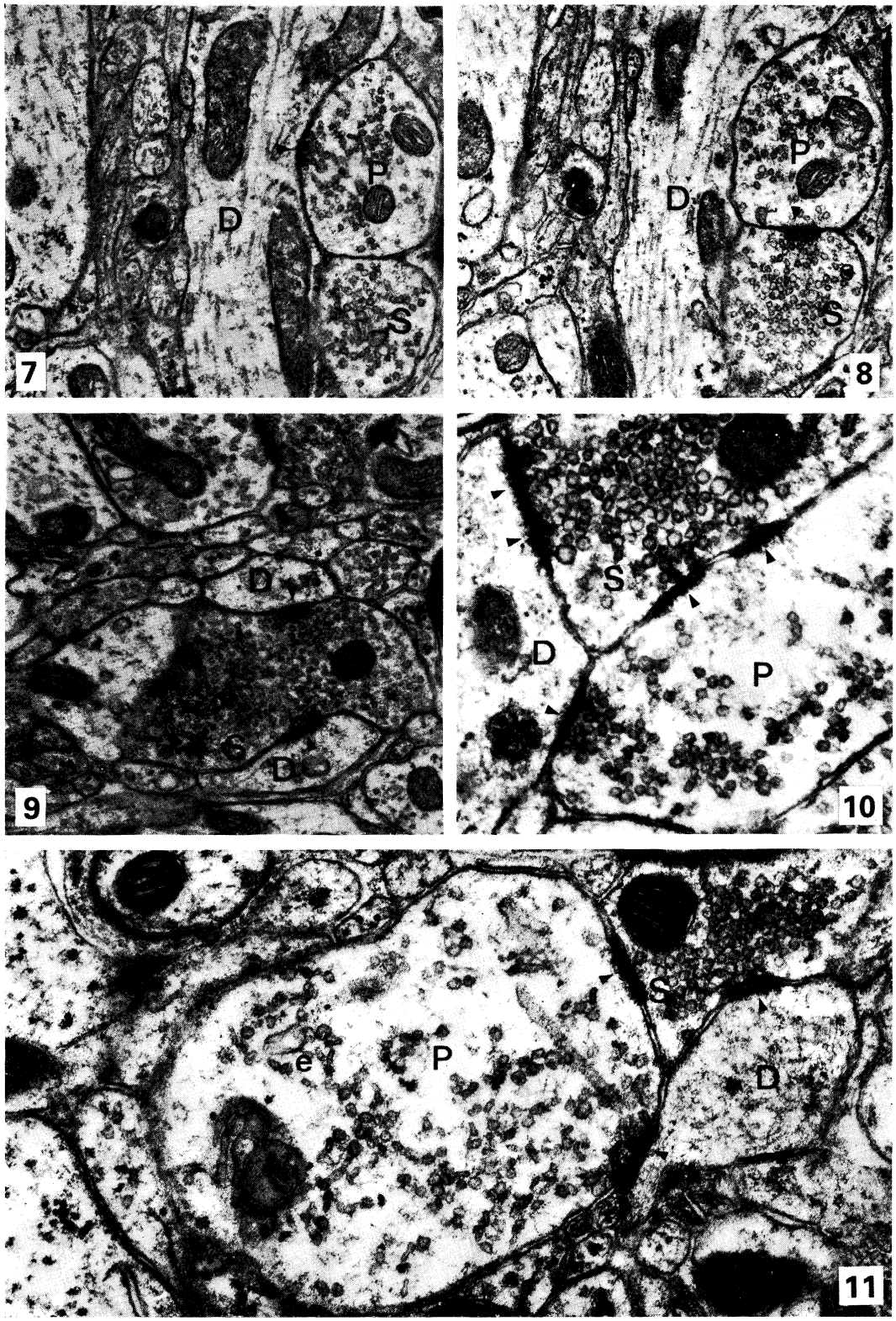
FIGURES 2 AND 3. For description see p. 360.







FIGURES 4–6. For description see p. 361.



FIGURES 7–11. For description see opposite.

adopted in order to study the degeneration in the centre-median nucleus of fibres from the globus pallidus only. Large lesions of the globus pallidus almost invariably caused some damage to the internal capsule, either by direct involvement or as the result of interruption of blood supply, and therefore resulted in degeneration of fibres from the cortex as well as from the globus pallidus. By first removing the motor cortex with a survival period sufficiently long to allow degeneration and removal of the terminals of axons from the cortex, it was considered that the second lesion would result in degeneration of fibres from the globus pallidus only.

Both the normal and experimental animals were perfused under hypothermia with a balanced salt solution followed by a mixture of 4 % formaldehyde and 1 % glutaraldehyde in a phosphate buffer at pH 7.0–7.3. After removal from the skull the brain was stored in the fixative at 4 °C before small blocks were taken. Great care was used in the removal of blocks from the thalamus as it is easy to misinterpret certain landmarks, particularly in the antero-posterior dimension. The brain was first divided into right and left halves and each hemisphere was then cut in the coronal plane at the level of the posterior commissure which was seen on the medial surface and which was known from the coordinates in the stereotaxic atlas of Olszewski (1952) to be just posterior to the centre-median nucleus. The cut surface was examined to confirm this and then a parallel cut was made 5 mm anterior to the first, resulting in a coronal slice which contained the centre-median and adjacent nuclei. If visual identification of the posterior aspect of the centre-median nucleus and the habenulo-peduncular tract was not confirmed at the first cut further thin slices were made. At the start of the investigation difficulty was experienced in identifying the centre-median nucleus with confidence, and it was decided therefore to trim the coronal slices into blocks 4 × 7 mm in cross section and 1 mm thick, which contained the centre-median nucleus together with parts of the adjoining thalamic nuclei; in this way identification of the nuclei could be made at the thick section stage before thin sections for electron microscopy were cut. In the ultrathin sections of material taken from these large blocks the

Description of plate 3

Figure 4. Narrow calibre, distal dendrite (D) cut longitudinally, contacted by numerous SR terminals (S) at asymmetrical synapses and also one P profile (P). Observe the difference between the spherical vesicles in the SR terminals, and the pleomorphic vesicles in the P profile. Centre-median nucleus. (Magn. × 30000.)

Figure 5. Distal dendrite (D) sectioned transversely completely encompassed by three SR boutons (S) all of which are presynaptic to it. Ventrolateral nucleus. (Magn. × 40000.)

Figure 6. A serial synapse: an SR profile (S) is pre-synaptic to a P profile (P) which in turn contacts a small dendrite (D). Contrast the morphology of the synaptic vesicles in the two profiles. Centre-median nucleus. (Magn. × 35000.)

Description of plate 4

Figures 7 and 8. Serial sections to show a serial synapse, i.e. SR bouton (S) is pre-synaptic to a P profile (P), and the latter is pre-synaptic to the dendrite (D). Note the ribosomes (r) within the P profile. Centre-median nucleus. (Magn. × 30000.)

Figure 9. SR axon bouton (S) pre-synaptic to two small dendrites (D) in the centre-median nucleus. (Magn. × 30000.)

Figure 10. A triadic synaptic array in the centre-median nucleus. The SR bouton (S) is pre-synaptic to a dendrite (D) and a P profile (P). The P profile is pre-synaptic to the dendrite. Compare the asymmetrical synaptic specializations at the SR axo-dendritic synapses with the symmetrical synaptic specialization at the P dendro-dendritic synapse. (Magn. × 38000.)

Figure 11. A triadic synaptic array in the centre-median nucleus. An SR terminal (S) contacts a dendrite (D) and a P profile (P) which is also pre-synaptic to the dendrite. The P profile contains sacs of smooth endoplasmic reticulum (e). (Magn. × 40000.)

standard of preservation of the tissue was not adequate (e.g. figure 3) and therefore the procedure was modified and the original slice was trimmed down until only this nucleus remained and it was divided into 1 mm^3 blocks. Small blocks of the ventrolateral and ventroposterior nuclei were taken from the thalamus adjoining the centre-median nucleus and further samples of these principal nuclei were obtained from thin slices of the cut surfaces of the remaining brain in front and behind the original coronal slice. Another method (Ralston & Herman 1969) was used in a few brains; a narrow gauge hypodermic needle pushed through a coronal slice of the thalamus containing the relevant nuclei, and the thin rod of material which was obtained was cut into small lengths. The advantage of this method was that one could check the position of the needle hole by staining with thionin the slice of the thalamus from which the sample was taken for light microscopy.

The blocks of tissue were rinsed in 10 % sucrose in phosphate buffer, post-fixed in osmium tetroxide and dehydrated (with block staining by uranyl acetate at the 70 % alcohol stage); they were embedded in Epon-Araldite. From the complete face of the hardened blocks a 1 μm 'thick' section was cut and stained with a mixture of methylene blue and Azure II (Richardson, Jarrett & Finke 1960). From examination of this section an appropriate area was chosen and thin sections approximately 50 nm thick were cut. For the qualitative study of the normal and experimental material large sections, 0.9 × 0.2 mm were used, three to six of which could be mounted on a film of Formvar on copper grids with single hole 1 × 2 mm. For the studies of serial sections smaller sections were used, approximately 0.1 × 0.2 mm, and these were collected in long ribbons and mounted on the same type of grids with a film of Formvar. Up to 50 such sections could be mounted on one grid in two or three ribbons, and series of up to 200 consecutive sections were obtained on five or six grids. All sections were stained on the grid with alkaline lead citrate (Reynolds 1963) and uranyl acetate (5 % solution in 50 % ethanol).

In all experiments in which lesions had been placed in the globus pallidus or in the cerebellum, the part of the brain containing the lesion was embedded in paraffin and sectioned at 20 μm. A 1:20 series was mounted and stained with thionin in order to determine the precise site and extent of the lesion. For the study of Golgi-impregnated material of the centre-median and ventrolateral nuclei the thalamus was dissected from normal brains which had been perfused as described above and cut into coronal slices 3–4 mm thick. They were impregnated by the Golgi-Kopsch modification of the Golgi technique (Colonnier 1964), dehydrated and embedded in low viscosity nitrocellulose. Sections were cut at 100 μm and mounted under cover slips using a neutral mountant. Sections of several Macaque monkey brains stained with thionin were available for the study of cell bodies in the nuclei.

Results

General morphology of ventrolateral and centre-median nuclei

It is important to state at the outset how striking are the similarities and how few and subtle the differences between the centre-median and ventrolateral nuclei, and this general account of normal morphology therefore applies to both nuclei, except where specific reference is made to the individual peculiarities of one or other nucleus. One obvious difference between these nuclei at lower magnifications with the electron microscope, however, is that the centre-median nucleus is traversed by more fibres than the ventrolateral and other relay nuclei; but perikarya

and neuropil appear evenly scattered throughout both nuclei. A systematic study of the cell bodies in the two nuclei has not been made, partly because with the small sections used throughout most of this study, few cell bodies were seen, and partly because most effort was concentrated upon the analysis of the glomeruli and interglomerular neuropil. Of approximately 100 somata photographed from each of the centre-median and ventrolateral nuclei, two distinct types at least could be distinguished. The first is a large cell approximately 15–20 μm in diameter, round or multipolar, and usually with more than one dendrite (figure 1, plate 1). The nucleus is pale and often has one or two marked indentations. A characteristic feature is the abundant cytoplasm with numerous organelles of all types and the large amount of granular endoplasmic reticulum arranged in stacks. Few synapses are present upon the cell somata, and most of these are the symmetrical type. These cells formed approximately two-thirds of the total sample. The second type (figure 3, plate 2) is much smaller, 5–8 × 10–12 μm, is frequently fusiform in shape, with one or two dendrites emerging from each pole. The nucleus is similar to that of the large type and has definite indentations, but the cytoplasm is very small in amount, often forming just a thin rim around the nucleus and containing very little granular endoplasmic reticulum. Many of the mitochondria appear rather pale or vacuolated. Of approximately the same frequency as the small cell type are perikarya intermediate in size and qualitative features, many being fusiform in shape. The nucleus appears similar to the other cell types but the cytoplasm is paler with an appreciable amount of endoplasmic reticulum, predominantly in the form of very small fragments and groups of ribosomes. Whether this intermediate type forms a separate group remains to be determined. Taken together the small and intermediate types formed approximately a third of the total number. On this small sample one is hesitant to make correlations with light microscopy or the functional nature of the cells, but it seems probable that the large type is the efferent relay cell and the small an interneuron. Vesicles have been seen in the type of small cell that may give rise to the P profile and also initial segments have been seen arising from both large and small types of cells (figure 2, plate 2). These observations are significant in view of the suggestion that the small cell type may be of an amacrine nature without an axon (Le Vay 1971; Wong 1970; Lieberman 1973). A light microscopical study of thionin-stained sections of the ventrolateral nucleus shows that both large and small cells are present, but the small cells are fewer in number and form a smaller proportion of the total population than the electron-microscopic observations would suggest.

The neuropil contains a high proportion of profiles with presumed synaptic vesicles, and the shape of these vesicles and the features of any associated synaptic specialization form the basis for classifying these profiles. Two groups of axon terminals make up the first category: small (SR) and large (LR) synaptic boutons are pre-synaptic at asymmetrical contacts and contain round synaptic vesicles. The second category also has two classes: F boutons and P profiles are pre-synaptic at symmetrical contacts and contain vesicles which are characteristically pleomorphic. F and P profiles are similar in some respects, and difficulties were experienced in differentiating them in the initial stages of this study; the use of a gonioscopic stage (Dennison 1971) helped to differentiate them and confirmed their disparate natures.

SR axon terminals (figures 4–6, plate 3; figures 7–11, plate 4; figures 13 and 14, plate 5) are small dark profiles, not more than 1.5 μm in diameter, with densely packed round vesicles; few contain mitochondria and those that do rarely possess more than two. Numerically these are the predominant vesicle-containing component of the neuropil, and they are pre-synaptic most frequently to small and medium sized dendrites (figures 4 and 5, plate 3; figure 9, plate 4)

and their spines, and also to P profiles (figure 6, plate 3; figures 7, 8, 10 and 11, plate 4; figure 13, plate 5). The synaptic contact is usually single, with a marked post-synaptic opacity, thus resembling the type I synapse of Gray (1959), an asymmetrical synapse. Generally SR terminals have only one synapse in a single thin section, but occasionally they may be pre-synaptic to

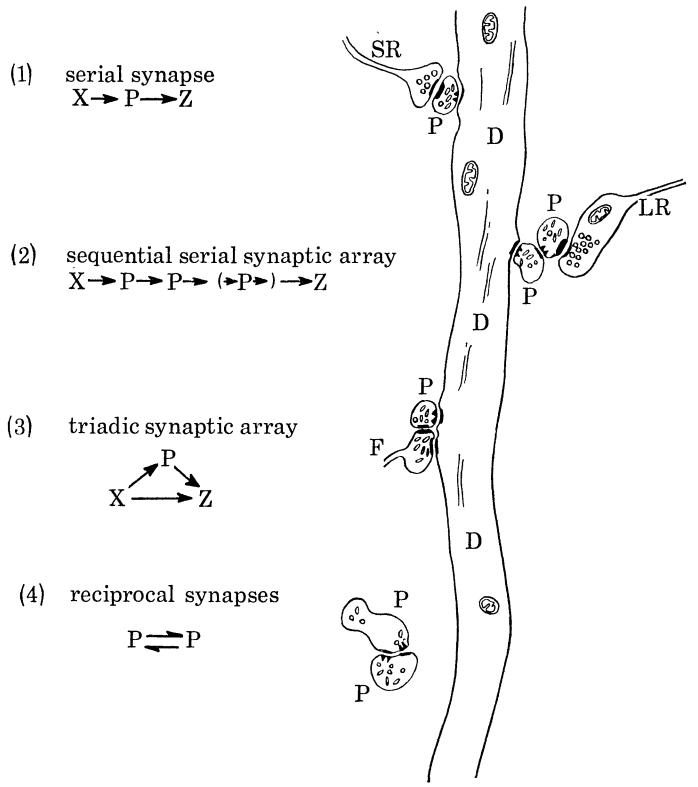


FIGURE 12. An explanatory diagram showing the various types of complex synaptic arrangement to be found in the centre-median and ventrolateral nuclei. X = SR, LR, F axon or P profile; Z = P profile or dendrite; P = P profile.

DESCRIPTION OF PLATE 5

FIGURE 13. Varicose P process (P) which is both post-synaptic to an SR axon (S) and pre-synaptic to a dendrite (D). Observe the ribosomes (r) and sacs of smooth endoplasmic reticulum (e). Centre-median nucleus. (Magn. × 40000.)

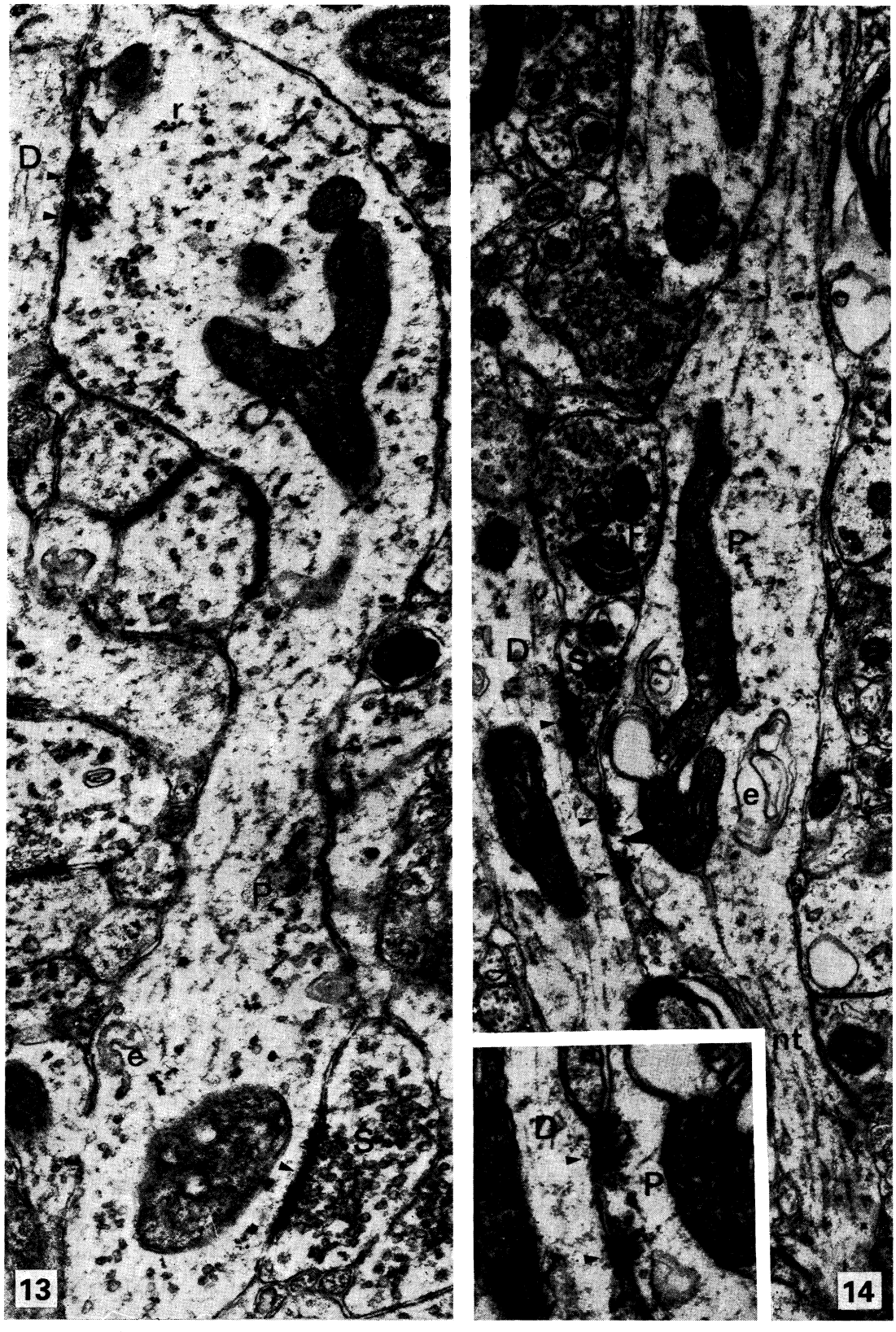
FIGURE 14. P profile (P) which is both post-synaptic to an F axon (F) and pre-synaptic to a dendrite (D). Compare the length of the synaptic contacts occurring post-synaptic to F and P profiles. Ventrolateral nucleus. (Magn. × 30000.) *Inset:* the dendro-dendritic synapse indicated by arrow in figure 18 at higher magnification. (Magn. × 60000.)

DESCRIPTION OF PLATE 6

FIGURE 15. The P profile [P(D)] is very similar in structure to a conventional dendrite, containing clusters of ribosomes (r) but also has a number of synaptic vesicles (sv) clustered near a symmetrical synapse with a small dendrite (D). Centre-median nucleus. (Magn. × 24000.)

FIGURE 16. The profile [P(D)] in figure 15 when followed in serial sections turns out to be a mainstem dendrite (D) here seen post-synaptic to an SR bouton (S) and in continuity with its cell soma (so). (Magn. × 24000.)

FIGURE 17. A varicose P process (P); two expansions are joined by a narrow portion containing neurotubules (nt). Note the sac of smooth endoplasmic reticulum (e). Centre-median nucleus. (Magn. × 18000.) The P profile is post-synaptic to an SR bouton (S) (the large arrow indicates the place). The upper inset shows this synapse in another serial section. The P profile is also pre-synaptic to a small dendrite (D). (The large arrowhead indicates the site). The lower inset demonstrates this synapse in another serial section. (Magn. of insets × 30000.)



FIGURES 13 AND 14. For description see opposite.

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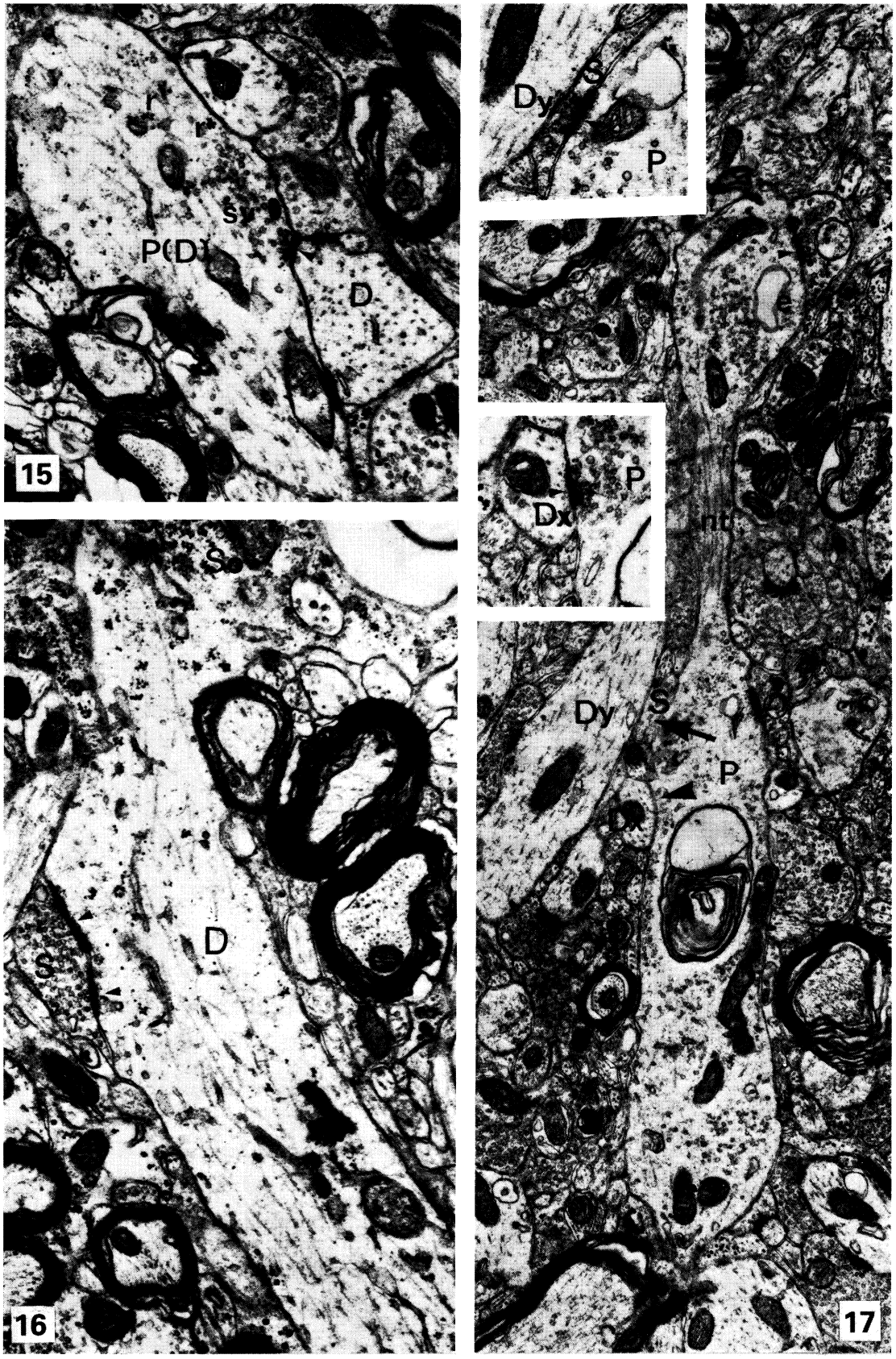
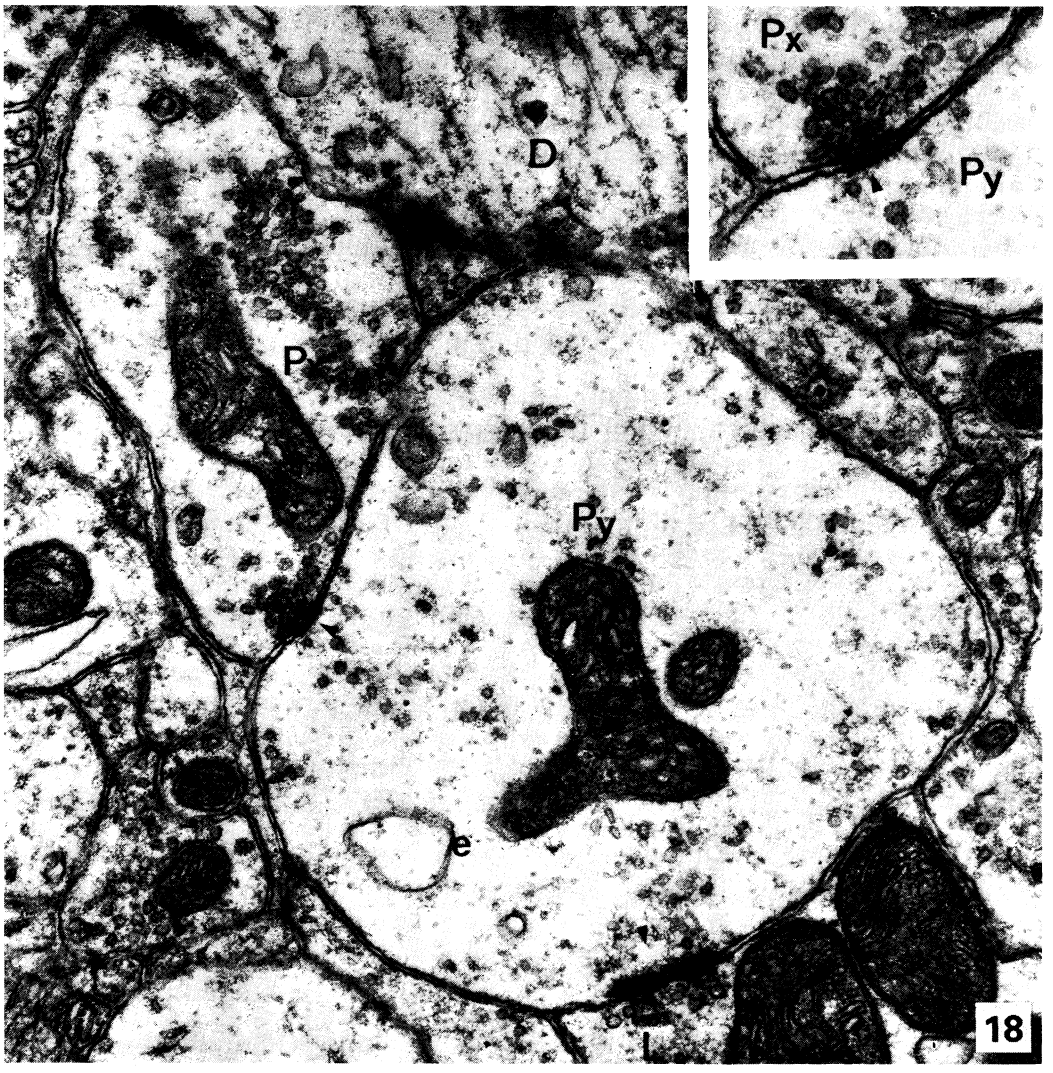
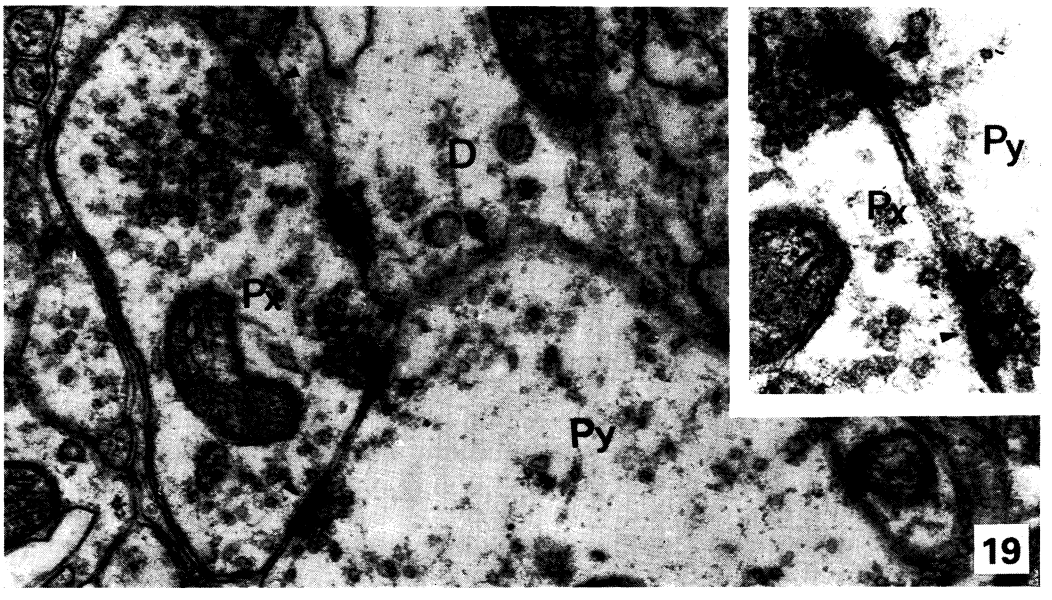
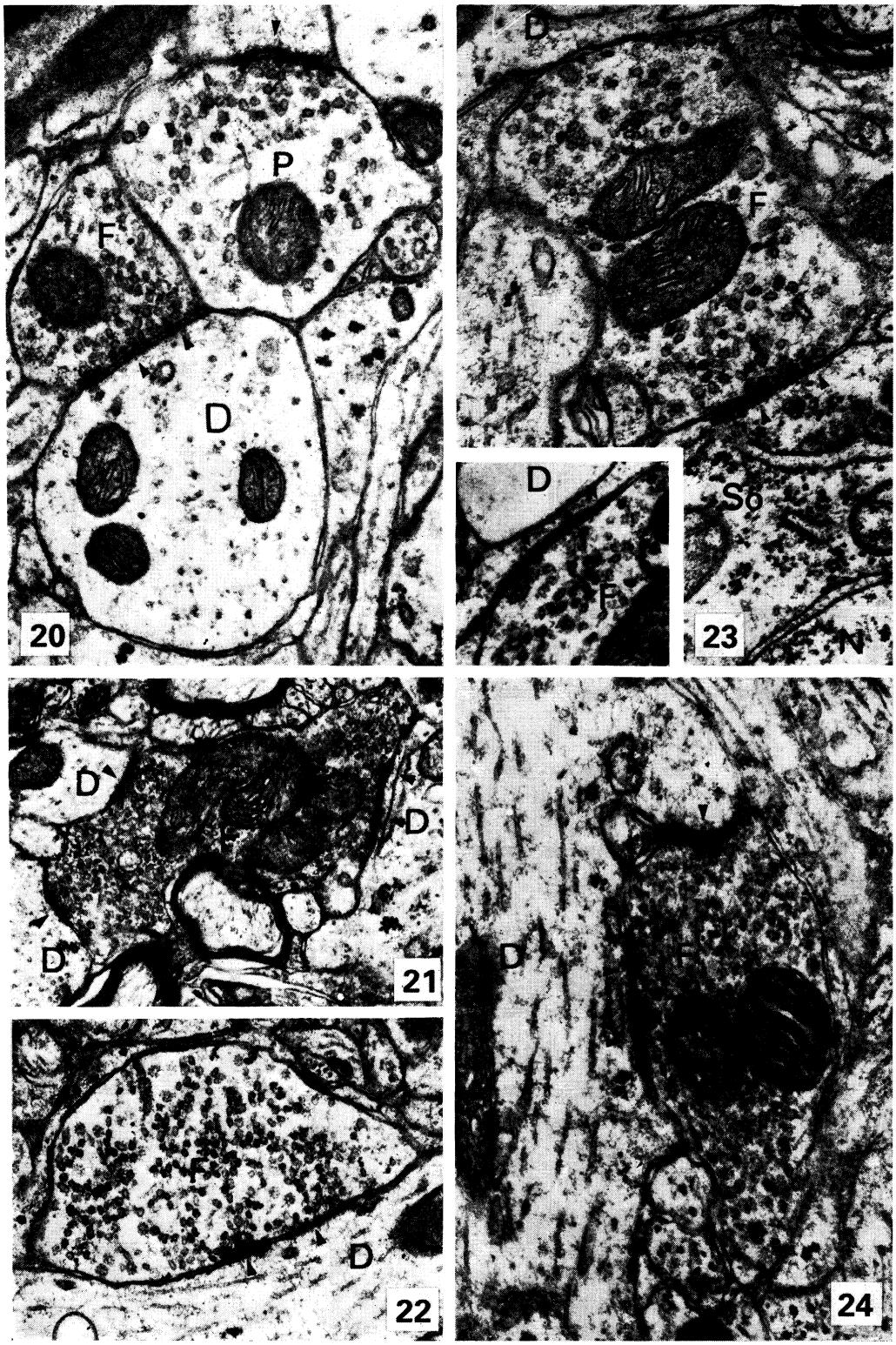


FIGURES 15–17. For description see p. 364.





FIGURES 18 AND 19. For description see p. 365.



FIGURES 20–24. For description see opposite.

several profiles, which may be two dendrites (figure 9, plate 4), a dendrite and its spine, or a dendrite and a P profile (figures 10 and 11, plate 4). SR terminals with more than one synapse are more common in the centre-median than in the ventro-lateral nucleus. SR terminals may occasionally take part in a triadic synaptic arrangement (figure 12), but this has only been observed in the centre-median nucleus (figure 10, plate 4). This complex (figure 12) consists of an SR bouton which is pre-synaptic to a P profile and the shaft or spine of a dendrite, the latter being post-synaptic to the P profile as well. SR profiles are never post-synaptic and are rarely found to have multiple synaptic contacts with the same post-synaptic profile. They are commonly situated in considerable numbers along the shafts of small diameter dendrites (figures 4 and 5, plate 3). Occasionally SR profiles occur at the periphery of glomeruli (figure 47, plate 13) where they can be pre-synaptic to P profiles or to the main dendrite as it leaves the glomerulus. SR boutons are the terminal expansions of extremely fine unmyelinated axons; no myelinated fibre has been traced unequivocally into continuity with an SR terminal, although many of these are terminals of extrinsic axons.

LR axon terminals are the largest vesicle-containing profiles in these nuclei, and as well as being present in every glomerulus they may occasionally have axo-dendritic or axo-somatic contacts in the adjacent neuropil. In single sections LR profiles can appear circular, ovoid, crescentic or oblong, but serial sections show them to be slightly elongated, flask-shaped or bulbous knobs, up to 3 μm in diameter and sometimes as long as 7 μm, flattened against and tending to surround the segment of dendritic shaft with which they have most synaptic contacts. In single sections a glomerulus may apparently contain several LR expansions, but in serial sections these are seen to be different parts of the same bouton which is often highly contorted owing to the multiple invaginations produced by the expansions and finger-like protrusions of P profiles, and the spines which radiate from the glomerular dendrite. Some LR axons are

Description of plate 7

Figures 18 and 19. Serial sections of a reciprocal synaptic array in a glomerulus in the ventrolateral nucleus. (Magn. × 40000; of insets, × 67000.)

In figure 18 a P profile (Px) is pre-synaptic to another P profile (Py). The inset shows this synapse at a higher magnification. Py is also post-synaptic to an LR terminal (L). Note the sac of endoplasmic reticulum (e).

In figure 19 (four sections distant from figure 18) Py is presynaptic to Px close to the site of the oppositely directed synaptic specialization in figure 18; compare the position of the arrowhead. Px is also pre-synaptic a second time to Py. These synapses are shown at a higher magnification in the inset.

Description of plate 8

Figure 20. Axo-dendritic symmetrical synapse between an F bouton (F) and a dendrite (D) in the centre-median nucleus. Compare this bouton's synaptic vesicles with those in the juxtaposed P profile (P) which makes a dendro-dendritic synapse. (Magn. × 40000.)

Figure 21. F axon bouton (F) which is pre-synaptic to three dendrites (D) in the centre-median nucleus. Observe how this profile is filled with small flat vesicles. The synaptic specializations appear rather straight. (Magn. × 30000.)

Figure 22. F axo-dendritic synapse in the centre-median nucleus. Note the straightness and length of the synaptic specializations – the larger one is 0.5 μm long. (Magn. × 30000.)

Figure 23. F axon terminal (F) which is pre-synaptic to a cell soma (So) in the centre-median nucleus. (Magn. × 45000.) Inset to figure 23 is a few serial sections distant from it, and at the opposite side of the F profile from the synapse shown in figure 23. The F terminal is pre-synaptic to a dendrite (D). The synaptic contact is rather straight and 0.5 μm in length. (Magn. × 45000.)

Figure 24. F axo-dendritic synapses in the centre-median nucleus. (Magn. × 40000.)

extrinsic in origin, as many of these terminals in the ventrolateral nucleus degenerated following the destruction of the cerebellum. After emerging from a myelinated sheath, *ca.* 0.25–0.75 μm diameter, LR axons often expand into one or more boutons *en passant*, each of which is related to a glomerular complex, before forming a terminal expansion. In one example the first synapse was only 0.3 μm from the end of the myelin sheath, and was an *en passant* axo-dendritic synapse in the neuropil just prior to the glomerular expansion. Up to five expansions have been observed, connected by narrow unmyelinated axon segments; they may share the same dendrite for their glomerular synaptic connections as well as sharing some of the same P profiles. An LR expansion was observed at a node of Ranvier making synaptic contacts with a dendrite. LR terminals contain large numbers of round synaptic vesicles, and a distinctive feature is their large number of darkly staining mitochondria. Neurofilaments may be found in the central core of a terminal and in the connecting segments. LR terminals are never post-synaptic, but always pre-synaptic to a large number of profiles. Within a glomerulus an LR expansion is always pre-synaptic to the main dendrite, to its spines, and to many, sometimes nearly all, of the P profiles within the complex. The LR terminal forms multiple synaptic contacts, as many as 30 or 40 within a glomerulus of which up to a dozen are on the dendritic shaft (excluding its spines). As well as regular synapses, the LR terminal also forms 'filamentous' (Colonnier & Guillery 1964) or 'adhesive' (Peters & Palay 1966) desmosome-like contacts with the dendrite.

P profiles (figures 13–17, plates 5 and 6) are irregularly shaped, pale, and are found in large numbers both within and outside glomeruli; they account for nearly 70 % of all intraglomerular profiles. P profiles contain pleomorphic vesicles which vary from circular or oval profiles, 40–50 nm diameter, to elliptical shapes up to 50 nm long and as narrow as 15 nm, but the majority are round. On a gonioscopic stage a thin section was rotated through 90° (+45° to −45° of the normal section plane) and photomicrographs of P profiles were taken at 15° intervals of tilt. These synaptic vesicles were found to be of the disc-like class described by Dennison (1971), and similar to those of the 'PSD' profiles in the rat dorsal lateral geniculate nucleus (Lieberman & Webster 1972; Lieberman 1973). P profiles owe their pale appearance to the lack of opacity of their cytoplasmic matrix and, by comparison with other types of vesicle-containing profile, their relatively small number of vesicles mostly aggregated near synaptic specializations. P profiles possess a few mitochondria which are usually smaller and paler than those in LR terminals, but similar to those in dendrites. Commonly P profiles contain one or more irregular sacs of smooth endoplasmic reticulum (figures 13 and 14, plate 5; figure 17, plate 6) and occasionally a small number of neurofilaments or neurotubules, the latter particularly in thin processes. Ribosomes are also sometimes found, either simply or clustered in rosettes, or very rarely attached to endoplasmic reticulum (figure 13, plate 5). P profiles are extremely variable in size, commonly varicose in contour and their course is often tortuous. Arising from very thin unmyelinated processes, P profiles form expansions which are joined by thin processes. Up to 30 P profiles may be present in one glomerulus, some being small protrusions which invaginate the LR terminal. A given process may have synaptic contacts in several glomeruli or be found to pass for a considerable distance through the neuropil, when they are straighter and more uniform in diameter. Such vesicles and ribosomes are also seen in larger calibre profiles, closer in character to proximal dendrites, which may also give or receive the occasional synapse and which have been observed in continuity with cell somata (Harding 1971; figures 15 and 16, plate 6). P profiles are post-synaptic to LR and F axons within

glomeruli, and to F and SR axons in the neuropil (figures 7–11, plate 4; figures 13 and 14, plate 5); these contacts can occur on a narrow portion of a profile, which has few vesicles and no pre-synaptic specialization. P profiles can be pre- or post-synaptic, or both concurrently to other P profiles; they are also pre-synaptic to the shafts and spines of glomerular and other dendrites and occasionally to cell somata. P profiles are often pre-synaptic to several profiles, but usually each post-synaptic profile is contacted only once. Multiple synapses may however occur upon a dendrite within a glomerulus. A small number of pleomorphic vesicles cluster around pre-synaptic dense projections. The pre- and post-synaptic membranes are both lightly thickened, while sub-synaptic electron-dense 'fuzz' is present in both profiles, and the synapses resemble the 'symmetrical' type described by Colonnier (1968). Reciprocal synapses (figure 12) occur in both the ventrolateral and centre-median nuclei (Harding 1971; figures 18 and 19, plate 7) between pairs of P profiles (cf. Famiglietti 1970). Two similar but separate symmetrical specializations adjoin each other but are polarized in opposite directions. Most reciprocal synapses are found inside glomeruli (figures 18 and 19, plate 7), but some occur in the inter-glomerular neuropil.

The nature of these P profiles, whether axonal or dendritic, is still uncertain but for many reasons they are best classified as dendritic. They contain disc-like vesicles similar to those found in undoubted dendrites in these nuclei (Harding 1971) and in the rat lateral geniculate nucleus (Lieberman & Webster 1972; Lieberman 1973). These processes have not been traced to a myelinated fibre or an axonal initial segment; they are the only vesicle-containing profiles in these nuclei to be post-synaptic to axons and to other profiles of their own type, and they are also unique in having reciprocal synaptic relations; axo-axonic synapses have only been seen when the post-synaptic axon is an initial segment (figure 2, plate 2) or a terminal expansion with vesicles and a synaptic thickening, but these profiles, which are usually varicose and tortuous for axons, are sometims post-synaptic where they are non-terminal and virtually devoid of vesicles. This conclusion is in essential agreement with that of several recent papers dealing with the thalamic nuclei of various species (Ralston & Herman 1969; Wong 1970; Le Vay 1971; Morest 1971; Famiglietti & Peters 1972; Lieberman & Webster 1972; Lieberman 1973; Wong-Riley 1972*a*) where it has been argued that dendritic terminals account for a large proportion of the pre-synaptic profiles.

F axon terminals (figures 20–24, plate 8) are the least common type of vesicle-containing profile; most are found in the interglomerular neuropil, but some are related to glomeruli. They are less common in the centre-median nucleus than in ventrolateral. Myelinated fibres, about 1 μm in diameter, have been found in continuity with *en passant* boutons of F processes, and the most proximal synapse may actually adjoin the last myelin tongue. F profiles are observed as either *en passant* or terminal expansions, about 1–2 μm diameter; a synaptic bouton has been found at the end of a narrow branch from an F axon segment that also possessed *en passant* synapses. F boutons are similar to P profiles in having pleomorphic synaptic vesicles, at least half of which are flat vesicles, while the remaining circular vesicle profiles are 20–40 nm in diameter, which are smaller than in P processes. These differences were confirmed with tilt analysis, which showed that F vesicles were cylindrical (Dennison 1971). F boutons usually contain three or four mitochondria, which are larger and darker than those in P profiles; *en passant* expansions and connecting segments also contain neurotubules and occasionally neurofilaments. Because of this considerable complement of intracellular inclusions, F boutons are rarely as pale as P profiles and they may contain a slightly denser

matrix. F boutons have never been seen to be post-synaptic, but their terminal expansions are pre-synaptic to several profiles which can be dendrites or P profiles. F terminals are more commonly pre-synaptic to the proximal parts of dendrites, their shafts and occasionally their spines (figure 37, plate 11) than to their more distal parts. They form the largest proportion of the terminals making axo-somatic synapses (figure 23, plate 8) and are also pre-synaptic to somatic spines (figures 25, 26, 28 and 29, plate 9) in the centre-median nucleus. F axon boutons may also contact an axon initial segment (figure 2, plate 2), and are sometimes found at the edges of glomeruli, where they may form triadic arrangements (figure 12) with P profiles and dendrites. Unlike the contacts formed by P profiles, F synaptic specializations are frequently long, up to 0.5 μm, but they are usually single, and conform to the symmetrical type (Colonnier 1968).

Dendrites and somatic spines

Dendritic appendages of various kinds have been described in a number of thalamic nuclei in several different species. Terms such as grape-like protrusion, dendritic protrusion, dendritic appendage or bulbous thorn (Szentágothai 1963; Peters & Palay 1966; Guillery 1966, 1969; Jones & Powell 1969*b*; Ralston & Herman 1969; Guillery & Colonnier 1970; Le Vay 1971; Wong-Riley 1972*a*; Famiglietti & Peters 1972; Špaček & Lieberman 1974) have been used when referring to larger irregularities or short side branches arising from dendritic shafts. Smaller appendages, often occurring on more distal dendrites and sometimes as excrescences

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Description of plate 9

Figure 25. Somatic spine (sp) post-synaptic to F bouton (F) in the centre-median nucleus. The spine has denser cytoplasm than the rest of the cell soma (So) but contains no organelles. (Magn. × 30000.)

Figure 26. Somatic spine (sp) post-synaptic to an F profile (F) in the centre-median nucleus. (Magn. × 40000.)

Figure 27. Narrow calibre distal dendrite in the ventrolateral nucleus with four spines (sp), all of which have dense cytoplasm but no organelles. Three of these spines are post-synaptic to SR terminals (S). Two of the axo-spinous contacts are associated with a second synapse at the base of the spine on the shaft of the parent dendrite, i.e. a dyadic arrangement; one of these dyads has a single axon bouton pre-synaptic at both contacts. (Magn. × 30000.)

Figure 28. F axon bouton (F) in the centre-median nucleus presynaptic to a somatic spine (sp) and also to the soma (So) at the base of the spine – a dyad. Note the sub-synaptic sac (c) within the spine. (Magn. × 42000.)

Figure 29. Somatic spine (sp) post-synaptic to an F bouton (F) in the centre-median nucleus. The soma (So) is that of a small type neuron. (Magn. × 25000.)

Description of plate 10

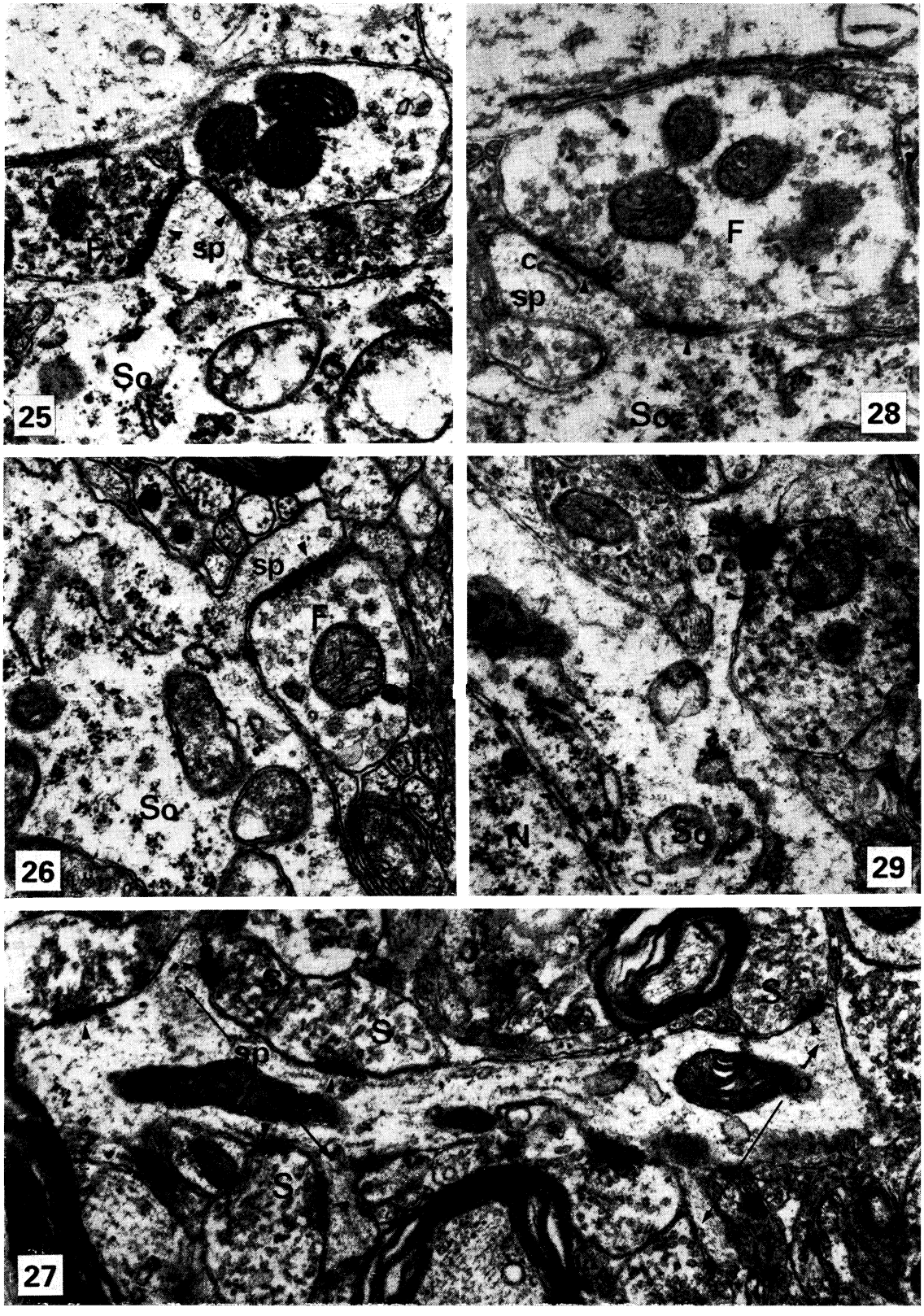
Figure 30. Two spines (sp) arising from a dendrite (D) in the centre-median nucleus. Both spines are accompanied by a subjacent multivesicular body (m) within the parent dendrite. (Magn. × 32000.)

Figure 31. A double spine (sp) in the centre-median nucleus. Both parts of the spine are contacted by an SR terminal (S). A multivesicular body (m) is situated directly beneath the spine in the dendrite (D). Note the floccularity of the matrix within the spine. (Magn. × 38000.)

Figure 32. An SR terminal (S) pre-synaptic to two spines (sp) arising from adjacent dendrites (D) within the neuropil of the centre-median nucleus. A multivesicular body (m) is associated with each spine. (Magn. × 30000.)

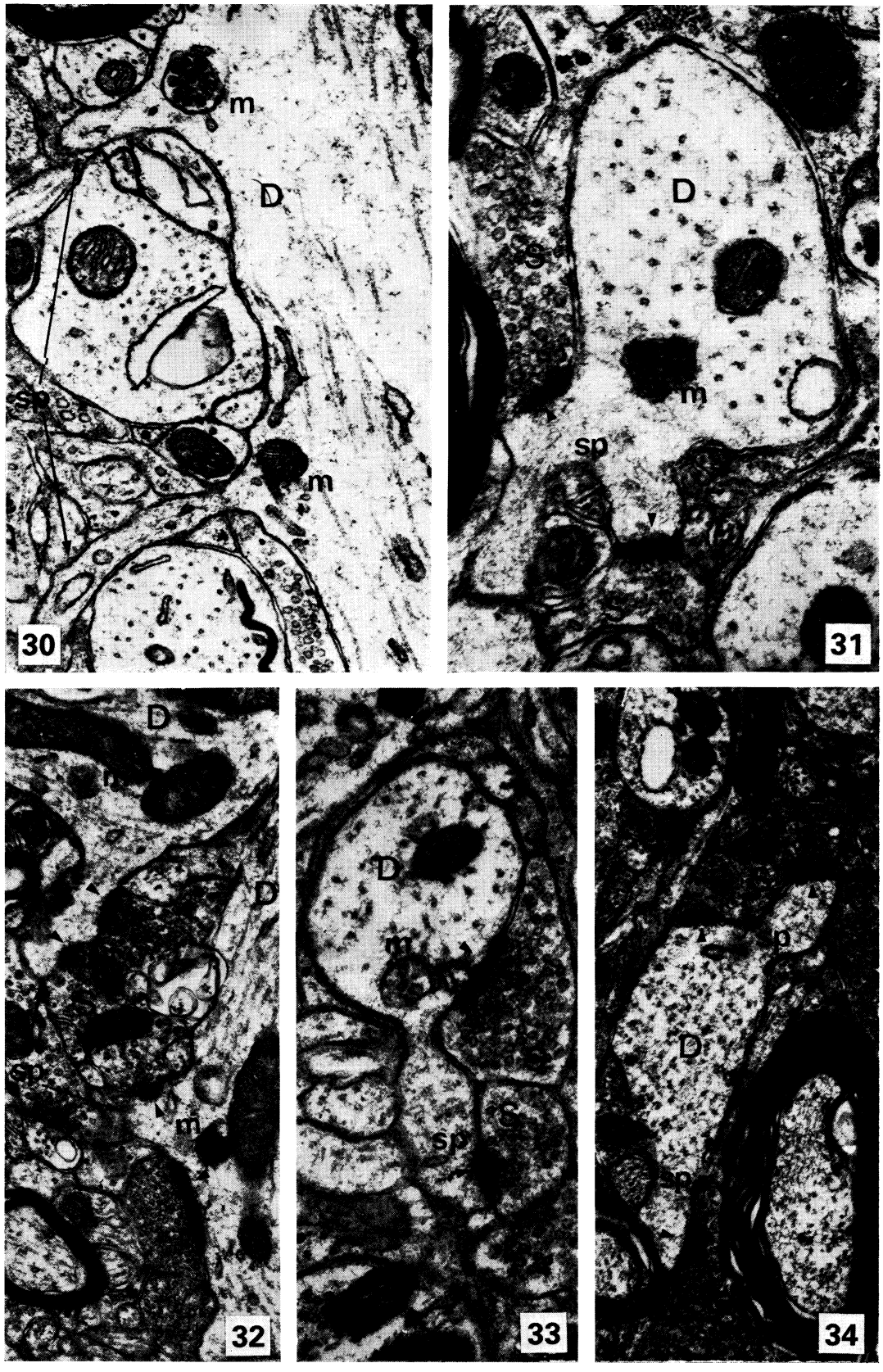
Figure 33. Dendritic spine (sp) with an associated multivesicular body (m) in the centre-median nucleus. Both the spine and its parent dendrite (D) are contacted by an SR terminal (S) – a dyad. (Magn. × 45000.)

Figure 34. Two spines (sp) arising from a dendrite (D) in the centre-median nucleus are contacted by SR terminals (S); one spine forms a synaptic dyad with a second contact from an SR bouton upon the nearby dendritic surface. (Magn. × 35000.)

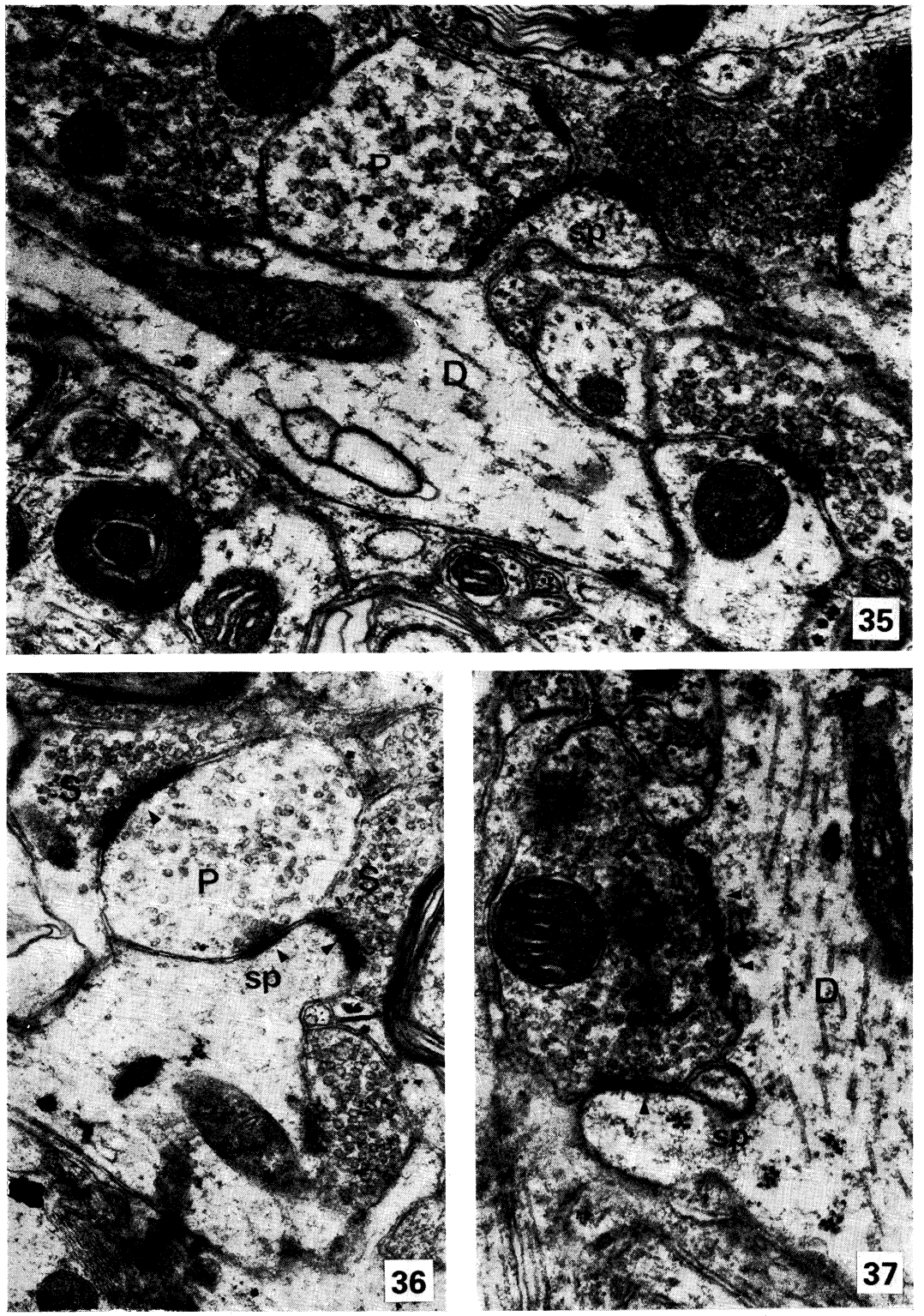


FIGURES 25–29. For description see opposite.

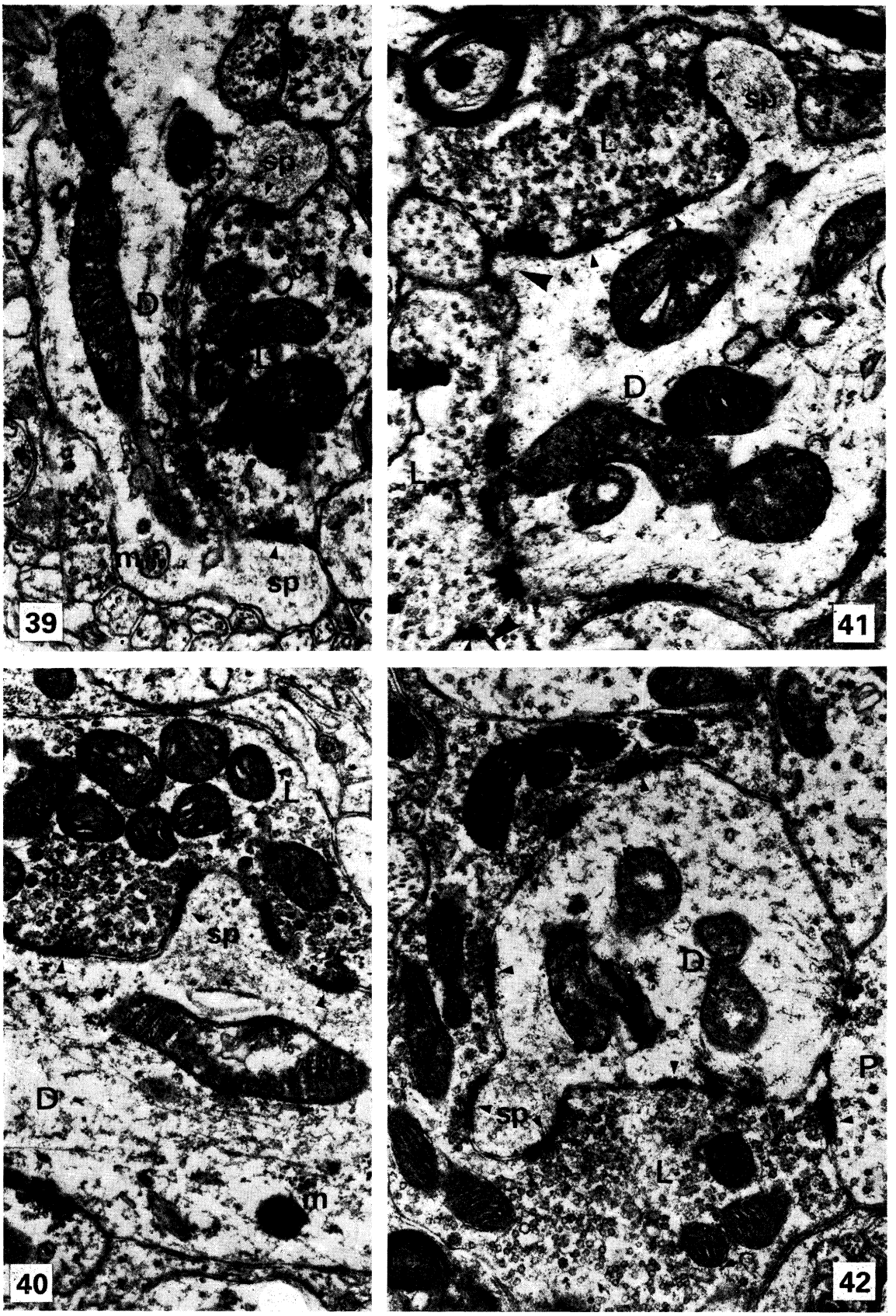
(*Facing p.* 368)



FIGURES 30-34. For description see p. 368.



FIGURES 35–37. For description see p. 369.



FIGURES 39–42. For description see opposite.

of dendritic protrusions (Szentágothai *et al.* 1966) are commonly referred to as spines, thorns or dentate appendages (Guillery 1969; Guillery & Colonnier 1970; Guillery & Scott 1971; Morest 1971; Wong-Riley 1972*a*). In the ventrolateral and centre-median nuclei of the monkey thalamus only the latter type of smaller appendage has been seen and this resembles the dendritic spine described in detail in the cerebral cortex (Gray 1959; Gray & Guillery 1963; Jones & Powell 1969*d*; Peters & Kaiserman-Abramof 1969, 1970). At the ultrastructural level these appendages, which will be called dendritic spines, are present both within and among the interglomerular neuropil.

A significant number of cell somata in the centre-median nucleus possess spines, and these structures project at right-angles from the surface (figures 25, 26, 28 and 29, plate 9). The cytoplasm is floccular and usually devoid of inclusions. Most synaptic spines are post-synaptic to F boutons, and as yet no example of an asymmetrical contact on a somatic spine has been found (cf. Peters & Kaiserman-Abramof 1970). In some cases (figure 28, plate 9) the pre-synaptic profile forms a second synapse on the cell soma nearby at the base of the spine (cf. Peters & Kaiserman-Abramof 1970) and on other occasions a separate profile forms a synapse in this position. Spines are more common in the neuropil of the centre-median nucleus than in the neuropil of the ventrolateral and other principal thalamic relay nuclei in the monkey. They vary considerably in size and shape (figures 30–37, plates 10 and 11): some are sessile or peg-like, while others are pedunculated. No correlation could be found between the length of a spine and the size of its parent dendrite, and most spines were seen to arise from small dendrites.

A striking observation is the frequent occurrence of multivesicular bodies (Palay & Palade 1955; Palay 1963) in spine-bearing dendrites (figures 30–33, plate 10); the parent dendrite

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Description of plate 11

Figure 35. A triadic synaptic array in relation to a dendritic spine (sp) in the centre-median nucleus. The spine is post-synaptic to a P profile (P) and an SR terminal (S); the latter is also pre-synaptic to the P profile. (Magn. × 32000.)

Figure 36. A serial synapse upon a spine (sp) in the centre-median nucleus. An SR terminal (S) makes a synaptic contact with a P profile (P) which is pre-synaptic to the spine. The spine is also post-synaptic to another SR terminal. (Magn. × 30000.)

Figure 37. A dyadic array in the centre-median nucleus in which an F bouton (F) is pre-synaptic to a spine (sp) and the parent dendrite (D) at the spine's base. (Magn. × 40000.)

Description of plate 12

Figure 39. Two spines (sp) arising from a dendrite (D) within a glomerulus are contacted by an LR terminal (L). Note the increased floccularity of the cytoplasmic matrix compared with the parent dendrite. A multivesicular body (m) is present next to one of the spines. Ventrolateral nucleus. (Magn. × 20000.)

Figure 40. An LR bouton (L) indented by a dendritic spine (sp) to which it is pre-synaptic; the LR terminal also makes synaptic contact with the parent dendrite nearby. Observe the multivesicular body (m) in the parent dendrite. Centre-median. (Magn. × 30000.)

Figure 41. A spiny intraglomerular dendrite (D) in the ventrolateral nucleus. Parts of three spines (sp) are present (two indicated by large arrowheads); in forty serial sections this dendrite was found to have seven spines, all post-synaptic to the LR bouton (L). (Magn. × 30000.)

Figure 42. Part of a glomerulus in the centre-median nucleus showing a typical peg-like dendritic spine (sp) indenting an LR terminal (L). Notice the extensive axo-spinous synaptic contacts as well as three synapses between the LR terminal and the parent dendrite (D) and one between the LR bouton and a post-synaptic P profile (P). (Magn. × 30000.)

associated with 20 % of spines contains this organelle often situated near the base of the appendage. In one example, two multivesicular bodies were found subjacent to two spines on the same dendrite (figure 30, plate 10). On several occasions when a spine has been observed to be continuous with the shaft of a dendrite which does not appear to contain a multivesicular body, this organelle has been found in the parent dendrite near to the attachment of the spine in a subsequent section, a few serial sections distant. Multivesicular bodies are not frequently encountered in dendrites and a random survey of 100 dendrites showed only ten multivesicular bodies. When taken together with the relative paucity of spines, therefore, this is very suggestive of a relation between the presence of spines and multivesicular bodies.

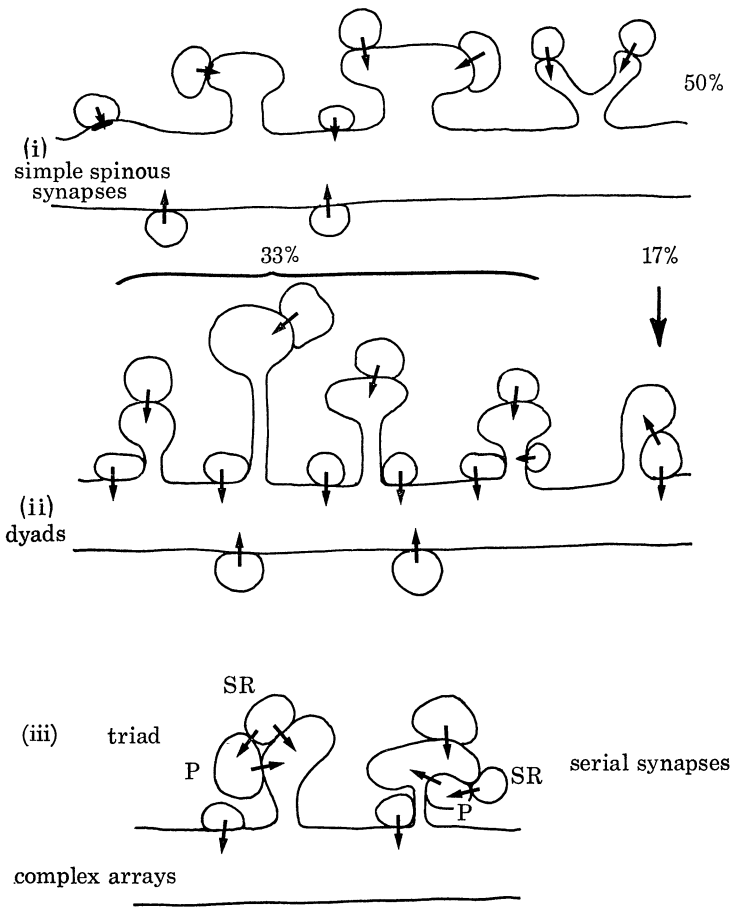


FIGURE 38. The synaptology of spines arising from dendrites in the neuropil of the centre-median nucleus represented as an hierarchical scheme.

(i) SR and F axons, and P profiles are pre-synaptic (arrows) to spines, which may be sessile, pedunculated or bilobed.

(ii) A synapse on a spine and a contact at its base on the parent dendrite make up a dyadic array; one terminal may be pre-synaptic at both synapses.

(iii) More complex spinous synaptic arrays include a triadic arrangement.

Spines are post-synaptic to SR or F (figure 37, plate 11) axon terminals and P profiles (figures 35 and 36, plate 11); the synaptic contact may be anywhere on the spine, but rarely occurs on the slender shaft of a long spine. If followed in serial sections a spine is always found to be post-synaptic; 80 % of spines are post-synaptic to at least one SR terminal at an asymmetrical synapse, whereas 25 % are post-synaptic to F boutons and P profiles at symmetrical

contacts (though not both on the same spine). It was estimated that more than half this second category are situated on large diameter dendrites ($\geqslant$ 2 μm), while three-quarters of the spines attached to large diameter dendrites are post-synaptic to an F axon terminal. Thus axo-spinous F terminals are predominantly associated with large proximal dendrites. Without examining spines with serial sections one cannot state that some may be post-synaptic *only* to F boutons, but of the spines which were observed post-synaptic to F boutons, not one was contacted by another type of terminal. As P profiles are considered to be dendritic those spines which are contacted by P processes are taking part in dendrospinous synapses, an arrangement which has been reported in the rat superior colliculus (Lund 1969), the olfactory bulb (Pinching & Powell 1971*a*) and the monkey motor cortex (Sloper 1971).

Further examination showed that the disposition of synapses on and near to spines was not a random arrangement. Fifty per cent of the spines observed in continuity with a parent dendrite were associated with at least two distinct synapses. The spine was post-synaptic at the first contact, while a second synapse was situated on the parent dendrite close to the basal attachment of the spine (figures 32–34, plate 10). More than a third of the synaptic dyads (figure 38) had only a single pre-synaptic process which contacted both the spine and the dendritic shaft (figure 37, plate 11); otherwise, the two pre-synaptic profiles were nearly always of the same type. A third synaptic contact sometimes occurred on the spine (figure 36, plate 11). In such a synaptic array two SR terminals would most frequently make up the 'complex', but P profiles and SR boutons could be present together, unlike the F axon terminals which were only observed pre-synaptic in a dyad with others of their own type. Two slightly more complicated arrangements have been encountered, the first (figure 36, plate 11) includes a basal synapse on the dendritic shaft and a peg-shaped spine which is post-synaptic to both an SR terminal and a P profile which is itself post-synaptic to another SR terminal. The second synaptic array is a triadic (figure 12) arrangement (figure 35, plate 11) in which the spine is contacted by an axon terminal at an asymmetrical synapse, while a P profile, besides being pre-synaptic to the spine, is also post-synaptic to this terminal. A tentative hierarchy or organization of spinous synapses has been presented in a schematic diagram of these examples (figure 38).

Although fewer in number, spines are also present in the neuropil of the ventrolateral nucleus (figure 37, plate 9), and the structure and connections of these are similar to those in the centre-median nucleus. All spines encountered were seen to arise from medium or small dendrites ($\leqslant$ 1.5 μm) and most were dentate. Multivesicular bodies were present in one third of the parent dendrites. The spines were post-synaptic to SR terminals and also occasionally to P profiles: in the majority of cases another synapse was also situated on the dendritic shaft at the base of the spine forming a dyad (figure 27, plate 9). In a few cases one profile was pre-synaptic at both synapses, and it was always an SR terminal. No spines were observed post-synaptic to F boutons, and none was found attached to large dendrites outside glomerular aggregations, where most F axo-spinous contacts were observed in the neuropil of the centre-median nucleus.

In the cat lateral geniculate nucleus, spines occasionally arise from dendritic protrusions within glomeruli (Szentágothai *et al.* 1966) but in both the ventrolateral and centre-median nuclei dendritic shafts commonly bear spines within glomerular aggregations (figures 39–42, plate 12). The frequency of these appendages varies; one glomerular dendrite was examined in transverse section and bore no spines through 68 serial sections (3.4 μm), while seven spines

were found on another single dendritic segment (figure 41, plate 12) within 40 sections (2 μm) in another glomerulus; several spines were often observed on a longitudinally sectioned dendritic segment, contacted by more than one LR expansion, and 11 spines were seen on a length of 20 μm when one dendrite was traced through a depth of 30 serial sections (1.5 μm). Glomerular spines are sometimes seen in continuity with a parent dendrite, but if not they may be recognized by their position, usually surrounded by an LR terminal which has been invaginated, and by their cytoplasm which is amorphous, floccular and moderately electron-dense. Although a spine apparatus is rarely found within the spine itself, it is not uncommon to find, subjacent to the spine in the parent dendrite, a similar structure which consists of an assemblage of parallel sacs alternating with electron-dense material. Multivesicular bodies are frequently seen within glomerular dendrites associated with spines, and two such organelles were found subjacent to two juxtaposed spines branching off one dendrite.

A considerable proportion of the plasma membrane encompassing a spine is devoted to post-synaptic specializations and when a spine invaginates an LR terminal the asymmetrical thickening may be very extensive. Within glomeruli spines are always post-synaptic to LR boutons, often at multiple contacts. Analogous to the spine-and-base dyadic synapses of a single terminal in the neuropil, LR boutons invariably synapse both with a spine and its parent dendrite and this axo-dendritic synapse is usually situated quite close to the base of the spine;

Description of plate 13

This and the following figures (up to and including figure 55, plate 15) are serial sections of a large glomerulus in the centre-median nucleus. See text and figures 56 and 57 for representative tracings and reconstruction; P profiles are numbered in accordance with the tracings. Numbers in the top corners of these figures indicate the number of the section in the series.

Figure 43. (Section 18.) Reciprocal synaptic arrangement between P profiles 13 and 19; the former is also post-synaptic to an SR terminal (S4), while the latter is post-synaptic to the LR terminal (see figure 56). (Magn. × 18000.)

Figures 44 and 45. (Sections 31 and 24.) Illustrating contacts between P profiles at dendro-dendritic synapses. Thus 17 is pre-synaptic to both 22 and 23, while 23 is pre-synaptic to 22, which is also contacted by the LR terminal (L); this is a P profile triad. Note also, that being post-synaptic to the LR terminal and pre-synaptic to the dendrite (D), profile 11 takes part in a triadic array. (Magn. × 18000.)

Figures 46 and 47. (Sections 21 and 7.) Further synaptic connections of P profiles, i.e., the serial synapse 7 → 5 → 12. The last, 12, is also post-synaptic to the LR terminal (L) and 5 is pre-synaptic to the main glomerular dendrite (D). (For the continuity of profile see figure 56, section 5.) (Magn. × 26000.)

Figure 48. (Section 11.) Sequential serial synaptic array S2 → 9 → 2 → 1; profile 2 is also post-synaptic to an SR terminal (S1). (Magn. × 24000.)

Description of plate 14

(See introductory remarks to plate 13.)

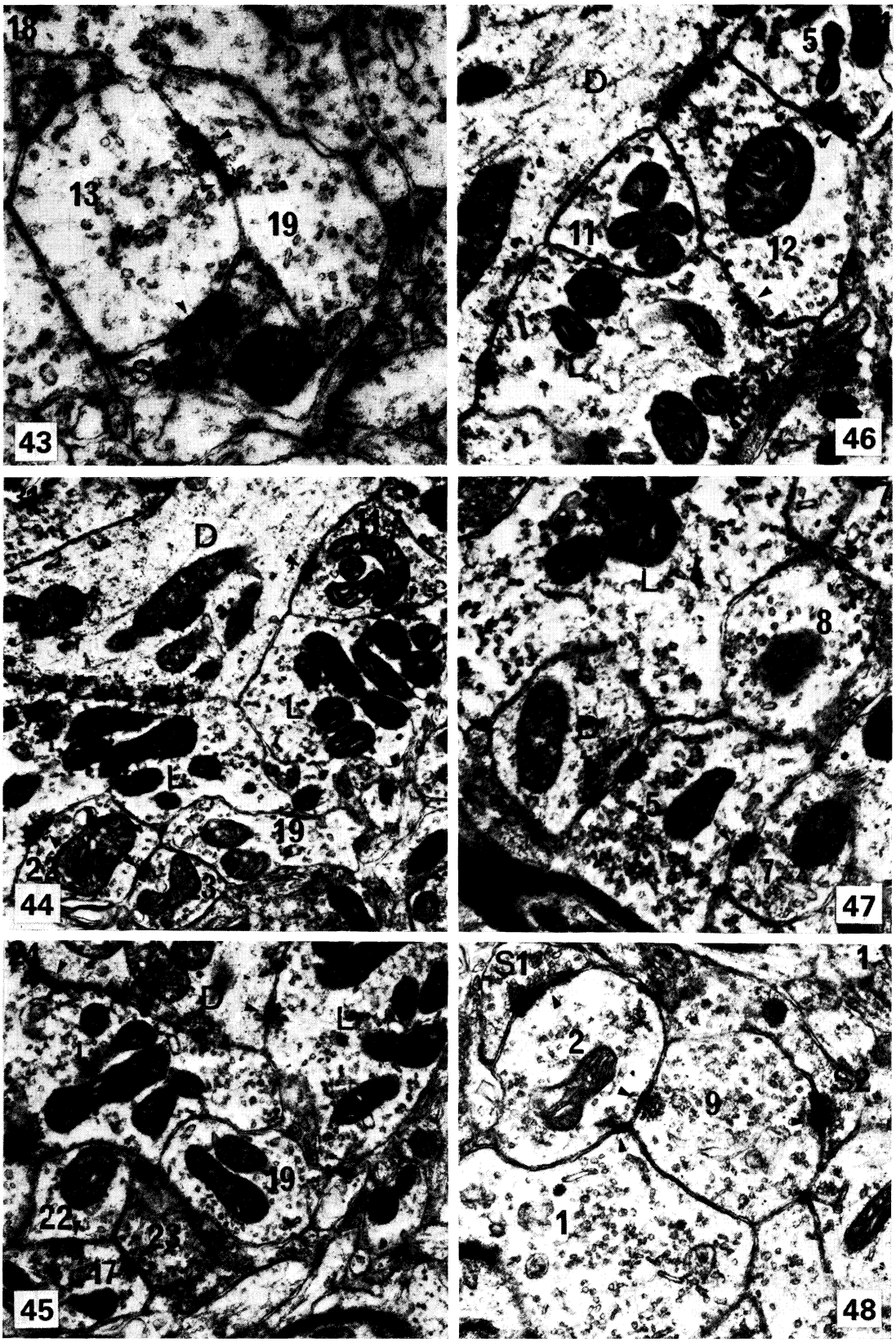
Figure 49. (Section 30.) P profile 27 has a complex series of synaptic contacts. In this section it is pre-synaptic to P profile 10, which is also post-synaptic to another P profile (see figure 50). (Magn. × 18000.)

Figure 50. (Section 34.) SR bouton S5 is pre-synaptic to P profile 25 which is pre-synaptic to 26, which is in turn pre-synaptic to 10 (see figure 49). (Magn. × 18000.)

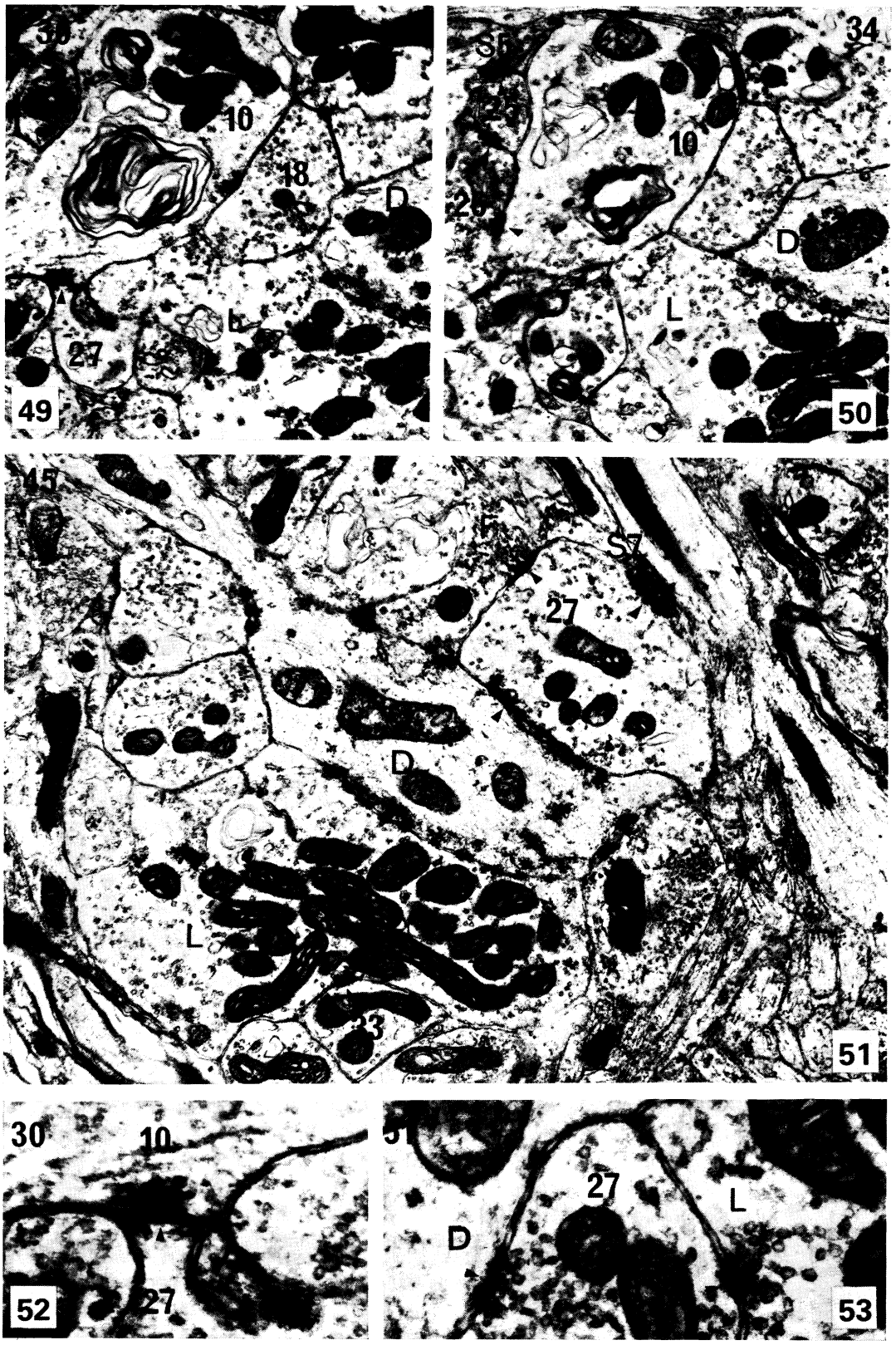
Figure 51. (Section 45.) P profile 27 is also post-synaptic to two axon terminals, an F bouton (F) and an SR terminal (S7), and contacts the main dendrite (D). (See figure 54, plate 15, for another part of the F triad.) (Magn. × 18000.)

Figure 52. (Section 30.) Higher magnification of part of figure 79 to show the dendro-dendritic synapse between P profiles 10 and 27. (Magn. × 58000.)

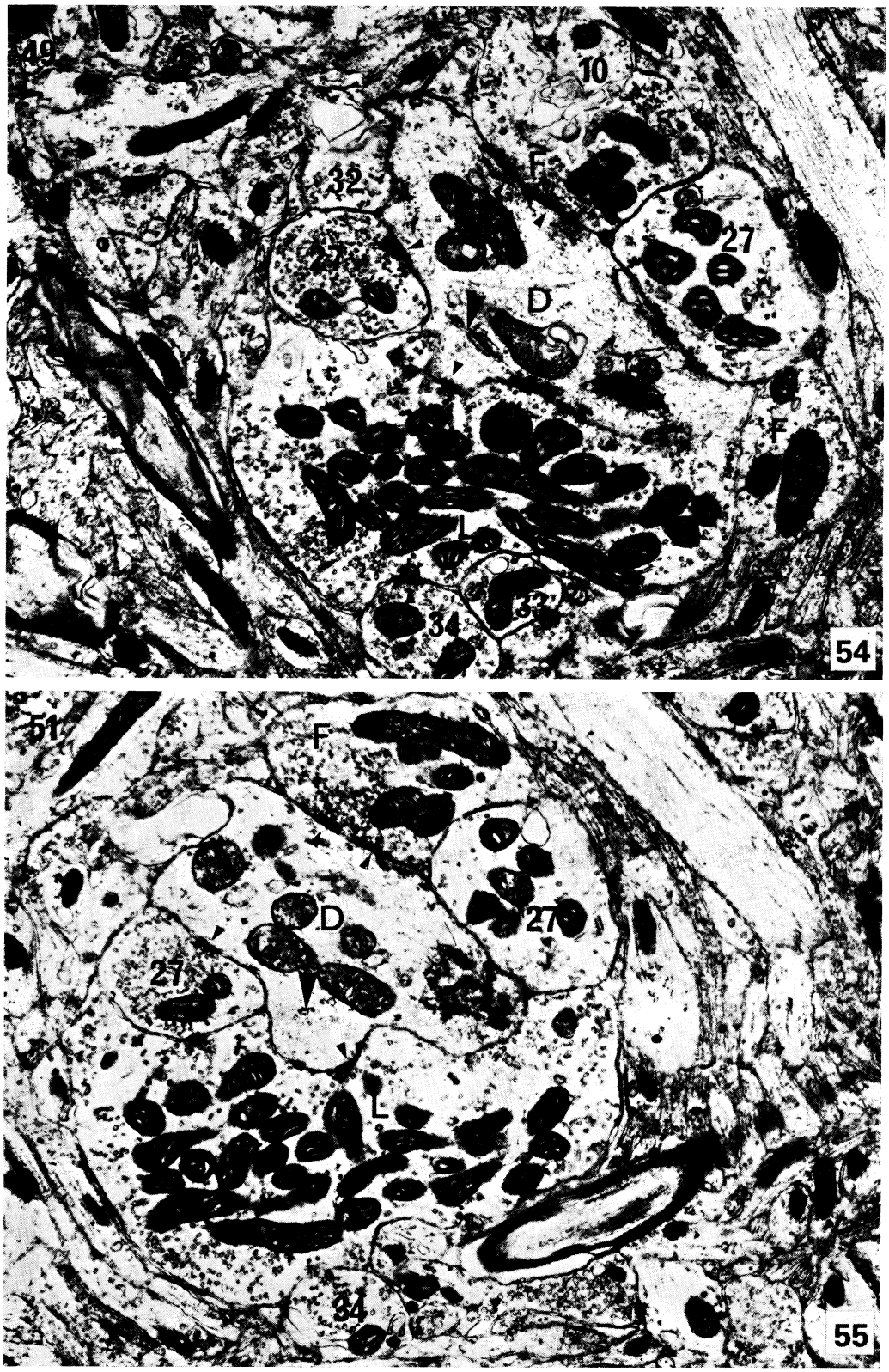
Figure 52. (Section 51.) Higher magnification of part of figure 55, plate 15, to show the synaptic specializations. (Magn. × 50000.)



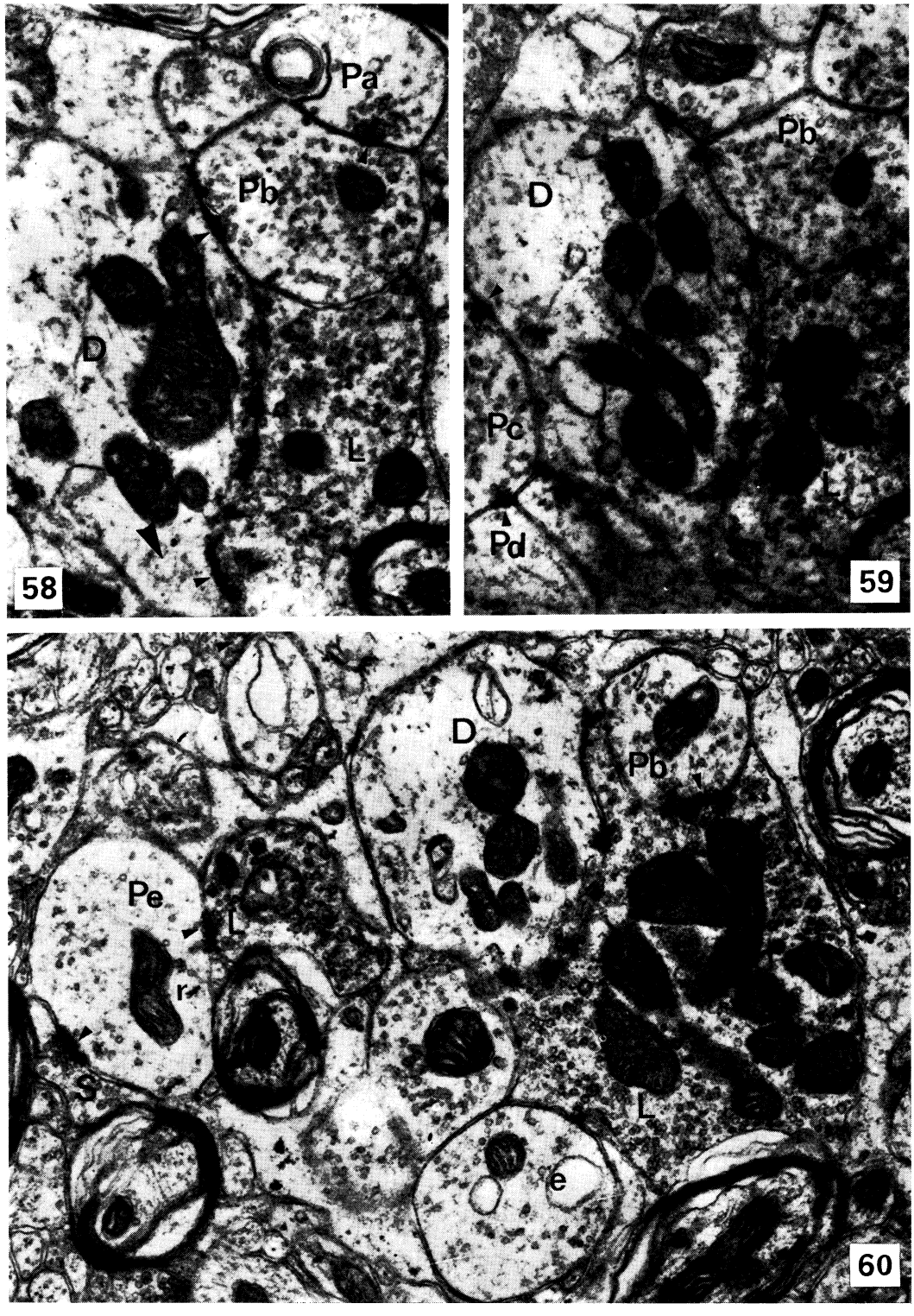
FIGURES 43–48. For description see opposite. (*Facing p.* 372)



FIGURES 49–53. For description see p. 372.



FIGURES 54 AND 55. For description see p. 373.



FIGURES 58–60. For description see opposite.

axo-spinous synapses account for nearly half the synaptic contacts between LR boutons and spiny dendrites within glomerular aggregations. In addition, glomerular spines can be post-synaptic to P profiles at dendro-spinous symmetrical synapses, and this may result in a triadic (figure 12) relationship between the spine, an LR bouton and a P profile, whereby both the LR bouton and the P profile are pre-synaptic to the spine and the P profile is post-synaptic to the LR terminal. The triadic arrangement between an axon, a pre-synaptic dendrite and a conventional dendrite, whether via a spine or not, seems to be an important facet of glomerular organization.

The glomeruli

All the thalamic glomeruli which have been described in the literature consist of an aggregation of pre- and post-synaptic profiles, partially surrounded and relatively isolated from the residual neuropil by a sheath of glial processes, a definition originally proposed in relation to the cat lateral geniculate nucleus (Szentágothai 1963). The glomeruli in the ventrolateral and centre-median nuclei have a similar constitution; an LR bouton, a dendrite, and a number of P profiles are always present, and occasionally towards the periphery, one or more SR and/or F axon terminals; sometimes more than one LR terminal or dendrite may be found. The basic framework of the glomeruli found in the ventrolateral and centre-median nuclei differs from the standard description of thalamic glomeruli which is based on observations of the cat lateral geniculate nucleus (Szentágothai *et al.* 1966; Peters & Palay 1966; Guillery 1969; Jones & Powell 1969*b*; Famiglietti & Peters 1972) in that here short dendritic side branches or bulbous thorns have not been observed; instead, each glomerulus generally contains only one dendritic process, usually a medium calibre dendritic shaft, and glomerular complexes are particularly common in association with secondary dendrites just distal to the bifurcation of the parent dendrite. Glomeruli are shaped rather like squat, bulbous cylinders, 3–5 μm in diameter and 7–10 μm in length, with a dendritic shaft running through the centre along the length of the complex, while the other vesicle-containing profiles are arranged around this dendrite. A given length of dendrite may be contacted by several LR boutons either unrelated to each other or *en passant* expansions of the same axon, or may be seen in continuity with a narrow dendritic

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Description of plate 15

(See introductory remarks to plate 13.)

Figure 54. (Section 49.) P profile 27 is pre-synaptic to the main glomerular dendrite (D); compare this contact with the longer synaptic specialization formed by the F bouton with the dendrite, which completes an F triad (see figure 52, plate 14). Magn. ×18000.)

Figure 55. (Section 51.) P profile 27 forms part of a triadic array; it is pre-synaptic to the dendrite (D) and post-synaptic to the LR terminal (L) which also contacts the dendritic spine (large arrowhead). (Magn. ×18000.)

Descriptions of plate 16

Plates 16 and 17 are concerned with serial sections from a glomerulus in the ventrolateral nucleus which illustrates both a triadic and a sequential synaptic array. (Magn. of all figures ×30000.)

Figure 58. The LR terminal (L) makes synaptic contact with the dendrite (D) on a spine (large arrowhead). A serial synaptic array is formed where P profile Pa is pre-synaptic to Pb which makes synaptic contact with the dendrite.

Figure 59. The LR terminal (L) is pre-synaptic to Pb, so forming a triadic array. Note the dendro-dendritic synapses between a P profile (Pc), the dendrite (D) and another P profile (Pd).

Figure 60. Another P profile (Pe) is post-synaptic to the LR terminal (L) (the continuity of this part of the LR bouton with the main part is shown in figure 61, plate 17) as well as an SR terminal (S).

segment which possesses the typical synaptic arrangements of distal dendrites in the neuropil, in that it is post-synaptic to numerous SR terminals. It is also quite common to observe only a single glomerular aggregation in conjunction with quite considerable lengths of dendritic shaft, and in such cases the dendritic shaft outside the glomerulus is comparatively devoid of synaptic contacts for a distance of several micrometres both proximal and distal to the complex. Frequently (in 19 of the 30 glomeruli in table 1) the dendritic shafts bear several spines within a glomerulus (figure 55, plate 15; figure 58, plate 16); but in one example, a glomerulus traced in serial sections through a depth of more than 2.5 μm, no spines were found while in another example ten spines were present in a similar space. The available evidence from light- and electron-microscopical studies suggests that these spiny dendrites which take part in synaptic glomeruli are the processes of thalamic relay cells.

TABLE 1. THIRTY SERIALLY SECTIONED GLOMERULI

nucleus	CM	VL
glomeruli	15	15
total profiles	210	196
Total P profiles	145 (68.5%)	132 (67.5%)
Total LR boutons	16	21
Total SR boutons	22	15
Total F boutons	3	6
Total dendrites	24	22
glomeruli with spinous dendrites	9	10
number of spines	25	47

TABLE 2. SYNAPTIC TYPES IN THIRTY SERIALLY SECTIONED GLOMERULI

nucleus	CM	VL
LR → D	88	132
→ spines)	(34) } = 159 (50%)	(55) } = 212 (65%)
LR → P	71	80
P → D	63 } = 126 (40%)	51 } = 92 (28%)
P → P	63 }	41 }
SR → P	25 (8%)	17 (5%)
F → D	4 } = 7 (2%)	4 } = 7 (2%)
F → P	3 }	3 }
total	317	328

In single sections, most glomeruli include less than ten profiles but if traced for at least 1 μm in serial sections the majority have between 10 and 30 apparently separate processes. Glomeruli vary considerably in the number of profiles which they contain, however, and although the 30 glomeruli analysed in depth from both the ventrolateral and centre-median nuclei (see tables 1–4) contained on average 13 profiles per complex, individual examples varied from less than 10 to more than 40 profiles. Such variation in size may be more apparent than real: an artefact of the sectioning angle and the limits imposed by the length of the ribbon of sections, and the larger the number of profiles observed in a glomerulus, the greater the likelihood that the major part of the complex is contained within the available ribbon of sections. This is undoubetdly so in the case illustrated in figures 43–55, plates 13–15, from which a considerable amount of information has been obtained because a fortuitous sectioning angle has allowed the glomerulus to be viewed side on to the central dendrite which is itself in longitudi-

nal section; we can be confident that this series of sections includes most of the glomerular aggregation.

A partial reconstruction of this glomerulus (figures 56 and 57) shows a dendrite of 1.5–2 μm diameter, almost entirely surrounded by an LR expansion which is considerably folded as a result of many invaginations by dendritic spines and the expansions of P processes. Perhaps the most obvious feature is the massive innervation of the central dendrite by the LR terminal by no less than 18 separate asymmetrical synaptic specializations; ten of these contacts are situated on the five spines arising from the dendrite within the glomerulus. The LR bouton is presynaptic at a further 23 axo-dendritic synapses on to P profiles; although four of the latter are contacted twice, this still means that 16 out of a total glomerular content of 35 P profiles are post-synaptic to the LR terminal. Another six P profiles are post-synaptic to SR axon terminals,

TABLE 3. SYNAPTIC ARRANGEMENTS IN THIRTY SERIALLY SECTIONED GLOMERULI

	number of glomeruli containing synaptic arrangements		number of synaptic arrangements		total	
type of synaptic arrangement	CM	VL	CM	VL	glomeruli	synaptic arrangement
reciprocal P ↔ P	5	3	7	3	8	10
triad L → P → D	9	9	16	18	18	34
serial X → P → Y	15	14	87	65	29	152
sequential serial; X → P → P–(...P → P...) → Y	8	7	13	10	15	23

X = LR, SR, and F axons or P profile.
Y = P profile or dendrite.
P = P profile.
L = LR axon.
D = dendrite.

TABLE 4. P PROFILES IN THIRTY SERIALLY SECTIONED GLOMERULI

	CM	VL	total
total P profiles	145	132	277 (100%)
those pre-synaptic	56	64	120 (43%)
those post-synaptic	110	104	214 (77%)
those post-synaptic to LR boutons	65	72	137 (50%)
those post-synaptic to SR or F axons	24	13	37 (13%)
those post-synaptic to P profiles	21	19	40 (14%)

while one P profile (27 in the figures) as well as being post-synaptic twice to the LR and once to the SR terminals, is also post-synaptic to an F bouton (figures 49–55, plates 14 and 15). On the other hand, 17 P profiles are pre-synaptic at 24 dendrodendritic synapses: 11 of these are single contacts between P profiles; there is one reciprocal synaptic arrangement between profiles 13 and 19 (figure 43, plate 13) and a further five P profiles are pre-synaptic to the central dendrite, four of them at multiple contacts. In this regard P process 27 is again interesting for it is both post-synaptic to a P profile and pre-synaptic at four separate synaptic contacts with the central dendrite. There is a considerable number, 20 in all, of *serial* synapses (figure 46, plate 13), a synaptic relationship occurring when a profile is pre-synaptic to another profile which is also pre-synaptic (of necessity a P profile, for this is the only type of vesicle-containing profile which

is both pre- and post-synaptic); this number includes three *triads* with P profiles post-synaptic to the LR bouton and also pre-synaptic to the central dendrite (figure 44, plate 13; figure 55, plate 15), and one triad with an F bouton in place of the LR bouton (figure 51, plate 14; figure 54, plate 15). There is also a sequence of three P profiles. The first two (17, 23) are pre-synaptic to the third (22), and P profile 17 is also pre-synaptic to 23 (figures 44 and 45, plate 13). There are also two examples of what are here termed *sequential serial* synapses, which are chains of serial synapses in which the second (i.e. post-synaptic profile) is pre-synaptic to a third profile, which is also pre-synaptic (etc.). The first group of sequential serial synapses (figures 49, 50 and 52, plate 14) has an SR terminal (35) presynaptic to a P profile (25) which is itself pre-synaptic to another P profile (26) which is in turn pre-synaptic to yet another P profile (27)

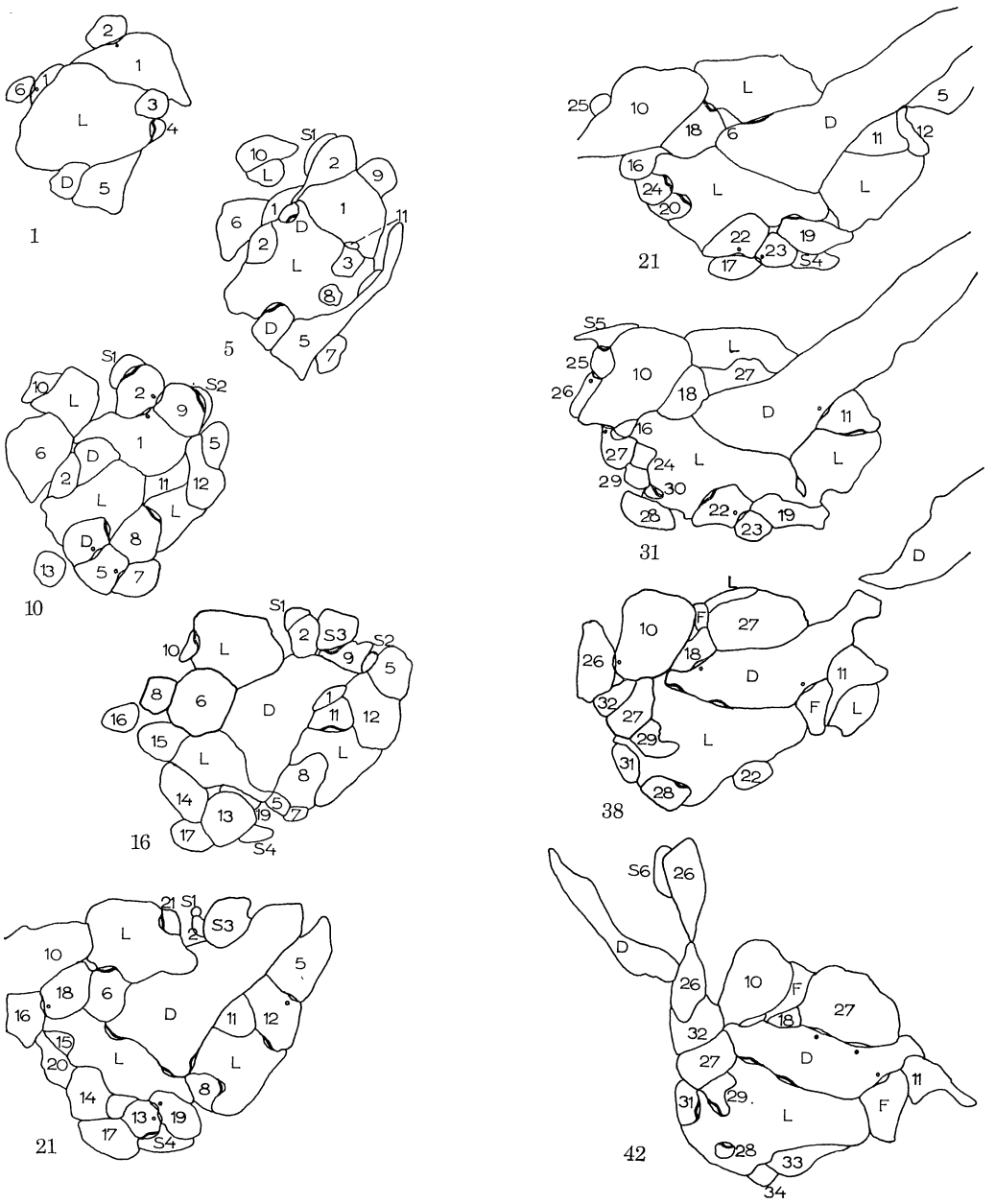
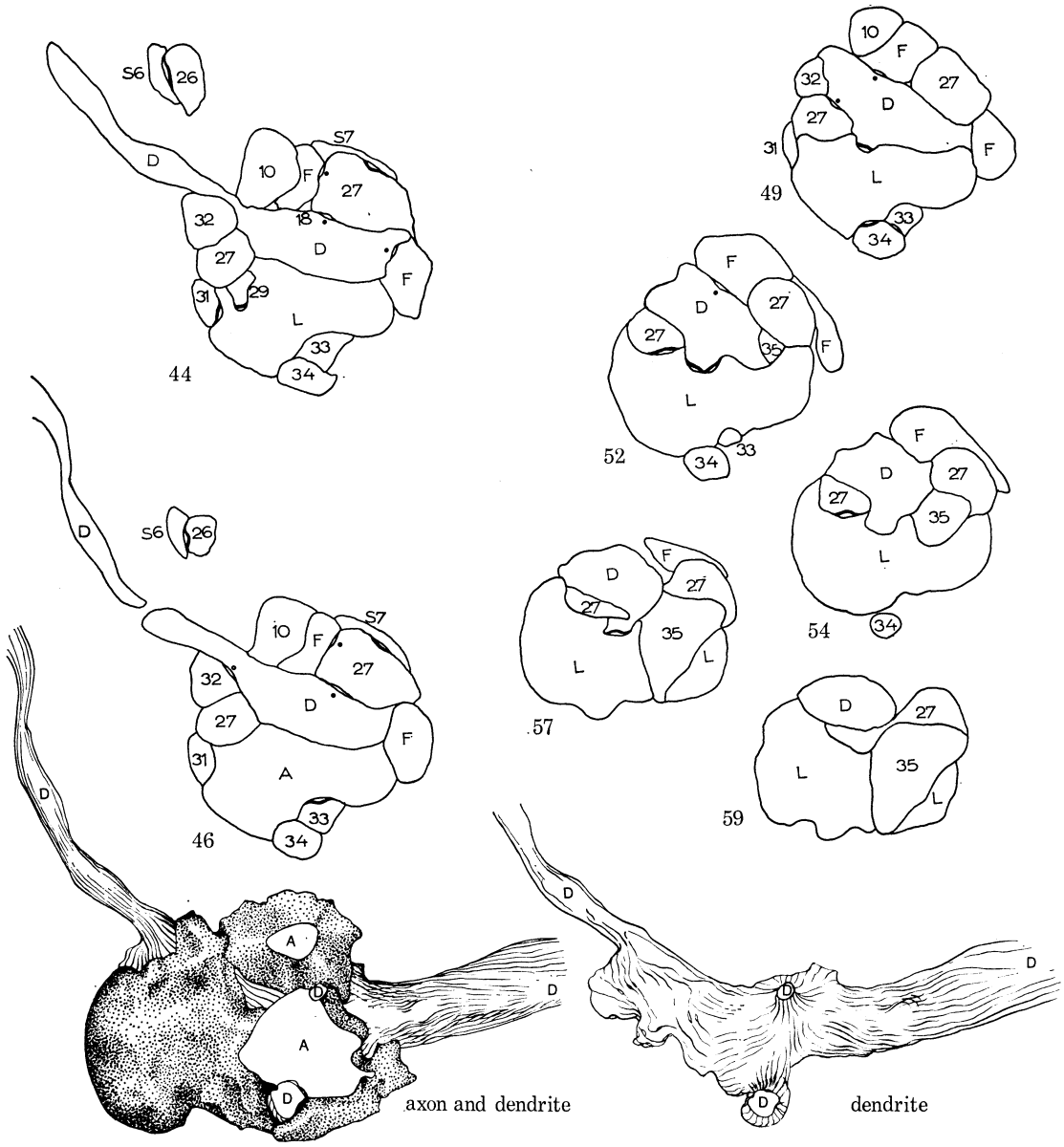


FIGURE 56. For description see opposite.



FIGURES 56 AND 57. Tracings of the 16 most representative serial sections of the large glomerulus from the centre-median nucleus illustrated in figures 43–55, plates 13–15. Occasional synapses have been added to these drawings from neighbouring unillustrated sections so that all observed synaptic specializations are shown. L, LR terminal; S, SR terminal; F, F bouton; 1–35, P profiles. Synapses are schematically shown: asymmetric; symmetric (post-synaptic on the right-hand side). The number of the section in the series is given by each illustrated section.

At the bottom of figure 58 are two reconstructions; on the right is shown an artist's impression of the dendrite (D) which courses through this glomerular aggregation; on the left another impression of the LR axon terminal wrapped around this dendrite. These drawings were made by studying tracings of the series of 60 sections.

which is finally pre-synaptic to the central dendrite; the other example is similar (figure 48, plate 13) but has only two pre- and post-synaptic P profiles interpolated between an SR terminal and the final dendritic P profile.

In contrast, a smaller glomerulus taken from the ventrolateral nucleus was viewed with the central dendrite cut transversely (figures 58–63, plates 16 and 17). Although a similar ribbon-length was examined (62 sections) only half the number of profiles observed in the previous example were identified in this complex, a probable consequence of the different sectioning angle. The LR terminal contacts the central dendrite nine times, three synapses are upon the three spines (figure 58, plate 16; figure 62, plate 17), and is pre-synaptic to 8 of the 13 P profiles in the complex. There are ten dendro-dendritic synapses in this glomerulus, five between pairs of P profiles and five with P profiles pre-synaptic to the central dendrite; there are as a result 11 serial synapses of which three are triads (figures 58 and 59, plate 16). There is also a sequential array of serial synapses with two intermediate P profiles (figure 60, plate 16; figures 61–63, plate 17); the first P profile (Pe) is post-synaptic to the LR terminal, while the second P profile (Pf) is pre-synaptic to the central dendrite. Thus complexity within glomeruli is not necessarily a function of size.

Table 2 summarizes the synaptic contacts identified in 30 glomeruli, 15 from each of the ventrolateral and centre-median nuclei, which have been examined in serial sections through a large part of their total extent. Axo-dendritic synapses between the LR boutons and the central dendrites are the most frequently occurring category of the synapses in glomeruli; spines make an important contribution to the dendritic post-synaptic surface, for they are post-synaptic at between one-third and one-half the contacts between LR boutons and spine-bearing dendrites in this sample (tables 1, 2; figure 66, plate 18; figure 67, plate 19). LR boutons are less frequently pre-synaptic to P profiles than to conventional dendrites in the population of glomeruli represented in tables 1–4, but P profiles have approximately equivalent numbers of pre-synaptic contacts with dendrites and other P processes. P profiles have more post-synaptic than pre-synaptic contacts, in the ratio 5:4 (table 2), but only 43 % of P profiles are pre-synaptic while 77 % are post-synaptic (table 4). Fifty per cent of the P profiles in the 30 glomeruli are post-synaptic to the LR boutons (table 4). Table 3 contains a survey of the synaptic patterns which are present in the 30 glomeruli, and such patterns have also been observed in other serially sectioned glomeruli and in single sections. The table shows that all but a few of the possible patterns occur within a single glomerulus.

All but one of the complexes in the sample contained serial synapses, 152 altogether with a mean of five per glomerulus; half of the glomeruli included sequential serial arrays, the greatest length being four intermediate (pre- and post-synaptic) P profiles between the initial pre-synaptic axon and the final post-synaptic dendrite. Ten reciprocal synapses were observed in eight of the glomeruli (figure 43, plate 13; figures 68 and 69, plate 19), and when one considers the comparatively smaller probability of finding reciprocal synaptic relations with random sectioning angles, these few become more significant. Perhaps more interesting from a functional point of view are triadic relationships, arrangements which occur when an LR bouton is both pre-synaptic to a dendrite and to a P profile which last is also pre-synaptic to the same dendrite; 34 LR and P profile triads were found in 18 of the glomeruli (e.g. figure 66, plate 18) suggesting that this is a typical, although far from a universal conformation of glomerular connections, for there were in all 277 P profiles in the 30 glomeruli. Other triadic arrangements also occur, either with an F axon (figure 51, plate 14; figure 68, plate 19) or a P profile

(figures 44 and 45, plate 13) in place of the LR bouton; the latter type of synaptic array is more common in the centre-median nucleus, where eight were found in six glomeruli, than in the ventrolateral nucleus.

Emphasis has been placed upon certain possible general principles of synaptic connectivity within glomerular aggregations in the centre-median and ventrolateral nuclei, but it should be remembered that the versatile nature of the synaptic contacts of P processes and their considerable numbers within glomeruli make for a much more complicated network of synaptic relationships in which there may be a combination of several of the simpler patterns considered previously. For example, two reciprocally related P profiles may be both post-synaptic to the same LR terminal and pre-synaptic to the same dendrite, while the latter is also post-synaptic to the LR terminal (figures 67–70, plate 19, and diagrammatically in figure 71*a*);

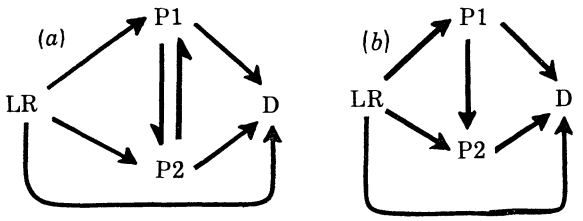


FIGURE 71. Schematic examples of various glomerular synaptic complexes; (*a*) and (*b*) only differ by one synaptic contact; both may be found, but (*b*) may be just part of (*a*). Electron micrographs of a glomerulus with a synaptic array similar to (*a*) are shown in figures 67–70, plate 19.

on the other hand, one also finds a sequential synaptic array with two intermediate pre- and post-synaptic P profiles which are both part of triads (figure 72*b*). The only difference between these two arrangements is the lack, in the second case (figure 71*b*), of areturn dendro-dendritic synapse from the second to the first of the P profiles, but we do not know whether the second synaptic array is really only part of the larger pattern similar to the first, its difference only apparent because of a possible technical inability to observe one synapse among seven. Sequential arrays of synapses between P profiles also result in further types of synaptic array. An example of a triad-like array with a sequence of P profiles has already been mentioned, and another example (figure 84, plate 24; figures 85 and 86, plate 25) shows a glomerulus cut obliquely so that little of the LR bouton could be observed; on the other hand a considerable complexity of P profile connections are found. There is a sequential synaptic arrangement of three pre-synaptic P profiles (Pa → Pb → Pc) which are all pre-synaptic to the central glomerular dendrite; in addition there are reciprocal synapses between Pb and Pc, and another reciprocal synaptic array within the same glomerulus (Pd ↔ Pe). Although glomeruli appear as separate entities in single sections, and the majority examined in serial sections, on a few occasions in the ventrolateral nucleus a definite synaptic overlap through the agency of P profiles has been observed between glomeruli. Two examples will be described: the LR boutons in the first case are apparently independent, while in the second example the LR terminals are *boutons en passant* from the same preterminal axon. The first example (figures 75–83, plates 20–24; figures 72–74), consists of three LR boutons, H, I and J, each of which was has several synaptic contacts with only one glomerular dendritic segment, respectively A, B and C, these dendritic profiles being unrelated in the depth of tissue studied. Axon terminal J forms two triadic synaptic arrays (figures 75 and 76, plate 20) with two P profiles and similarly I takes part in another triad (figure 83, plate 24) with a further P process (16). However, I has two expansions, and

while the first lobe is pre-synaptic to B, the second is pre-synaptic to a P profile (12) which is itself pre-synaptic to C (figure 80, plate 22); moreover the first lobe of I is also pre-synaptic to another P process (5) which is also pre-synaptic to a spine from dendrite C (figure 81, plate 23); and further, terminal H is pre-synaptic to P profile 4 (figure 77, plate 20) which is pre-synaptic to 5 also (figure 79, plate 22). It is apparent that the dendrite C is not only directly contacted by one LR bouton (J) but also affected in some way by two others: one (I) with a single interpolated P profile on two occasions, the other (H) with two interpolated P profiles. In 75 serial sections, however, there was no evidence of a synaptic contact directly between the dendrite C and either the H or I axon boutons.

The second example (figures 87–93, plates 26 and 27, and figure 94) concerns a long segment of dendrite, 15 μm of which was observed in longitudinal section passing through 47 sections. In all, nine LR expansions contact this dendrite at 26 synapses, 11 of these on to the ten spines attached to the dendritic shaft; however, five of the axon terminals (L2–L6) are *boutons en passant*. Both L2 and L4 are pre-synaptic to the same P process (P3) which, as well as taking part in two sequential serial synaptic arrays and a reciprocal synaptic arrangement, is also pre-synaptic at two contacts with the main dendrite (figures 92 and 93, plate 27): in other words, two triads are subserved by the same P profile and two *en passant* LR boutons. The axon boutons L3 and L5 are also somewhat linked for they are each pre-synaptic to a P profile, P5 and P6 respectively, each of which is pre-synaptic to a large varicose dendrite that contains discoid vesicles (P8: figures 88 and 89, plates 26 and 27).

These examples show that P profiles are not only interpolated between LR boutons and adjacent glomerular dendrites, but also between LR terminals and other dendrites not synaptically contacted by this same LR terminal, but instead being post-synaptic to another unrelated LR bouton which may form part of a separate synaptic complex. Moreover, a given afferent axon may give a series of terminal expansions contacting a single dendritic shaft, each expansion being part of a different synaptic complex, and these complexes may share some of the same P processes.

Description of plate 17

Figure 61. A further synaptic contact formed by the LR terminal (L) with the shaft of the glomerular dendrite (D). This section also shows the continuity between the main body of the LR bouton and that portion which is pre-synaptic to Pe in figure 60.

Figure 62. While the LR terminal (L) makes synaptic contact with another profile (Pg) and the glomerular dendrite again, the P profile Pf is pre-synaptic to the main dendrite (D) on a small spine (large arrowhead).

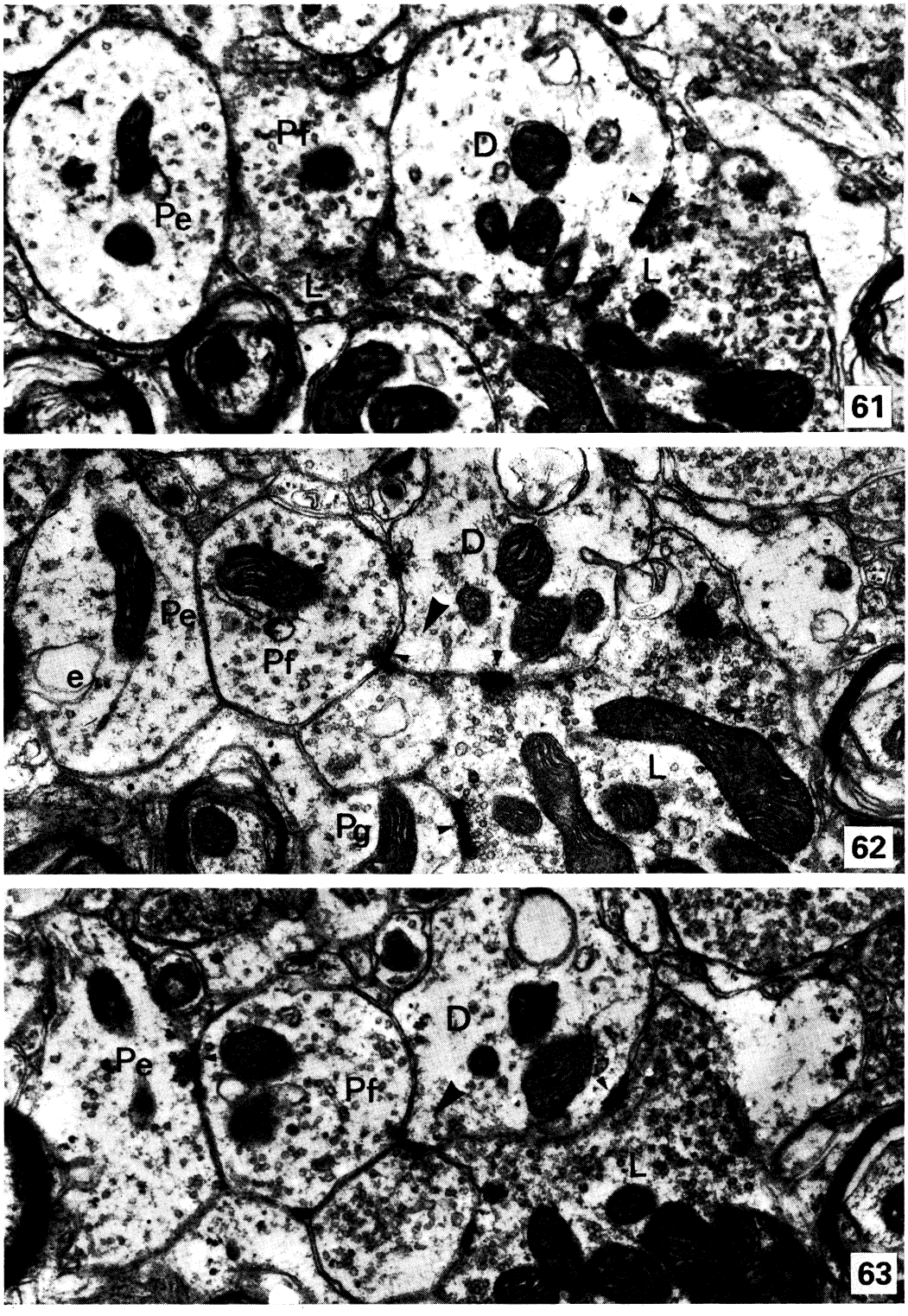
Figure 63. A dendro-dendritic synapse from Pe on to Pf – thus there is a sequential synaptic array in which the LR terminal (L) has made a synapse upon a P profile (Pe) which is pre-synaptic to another (Pf) which in turn has a synaptic contact with the glomerular dendrite (see figure 60).

Description of plate 18

Figure 64. A triad from a glomerulus in the centre-median nucleus. Note that the LR terminal (L) forms a synapse with both the spine (sp) and the shaft of the dendrite (D) and with a P profile (P). (Magn. × 30000.)

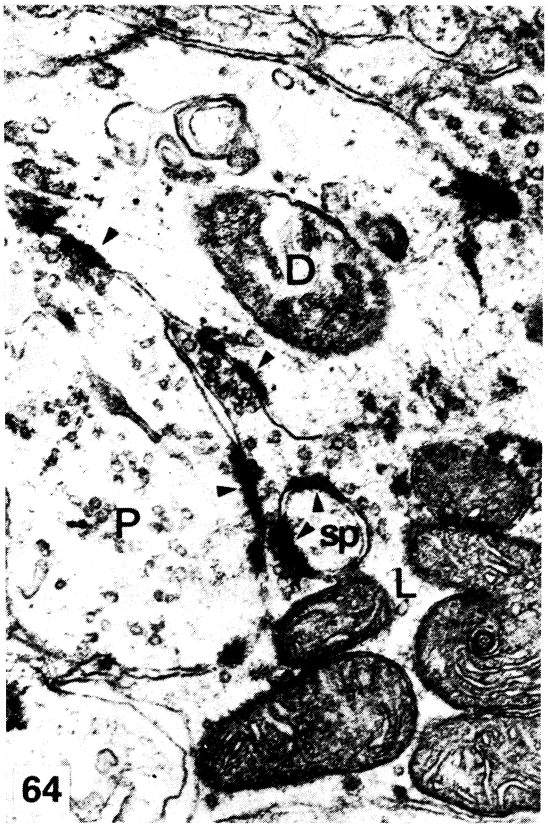
Figure 65. Part of a glomerulus in the ventrolateral nucleus with a triadic array in which an F axon bouton (F) makes a synaptic contact with the main dendrite (D) and a P profile (P) which is also pre-synaptic to the dendrite. Note the dendritic spine (sp) post-synaptic to the LR terminal (L). (Magn. × 18000.)

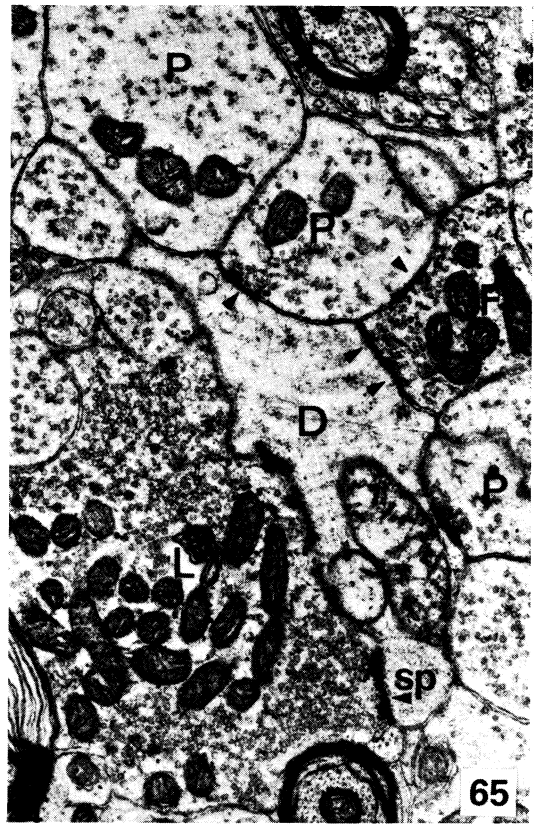
Figure 66. A glomerular dendrite (D) with a spine (sp) which invaginates the LR terminal (L). There is a triadic arrangement involving the LR bouton, the dendrite and a P profile (P). Ventrolateral nucleus. (Magn. × 30000.)

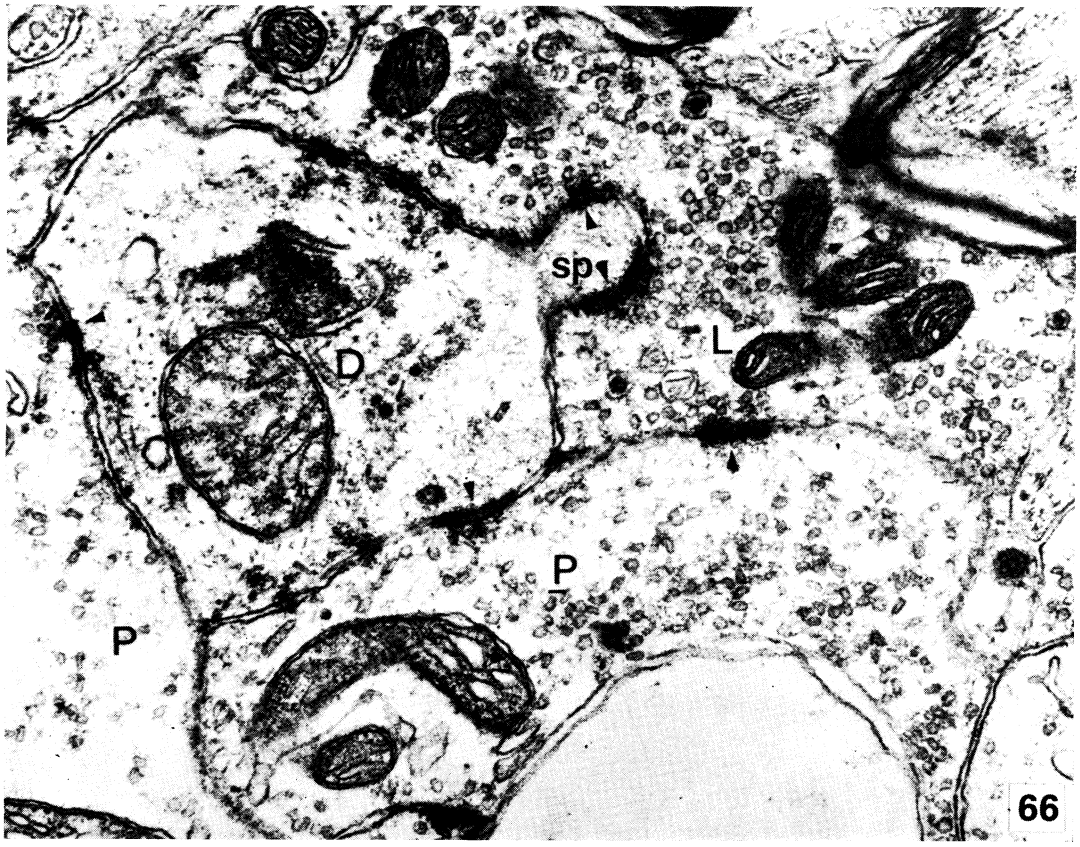


FIGURES 61–63. For description see opposite.

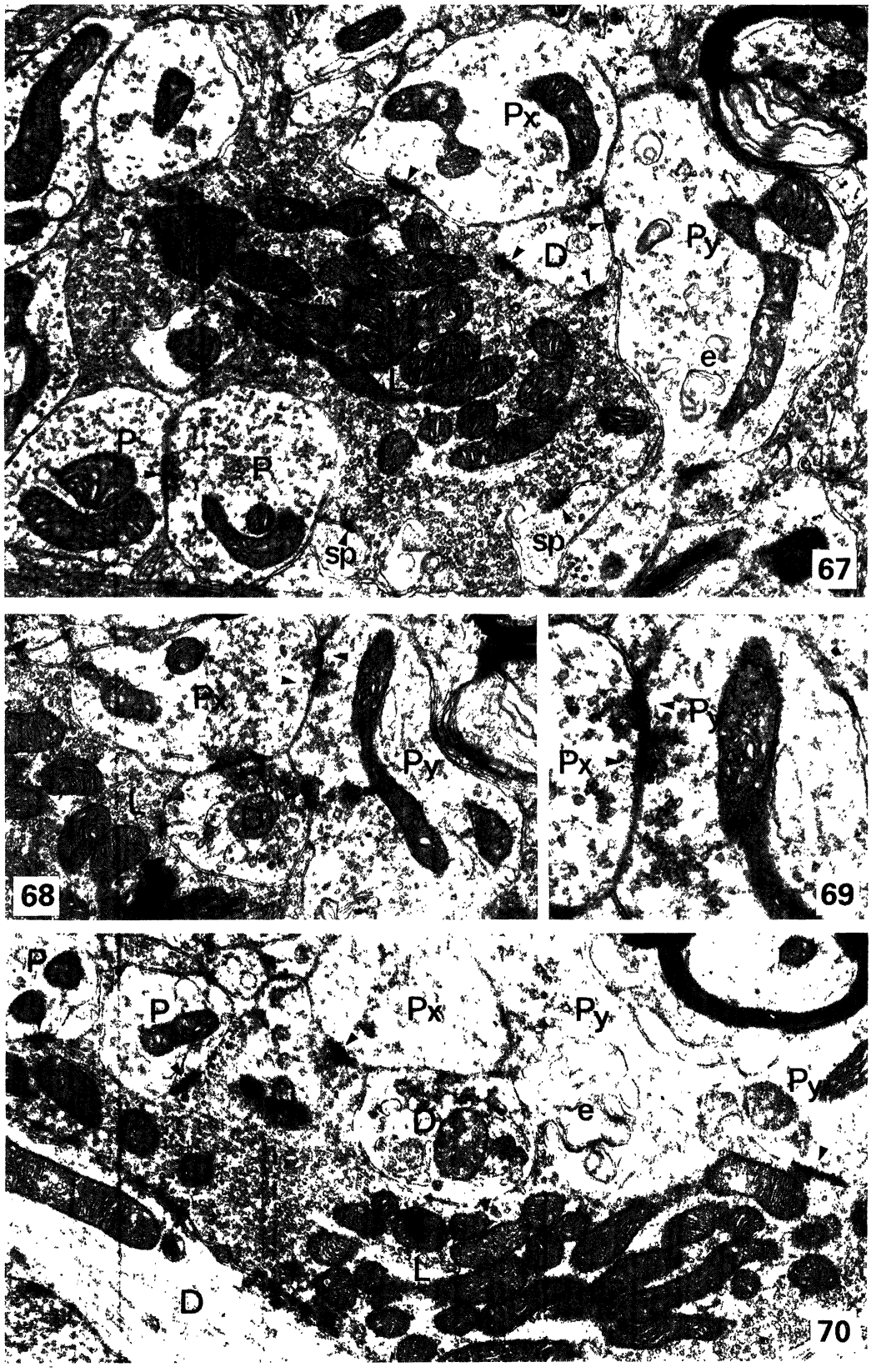
(*Facing p.* 380)



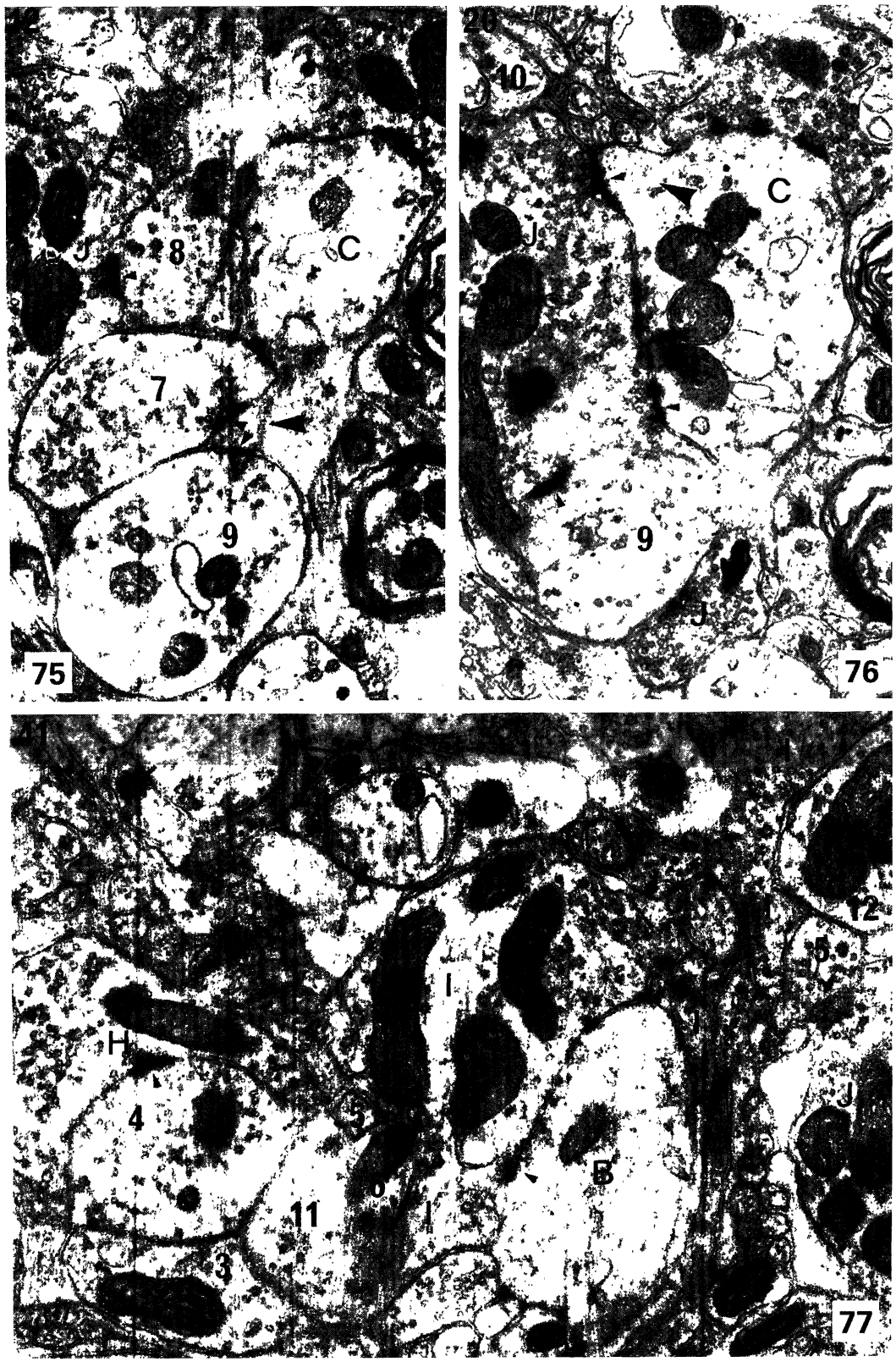




FIGURES 64–66. For description see p. 380.



FIGURES 67–70. For description see p. 381.



FIGURES 75–77. For description see opposite.

Experimental results

General features

The phrase 'terminal degeneration' is used here when referring to degenerative changes in profiles which contain synaptic vesicles and are undoubtedly pre-synaptic. Although the ventrolateral nucleus has reciprocal connections with the motor cortex, at the short survival periods used here, up to eight days, little sign of retrograde cell degeneration was found; no cell somata appeared to be affected, and very few dark dendrites were observed. Terminal degeneration was present only in the cerebral hemisphere in which a lesion had been placed in the cortex or globus pallidus, and damage of the cerebellum resulted in degeneration in the contralateral hemisphere. Sections were examined from blocks which sampled the major part of these nuclei, but no attempt has been made to differentiate between their various subdivisions.

A critical factor was the length of post-operative survival, five to six days resulting in optimal degeneration in each type of experiment. Only myelinated fibres and small (SR) or large (LR) axon terminals were found to degenerate; P or F profiles were never affected. There was a definite tendency for degenerating terminals to occur in clusters (figures 110–112, plate 31) while occasionally two such profiles were pre-synaptic to the same process. Degenerating terminals were found to synapse only upon dendrites, being pre-synaptic either to conventional dendrites or to P profiles. On other occasions, a pair of degenerating terminals have been found connected by a thin strand of dense cytoplasm (figures 111 and 112, plate 31), which suggests two *en passant* terminal boutons and their unmyelinated connection. Degenerating myelinated fibres

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Description of plate 19

Serial sections of a glomerulus in the centre-median nucleus.

Figure 67. In this section the LR bouton (L) is pre-synaptic to the dendrite (D), to two of its spines (sp) and to a P profile (Px). There is also a dendro-dendritic synapse from the P profile (Py) on to the dendrite. (Magn. × 18000.)

Figure 68. Another serial section showing four dendro-dendritic synapses; two form a reciprocal synaptic arrangement between Px and Py, while two arise where Px and Py contact the dendrite (D). (Magn. × 18000.)

Figure 69. The reciprocal synapses in figure 68 at higher magnification. (Magn. × 36000.)

Figure 70. In this section the LR terminal (L) is pre-synaptic to four P profiles, including Px again and also Py – note the large sac of smooth endoplasmic reticulum (e) within Py. (Magn. × 18000.)

In summary there is a double triad in which the intermediate P profiles also form a reciprocal synaptic arrangement (see figure 71 for a diagram of this synaptic complex.)

Description of plate 20

This plate and those following up to and including figure 83, plate 24, are serial sections of three neighbouring glomeruli in the ventrolateral nucleus, each consisting of an LR terminal (H, I and J) and a dendrite (A, B and C respectively). These figures illustrate how the glomeruli are interrelated. Representative tracings from this series of sections are shown in figures 72–4; P profiles are therein numbered in sequence and the numbers in these electron-micrographs are taken from this scheme. All plates × 30000; the section numbers are placed in the top corners of these figures. Large arrowheads indicate spines.

Figure 75. (Section 2.) LR terminal J makes a synapse with P profile 8; the spine arising from dendrite C is post-synaptic to two P profiles, 7 and 9.

Figure 76. (Section 20.) Another spine of dendrite C is post-synaptic to the LR terminal J which has a synaptic contact with the dendritic shaft and P profile 9, thus forming a triad.

Figure 77. (Section 41.) LR terminal H is pre-synaptic to P profile 4; LR terminal I makes a synaptic contact with the dendrite B. Note the process of LR terminal I next to P profiles 5 and 12.

are present but none has been traced into continuity with a degenerating terminal. Glial profiles form a prominent feature, and the glomeruli become surrounded by thickened bands of glia rather than thin lamellae, and thick wedges or tongues of glial processes appear throughout the neuropil. Often they contain glycogen granules and dense fragments of degenerated afferent nerve fibres and terminals (figure 111, plate 31).

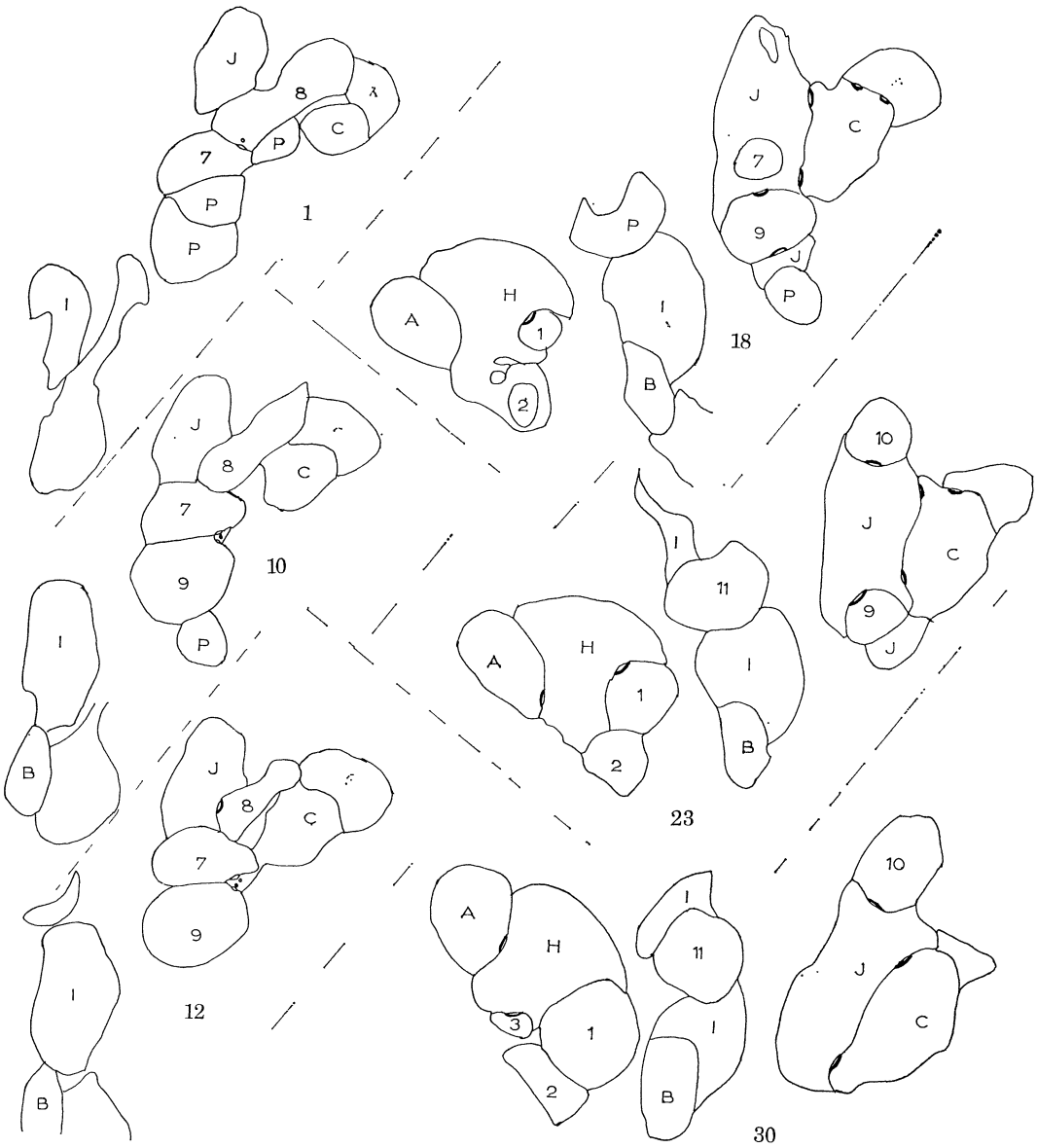


FIGURE 72. For description see p. 384.

With one exception which is described separately below, in all the experimental animals which were subjected to unilateral damage of the cortex or globus pallidus, only SR terminals were subsequently found to degenerate. The four separate populations of SR terminals, those of the afferent fibres to the ventrolateral and centre-median nuclei from the cortex and globus pallidus, in their process of degeneration and in the profiles to which they are pre-synaptic, are so markedly similar that they will be described together.

Degenerating axon terminals in the ventrolateral and centre-median nuclei after damage of the motor cortex and globus pallidus

By obtaining material from animals sacrificed at progressive intervals of post-operative survival, from 4 to 8 days, it has been possible to study the time course and the process of terminal degeneration of cortico-fugal fibres within the ventrolateral and centre-median nuclei.

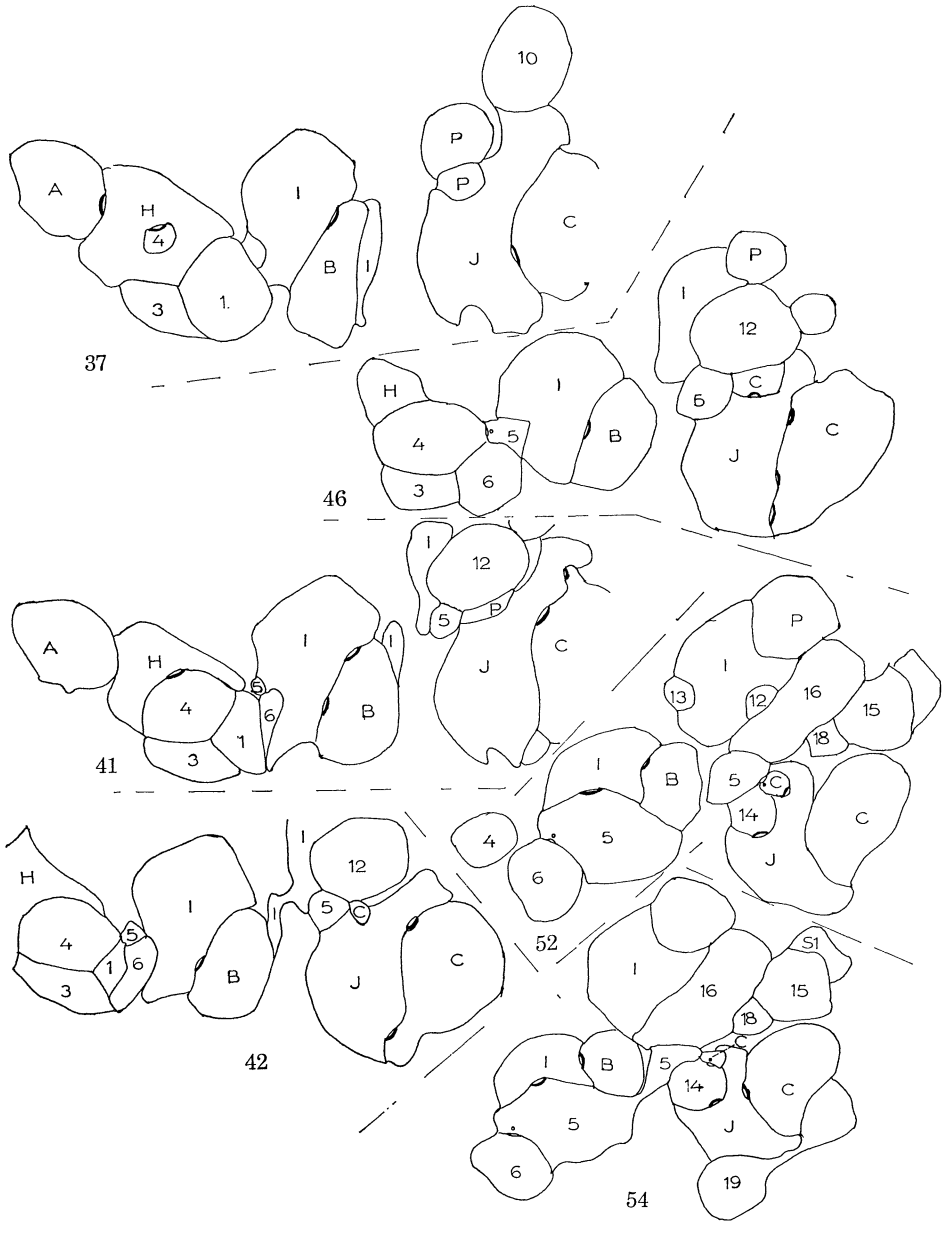
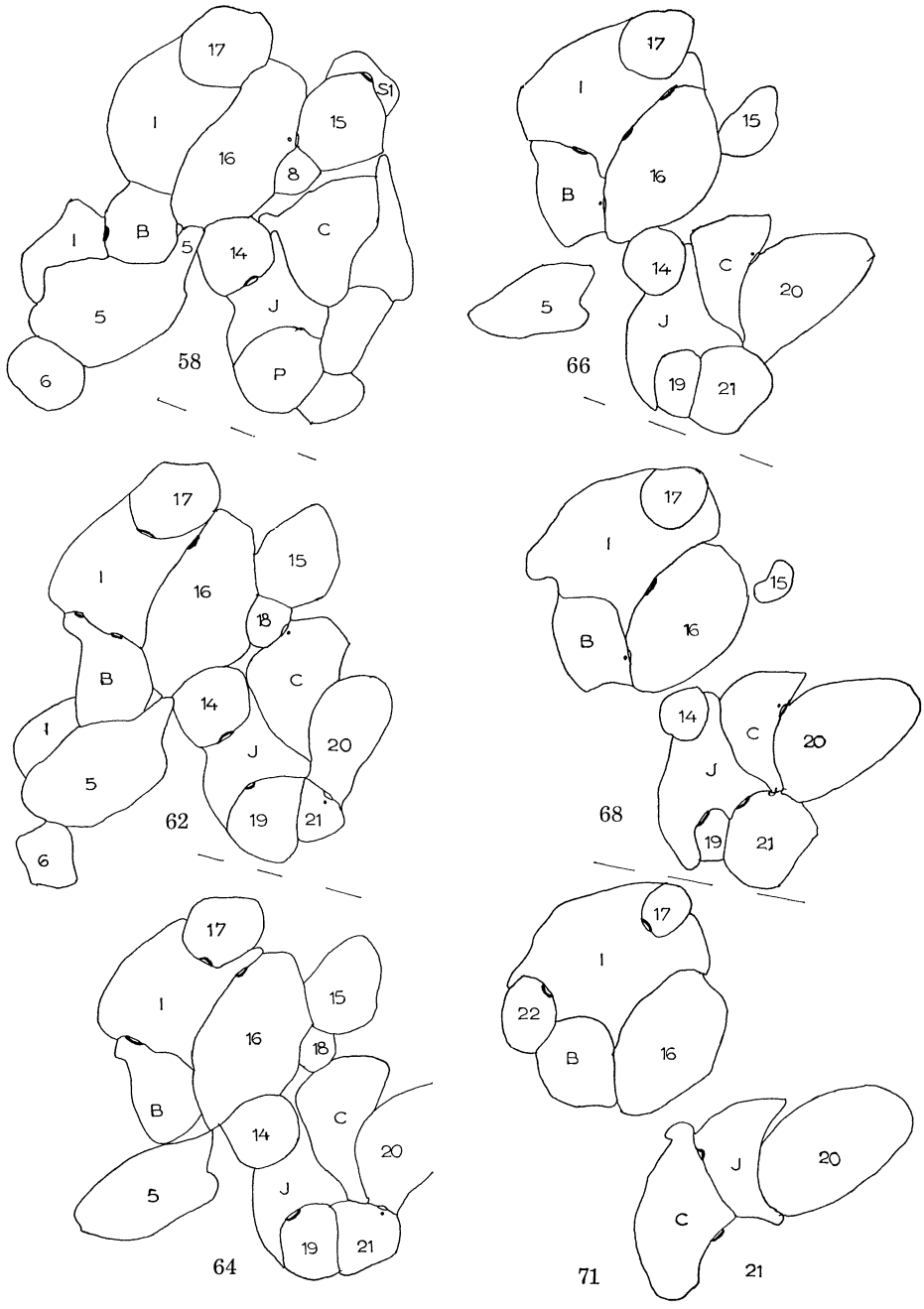


FIGURE 73. For description see p. 384.

Although the sequence of experiments designed to elucidate the termination of pallido-thalamic afferents within these nuclei is less complete, the process of degeneration appears to be essentially the same. At any given survival time the total population of affected terminals usually includes profiles at various stages of degeneration, but the majority of degenerating terminals



FIGURES 72–74. Tracings from serial sections of three glomeruli from the ventrolateral nucleus which are connected by P profile synapses (see text). Electron micrographs of certain aspects of this series of sections are shown in figures 76–83, plates 20–24. LR terminals are H, I, J: respective dendrites are A, B, C. The labelling scheme is otherwise similar to figures 56 and 57.

DESCRIPTION OF PLATE 21

(See introductory remarks to plate 20.)

FIGURE 78. A montage showing the three glomeruli in section 23. LR terminal H is pre-synaptic to the dendrite A and P profile 1. LR terminal I is pre-synaptic to the dendrite B. LR terminal J is pre-synaptic to the dendrite C (shaft and a spine), and P profiles 9 and 10.

DESCRIPTION OF PLATE 22

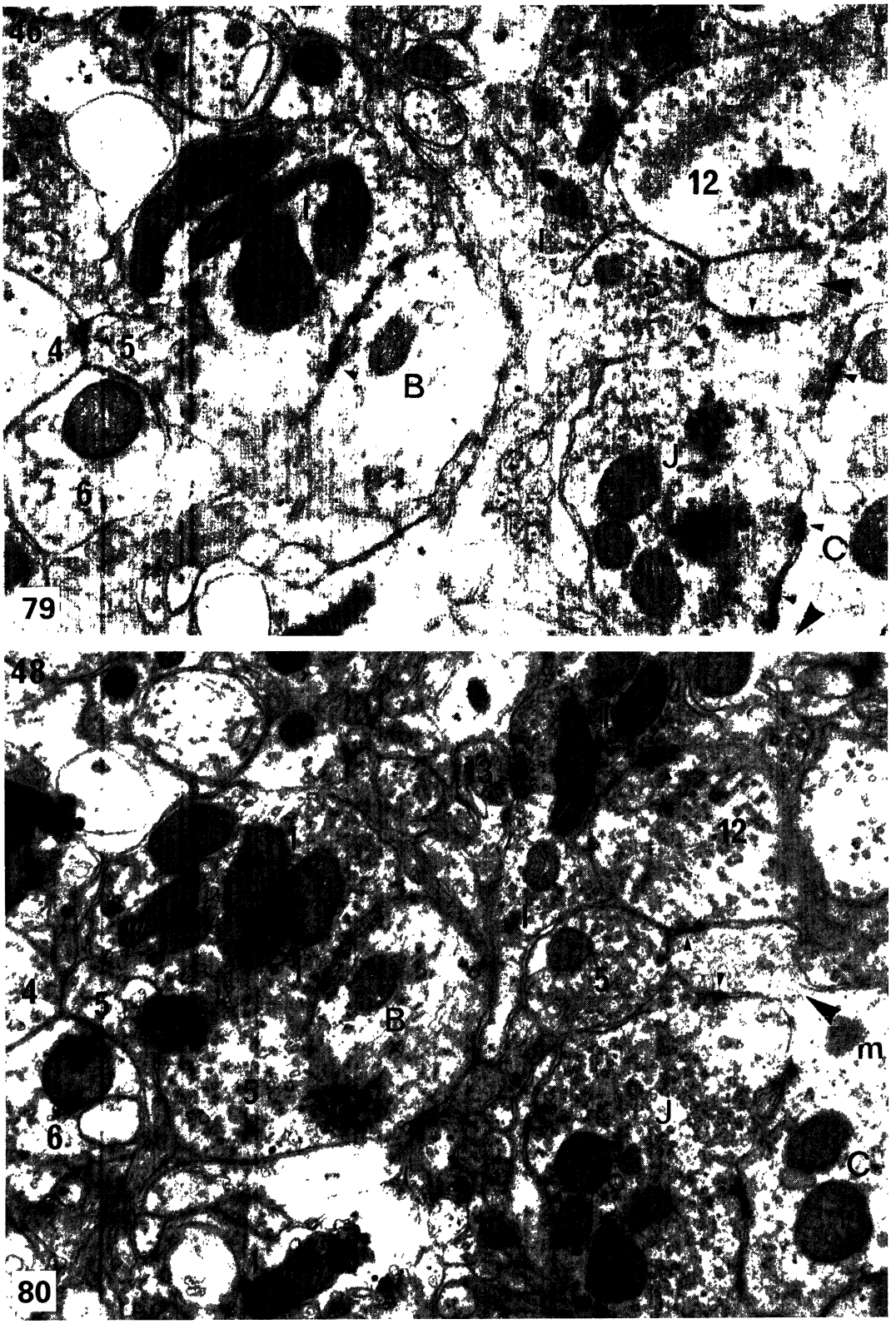
(See introductory remarks to plate 20.)

FIGURE 79. (Section 46.) LR terminal J has further synapses upon the shaft of dendrite C and on another spine. P profile 4 is pre-synaptic to P profile 5 (see figure 80; figures 81 and 82, plate 23, and figure 73 for demonstration of the continuity of P profile 5).

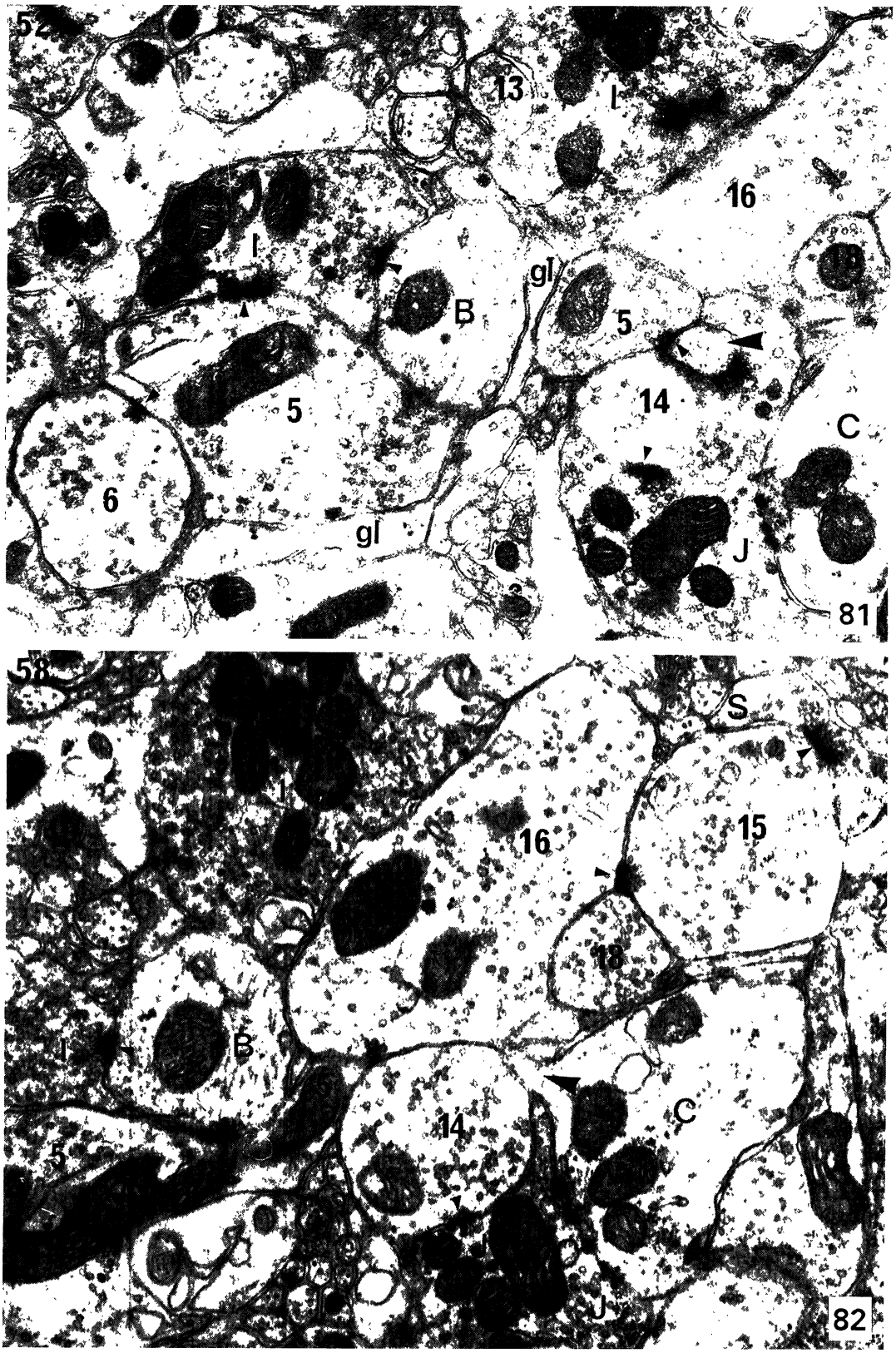
FIGURE 80. (Section 48.) The dendritic spine seen in figure 79 is now in continuity with dendrite C – note the subjacent multivesicular body (m). This spine is also receiving a synaptic contact from P profile 12 in a dendrospinous synapse. Since the right hand part of LR terminal I is pre-synaptic to P profile 12, this LR bouton has effects in two glomeruli, i.e., that concerning dendrite B and that of dendrite C (plates 20, 21, and figures 72–74.)

FIGURE 78. For description see opposite.

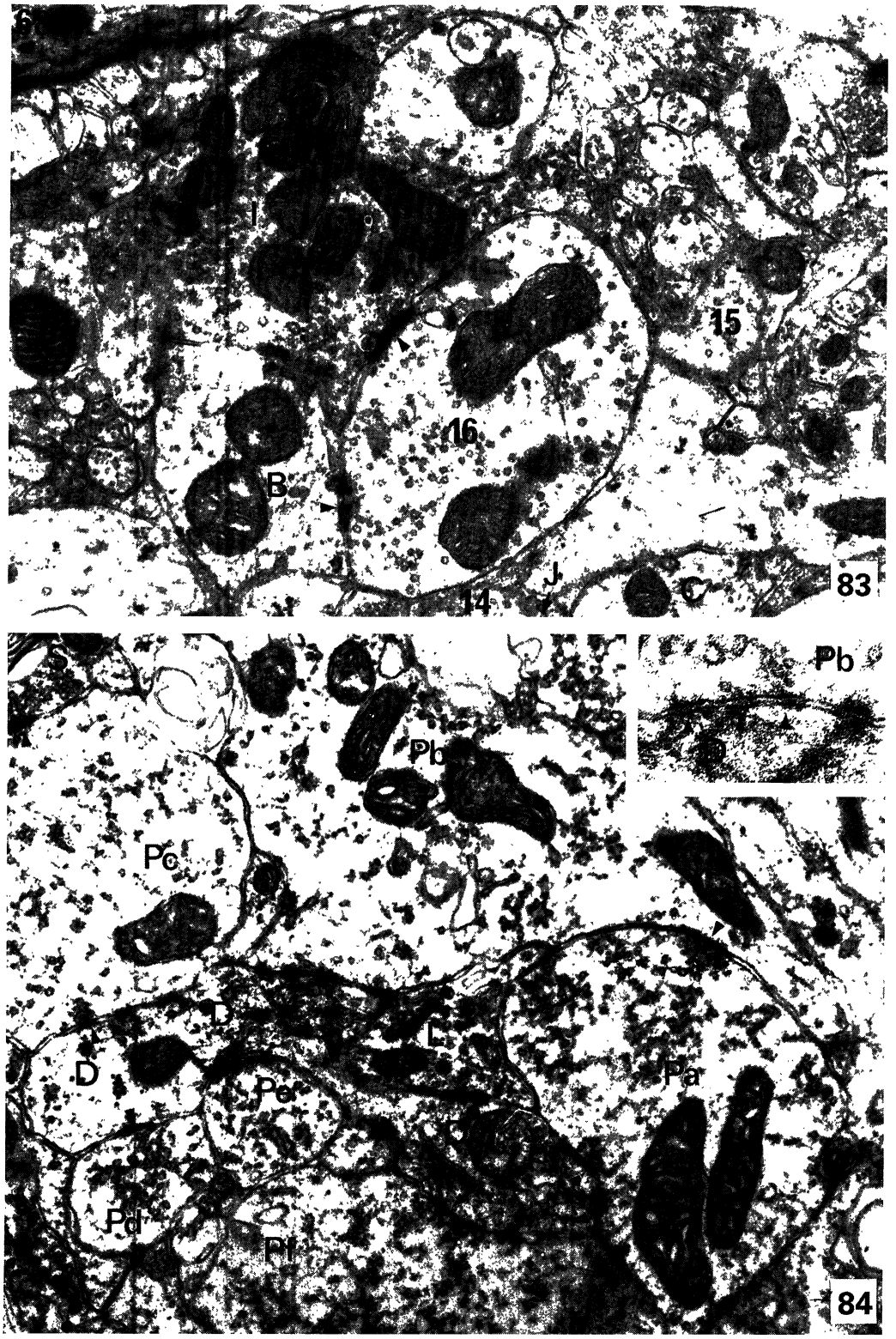
(*Facing p.* 384)



FIGURES 79 AND 80. For description see p. 384.



FIGURES 81 AND 82. For description see p. 385.



FIGURES 83 AND 84. For description see opposite.

follow a similar trend of disintegration; other terminals at differing degrees of dissolution from the broad mass of affected profiles may begin to degenerate later, or degenerate at a slower rate than the majority, but the sequence of events which comprise the degenerative process, in all cases, appears to be the same.

At 4 days slight changes are present in many SR axon terminals (figure 110, plate 31). Their synaptic vesicles are more closely packed than normal, for the vesicles are beginning to enlarge, while the terminals start to shrink, and sometimes assume a scalloped appearance. Often the vesicles are slightly paler at their centres than normal, for their diameters have become larger than the thickness of the section (figure 96, plate 28). Along with this glassy appearance, they become more irregular in size and shape (figures 95–98, plate 28). There is also an increase in density of the cytoplasmic matrix, especially after a survival period of 5 days (figure 98, plate 28); rarely filamentous material is present in the matrix (figure 97, plate 28). Mitochondria are less easily seen against the dark ground substance and begin to swell, become internally disorganized and finally break up. By 5–6 days post-operatively the terminal is considerably shrunken. Swollen glial processes surround degenerating profiles and begin to engulf them (figure 97, plate 28). Synaptic vesicles may at this stage resemble pale discs against the electron-dense background (figure 100, plate 29) and are beginning to disappear. Later, between 6 and 8 days, severe changes are apparent including an increase in the number and size of glial profiles, and all degenerating terminals are shrunken 'black' structureless masses, partially engulfed by glial processes (figures 99, 100 and 102, plate 29). The post-synaptic profile remains unaffected, as does the post-synaptic specialization which is an (originally) asymmetrical thickening. Some terminals become shrivelled to wafer-thin slivers of dark amorphous material, which adhere to the post-synaptic profiles only at their synaptic specializations (figures 104 and 105, plate 30). Gradually glial processes engulf and remove the degenerating pre-synaptic profiles, and some degenerating terminals are partially disengaged from their synaptic contact by a pale astrocytic protrusion which is inserted between the terminal and the synaptic cleft (figure 107, plate 30). Both the post-synaptic specialization and the dense material

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Description of plate 23

(See introductory remarks to plate 20.)

Figure 81. (Section 32.) Another spine arising from dendrite C (its pedicle is shown in figure 82) is contacted by P profile 5. This profile is also post-synaptic to P profile 6 and to LR terminal I. P profile 5 is therefore involved in all three glomeruli (see text). P profile 14 receives a synapse from LR terminal J; this P profile forms a triad as it is pre-synaptic to the spine in another section (see figure 73).

Figure 82. (Section 58.) An SR terminal is pre-synaptic to P profile 15 which makes a synaptic contact with P profile 16. LR terminal J is pre-synaptic to P profile 14.

Description of plate 24

(See introductory remarks to plate 20.)

Figure 83. (Section 68.) P profile 16 is post-synaptic to LR bouton I and pre-synaptic to dendrite B, so forming a triad, and also a sequential synapse: S → 15 → 16 → B (see figure 82, plate 23).

Figure 84. A serial section of a glomerulus in the centre-median nucleus (see also figures 85 and 86, plate 25). The glomerulus is sectioned obliquely giving good views of the P profiles but showing little of the LR bouton. In this section there are several dendro-dendritic synapses between P profiles (i.e. Pa, Pc, Pd and Pf) and the dendrite D; in addition Pa is pre-synaptic to Pb. (Magn. × 30000.)

The inset shows the dendro-dendritic synapse from Pb on to the dendrite D in the next serial section at a higher magnification. (Magn. × 60000.)

within the cleft persist, and can be found fortuitously adjacent to some inappropriate 'pre'-synaptic profile, such as a dendrite or a myelinated fibre (Pinching & Powell 1972). These persistent, exposed membrane thickenings (figures 103, 106, 108, 109, plate 30) were most obvious at late survival periods or in long-term material with survivals of several months. Degenerating myelinated fibres have more or less an unchanging appearance at all survival periods, containing dense cytoplasm and swollen or fragmented mitochondria.

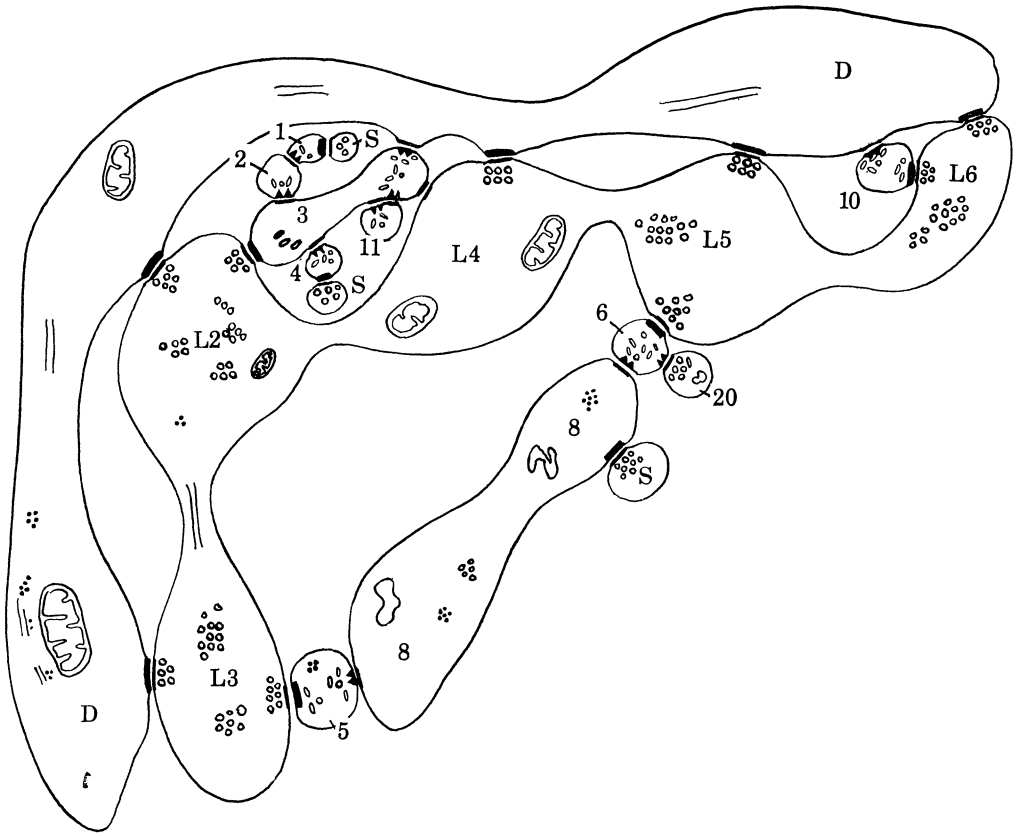


FIGURE 94. Diagram of five *en passant* boutons (L2–L6) which form a series of glomeruli along a single main dendrite (D) in the ventrolateral nucleus. Nine LR boutons in all were found in 50 serial sections to contact this dendrite. The associated P profiles (1–20) partially interconnect between these glomeruli (see plates 26 and 27).

Schematic synapses:

asymmetric;

symmetric (post-synaptic on right hand side).

The results of the experiments in which the motor cortex had been removed several months before placing a stereotaxic lesion in the globus pallidus are in agreement with those in which lesions were placed only in the globus pallidus, and are included in the totals shown in table 5. Only material from the centre-median nucleus was examined after these combined lesions, for, unlike the centre-median, the ventrolateral nucleus sends afferent fibres to the motor cortex, and it is well known that severe retrograde cell degeneration occurs in the latter nucleus after decortication. Electron-microscopical examination of the centre-median nucleus several months after removal of the somatic sensory and motor areas has failed to provide any

evidence of such retrograde changes, for no dark cells and very few 'grey' dendrites were found, nor was there any marked disorganization of the glomerular or interglomerular neuropil (cf. Pasik, Pasik, Hámori & Szentágothai (1973), and Wong-Riley (1972*c*) for the lateral geniculate nucleus).

TABLE 5. ANALYSIS OF DEGENERATING CORTICAL AND PALLIDAL TERMINALS IN THE THALAMUS

(*a*) total degenerating terminals: those with more than 1 synapse (%)

Lesion ...	VL	CM	VP
Cortex	257:5 (2%)	363:65 (18%)	155:3 (2%)
Pallidus	222:9 (4%)	208:8 (4%)	

(*b*) total post-synaptic profiles: those which are P profiles (%)

Lesion ...	VL	CM	VP
Cortex	262:25 (9½%)	442:81 (18½%)	158:10 (6½%)
Pallidus	231:21 (9%)	216:5 (2½%)	

(*c*) total post-synaptic dendrites: those with another synapse (%)

Lesion ...	VL	CM	VP
Cortex	238:1114 (48%)	361:45 (12½%)	148:61 (41½%)
Pallidus	210:87 (41½%)	211:87 (41%)	

In any experimental brain degenerating profiles make up only a small proportion of the total number of SR terminals that can be identified. In the centre-median nucleus, even after the combined lesions, when, as well as degenerating pallidal terminals, most of the cortical terminals should have degenerated and been removed, considerable numbers of normal SR terminals are observed. It is possible that the time course of the degenerative process is so variable that many more SR terminals degenerate than were observed to do so at the survival periods which were studied. Alternatively, such unaffected SR boutons, in common with LR, F and P profiles, which were also unaffected in these experiments, may be the terminals of cells whose somata reside in regions of the brain other than the motor cortex or globus pallidus, and they may be the terminals of axon collaterals of thalamo-cortical relay cells.

With regard to the nature of the degeneration it has been possible to treat the four sets of SR synaptic boutons, the cortico- and pallido-thalamic afferents to the ventrolateral and centre-median nuclei, as a homogeneous group. However, when one considers the types and number of profiles which are post-synaptic to these degenerating terminals, certain differences emerge. A summary of the results is presented in table 5, which is a compilation of all the degenerating terminals of cortical or pallidal origin which were photographed, and which strictly comply with three criteria: they are unequivocally degenerating, they are pre-synaptic at a definite synaptic specialization, and all the post-synaptic profiles are clearly recognizable. The tabulated figures are a rigorously selected sample of a larger number of observations of degenerating profiles, as many were not photographed because they were found wanting in one or other test, while others were photographed but later excluded from the sample for similar reasons.

In a single thin section, degenerating terminals are usually pre-synaptic to only a single process, which can be a dendrite or a P profile. Dendrites are contacted either on their shafts or occasionally on a spine (figure 119, plate 33). As spines are difficult to recognize unless they

are in continuity with their parent dendrites, only a few have been identified unequivocally post-synaptic to degenerating profiles, of both cortical and pallidal origin, in the ventrolateral nucleus and none in the centre-median nucleus. In both nuclei, however, many post-synaptic profiles are very small, and their cytoplasm is both devoid of inclusions and relatively electron-dense (figure 111, plate 31), so it seems probable that a higher proportion of degenerating terminals are pre-synaptic to spines than can be identified. Dendritic profiles which are post-synaptic to degenerating terminals are generally fairly distal portions, for they are usually of fairly narrow calibre, and a considerable proportion of them are also contacted by other synaptic boutons. However, only 12.5 % of the dendritic profiles which are post-synaptic to cortico-fugal terminals in the centre-median nucleus are contacted by another terminal, but of the dendritic profiles which are post-synaptic to pallido-thalamic terminals in this nucleus, 41 % possess a second synaptic contact. Of the dendrites which are post-synaptic to cortico- and pallido-thalamic terminals in the ventrolateral nucleus, 48 % and 41 % respectively of such dendritic profiles are secondarily contacted. However, since dendritic spines are more common in the centre-median than the ventrolateral nucleus, and because spines, as compared with dendritic shafts, are less commonly contacted by a second pre-synaptic profile, it is possible that the cortical fibres afferent to the centre-median nucleus terminate more frequently upon spines than the observations would indicate. Nevertheless, from the standpoint of the frequency of their synaptic connections, the group of post-synaptic dendritic profiles contacted by the cortical projection to the centre-median is significantly different ($P < 0.001$) from the population of dendrites post-synaptic to the other three types of SR terminals observed in the ventrolateral and centre-median nuclei.

Other differences are apparent between the several types of degenerating SR boutons in these experiments, for the cortico-thalamic terminals in the centre-median nucleus synapse upon a higher proportion of P profiles (18.5 % of the post-synaptic profiles) (figures 113–116, plate 32) than do the pallido-thalamic terminals (2.5 %). This difference is highly significant ($P < 0.001$) as is the difference between these results and the corresponding percentages of processes post-synaptic to cortico- and pallido-thalamic terminals in the ventrolateral nucleus, which are P profiles (respectively 9.5 % and 9 %). In one further respect the terminals of the

Description of plate 25

Further serial sections of a glomerulus in the centre-median nucleus (see figure 84, plate 24).

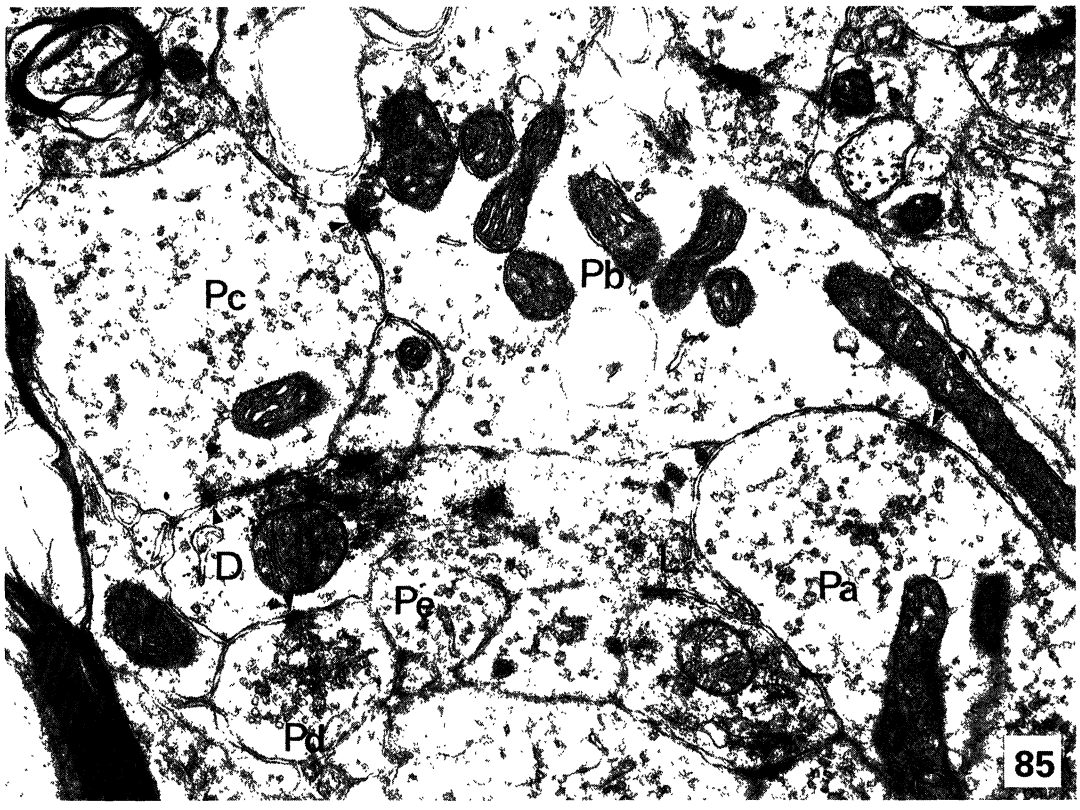
Figure 85. A sequential serial synaptic array. P profile Pa is pre-synaptic to P profile Pb; the latter is pre-synaptic to Pc (see figure 86 for return reciprocal synapse) which is pre-synaptic to the dendrite (D). (Magn. × 30000.

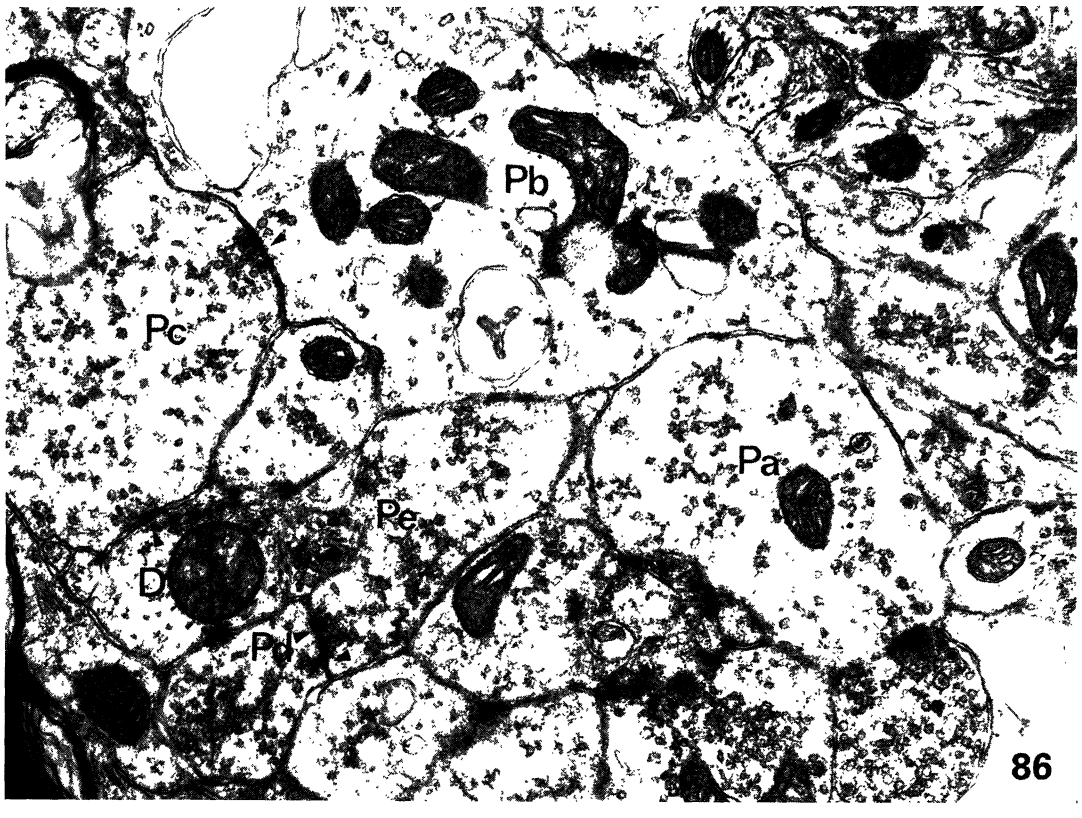
Figure 86. The return synapse (Pc pre-synaptic to Pb) of a reciprocal synaptic array and further reciprocal synapses between P profiles Pd and Pe. (Magn. × 30000.)

Description of plate 26

Figure 87. Montage to show a longitudinally sectioned dendrite (D). In all nine LR boutons contact this dendrite; five are *en passant* (see text and schematic diagram, figure 94). Three *en passant* LR terminals are seen here (L2, 4, 5). Note the spines (sp); those adjacent to P3 and L4 are shown at higher magnification in figure 93, plate 27. A narrow process from P profile P3 is post-synaptic to another P profile (arrowheads). (Magn. × 10000.)

Figure 88. Montage to show a large P profile P8, which runs alongside the large dendrite (D) in figure 87, which is 17 serial sections away. P8 contains synaptic vesicles (sv), ribosomes (v) and sacs of smooth endoplasmic reticulum (e) and is post-synaptic at an axo-dendro-dendritic serial synapse (arrowhead) which is shown at higher magnification in figure 90, plate 27. (Magn. × 10000.)

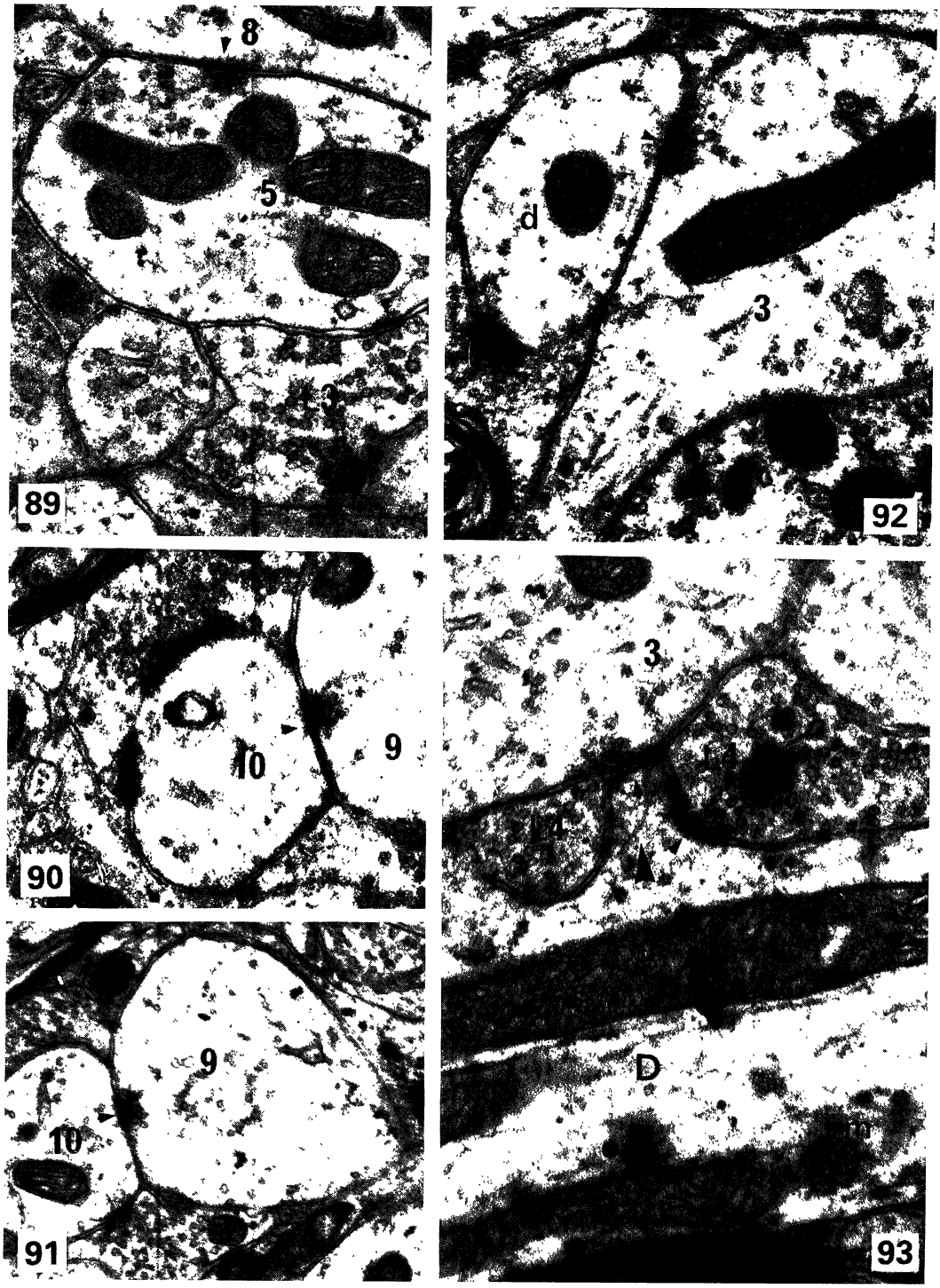




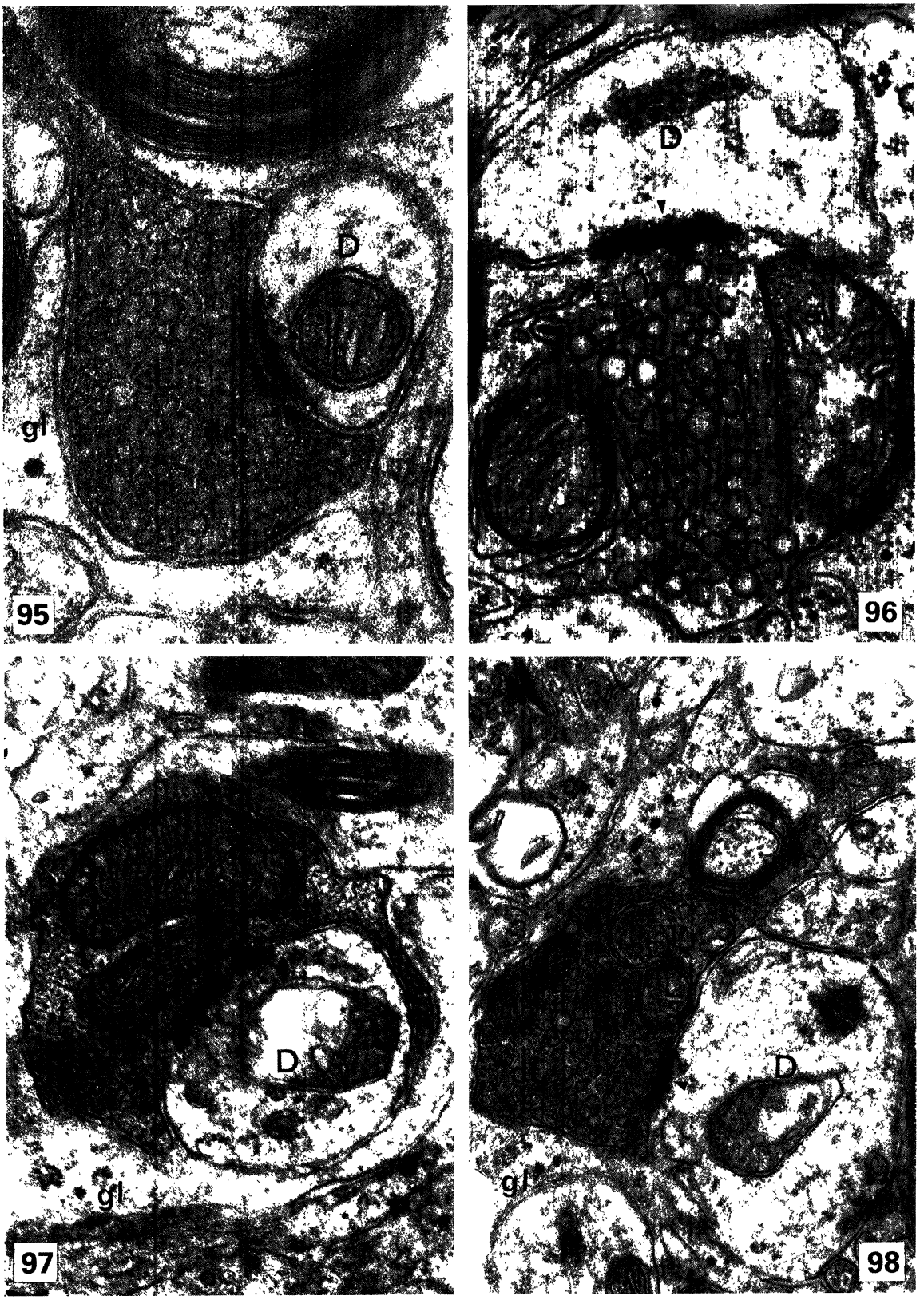
FIGURES 85 AND 86. For description see opposite.

(*Facing p.* 388)

FIGURES 87 AND 88. For description see p. 388.



FIGURES 89–93. For description see p. 389.



FIGURES 95–98. For description see opposite.

cortico-thalamic afferents in the centre-median nucleus differ significantly ($P < 0.001$) from the terminations of the other three fibre pathways to the thalamus from the motor cortex and globus pallidus; 18 % of the degenerating SR boutons in the centre-median nucleus have more than one synaptic specialization (figures 120 and 121, plate 33) as against only 2–4 % of the other types of SR bouton (table 5). In normal material SR profiles possessing multiple synapses are more common in the centre-median nucleus than in the ventrolateral; SR boutons also take part in triadic synapses, but these have only been observed in the centre-median nucleus where the arrangement consists of an SR terminal pre-synaptic to both a dendrite and a P profile, which is itself pre-synaptic to the same dendrite. Degenerating SR boutons of cortical origin have also been found to form part of such a triadic conformation in the centre-median nucleus (figures 113 and 114, plate 32) and it seems that the statistically significant disparities resulting from this analysis of the degenerating SR terminals in the ventrolateral and centre-median nuclei mirror the subtle differences observed in the normal study of these nuclei.

These quantitative data clearly demonstrate certain differences between the projections of the cortex and globus pallidus upon the ventrolateral principal nucleus and the intralaminar centre-median nucleus. The axons from both the cortex and the globus pallidus terminate in the same manner (table 5) within the ventrolateral nucleus; but within the centre-median nucleus the terminals of fibres from the cortex differ from those from the globus pallidus in more often having multiple synapses, ending on a higher proportion of P profiles, and being pre-synaptic to dendritic profiles which less frequently have a second synapse. The cortical projection to the two nuclei differs in similar ways, and the afferent fibre pathway from the globus pallidus to the centre-median differs from that to the ventrolateral nucleus, in that within the centre-median

Description of plate 27

Some synaptic details from the complex of glomerular aggregations associated with the main dendrite (D) in figure 87, plate 26. (Magnification of all figures × 45000.)

Figure 89. LR terminal L3 is pre-synaptic to a P profile (P5) which is also pre-synaptic to the large P profile (P8) seen in figure 88, plate 26.

Figures 90 and 91. Nearby serial sections showing two synaptic contacts from P profile P9 on to P10.

Figure 92. P profile P3 makes synaptic contact with a small dendrite (d).

Figure 93. P profile P3 forms a synapse with a dendritic spine (arrowhead). Note the subjacent multivesicular body (m). LR terminal L4, which also has a synaptic contact with P3 at another level thus forming a triad, makes a synapse upon the side of the spine.

Description of plate 28

Early degenerating SR terminals

Figure 95. An early degenerating SR terminal (dt) pre-synaptic to a small dendrite (D) in the centre-median nucleus, 5 days after electrolytic destruction of the ipsilateral globus pallidus. With shrinkage of the terminal and enlargement of the synaptic vesicles the latter have become crowded closely together. (Magn. × 67500.)

Figure 96. An early degenerating SR terminal (dt) pre-synaptic to a small dendrite (D) in the centre-median nucleus, 5 days after ablation of the motor cortex. The synaptic vesicles vary in size, many being considerably enlarged with a pale glassy appearance. (Magn. × 60000.)

Figure 97. Early degenerating SR terminal (dt) in the ventroposterior nucleus 5 days after ablation of the ipsilateral sensorimotor cortex. The shrunken terminal contains filaments (f) cut transversely. (Magn. × 45000.)

Figure 98. Early degenerating terminal (dt) in the ventrolateral nucleus 5 days after destruction of the globus pallidus. Glial processes (gl) surround the terminal which has a darkened matrix containing enlarged pale vesicles and partially disorganized mitochondria. (Magn. × 40000.)

nucleus terminals of axons from the globus pallidus are pre-synaptic to proportionately fewer P profiles.

A single exception to the findings of this experimental study is considered separately. In this one brain, perfused six days after unilateral ablation of the motor cortex, early filamentous degeneration of LR boutons was observed in sections of a restricted part of the ventrolateral nucleus. Although a survey was made throughout most of this nucleus, only two blocks contained these degenerating terminals which were very similar in appearance to the degenerating terminals of afferent cerebello-thalamic fibres in this nucleus. Considerable numbers of LR terminals in the affected area showed early filamentous changes whereas few smaller SR terminals were seen to degenerate. In other areas of the ventrolateral nucleus little degeneration was observed, and none of it was filamentous in type. The ipsilateral centre-median nucleus in this brain was also examined and a small number of degenerating SR terminals were found. The cause of the degeneration of LR terminals in a circumscribed part of the ventrolateral nucleus in a single experiment is uncertain, but since degeneration of similar large axon terminals (termed 'RL') has been described in the pulvinar of the squirrel monkey after experimental damage of the parieto-temporal cortex (Mathers 1972), such filamentous degeneration might be the result of interruption of fibres from more anterior cortical areas of the frontal lobe, or to coincidental fortuitous degeneration of fibres from the cerebellum.

Cortico-thalamic axon terminals in the ventroposterior nucleus

In some experiments in which the motor cortex was damaged, the somatic sensory cortex was also removed in order to produce degeneration of cortico-thalamic terminals in the ventroposterior nucleus. The purpose of these experiments was to provide a comparison with the ventrolateral nucleus, for both the ventrolateral and ventroposterior nuclei are principal relay nuclei, and also because the corticothalamic terminals in the monkey ventrolateral and centre-median nuclei were found to be very similar to those described in the ventroposterior nucleus of the cat (Jones & Powell 1969*c*). A brief survey of the normal fine structure of the ventroposterior nucleus in the monkey showed it to be very similar to other principal thalamic nuclei. Corticofugal fibres terminate in the ventroposterior nucleus as small dark (SR) boutons (figures 117–119, plate 33) which are filled with round synaptic vesicles, and possess asymmetrical membrane thickenings. The terminals are generally situated in the extra-glomerular neuropil, and are pre-synaptic to P profiles and dendrites (figures 117–119, plate 33). Degeneration is very dense in the ventroposterior nucleus, with a density of approximately one terminal degenerating per 500 μm^2, and there is a marked tendency for degenerating profiles to occur in clusters; two degenerating terminals have been observed pre-synaptic to the same post-synaptic profile.

Terminals of axons from the cerebellum in the ventrolateral nucleus

Within a few days following the unilateral destruction of the dentate and other deep nuclei of the cerebellum, terminal degeneration is seen in the contralateral ventrolateral nucleus of the thalamus. No evidence of degenerating terminals was seen in the contralateral centre-median nucleus, but degenerating myelinated fibres were fairly common, in agreement with the results of experimental light-microscopical investigations (Mehler, Vernier & Nauta 1958; Mehler 1966). Degenerating boutons of axons from the cerebellum were frequently found in association with glomeruli and both their position and their fine structure identified them as

LR axon terminals. The frequency of degeneration varies considerably within the ventrolateral nucleus; in some areas three degenerating terminals may be found in an area of only 100 μm^2, but even in such densely affected areas, some LR terminals remain unaffected by cerebellar ablation.

A complete analysis of the time course and process of degeneration has not been undertaken, as brains with a post-operative survival period of five days only were available. Of the three brains, two had only partial damage of the dentate nucleus, and in these relatively few degenerating profiles were present in the ventrolateral nucleus. In the third experiment the dentate nucleus had been completely removed and the superior cerebellar peduncle was extensively involved; the nucleus interpositus showed complete cell loss and severe gliosis, while in the nucleus fastigius only a third or so of the normal number of neurones remained. Although this material is all from experiments with the same survival period, it provides evidence of a considerable range of ultrastructural changes which are in general agreement with more comprehensive observations of filamentous degeneration in the lateral geniculate nucleus (Colonnier & Guillery 1964; Wong-Riley 1972*b*). Many degenerating profiles were much paler than normal LR terminals, in large part due to a considerable loss of synaptic vesicles; the remaining vesicles were enlarged and glassy in appearance, and usually aggregated near synaptic contacts (figures 122–124, plate 34). Often considerable amounts of glycogen are present within degenerating boutons, while less frequently one finds a number of coated vesicles, some of them apparently budding off the limiting membrane of the terminal, other than the cleft region. Many degenerating profiles are filled with filaments, arranged in rings and whorls; in general, the number of filaments is in inverse ratio to the number of vesicles, and it seems that profiles with considerable numbers of enlarged vesicles are at an earlier stage of degeneration than those which are packed with filaments. Some degenerating terminals appear slightly shrunken, with their intracellular contents crowded closely together in a fairly electron-dense cytoplasmic matrix (figures 127 and 128, plate 35). Others are electron-opaque, much reduced in size, and are partially engulfed by glial processes, which gradually insinuate themselves between the degenerating terminal and the post-synaptic thickening, which remains intact. The degenerating terminals of cerebellar afferents form both conventional synaptic contacts and filamentous (Colonnier & Guillery 1964) desmosome-like contacts (figure 122, plate 34). A single cerebellar axon terminal often forms several synapses (figures 122–124, plate 34), in 40 % of the sample counted; as many as three profiles may be post-synaptic to a degenerating terminal in a single section, while 20 % of the observed degenerating terminals have two separate synaptic contacts with a single post-synaptic profile. Thin myelinated fibres, 0.5–1.0 μm diameter, also exhibit both filamentous and dense degeneration; on occasions, such degenerating fibres have been seen in continuity with a degenerating synaptic bouton (figures 125 and 126, plate 35). Cerebellar axon terminals are pre-synaptic to both P profiles and medium-sized dendrites and their spines; the dendrites are frequently part of glomerular complexes and appear to be quite proximal portions of the main dendrites of the thalamic neurones, for they have sometimes been seen in continuity with their cell soma.

Discussion

The ultrastructure of the intralaminar centre-median nucleus and the ventrolateral main relay nucleus has been found to be essentially similar in both composition and organization, a conclusion which may seem surprising in view of the well known functional differences between specific main relay nuclei and non-specific intralaminar nuclei (Morison & Dempsey 1942; Jasper 1960). As these two nuclei are morphologically similar to other sensory relay nuclei, these observations strengthen the argument in favour of a basic ultrastructural framework common to most if not all the thalamic nuclei. Glomeruli have been described, with slight variations in numbers rather than in types of contained profile, in all thalamic nuclei that have so far been studied, and the very complexity of their organization is by itself strong evidence in favour of the complex nature of the processing of information in the thalamus. Both the ventrolateral and centre-median nuclei contain four types of synaptic profiles, which are very similar to the published descriptions and illustrations of synaptic profiles from other thalamic nuclei in various mammalian species. Table 6 sets out the terms used by various authors and is arranged

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Description of plate 29

Late degenerating SR terminals

Figure 99. Late degenerating terminal (dt) pre-synaptic to a P profile (P) in the centre-median nucleus, 6 days after destruction of the ipsilateral motor cortex. The intracellular contents are disorganized and indistinct, since the matrix is now very electron-dense. (Magn. × 40000.)

Figure 100. Late degenerating terminal (dt) pre-synaptic to a dendrite (D) in the centre-median nucleus, 6 days after the destruction of the motor cortex. The intracellular matrix is so dark that the synaptic vesicles appear only as pale discs. (Magn. × 40000.)

Figure 101. Late degenerating terminal (dt) in the ventrolateral nucleus, 7 days after ablation of the motor cortex. The terminal is very shrunken and dark, with no internal structure discernible, and is being engulfed by the glial process (gl). (Magn. × 45000.)

Figure 102. Late degenerating terminal (dt) pre-synaptic to a small dendritic profile (D) in the centre-median nucleus, 6 days after destruction of the motor cortex. The highly shrunken and darkened terminal is almost entirely engulfed by a glial process (gl). (Magn. × 40000.)

Description of plate 30

Figure 103. A dendrite (D) in the centre-median nucleus with a persisting exposed post-synaptic thickening (arrowheads) opposed to two profiles (u, v) which are not degenerating. Although there is cleft material, there are no pre-synaptic specializations; and whereas profile v contains a few vesicles, profile u does not, even when traced through in several serial sections on either side of this particular section. (Magn. × 78300.)

Figure 104. A degenerating terminal (dt) in the ventrolateral nucleus, shrunken to an almost indistinct fragment, 4 days after destruction of the globus pallidus. (Magn. × 40000.)

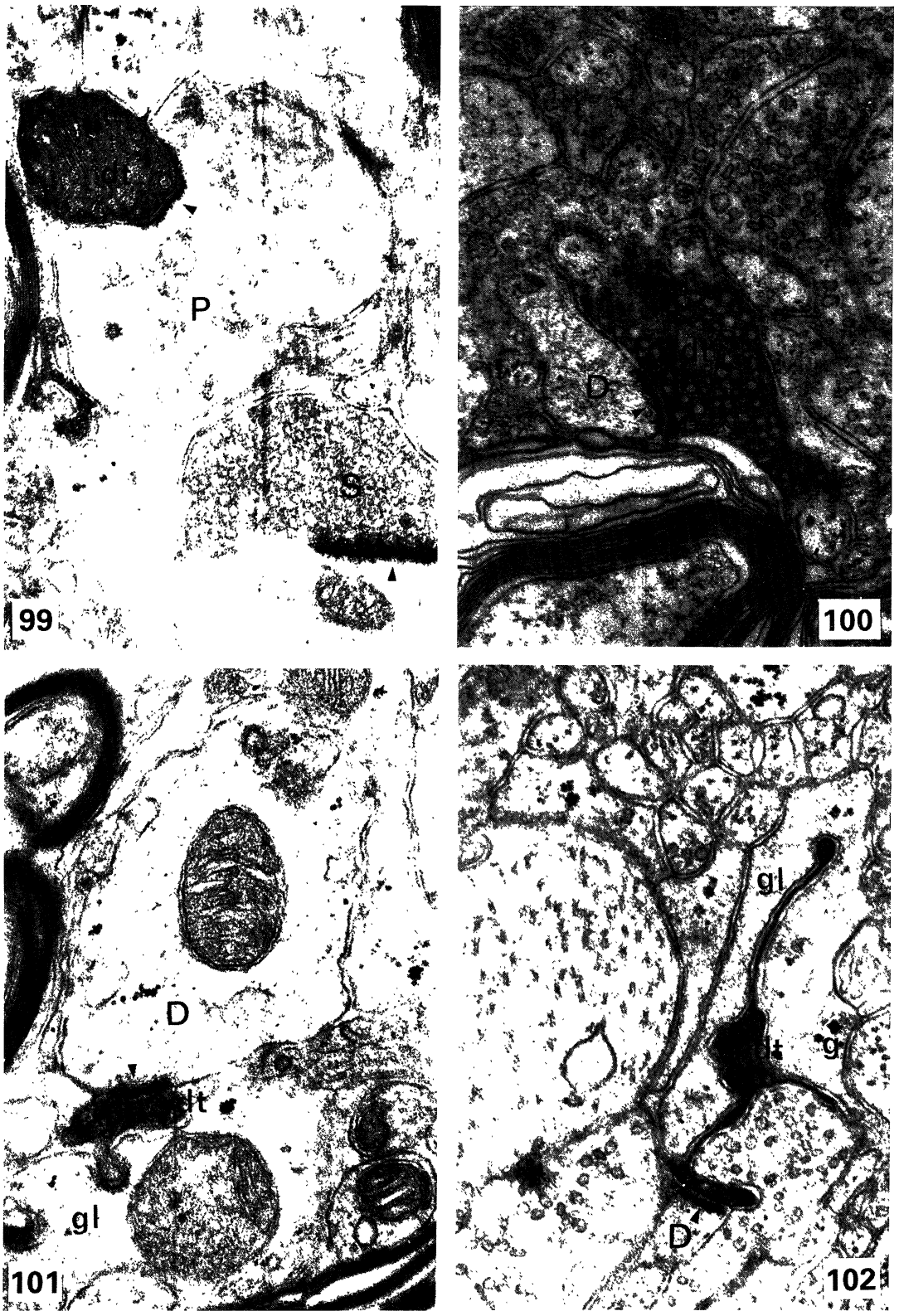
Figure 105. This degenerating terminal (dt) in the centre-median nucleus has shrivelled to just a sliver of electron-dense material. (Magn. × 42000.)

Figure 106. A persisting synaptic thickening in a dendrite (D) apposed to a glial cell (gl) in the centre-median nucleus, 4 days after destruction of the globus pallidus. (Magn. × 45000.)

Figure 107. A degenerating terminal (dt) being engulfed by an astrocytic process (gl) which is forming a wedge between the terminal and its opposed post-synaptic thickening so that the terminal and the post-synaptic thickening are becoming disengaged. Centre-median nucleus, 5 days following destruction of the globus pallidus. (Magn. × 30000.)

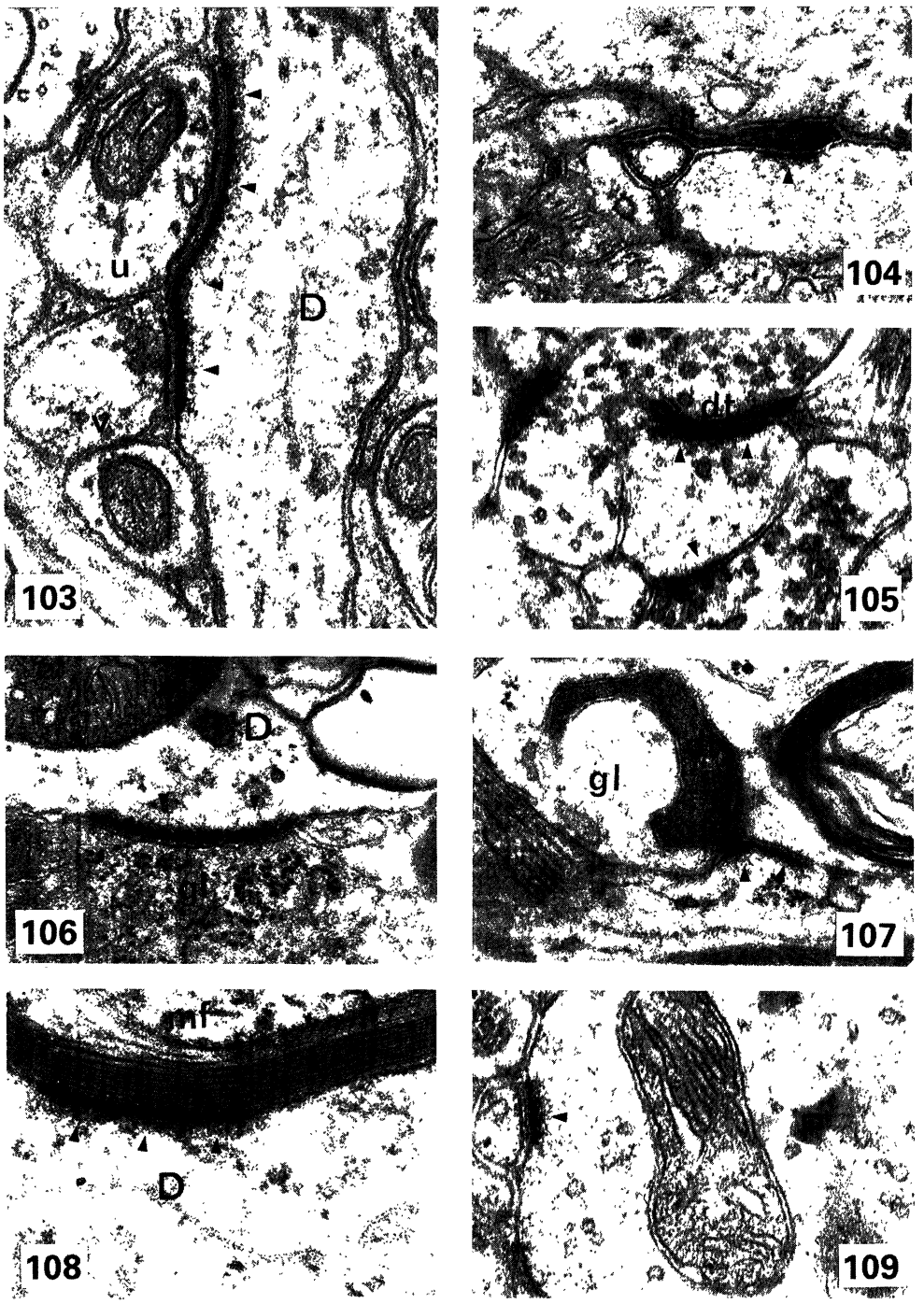
Figure 108. A persisting post-synaptic thickening directly apposed to the myelin sheath of a medullated fibre (mf). Centre-median nucleus, 5 days after destruction of the globus pallidus. (Magn. × 90000.)

Figure 109. A small persisting post-synaptic thickening (arrowhead) in a P profile (P) in the ventrolateral nucleus, 4 days after destruction of the globus pallidus. (Magn. × 48000.)

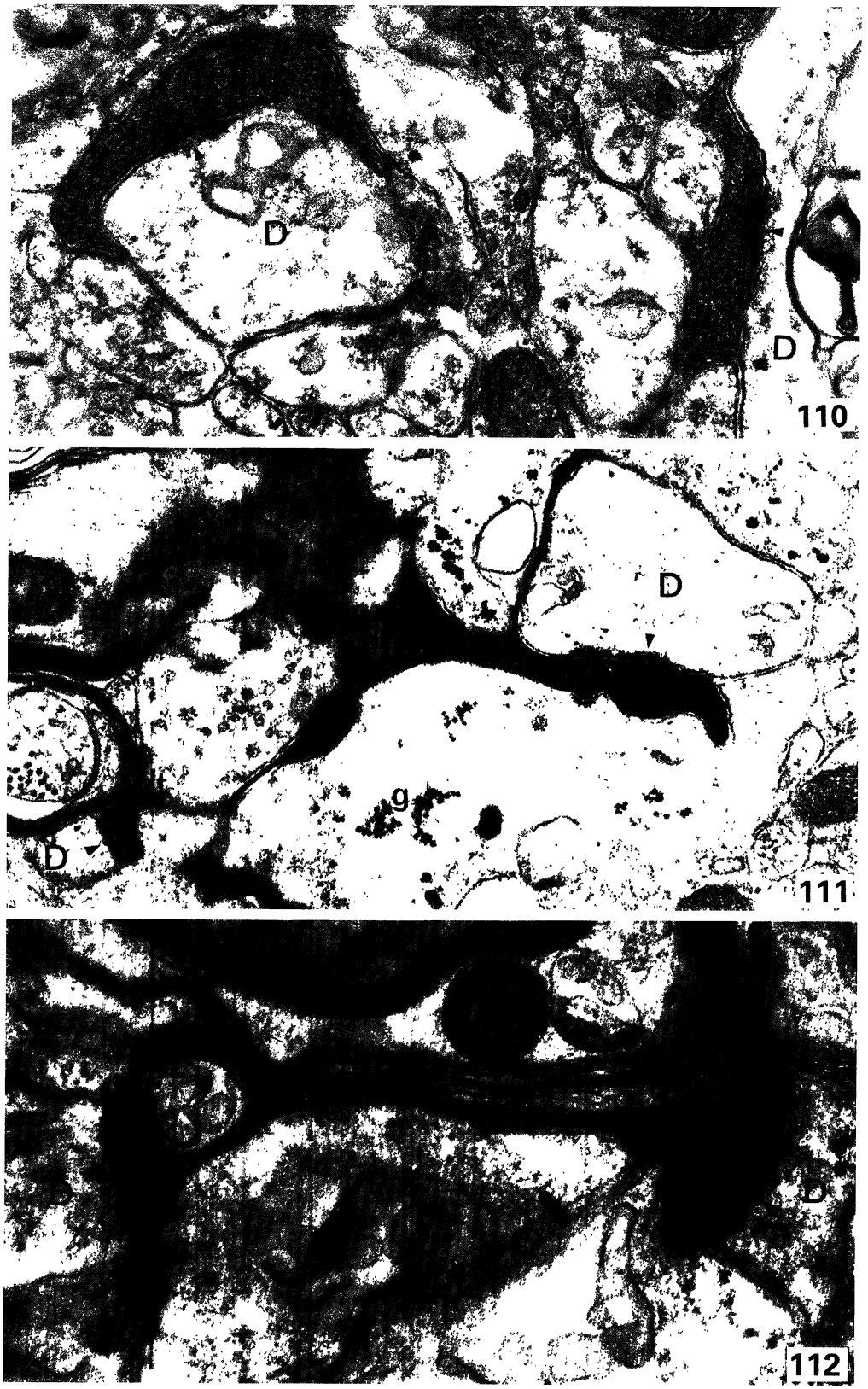


FIGURES 99–102. For description see opposite.

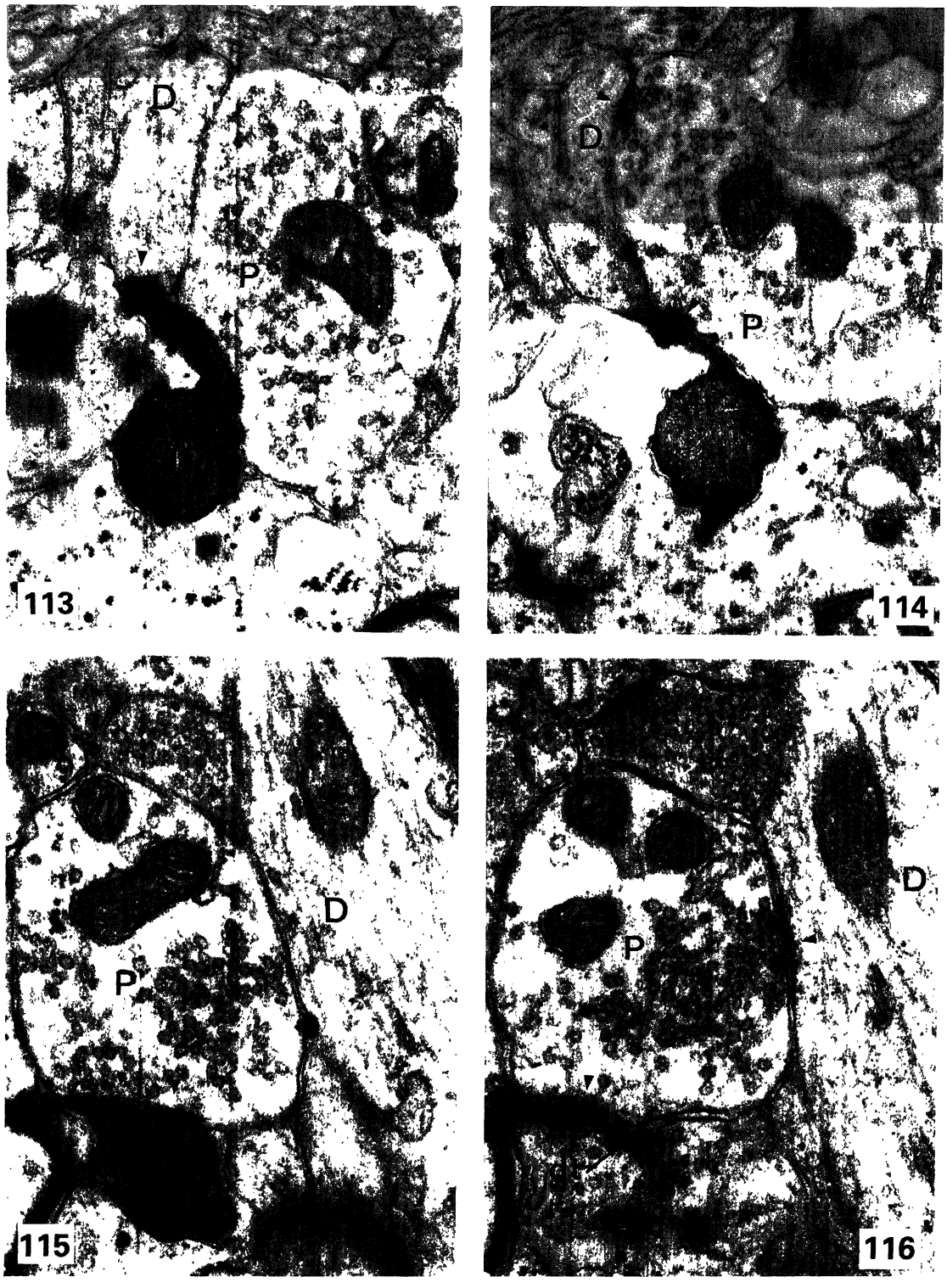
(*Facing p.* 392)



FIGURES 103–109. For description see p. 392.



FIGURES 110–112. For description see p. 393.



FIGURES 113–116. For description see opposite.

so that the equivalent findings of different studies can as far as possible be directly compared. Early work was largely concerned with the lateral geniculate nucleus of the cat thalamus (Szentágothai 1963; Peters & Palay 1966; Szentágothai *et al.* 1966), and there was considerable overlap between the various descriptions (Guillery 1969). Guillery described two types of axon terminals, 'RLP' and 'RSD', large and small terminal profiles respectively, containing round synaptic vesicles and little has been added to the description of these two classes of terminal. The nature of other profiles, containing irregularly shaped vesicles, has been controversial until quite recently. Guillery (1969) described two types of synaptic profile with flattened vesicle in the cat lateral geniculate nucleus, which could be differentiated with difficulty, but such a subdivision was not possible in the monkey lateral geniculate nucleus (Guillery & Colonnier 1970). Jones & Powell (1969*b*) described a pale profile, which like Guillery's (1969) 'F_2' process contained smooth endoplasmic reticulum, but they also observed occasional ribosomes and granular endoplasmic reticulum in the parent processes of the pale terminals which made them consider, but later reject, the possibility that these pale profiles were dendritic; their description was essentially the same as that provided by Ralston & Herman (1969) of the cat ventrobasal nucleus, but the latter authors interpreted the pale profiles to be dendritic and were the first to distinguish them from a group of axon terminals containing flat vesicles. Wong-Riley (1972*a*) in describing the squirrel monkey lateral geniculate nucleus concurred with this interpretation, but admitted uncertainty in distinguishing dendritic profiles containing vesicles from axon terminals that contain flat vesicles. Famiglietti & Peters (1972) measured synaptic vesicles and deduced that the dendritic profiles (which they term 'ID' profiles) possess vesicles which are less flat than the non-spherical synaptic vesicles in axon terminals (their 'IA' terminals), and both types of profile were thought to be part of the Golgi type II cell. Morest (1971) drew similar conclusions and he recognized a Golgi type II axon and dendrite from an analysis of Golgi preparations and a comparison with electron-microscopic observations.

In the early stages of the present study it was clear that on morphological grounds the pale profiles were a heterogeneous population, and the tilting experiments of Dennison (1971) prompted attempts to examine the present material with a gonioscopic stage in a manner

Description of plate 31

Figure 110. Two degenerating SR terminals (dt), both pre-synaptic to dendrites (D) in the ventrolateral nucleus, 4 days after destruction of the globus pallidus. (Magn. × 45000.)

Figure 111. Two neighbouring late degenerating terminals (dt) both pre-synaptic to dendrites (D) in the centre-median nucleus, 6 days after destruction of the motor cortex. They are probably connected by a narrow cytoplasmic bridge. (Magn. × 30800.)

Figure 112. A thin sliver of cytoplasm connects two late degenerating terminals (dt) in the centre-median nucleus, 6 days after ablation of the motor cortex. (Magn. × 48000.)

Description of plate 32

Figures 113 and 114. Neighbouring serial sections to show a degenerating terminal (dt) forming a triadic synaptic complex: pre-synaptic to a dendrite (D) and a P profile (P) (figure 113) which is also pre-synaptic to the dendrite (figure 114). Centre-median nucleus, 6 days after destruction of the motor cortex. (Magn. × 40000.)

Figures 115 and 116. Neighbouring serial sections to show a degenerating terminal (dt) as part of a serial synapse. The degenerating terminal makes a synapse with the P profile (figure 115) which in turn makes a synapse upon a dendrite (D) in figure 116. Centre-median nucleus, 6 days' survival after destruction of the motor cortex. (Magn. × 48000.)

TABLE 6

	lateral geniculate nucleus									medial geniculate nucleus			ventro-posterior	ventro-basal	centre-median ventrolateral ventroposterior
	cat					monkey			rat	cat			cat	cat	monkey
Author†...	1	2	3	4	5	6	7	8	9	4	10	11	4	12	13
	all profiles are considered axonal unless otherwise stated														presented results
profile 1	type 3 (α_1)‡	At	RSD	SD (α_1)	C (α_1)	RSD	RSD	SD	—	SD (α_2)	afferent axons	SD	SD (α_3)	as	SR = small axon round synaptic vesicles (α_4 and β)
profile 2	type 1 (γ)	central axon	RLP	LD	OCA NOCA (γ)	RLP (γ)	RLP (γ)	RL (γ)	R	LD		LD (δ)	LD	AS (ϵ)	LR = large bouton: round synaptic vesicles (Ω)
profile 3	type 2	peri-pheral axon	F_2	pale	ID = dendrite	F	F_2	F_2	P = presyn. dendrite	pale	Golgi type II dendrite	pale (? process)	pale	SS = pre-syn. dendrite	P = pre-synaptic dendritic profile: discoid vesicles
profile 4		A	F_1		IA		F_1	Fs = dendrite F_1	F					VS	F = axon cylindrical synaptic vesicles

(At present not shown to degenerate after any extrinsic lesion (see Pasik *et al.* 1973)

† LITERATURE

1 Szentágothai *et al.* (1966).
2 Peters & Palay (1966).
3 Guillery (1969).
4 Jones & Powell (1969*b*).
5 Famiglietti & Peters (1972).
6 Guillery & Colonnier (1970).
7 Le Vay (1971).
8 Wong-Riley (1972*b*).
9 Lieberman & Webster (1972).
10 Morest (1971).
11 Jones & Rockel (1971).
12 Ralston & Herman (1969).
13 Harding (1973*a*, *b*).

‡ KEY

α Degenerate after cortical lesions (1, visual; 2, auditory; 3, sensory; 4, motor and sensory).
β Degenerate after pallidal lesions.
γ Degenerate after optic enucleation.
δ Degenerate after inferior collicular ablation.
ϵ Degenerate after dorsal column nucleus ablation.
Ω Degenerate after ablation of deep cerebellar nuclei (ventrolateral nucleus only).

similar to that of Lieberman & Webster (1974) who tilted sections of rat lateral geniculate nucleus. It was found that two different classes of profiles had synaptic vesicles which differed in shape, and this helped in the differentiation of two types of synaptic profile (termed here F and P profiles). The F terminals fulfil the criteria for axonal processes and have been observed issuing from myelinated fibres. P processes are interpreted to be the terminal portions of dendrites, although the evidence is not conclusive. A proximal dendrite, connected to its parent cell soma, has been described (Harding 1971) which gives off synapses and contains synaptic vesicles similar to those present in P profiles (cf. Wong 1970; Le Vay 1971), but it has not proved possible in the ventrolateral and centre-median nuclei as in the lateral geniculate nucleus of the rat (Lieberman & Webster 1972) and cat (Famiglietti & Peters 1972) to trace a P profile from within a glomerulus unequivocally back to a mainstem or primary dendrite even with serial sections, probably because P profiles are, in parts, very thin and tortuous. Their thin non-terminal processes, and the fine calibre processes to which the expanded terminal portions found within glomeruli are usually traced, are similar to the narrow sheet-like dendrites and the gemmules with their very long thin stalks that arise from the periglomerular cells of the olfactory bulb (Pinching & Powell 1971*b*), and these gemmules also take part in reciprocal synapses. It is the latter reciprocal synaptic arrangements which form the most decisive evidence in favour of the dendritic nature of the P profiles, and is of particular interest with regard to their function.

Reciprocal dendro-dendritic synapses were first described occurring between mitral and granule cells in the olfactoy bulb (Hirata 1964; Andres 1965; Rall, Shepherd, Reese & Brightman 1966) and have since been found in many other sites (cf. Shepherd 1974). In the thalamus, Famiglietti (1970) has described rare reciprocal dendro-dendritic synapses in the cat lateral geniculate nucleus, and although both opposing synaptic specializations and their associated synaptic vesicles were similar in appearance, in contrast to those in the olfactory bulb, other morphological criteria were in Famiglietti's view suggestive evidence that the two opposing dendrites had different origins. Lieberman & Webster (1972) also mention reciprocal dendro-dendritic synapses between 'PSD' (pre-synaptic dendritic) profiles containing discoid vesicles in the rat lateral geniculate nucleus. In the present study examples of reciprocal dendro-dendritic synapses have been seen both within glomeruli and in the interglomerular neuropil of both the ventrolateral and centre-median nuclei (Harding 1971). In the rat lateral geniculate nucleus and the monkey ventrolateral and centre-median nuclei the two synaptic contacts which comprise the reciprocal arrangement have a similar structure and there are no other morphological grounds for distinguishing between the two P profiles responsible for these synapses. In the ventrolateral and centre-median nuclei reciprocal synapses are far from rare, and are a prominent feature of glomerular complexes where they form part of more complex synaptic arrangements. These reciprocal synapses are involved in triadic arrays and in the lengthy sequences of serial synapses which are an important feature of dendritic synaptic relations in the thalamus, such as the sequential serial synapses in the ventrolateral and centre-median nuclei (Harding 1973*a*) and the *iso*-synaptic relations in the cat lateral geniculate nucleus (Famiglietti & Peters 1972).

Although it has been concluded that F and P profiles are axon terminals and dendritic processes respectively, the cells of origin of these profiles are not known. It is highly likely that both processes are intrinsic to the thalamus, for they do not degenerate as a consequence of lesions of the motor cortex, globus pallidus or cerebellum. In a study of thalamic interneurons, Pasik

et al. (1973) have shown that at long survival periods after destruction of the visual cortex, when retrograde degeneration has resulted in the dissolution of thalamocortical relay cells and their dendrites in the monkey lateral geniculate nucleus, such pale profiles remain unaffected. Morest (1971), from studies of Golgi preparations and electron-microscopy, considered that both profiles are processes of the same cell, the Golgi type II cell, and a similar view is held by Famiglietti & Peters (1972) although they showed a statistically significant difference in the measured flatness of the two populations of synaptic vesicles in the 'IA' and 'ID' profiles. Differences in vesicle morphology in these profiles have been confirmed and extended by tilting experiments (Lieberman & Webster 1972; Harding 1973*a*), and as F boutons and P profiles contain morphologically distinct vesicles and possess markedly different synaptic specializations, it would seem more likely that these profiles take origin from different classes of cell. If there are two intrinsic interneurons in the ventrolateral and centre-median nuclei, the postulated correlation between synaptic structure and function would support the suggestion that they are both inhibitory (Uchizono 1965; Larramendi, Fickenscher & Lemkey-Johnston 1967). In the ventrolateral nucleus of the cat there is evidence from Golgi studies of two types of Golgi type II cell (Kiss & Tömböl 1972). If F boutons and P profiles belong to these two varieties of Golgi type II cell, this would explain the overlap of the presumed equivalents in Golgi preparations of the lateral and medial geniculate nuclei, where it was not possible to make such distinctions between classes of Golgi type II cells, as is also the case in the centre-median nucleus. The light-microscopical evidence may implicate the Golgi type II a cells as the origins of P profiles but it is by no means conclusive when one considers the incomplete nature of the electron-microscopical description of P cells. There is some evidence that F axons may arise from the reticular nucleus of the thalamus; from the study of Golgi-impregnated material, Cajal (1911) and Scheibel & Scheibel (1966) considered that the axons of the cells of the reticular nucleus pass medially into the principal and intralaminar nuclei of the thalamus and this has recently been established experimentally by the use of axonal transport methods (Jones 1975). Whatever the location of the parent cells of the F boutons and P profiles the present electron-microscopical evidence shows that within the ventrolateral and centre-median nuclei there are synaptic contacts between three cell types: one is the relay cell, the other two are F and P interneurons.

Description of plate 33

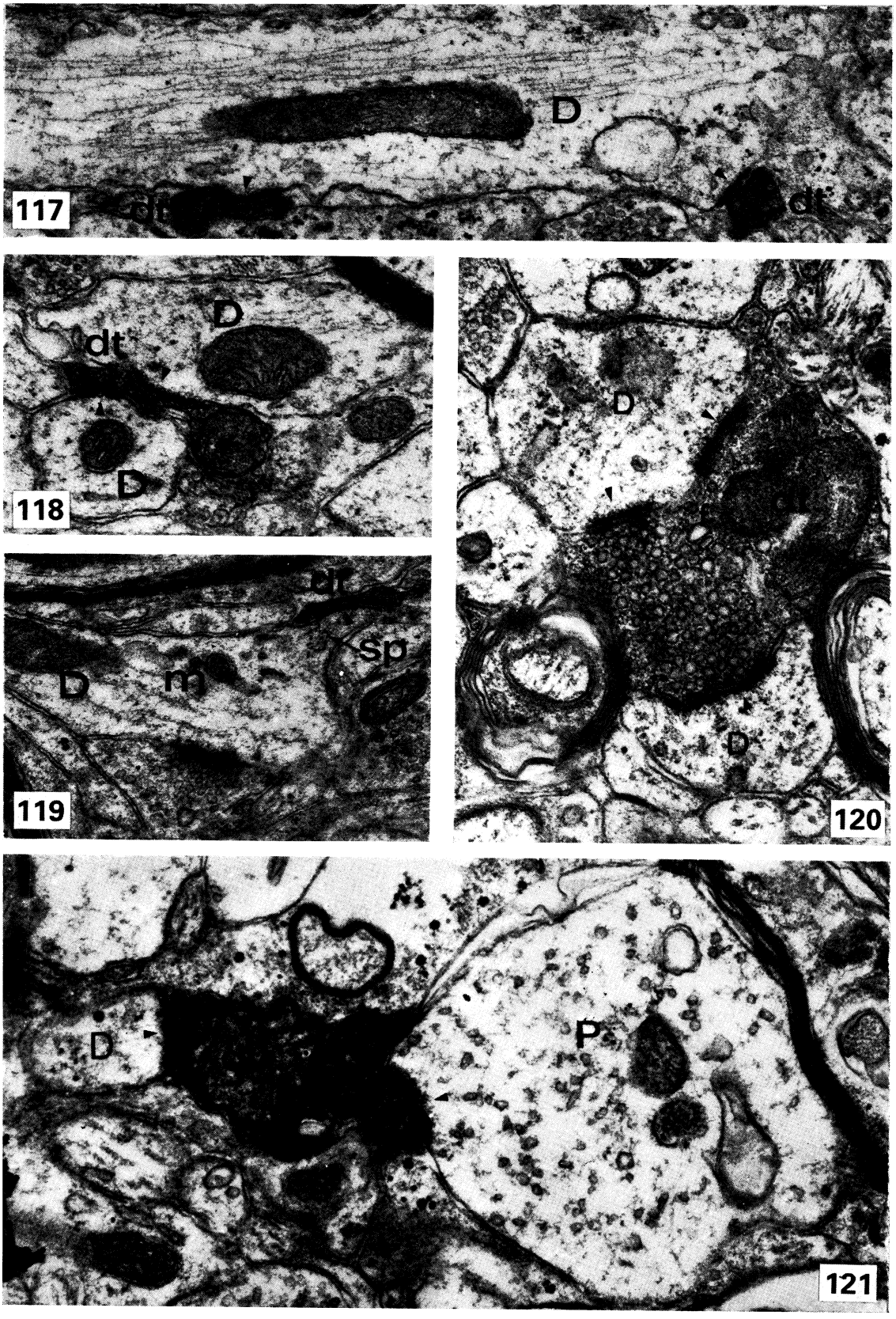
Figure 117. Two neighbouring degenerating terminals (dt) presynaptic to the same dendrite (D) in the ventroposterior nucleus, 7 days after the destruction of the somatosensory cortex. (Magn. × 30000.)

Figure 118. A late degenerating terminal (dt) pre-synaptic to two small dendrites (D) in the ventroposterior nucleus 7 days after removal of the somatosensory cortex. (Magn. × 38500.)

Figure 119. A dendritic spine (sp) receives a synaptic contact from a degenerating terminal (dt) in the ventroposterior nucleus, 7 days after destruction of the somatosensory cortex. Note the multivesicular body (m) subjacent to the spine. (Magn. × 30000.)

Figure 120. A degenerating terminal (dt) pre-synaptic to two dendrites (D) and containing enlarged pale synaptic vesicles and filaments (f). Centre-median nucleus, 6 days after destruction of the motor cortex. (Magn. × 40000.)

Figure 121. Late degenerating terminal (dt) pre-synaptic to a P profile (P) and a small dendritic profile (D) in the centre-median nucleus, 6 days after destruction of the motor cortex. (Magn. × 40000.)



FIGURES 117–121. For description see opposite.

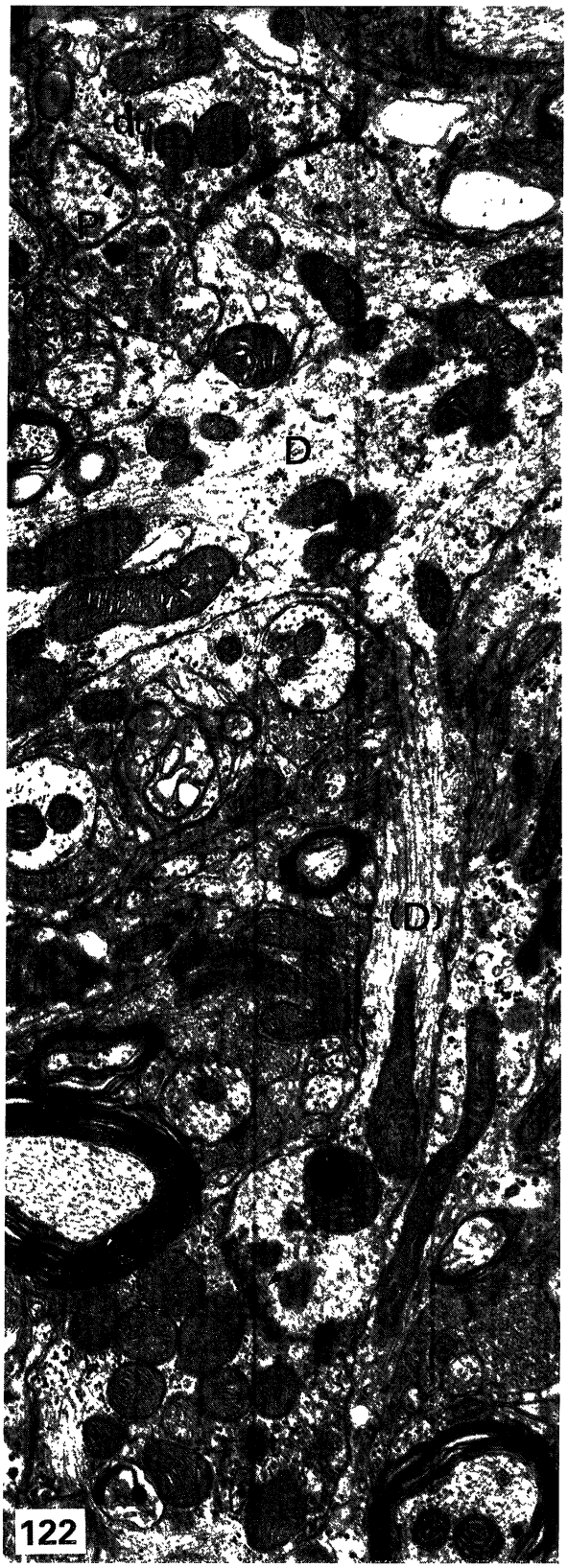
(*Facing p.* 396)

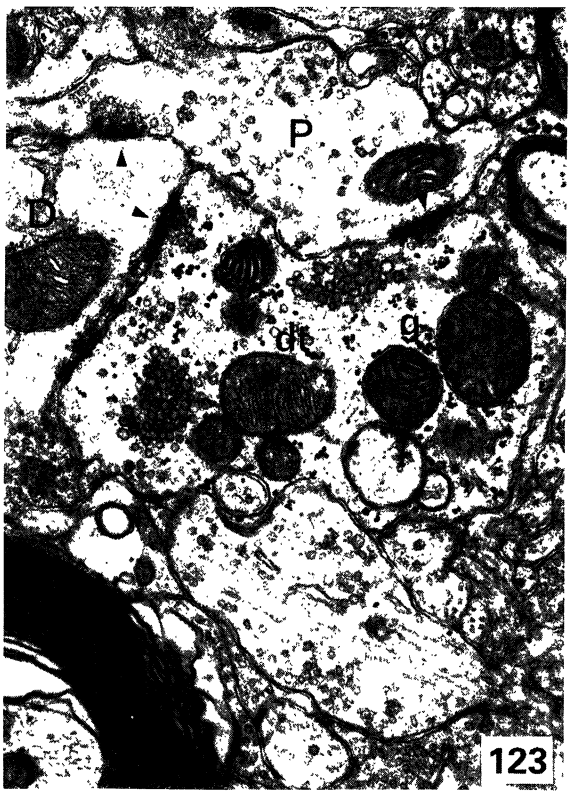
Description of plate 34

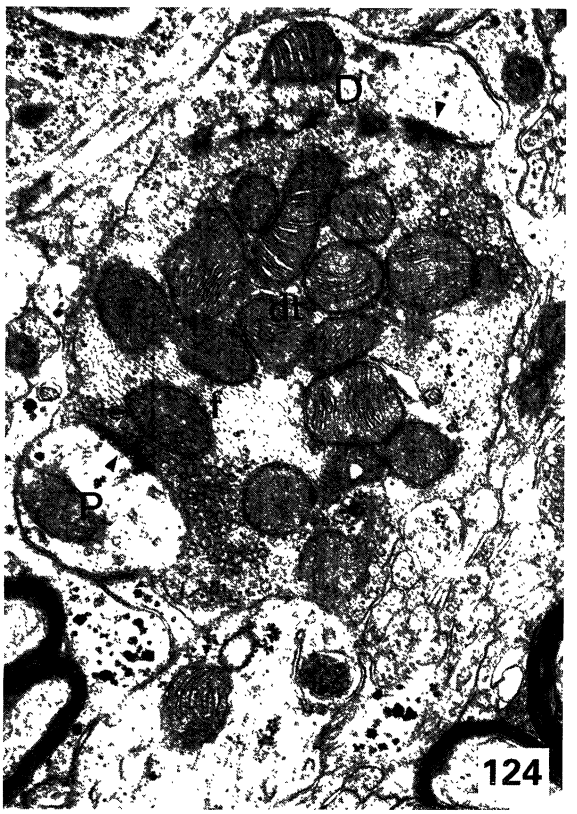
Figure 122. A dendrite (D) and its branch (D) which receive synapses from two degenerating LR terminals (dt). One of these terminals is also pre-synaptic to a P profile (P). Ventrolateral nucleus, 5 days after damage of the deep nuclei of the cerebellum. (Magn. × 18000.)

Figure 123. A degenerating LR terminal (dt) within a glomerulus, forming a triadic synaptic arrangement with a P profile (P) and dendrite (D). Observe the reduced number of enlarged synaptic vesicles and the considerable numbers of glycogen granules (g). Ventrolateral nucleus, 5 days after destruction of the deep nuclei of the cerebellum. (Magn. × 22000.)

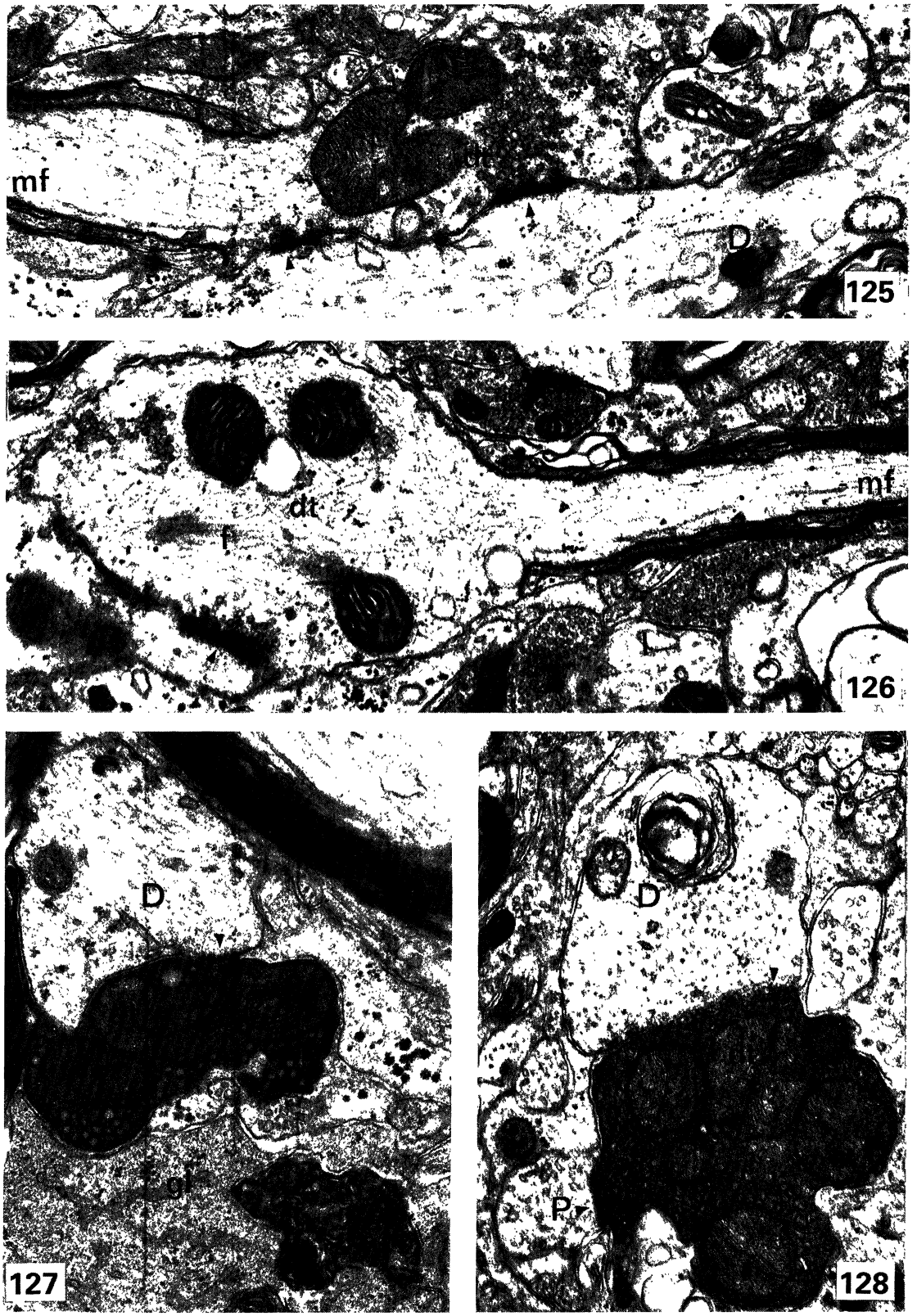
Figure 124. Degenerating LR terminal (dt) pre-synaptic to a dendrite (D) and a P profile (P) within a glomerulus. The terminal is filled with filaments (f). Ventrolateral nucleus, 5 days following destruction of the deep cerebellar nuclei. (Magn. × 26800.)







FIGURES 122–124. For description see opposite.



FIGURES 125–128. For description see opposite.

Dendritic spines

A detailed account has been given of the morphology and synaptology of the dendritic spines present in the ventrolateral and centre-median nuclei as spines in the thalamus have received relatively little attention (Špaček & Lieberman 1974) and also because dendritic spines are a prominent feature of the centre-median nucleus. The electron-microscopical description of dendritic spines closely parallels the findings from a study of Golgi-impregnated material of the same nuclei in the monkey (T. Tömböl, personal communication). With the electron microscope spines are found to be considerably more common in the centre-median nucleus than the ventrolateral nucleus, most arising from small dendritic shafts, which is in accord with observations in Golgi preparations of dendritic spines attached to secondary but not primary dendrites of relay cells. Spines are a prominent feature of the glomerular complex where a single LR terminal makes numerous synaptic contacts with a relay cell dendrite and its associated spines, and it is interesting that in Golgi preparations one type of axon is found closely related to the spinous appendages and shafts of the proximal portion of the relay cell secondary dendrites, from which one may deduce that this is a major site of glomerular integration. Multivesicular bodies are frequently present in the dendritic shaft subjacent to the spine and there are several reasons for regarding this relationship as a significant one. Not only are multivesicular bodies commonly encountered subjacent to spines arising from intraglomerular dendrites, but in the interglomerular neuropil 20 % of the spines observed in the centre-median nucleus and a third of the spines found in the ventrolateral nucleus have this property. When serial sections were used to trace spines where the parent dendrite did not apparently contain a multivesicular body, subsequent sections often revealed this organelle subjacent to the spine. Although multivesicular bodies have been described in detail in various parts of the central nervous system (Palay 1963) no proposals have been made concerning their function, nor has such a relationship between this organelle and any particular part of the neurone been recognized. The significance of this association remains to be determined, but the relative lack of a spine apparatus in the spines of the centre-median and ventrolateral nuclei may provide a clue.

Like spines in other areas of the brain, most spines in the ventrolateral and centre-median nucleus (and every spine traced through with serial sections) receive synaptic contacts. Although every glomerular spine is post-synaptic to an LR terminal, only 80 % of interglomerular dendritic spines encountered in the centre-median nucleus were post-synaptic to SR terminals at asymmetrical synapses; the remainder were post-synaptic to P or F profiles. All the spines

Description of plate 35

Figure 125. A degenerating terminal (dt) issuing from a myelinated fibre (mf) and making a contact with a dendrite (D) in the ventrolateral nucleus, 5 days after damage of the cerebellar nuclei. (Magn. × 30000.)

Figure 126. A myelinated fibre (mf) continuous with a degenerating axon bouton (dt), filled with filaments (f), which makes synaptic contact with a dendrite (D) in the ventrolateral nucleus 5 days after destruction of the cerebellar nuclei (Magn. × 30000.)

Figure 127. A late degenerating terminal (dt) making a synapse upon a dendrite (D) in the ventrolateral nucleus, 5 days after destruction of the cerebellar nuclei. The terminal has shrunk and its cytoplasm is so dense that filamentous material is not visible, and synaptic vesicles appear indistinctly as pale discs. Observe the glial process (gl) encroaching upon the terminal. (Magn. × 30000.)

Figure 128. A late degenerating terminal (dt) pre-synaptic to a dendrite (D) and a P profile (P) in the ventrolateral nucleus, 5 days after destruction of the deep nuclei of the cerebellum. (Magn. × 30000.)

observed in the ventrolateral nucleus were post-synaptic to SR or LR terminals. The significance of these observations is uncertain without serial sections through every spine to ascertain whether the random plane of section misses an asymmetrical synapse. Although P profiles are pre-synaptic to spines which also carry an SR terminal, F boutons are only pre-synaptic to spines by themselves or in company with another F terminal. It thus seems highly likely that some spines in the centre-median nucleus are only post-synaptic to F boutons, which would be inhibitory if the proposed correlation between symmetric synaptic specializations and inhibitory action is correct. Although spines which receive only symmetrical synapses have been seen upon cell bodies (Peters & Kaiserman-Abramof 1970) and upon axon initial segments (Westrum 1970; Kemp & Powell 1971), no analogous situation involving *dendritic* spines has previously been reported. There is a relationship between F axo-spinous contacts and the calibre of the parent dendritic shaft; in the centre-median nucleus 75 % of spines arising from proximal primary dendrites and all somatic spines seen to be post-synaptic are contacted by F boutons, which is not surprising in view of the fact that the majority of F synapses are located on cell somata and proximal dendrites. In the ventrolateral nucleus no F axo-spinous synapses are seen, nor are any spines found attached to cell somata or proximal dendrites. In both nuclei dendro-spinous contacts involving pre-synaptic P dendritic profiles are not uncommon.

Although only 50 % of spines were observed to form part of a synaptic dyad (figure 38) this percentage becomes more impressive if one realizes that most spine dyads were found in random single sections. The observation that one-third of dyads involved only a single pre-synaptic axonal profile suggests that this spinous dyadic relationship is a functionally significant one. It could be argued that the majority of dyads, which are post-synaptic to two separate terminals, are merely fortuitous findings resulting from the locations of spines on dendritic shafts which are heavily studded with synaptic contacts. Such a proposal would not explain why the dyadic pair of pre-synaptic profiles are nearly always of the same type of terminal, whether SR or F boutons; nor would it account for the finding that dyadic synaptic arrangements are also located on somatic spines and proximal dendrites, which relatively rarely bear synaptic contacts. If chance played a significant rôle in the occurrence of dyadic patterns one would expect to find such arrangements elsewhere, such as in the cerebral cortex, but such a constant relationship has not been found although stellate cell varicose dendrites are usually studded with synapses. However, Peters & Kaiserman-Abramof (1970) in the study of the small pyramidal neurones of the rat cerebral cortex mentioned that somatic spines were post-synaptic at a symmetrical synapse and that there might be a second synapse on the adjacent perikaryal membrane.

Whatever the effect of a synaptic impulse is upon a spine, it must overcome the resistance of the spine pedicle before it can affect the parent dendritic shaft. On account of the narrow calibre of many spine pedicles, and thus their high resistance, Diamond, Gray & Yasargil (1970) have proposed that spinous appendages serve the function of isolating a synaptic input from ongoing activity in the dendritic shaft, thus enabling a spine to function as a relatively noise-free input. Such a theory is difficult to reconcile with the occurrence of dyadic synaptic arrangements in which a single pre-synaptic terminal may affect spine and parent dendrite simultaneously, the axo-dendritic synapse apparently short-circuiting the axo-spinous contact. It is also possible that some pairs of pre-synaptic terminals which form dyadic arrays originate from the same pre-terminal axon, and the resultant effect would be functionally equivalent to the dyad with a single pre-synaptic terminal. The glomerular spines are a particular instance of

such short circuits: a single large profile, the LR terminal has multiple synaptic contacts with a dendritic shaft, which would be activated simultaneously with the spines. If spines are not mechanisms to isolate, but rather to weight the various synaptic inputs (Rall 1970) then a dyadic array with a pre-synaptic SR bouton seems to represent nil weighting since the shaft synapse is active whatever the length resistance of the spine pedicle. *Perhaps the delay with which any potential change must reach the dendritic shaft following the simultaneous firing of both shaft and spine synapses is the significant point as these spines would be a means of lengthening the period of synaptic influence rather than isolating or dissipating it.*

The glomerulus

Emphasis has been placed upon the similarity of the elements constituting the basic framework of glomeruli in various thalamic nuclei, but the differences in detail which do exist between the glomeruli present in the individual thalamic nuclei should also be considered. In the ventrolateral and centre-median nuclei there is little evidence of the dendritic bulbous protrusions or short side branches which are a frequent component of glomeruli within the feline lateral geniculate nucleus (Peters & Palay 1966; Famiglietti & Peters 1972) but instead the axon terminals and pre-synaptic dendritic profiles are grouped around a central dendrite. In this respect the ventrolateral and centre-median nuclei are more like the feline ventroposterior and medial geniculate nuclei which have central dendritic elements (Jones & Powell 1969*b*; Jones & Rockel 1971), although both shafts and side branches, rather than a centrally placed axon. Examination of the monkey ventroposterior nucleus shows that the glomeruli there also have central dendrites, but dendritic protrusions were not seen whereas in the lateral geniculate nucleus they were easily found. The most impressive feature of glomeruli is their complexity, and this has become particularly evident from the use of serial sections (Ralston & Herman 1969; Le Vay 1971; Famiglietti & Peters 1972; Špaček & Lieberman 1974). Various models of glomerular organization have been proposed in an attempt to formulate a functional hypothesis, and whether or not these models reflect differences in detailed synaptology between the individual thalamic nuclei studied, it is clear that the glomerulus represents a focus of synaptic activity between numerous pre- and post-synaptic profiles which are principally of three types. The first is an extrinsic (main relay nuclei certainly, centre-median nucleus probably) presumably excitatory axon terminal, which is presynaptic to both the other elements, the dendrite of a relay cell and the pre-synaptic dendrites of an intrinsic presumably inhibitory interneuron. The LR axon terminal is the pre-synaptic element at more than half the glomerular synapses, and as 60 % of these contacts are upon the conventional dendrite it is clear that the principal event within a glomerulus is the transmission of information from an ascending afferent pathway to the relay cell. The relay cell is activated at two sites, the dendritic shafts and the spines which are carried by at least half of the intraglomerular dendrites in the ventrolateral and centre-median nuclei. Spines have been a major finding in the present study, but whether their greater frequency in the ventrolateral and centre-median nuclei is more apparent than real is unclear because spines arising from intraglomerular dendrites are also not difficult to find in the ventroposterior and lateral geniculate nuclei in the monkey. The functional importance of spines in glomeruli cannot be denied, for when present they are always post-synaptic (Špaček & Lieberman 1974) and they may receive half the synaptic contacts of an LR bouton within a single glomerulus. The population of P profiles presents the greatest problem, as their large numbers and varied synaptic properties make for such complex

synaptic inter-relationships. Famiglietti & Peters (1972) have suggested that the triadic synaptic array, between optic axon terminal, 'ID' terminal (pre-synaptic dendrite) and thalamocortical relay dendrite, is crucially important in the glomeruli of the feline lateral geniculate nucleus. Such an arrangement, analogous to the LR bouton-P profile triad in the ventrolateral and centre-median nuclei, they consider to be 'the principal unit of centripetal transmission',

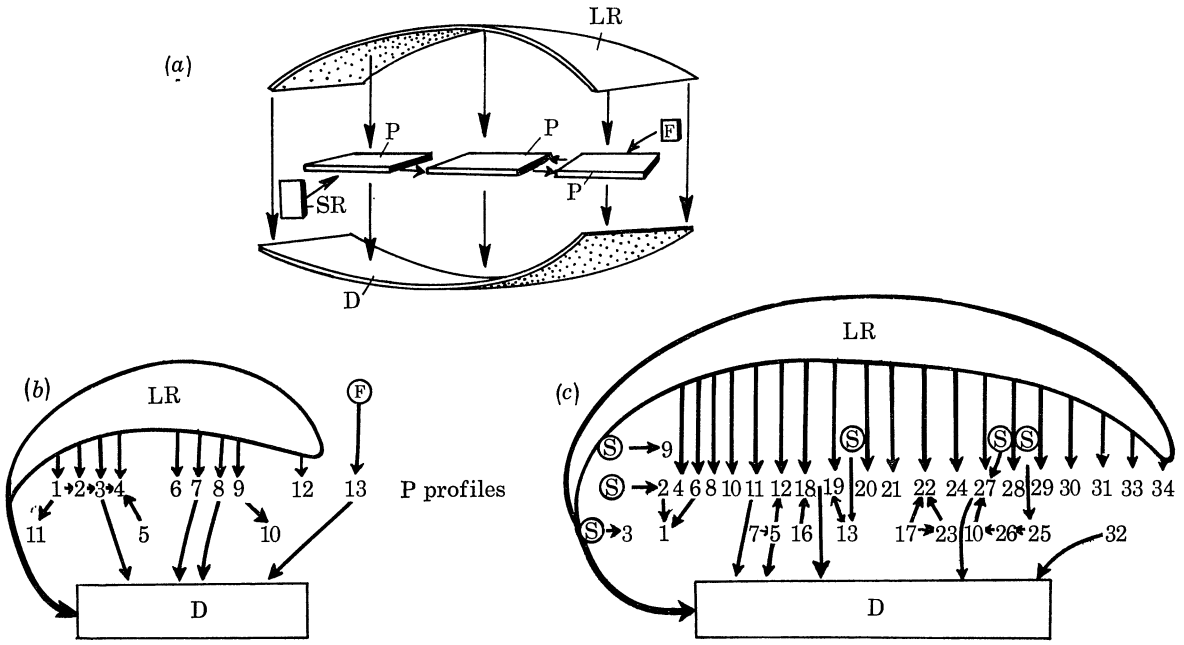


FIGURE 129. A simple anatomical model of the glomeruli in the centre-median and ventrolateral nuclei.
(*a*) In this hypothetical model (see text) the LR terminal (LR) makes synaptic contact with the main relay dendrite (D) and a population of P profiles (P). The latter have complex synaptic interconnections, may also receive contacts from F and SR boutons, and are pre-synaptic to the main relay dendrite. It is proposed that the P profiles function as a group interposed between main ascending afferent (LR) and main relay cell dendrite (D).
(*b*) and (*c*) are examples of glomeruli studied with long ribbons of serial sections, their synaptic connections schematically illustrated as support for the hypothetical model in (*a*). (*c*) is the large glomerulus from the centre-median nucleus shown in figures 43–55, plates 13–15, and schematically outlined in figures 56 and 57.

and suggest that the triad 'essentially defines the morphological nature' of the lateral geniculate nucleus. The first part of the statement by Famiglietti & Peters is an attractive hypothesis, but is probably an over-simplification when considered with the present data from the ventrolateral and centre-median nuclei. If triads are the fundamental units, how commonly should they be observed? Only 60 % of the sample of glomeruli contained them, although a single glomerulus could have up to three. Since the central glomerular dendrite is always post-synaptic to the LR bouton and 50 % of P profiles are found to be post-synaptic to the LR bouton, it is significant, even when one takes into consideration the technical bias of this analysis, that only 12 % of P profiles take part in triads with LR boutons. There are, however, certain other properties of glomeruli: triads with P or F processes in place of LR boutons, or with three P profiles; sequential synaptic arrays, with three or more serial synapses which are nearly as common as triads in the ventrolateral and centre-median nuclei (although similar 'iso-synaptic' contacts were reported to be only occasional in the lateral geniculate nucleus (Famiglietti & Peters 1972)); finally, there are a significant number of reciprocal dendro-dendritic synapses in glomeruli.

A useful morphological model must reconcile these various data and offer an explanation for the complex admixtures of the several types of synaptic array which take place within a glomerulus. It is for these reasons that a concept of a repeating unit, a single P profile intercalated between axon bouton and relay cell dendrite is inadequate. If the glomerulus is considered *as a whole* however it is possible to put forward the hypothesis (figure 129*a*) that within a glomerulus there is a system of pre-synaptic dendrites intercalated between the axon bouton and the relay cell dendrite. In the ventrolateral and centre-median nuclei the available evidence strongly suggests that the LR bouton is pre-synaptic to most, though not necessarily all of the P profiles – two-thirds of P profiles found to be post-synaptic within the sample of serially sectioned glomeruli. There are also many contacts between P profiles, and an equivalent number of dendrodendritic synapses with the relay cell dendrite; the triads and sequential serial arrays are a manifestation of the complex interaction occurring between individual members of the glomerular set of P processes. Unlike the earlier concept of a triadic unit, this hypothesis can include complex synaptic arrangements. Thus, in figure 129*b*, the glomerulus has 13 P profiles: the LR bouton is pre-synaptic to eight, of which three are pre-synaptic to the relay dendrite, but four P profiles also form a sequential array and of these the first three are post-synaptic to the LR bouton and the third contacts the relay dendrite. Figure 129*c* is a similar treatment of the large glomerulus illustrated in figures 43–55, plates 13–15. Some P processes do not appear to be post-synaptic to the LR terminal, but this may be partly explained by experimental error, and partly because some presynaptic dendrites are post-synaptic to SR and F axons at the glomerular periphery, and other P processes may be contacted in other glomerular complexes. Compared with the number that are post-synaptic, fewer P profiles are pre-synaptic, but similar technical considerations will apply, and a proportion of P processes may be pre-synaptic to dendrites in other glomeruli. The link between glomeruli can be very close, as when one axon forms several *en passant* LR expansions all of which contact the same relay dendrite while some share the same P profiles.

The inter-glomerular neuropil

Although the non-glomerular neuropil accounts for at least half of the volume of ventrolateral nucleus and still more of the centre-median where it is penetrated by considerable fibre tracts, an analysis of its synaptic organization presents several problems, particularly because of the inability to differentiate between the various small calibre dendrites. There are at least three types of cell from which these could be arising, the relay cell and two interneurons; of the latter they could be dendrites of the F axon cell, if this is not in the reticular nucleus, and they could also include those parts of the dendrites of P cells where the presynaptic specializations are not apparent. The synapses which are present may be either from axon terminals of the SR and F type, or they may be from presynaptic dendrites; some of the SR axons certainly arise in the cerebral cortex and globus pallidus, and it is possible that others arise elsewhere (e.g. the substantia nigra in the case of the ventrolateral nucleus) or are collaterals of the relay cells. Observations of Golgi-impregnated material indicate that all types of dendrites in the neuropil are contacted by cortico-thalamic fibres (Kiss & Tömböl 1972) which would suggest that dendrites of interneurons as well as of relay cells are influenced by SR axon terminals of extrinsic origin, and this is in accord with the electron microscopical finding of degenerating SR terminals making a synapse upon P profiles after damage of the cortex.

Figure 130 is a schematic summary of the major types of pre- and post-synaptic profiles in

the two subdivisions of thalamic nuclei, the glomeruli and neuropil. In relation to the relay cell the demarcation between the glomeruli, within which the fibres of the ascending pathways to the nucleus terminate as LR boutons, and the intraglomerular neuropil is clearly observed. The latter can be considered in two parts, on the basis of the type of axon terminal making the predominant synapses. The first area, the cell soma and proximal primary dendrite, is the main sphere of influence of the F axon. The second and larger subdivision, concerned with the finer arborizations of the relay cell dendrites, is the region in which most SR terminals form synapses.

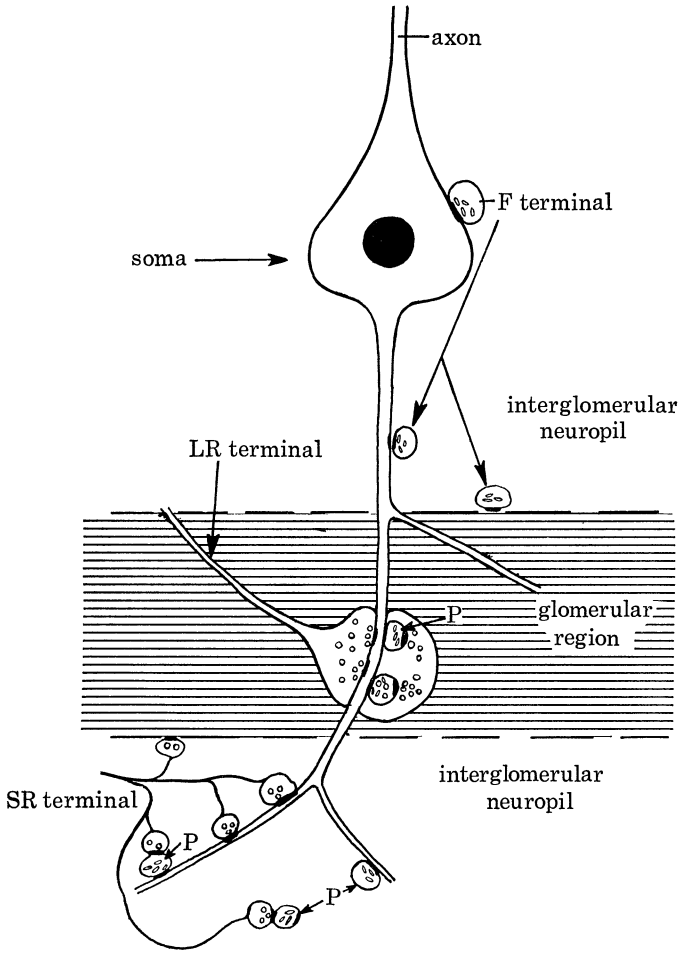


FIGURE 130. A schematic representation showing the distribution of the various afferents impinging upon a thalamic relay cell. The interglomerular neuropil can be considered in two parts: the cell somata and main stem dendrites receive synapses mainly from inhibitory F axons; the peripheral dendrites by excitatory SR axons (some of which are terminals of axons from cells in the motor cortex or globus pallidus) and intrinsic P profiles. The glomerular region is the site of termination of the main ascending afferents (cerebello-thalamic fibres in the ventrolateral nucleus) as LR boutons. The origin of the LR terminals in the centre-median nucleus is still speculative.

It thus appears that whereas information from more peripheral levels of the central nervous system reaches the thalamic relay cells through the glomerulus, modifying and integrating influences from other parts of the cerebral hemisphere affect the relay cell's more distal dendrites in the inter-glomerular neuropil. In addition, in the glomeruli and upon both the proximal and distal parts of the neurons in the neuropil pre-synaptic P profiles make synaptic contacts, and it is possible that a pre-synaptic dendrite may make a synapse upon the dendrites of different

cells, either by passing between adjoining glomeruli or within the neuropil. These pre-synaptic dendrites may in turn receive synapses from either LR boutons within glomeruli or from SR terminals in the neuropil.

Experimental findings

Cortico-thalamic pathways to the ventrolateral and centre-median nuclei in the monkey terminate as SR profiles, which was not unexpected in view of previous descriptions in various feline thalamic nuclei (Szentágothai *et al.* 1966; Guillery 1969; Jones & Powell 1969*c*; Famiglietti & Peters 1972; Rinvik 1972) and in the lateral geniculate nucleus of the monkey (Wong-Riley 1972*c*) of degenerating small dark boutons with asymmetrical synaptic thickenings following cortical lesions. If the postulated correlation between vesicle morphology and synaptic function is correct (Uchizono 1965; Larramendi *et al.* 1967) these should be excitatory. It was surprising, however, to find that the terminals of pallido-thalamic fibres within the ventrolateral and centre-median nuclei also form part of the large population of SR profiles, and this indicates an important difference between the ventrolateral nucleus and other main relay nuclei. The latter receive two extensive afferent pathways, an ascending sensory pathway and a descending corticofugal pathway, whereas the ventrolateral nucleus also receives a third afferent fibre connection from the globus pallidus. It is significant that in experiments in which the somatic sensory cortex was damaged in addition to the motor area the density of the degenerating terminals in the ventral posterior nucleus was much greater than in the ventrolateral. This observation suggests that in the principal nuclei which receive axons ending as SR boutons predominantly from the cortex these are equivalent to the *sum* of those from the motor cortex and globus pallidus together in the ventrolateral nucleus. In other words, the *total* number of fibres to the various principal nuclei from other sites in the cerebral hemisphere may be of the same order, whether they are from a single source such as the cortex or from more than one as in the case of the motor cortex and globus pallidus.

The dendrites post-synaptic to cortico-thalamic terminals in the centre-median nucleus are a quite distinct group from those dendrites contacted by other types of degenerating SR boutons, the pallido-thalamic terminals in both the ventrolateral and centre-median nuclei and corticothalamic terminals in the ventrolateral nucleus (and also the ventroposterior nucleus): they are four times less often post-synaptic at more than one contact, a finding which will admit of two separate but by no means mutually exclusive interpretations. It may indicate either that the cortico-thalamic SR boutons in the centre-median nucleus contact a different class of neuron from those synaptically involved with the other types of extrinsic SR terminal, or that they synapse on a different part of a similar type of neuron. In view of the numerous spines to be found in the centre-median nucleus it is quite possible that these data are a reflexion of a differential innervation by extrinsic terminals upon centre-median cells: the pallido-thalamic terminals contact the shafts whereas the cortico-thalamic terminals contact the spines (which are less often plurally post-synaptic) of the same type of neuron. The cortico-thalamic terminals in the centre-median nucleus also differ strikingly from other classes of extrinsic SR bouton studied here, as they have a second synapse four times as frequently. This observation parallels the greater frequency of multi-synaptic SR boutons in the normal centre-median nucleus compared with the ventrolateral nucleus, as both normal and degenerating SR terminals have been seen to form triadic arrays in the centre-median neuropil. It is tempting therefore to equate triad-forming SR boutons with cortico-thalamic terminals, and there is

supporting evidence for this concept since P profiles are twice as often post-synaptic to cortico-thalamic terminals in the centre-median nucleus as they are to cortico- and pallido-thalamic axon terminals in the ventrolateral nucleus, and P profiles form part of the triadic arrays. As P profiles are probably the terminal portions of dendrites of thalamic interneurons this may be a further demonstration of the differential nature of afferent inputs to the various classes of thalamic neurons. However, triadic arrays require multi-contacted dendrites and cortico-thalamic terminals in the centre-median nucleus synapse on dendrites which are far less frequently secondarily contacted than is the case for other classes of extrinsic SR boutons. Triads are particularly associated with spines in the centre-median nucleus and so we could be failing to observe further synapses which are found on the shaft of the parent dendrite from which a spine arises. Whatever the functional significance of the difference in termination of the cortico-thalamic terminals between the centre-median and relay nuclei proves to be, it should be noted that in the relay nuclei the cortico-thalamic fibres constitute a reciprocal connection between the thalamus and the cortex, whereas there is little evidence that the centre-median is projecting to the cortex.

The cerebello-thalamic pathway terminates in the ventrolateral nucleus as LR boutons within glomeruli, and is equivalent to the ascending pathways which terminate as LR boutons in glomeruli in the sensory relay nuclei. Many LR terminals in the ventrolateral nucleus remain unaffected by cerebellar lesions, however, and although technical factors may be partly responsible, it is possible that there is another origin for these axons. One of these may be the substantia nigra as there is light-microscopical evidence of a pathway to the pars medialis of the ventrolateral nucleus (see, for example, Cole, Nauta & Mehler 1964; Carpenter & Strominger 1967; Faull & Carman 1968; Rinvik 1975). Technical difficulties have prevented us from separating out the architectonic subdivisions of the ventrolateral nucleus for individual study, but the material has been taken mainly from the pars medialis and pars oralis of the ventrolateral nucleus. Nigro-thalamic fibres may well terminate as LR boutons in the ventrolateral nucleus, but they could end as SR boutons as our observations indicate that many SR terminals appear normal after destruction of the motor cortex or globus pallidus or even after both in the case of the centre-median nucleus. Such unaccounted SR boutons may also arise from collateral fibres of thalamic relay neurones: thalamo-cortical in the case of the ventrolateral nucleus, and thalamo-striate in the centre-median nucleus. If this is so one might expect such thalamic collateral terminals to have a similar morphology to those boutons found at the termination of these pathways in the cortex and striatum, which have been shown to have asymmetrical synaptic contacts and round synaptic vesicles (Sloper 1973; Kemp & Powell 1971).

No degeneration of LR terminals was found in the centre-median nucleus after lesions of the motor cortex or globus pallidus, and it would seem likely therefore that these are the terminals of axons arising in the midbrain tegmentum (Nauta & Kuypers 1957).

Functional correlations

In view of the complexity of the synaptic organization within the nuclei of the thalamus, it is not surprising that different interpretations have been made of the interrelations between the neuronal processes (see, for example, Le Vay 1971; Famiglietti & Peters 1972; Špaček & Lieberman 1974) and that several hypotheses have been proposed to explain the functional properties of the constituent neurons.

The rôle of the P profiles and of the glomeruli are two problems which are interdependent since the synapses related to the P processes form a major feature of the glomeruli. The primary processing of the ascending afferent input to thalamic nuclei occurs within glomeruli but one cannot formulate the integrative mechanism until one has decided upon the mode of operation of the P profiles. The putative cells of origin of P processes in the ventrolateral and centre-median nuclei, Golgi type II cells, have been shown to possess axons in Golgi-stained preparations and similar results have been reported for analogous interneurons in other thalamic nuclei (Tömböl 1966–67; Morest 1971; Ralston 1971; Famiglietti & Peters 1972; Pasik *et al.* 1973). However, apart from figure 3 there is only one previous report of an electron microscopically identified axon initial segment arising from this type of cell (Morest 1971) and it has therefore been suggested that these interneurons may be amacrine type cells (Le Vay 1971; Schiebel, Schiebel & Davis 1972; Wong 1970; Lieberman 1973). Ralston (1971) has proposed that the cells of origin of the pre-synaptic dendrites may exert effects upon the other neurons through both their axons and their dendrites. The action potential arising in the initial segment would be conducted along the axon and would also invade the proximal dendrites to cause release of transmitter. The action potential would not reach the finer terminal dendrites, however, and they would be influenced only by the boutons making synapses upon them. If these peripheral dendrites were sufficiently depolarized by the terminals to which they were post-synaptic, even locally, they would release transmitter and each dendritic branch could act independently. Morest (1971) has also pointed out that the reciprocal nature of dendro-dendritic synapses argues for a specialized and localized function. This functional dissociation of pre-synaptic dendrites from the rest of the cell is an attractive hypothesis, particularly in view of the peculiar anatomy of P processes, which both in Golgi preparations and with electron microscopy appear tortuous, irregular dendritic appendages, attached by long narrow stems to parent dendritic shafts (Guillery 1966; Famiglietti & Peters 1972; Lieberman & Webster 1972; Grossman, Lieberman & Webster 1973). Grossman *et al.* (1973) have commented upon the similarities between pre-synaptic dendritic appendages and spines arising from conventional dendrites, and have postulated that they may have analogous functional properties.

A combination of Ralston's hypothesis of local dendritic activation with the present analysis of glomerular structure provides the basis for a functional model (figure 131) of the complex glomeruli found not only in the ventrolateral and centre-median nuclei but in the principal nuclei in general. The multi-synaptic LR terminal, the ascending excitatory input to the glomerulus, forms numerous synapses with the relay cell dendrite and the P profiles. Some of the latter are connected by irregular processes to pre- and post-synaptic P profiles in adjoining glomeruli, while others receive synapses at the periphery of the glomeruli from SR and F axon terminals, but their morphological characteristics strongly suggest that *the P profiles within one glomerulus function as a group* (figure 129). The initial event in glomerular transmission occurs when an action potential reaches the LR terminal, causing release of transmitter from its many synapses which depolarize the central dendrite and most (perhaps all) of the P profiles within that glomerulus (figure 131 – 1). If Ralston's hypothesis for the local firing of dendritic synapses is correct, depolarization of the P profiles will cause them in their turn to release transmitter (thought to be inhibitory in function) and therefore, after a further synaptic delay, the central dendrite will suffer a hyperpolarizing influence (figure 131–2). However, there are also numerous synapses between P profiles so that after a similar synaptic delay the P profiles themselves will be inhibited, i.e. disinhibition. In other words, as the relay dendrite becomes hyperpolarized,

the cause of this potential change will be diminished or removed, so allowing the glomerular central dendrite once more to become fully receptive to the excitatory influence of the LR terminal (figure 131 – 3).

Such a mechanism would introduce an important time factor and this has also been recognized by Colonnier (1974) in a theoretical discussion of the significance of the synaptic organization within a glomerulus. Essentially there is a switch which is closed for a short period of time during which information flows from a more peripheral pathway to the relay cell; the switch is then opened by dendritic synaptic inhibition which gradually dissipates itself, allowing the switch to close once more. But between the initial current flow and the opening of the switch there is a time lag with a minimum of one synaptic delay. There is a similar time lag between the onset

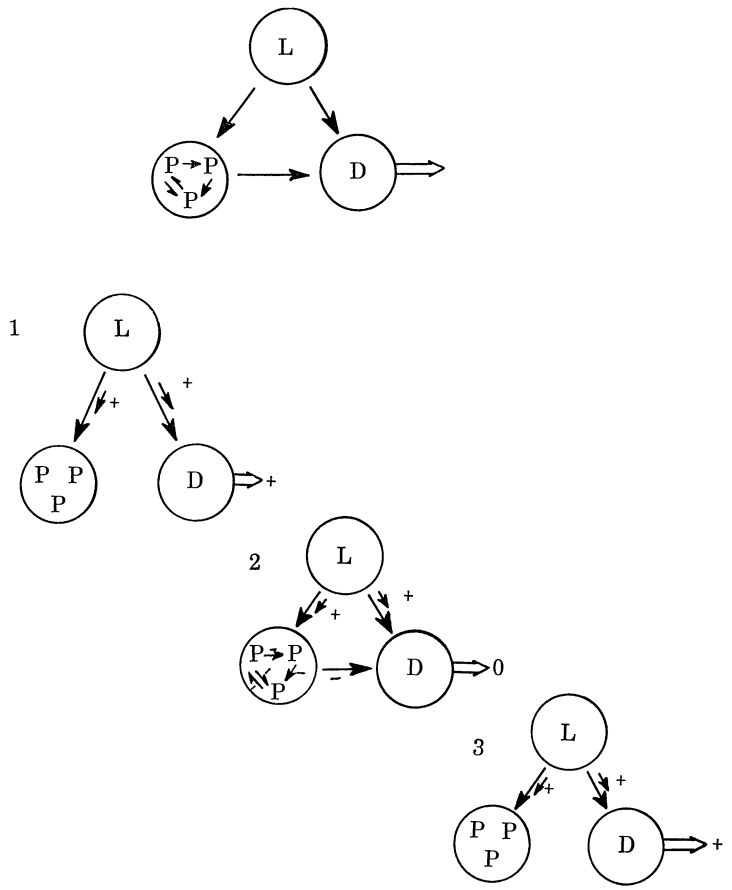


FIGURE 131. A hypothetical functional model of the glomerulus. The top figure shows the anatomical connections, considering the glomerulus to be as figure 129*a*. 1–3 suggest a possible explanation of glomerular function, shown in a series of steps (see text).

of the P profile inhibition of the conventional dendrite and their inhibition of each other. So we arrive at a cyclical series of events: excitation followed by inhibition, then excitation again if the relay neuron becomes sufficiently depolarized, the ratio of these two parts of the cycle being determined by the effectiveness of the inhibition of the P profiles upon the relay dendrite relative to that exerted upon each other. Modification of this influence may occur by the SR and F axon terminals either at the periphery of the glomerulus or through the synapses they make upon dendrites of relay cells and interneurons in the neuropil, which may augment or

depress the level of inhibitory effectiveness (figure 130). The interglomerular connections made by P processes suggest that dendritic inhibitory effects in groups of glomeruli are interrelated, a possible means for synchronizing the activation of various relay cell dendrites by several afferent axon terminals. Whether such related glomeruli form around dendrites of the same or different cells is not yet known, but it has been found that LR expansions formed *en passant* by a single fibre in adjoining glomerular aggregations and making synapses with the same dendrite, will share some of the same P processes.

This model of the sequence of events within a glomerulus could account for the excitatory post-synaptic potential (e.p.s.p.) followed by a long lasting inhibitory post-synaptic potential (i.p.s.p.) which has been found to be a characteristic feature of the response to stimulation of ascending afferent fibres of relay cells in all the principal nuclei of the thalamus, including the ventrolateral (see, for example, Andersen, Eccles & Sears 1964; Burke & Sefton 1966*a*; Purpura, Frigyesi, McMurtry & Scarff 1966; Singer, Pöppel & Creutzfeldt 1972). The longer duration of the i.p.s.ps could be due to the complex synaptic interrelation of the numerous P profiles within the glomerulus, which would result in their having a prolonged influence upon the relay dendrite. The anatomical observations could also account for the finding in the ventrolateral nucleus that the i.p.s.p. due to stimulation of the afferent fibres in the cerebellum was not dependent upon prior discharge of the relay cell (Purpura *et al.* 1966). Also relevant to the termination of the ascending afferent fibres upon P processes within glomeruli are the results of intracellular studies of the lateral geniculate nucleus in the cat by Singer *et al* (1972) which suggest direct excitation of interneurons by optic tract stimulation, as the i.p.s.ps could be consistently elicited by a lower threshold of electrical stimulation than was required for generating an orthodromic action potential in a relay cell, and the i.p.s.p. sometimes occurred before the excitatory response and resulted in a long lasting maintained inhibition.

The e.p.s.ps and action potentials of interneurons in response to stimulation of an ascending pathway (Andersen *et al.* 1964; Burke & Sefton 1966*a*; Purpura 1972; 1973) could be explained by assuming that there was sufficient depolarization of P processes to result in spread to their cell somata. The anatomical evidence indicates that these physiologically identified interneurons should be the cells of origin of the P profiles because the neurons giving off the F axon terminals would not be activated directly by the ascending LR terminals as the latter rarely make synapses outside the glomeruli in the principal nuclei, and the ascending pathways do not give off collaterals to the reticular nucleus (Jones & Powell 1971).

In addition to the functional correlates of the glomerular synaptic organization which have been discussed, there is the possibility of inhibitory interneurons being activated by axon collaterals of the relay cell as suggested by the results of physiological studies (Andersen *et al.* 1964; Burke & Sefton 1966*b*). Part of the post-synaptic inhibition of the relay cell may well occur through such a pathway in addition to the influence of the P processes within the glomeruli, and the finding of such inhibition on stimulation of the subcortical white matter 13 days after removal of the cortex (Andersen *et al.* 1964) can at present be explained only on this basis. This extra inhibitory mechanism might be one of the factors contributing to the long duration of the inhibitory process. The axon collaterals could arise and terminate either in the principal nuclei or in the reticular nucleus of the thalamus. Within the principal nuclei the collaterals could end as SR boutons upon P processes at the edge of glomeruli or within the neuropil, and they could also terminate upon the cells of origin of the F axons, the terminals of which make synapses upon the somata and proximal dendrites of relay cells. The reticular

nucleus may be involved in this pathway because of the evidence for thalamic relay cell axons giving off collaterals within the reticular nucleus and for the cells of this nucleus sending their axons into the principal nuclei (Schiebel *et al.* 1972; Jones 1975) together with burst discharges of cells in the nucleus synchronous with the inhibition of the relay cells upon sensory stimulation (Massion & Rispal-Padel 1972; Frigyesi & Schwarts 1972).

Lateral inhibition of relay cells has been found in the principal nuclei and has been studied in detail in the lateral geniculate nucleus of the cat (see, for example, Singer *et al.* 1972). For several reasons Singer *et al.* concluded that the inhibition was post-synaptic and that there was direct activation of interneurons by optic tract fibres. The finding of P processes passing from one glomerulus to another in the lateral geniculate nucleus of the monkey (Le Vay 1971), cat (Famiglietti & Peters 1972) and rat (Lieberman 1973) together with similar findings in the present study suggest that this might be one pathway for the post-synaptic inhibition of adjoining relay cells. The observation of Singer *et al.* (1972) that the e.p.s.ps of relay cells in response to light stimulation occasionally had smaller amplitudes during the rising phase of the large hyper-polarizing potential than those occurring spontaneously led them to suggest that the decrease could be due to 'the shunting effects of i.p.s.ps generated at dendritic sites close to the excitatory synapses.' The synapses which P processes from some glomeruli make on to relay cell dendrites in adjoining glomeruli may be the anatomical basis for the 'shunting effects'. The post-synaptic inhibition of adjoining relay cells could also be through axon collaterals and inhibitory interneurons.

The termination of the fibres from the cerebral cortex and the globus pallidus as SR boutons upon dendrites and P profiles in the neuropil and at the edge of glomeruli is in contrast to that of the ascending afferent fibres in the glomerulus and would indicate a difference in influence between these major afferent pathways to the centre-median and ventrolateral nuclei, which is in accord with electrophysiological observations. Electrical stimulation of the cortex has been shown to have both a facilitatory and inhibitory influence upon the relay cells of the principal nuclei. The facilitatory influence would be through the synapses which the corticothalamic fibres make upon the peripheral parts of the relay cell dendrites, the depolarization of which would augment the effects of the ascending axon terminals within the glomeruli (Kalil & Chase 1970; Andersen, Junge & Sveen 1972). The inhibitory effects would be mediated through more than one pathway and through interneurons (Purpura *et al.* 1966); the fibres from the cortex which end within the principal nuclei upon P processes in the neuropil or at the edge of glomeruli or upon the dendrites of F axon cells could be one pathway responsible for the inhibition, but it might also be through collaterals of the cortico-thalamic fibres which end in the reticular nucleus and there activate the cells of origin of the F axons. The different termination of axons from the cortex and the globus pallidus, as compared with those of the ascending pathways, could also explain the difference in response to stimulation of these pathways as found in intracellular studies; on stimulation of the afferent fibres from the cerebellum a monosynaptic e.p.s.p. followed by prolonged i.p.s.p. is recorded in relay cells of the ventrolateral nucleus but similar cells only produce a monosynaptic e.p.s.p. in response to stimulation of fibres from the globus pallidus (Purpura 1972); the complex and longer latency effects of stimulation of the cortex (Frigyesi & Schwartz 1972) could be due to further interconnections between the P processes and dendrites in the neuropil. The findings in table 5, on the types of profiles upon which fibres from the cortex and globus pallidus terminate in the two nuclei, suggest that the axons from these two sources would have similar effects in the ventrolateral

nucleus but that in the centre-median nucleus the fibres from the cortex would have more inhibitory influence and less excitatory, and the reverse would be true of those from the globus pallidus.

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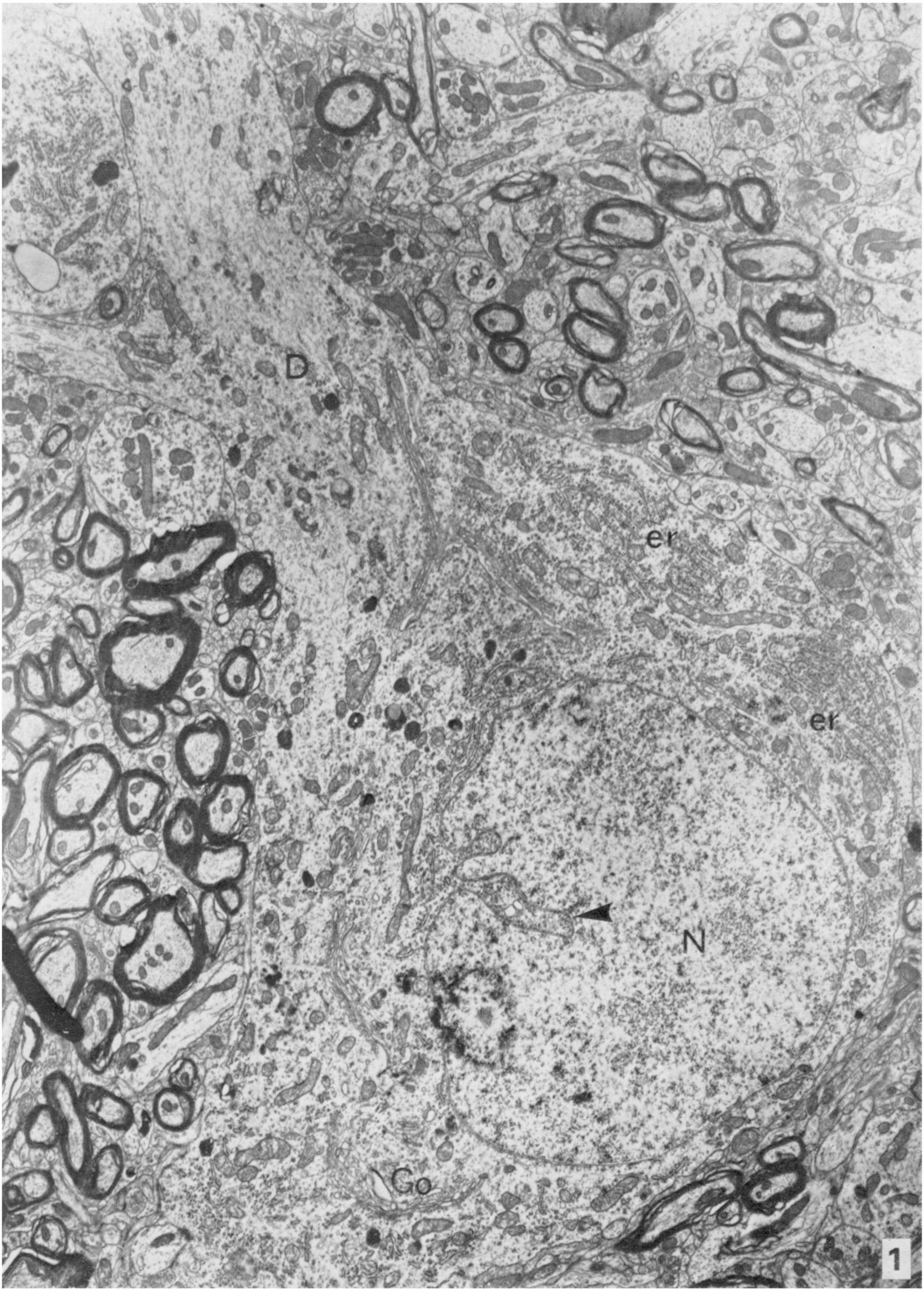
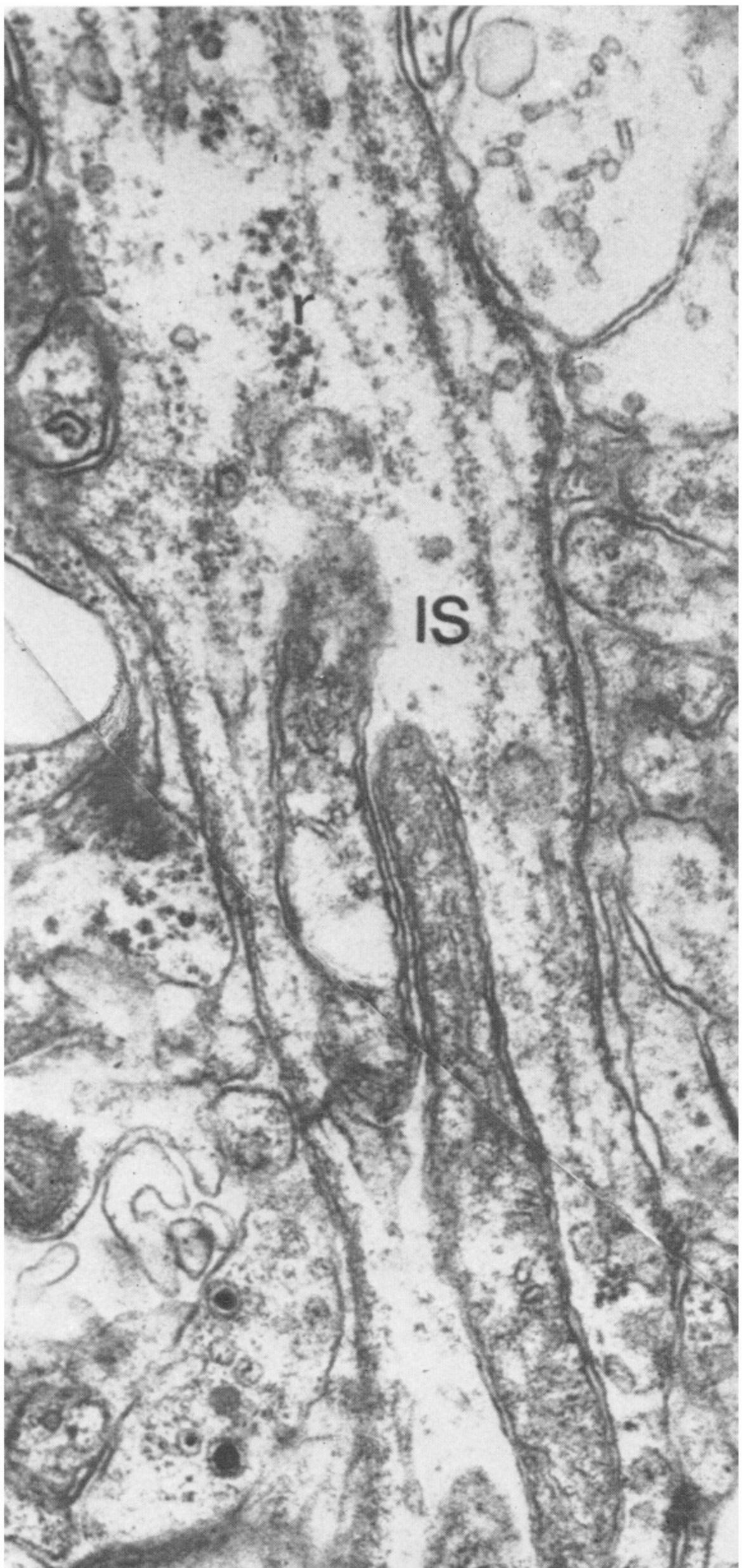
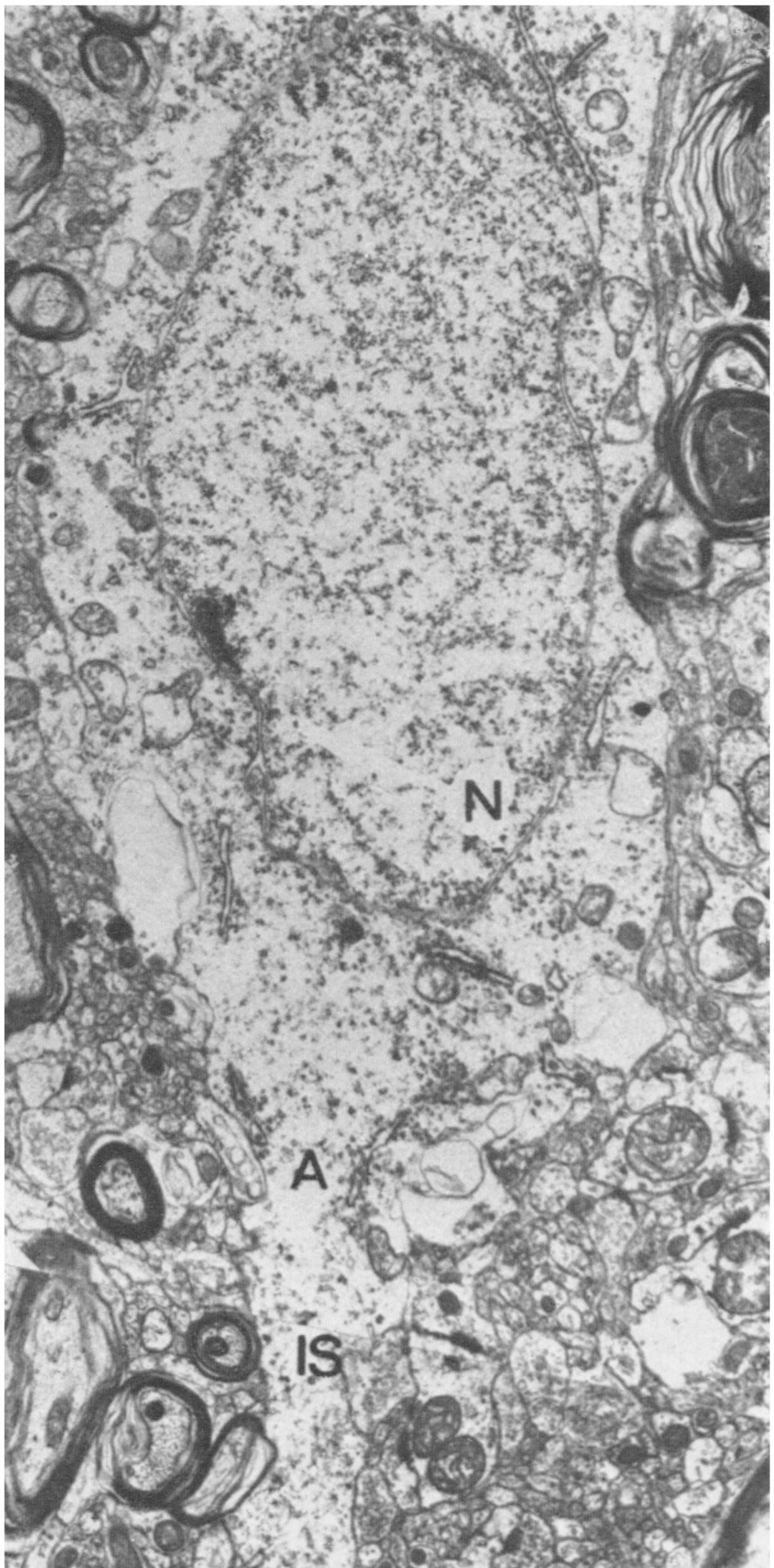
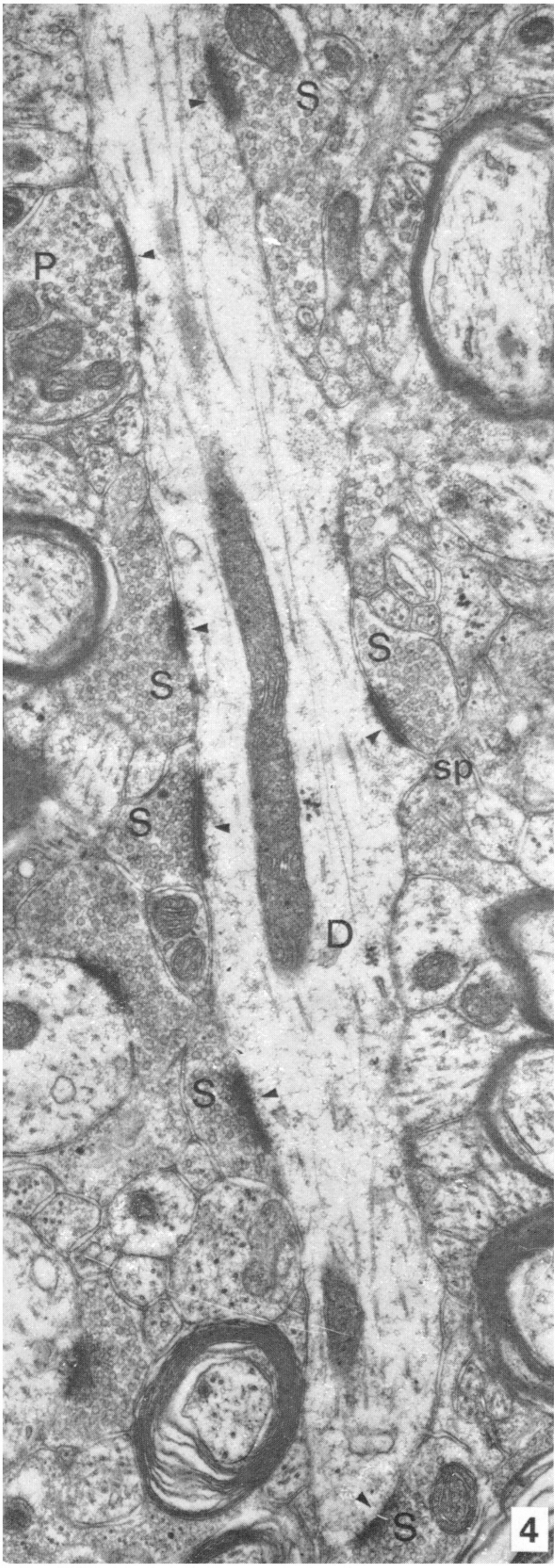


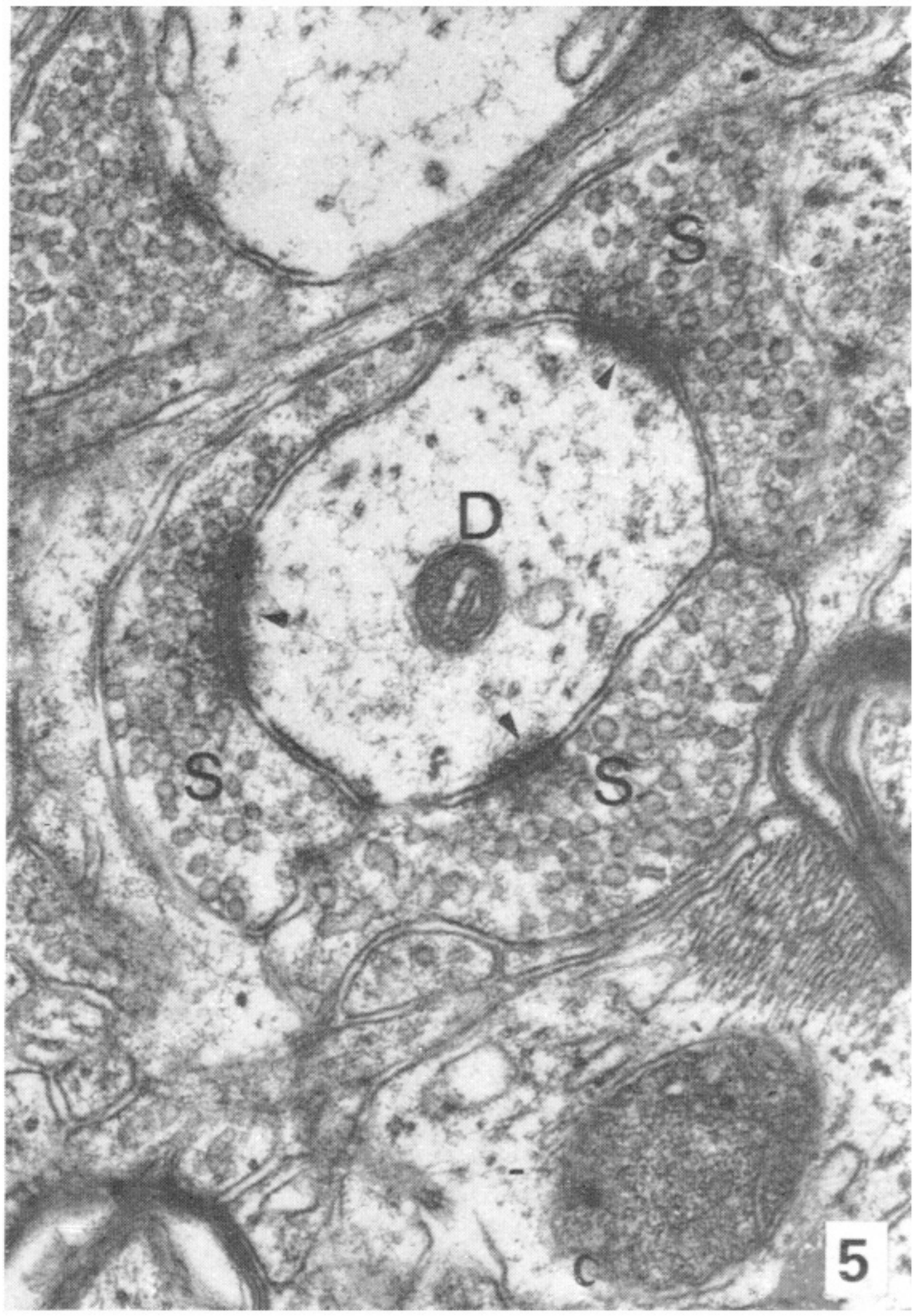
FIGURE 1. For description see opposite.

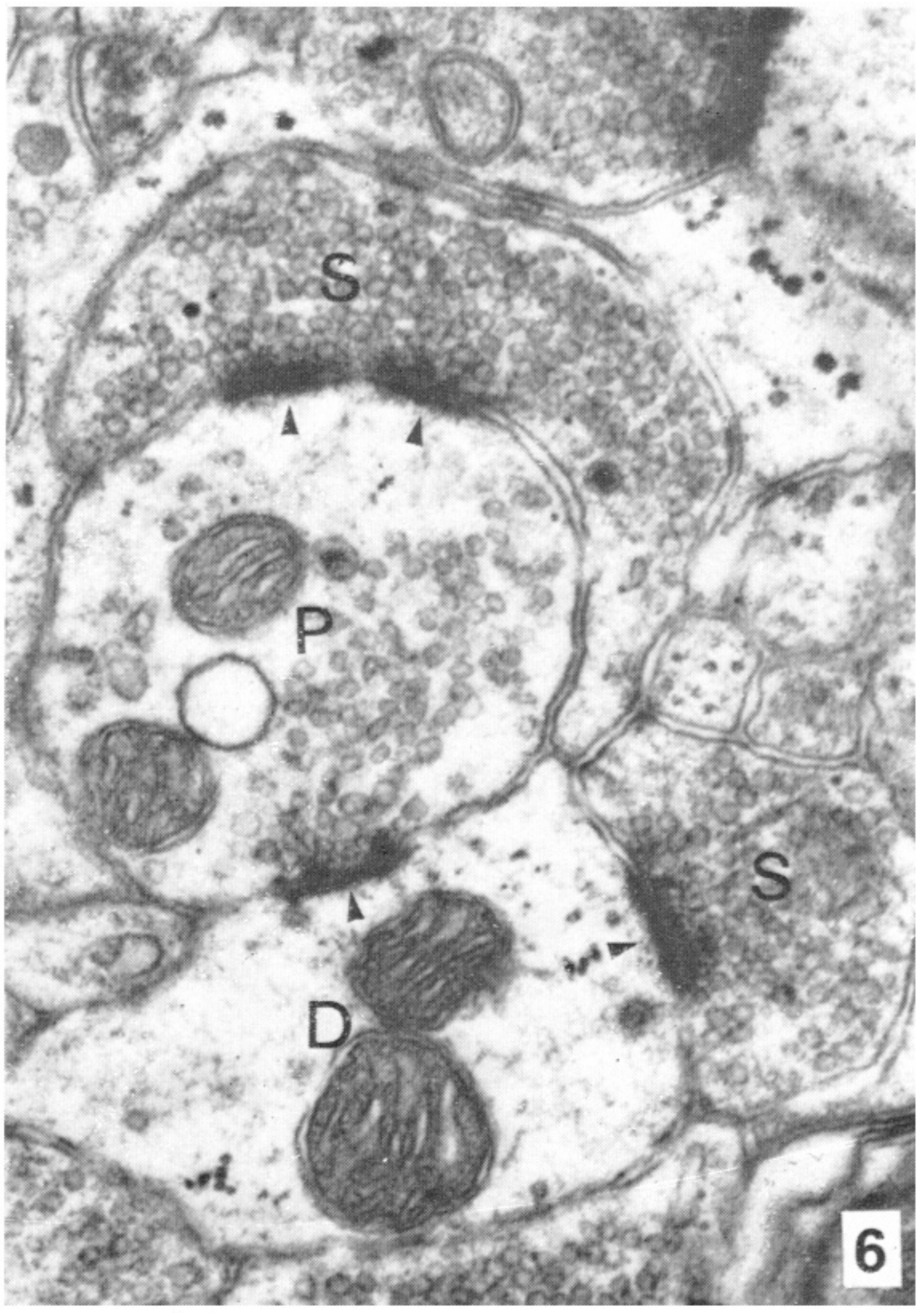




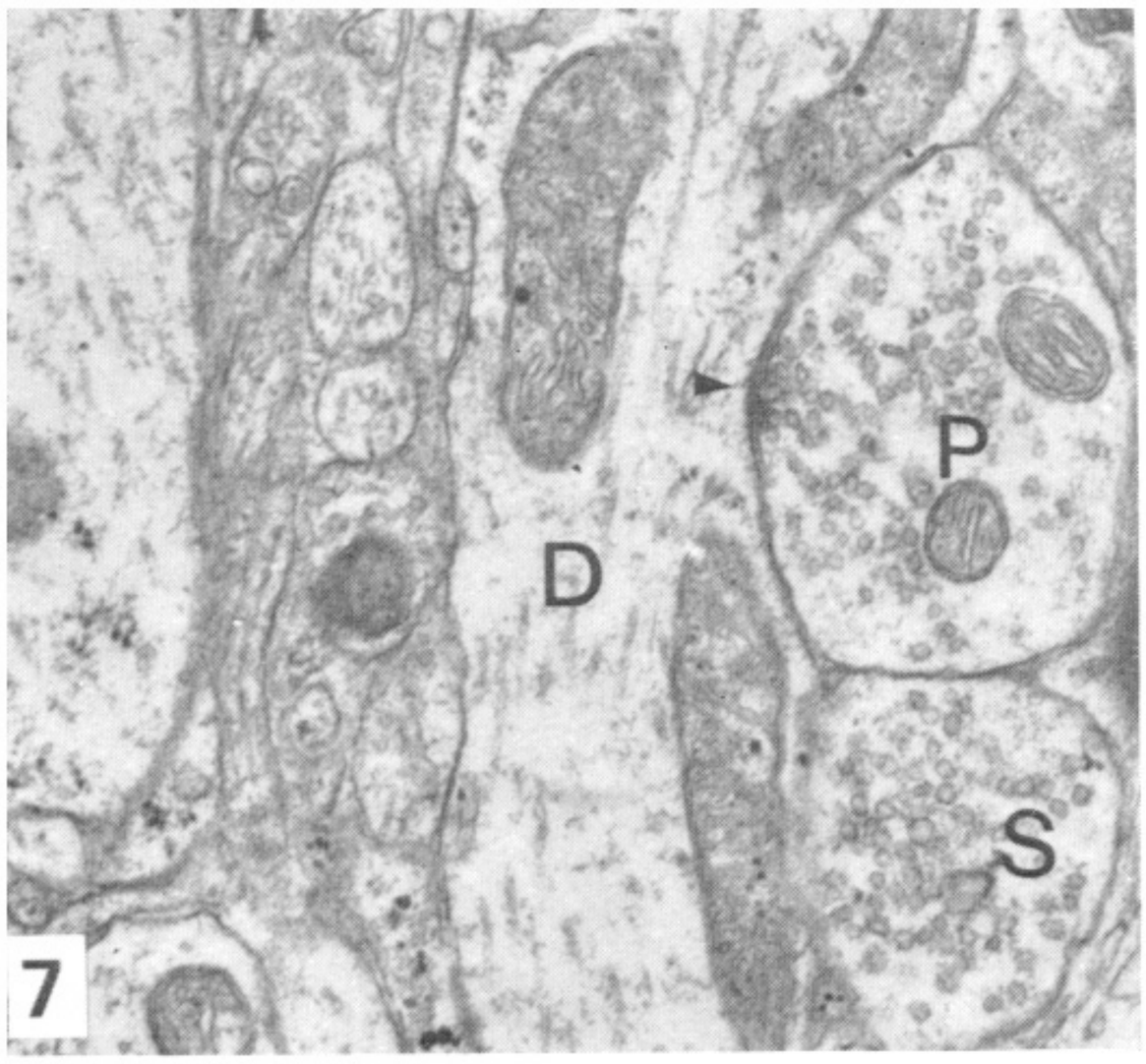
FIGURES 2 AND 3. For description see p. 360.

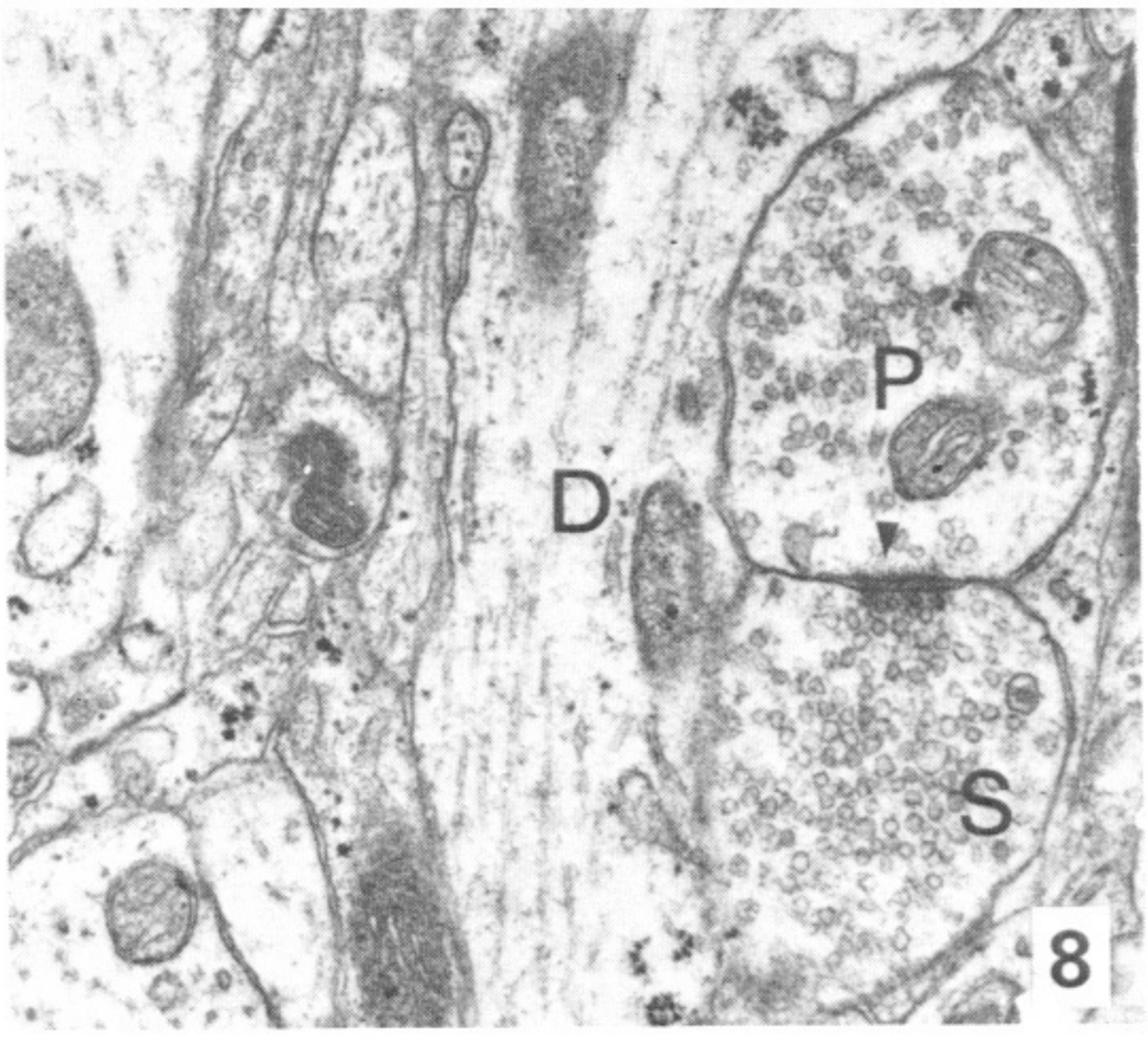


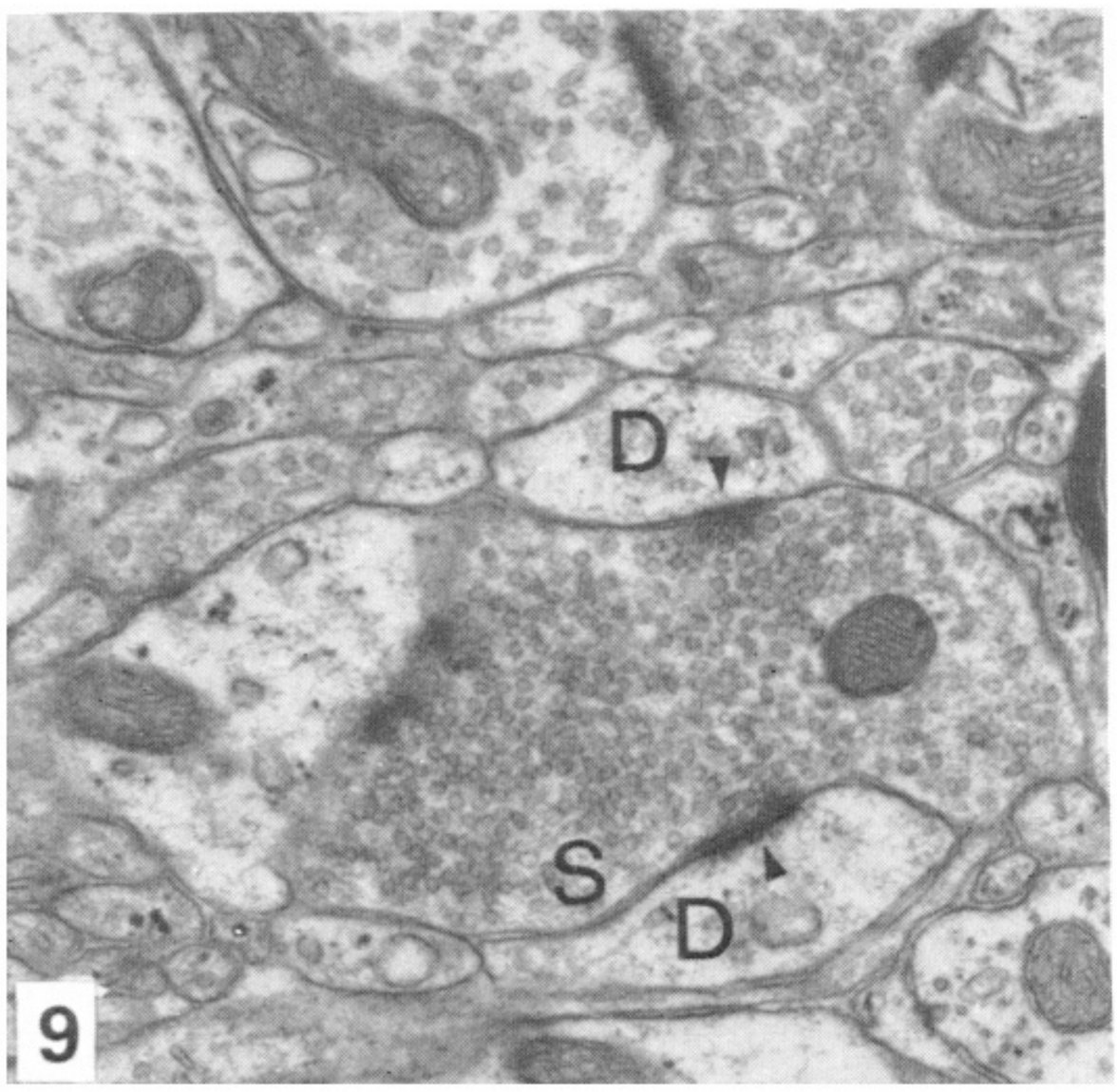


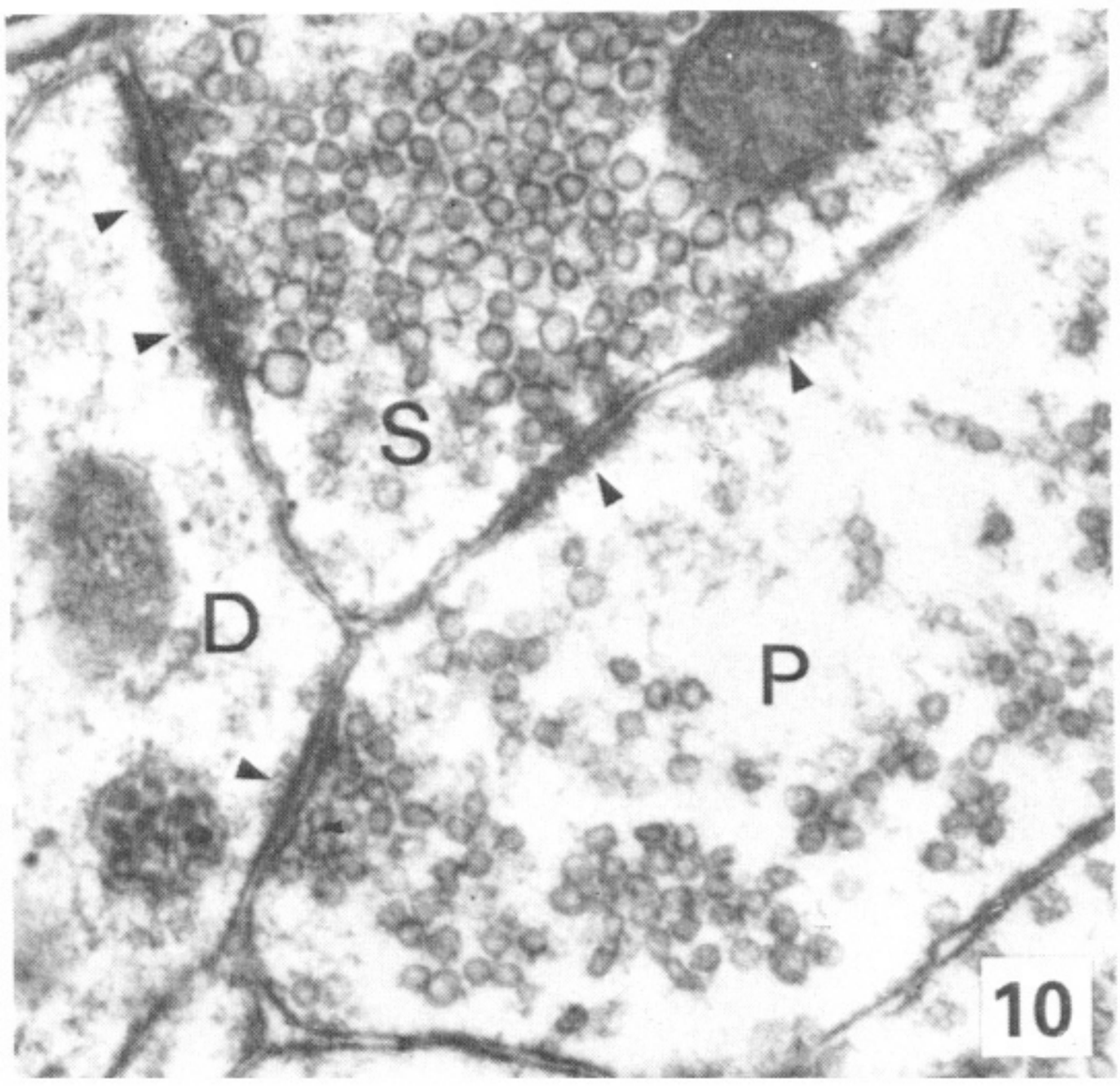


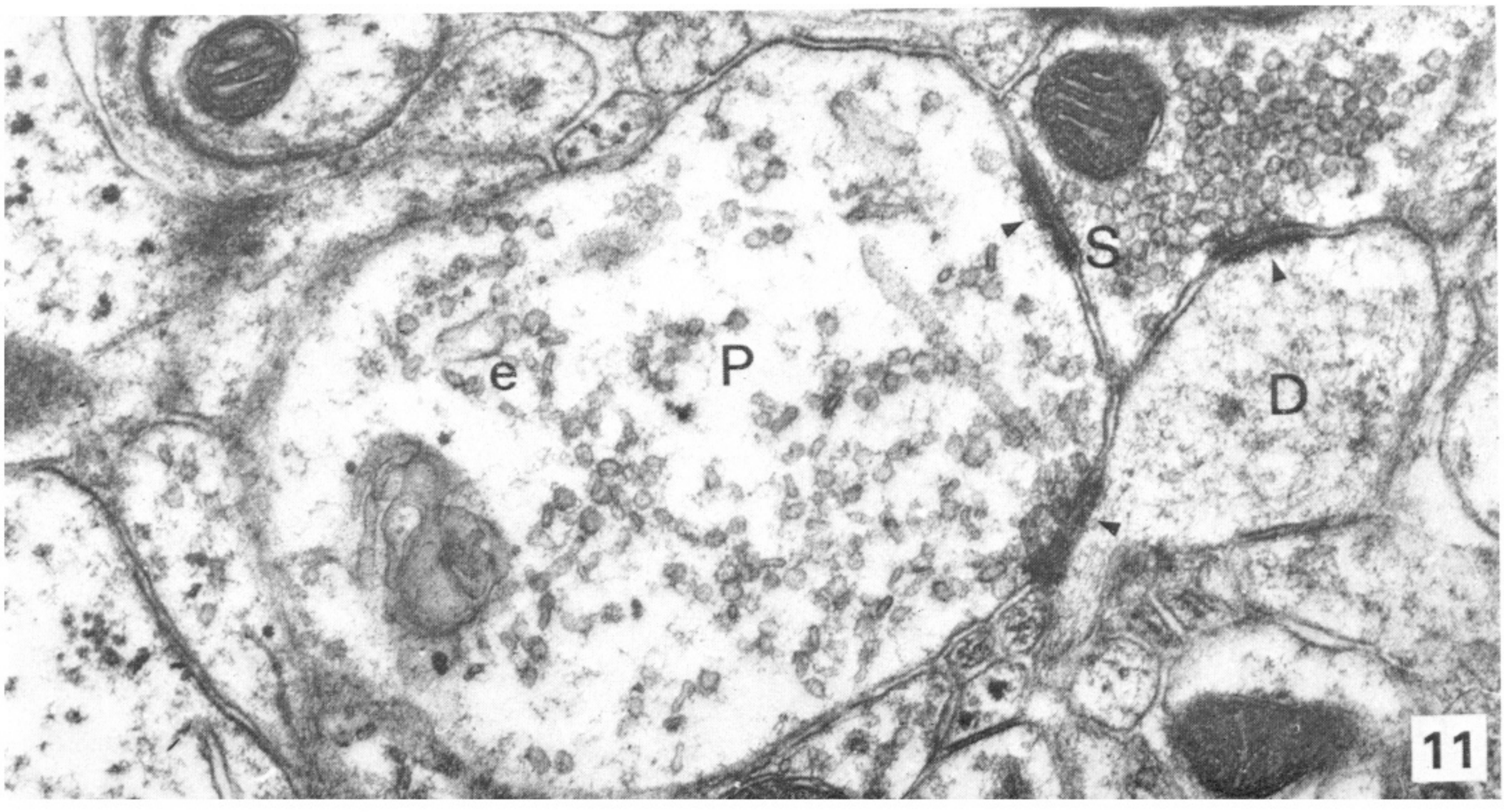
FIGURES 4–6. For description see p. 361.



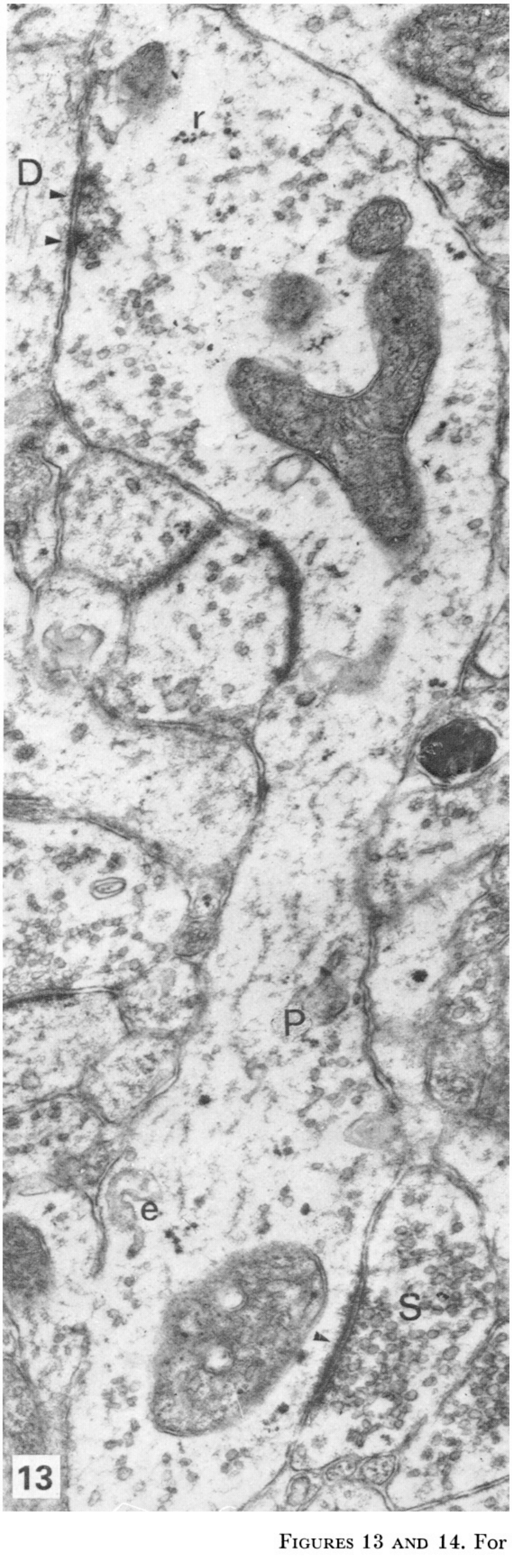


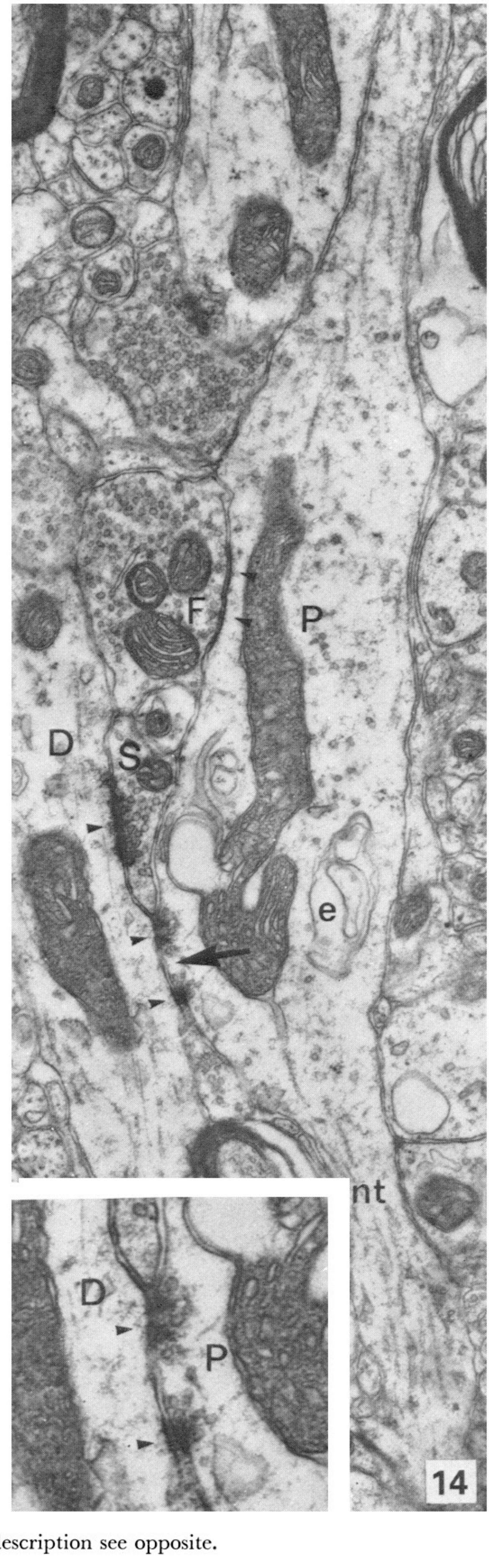




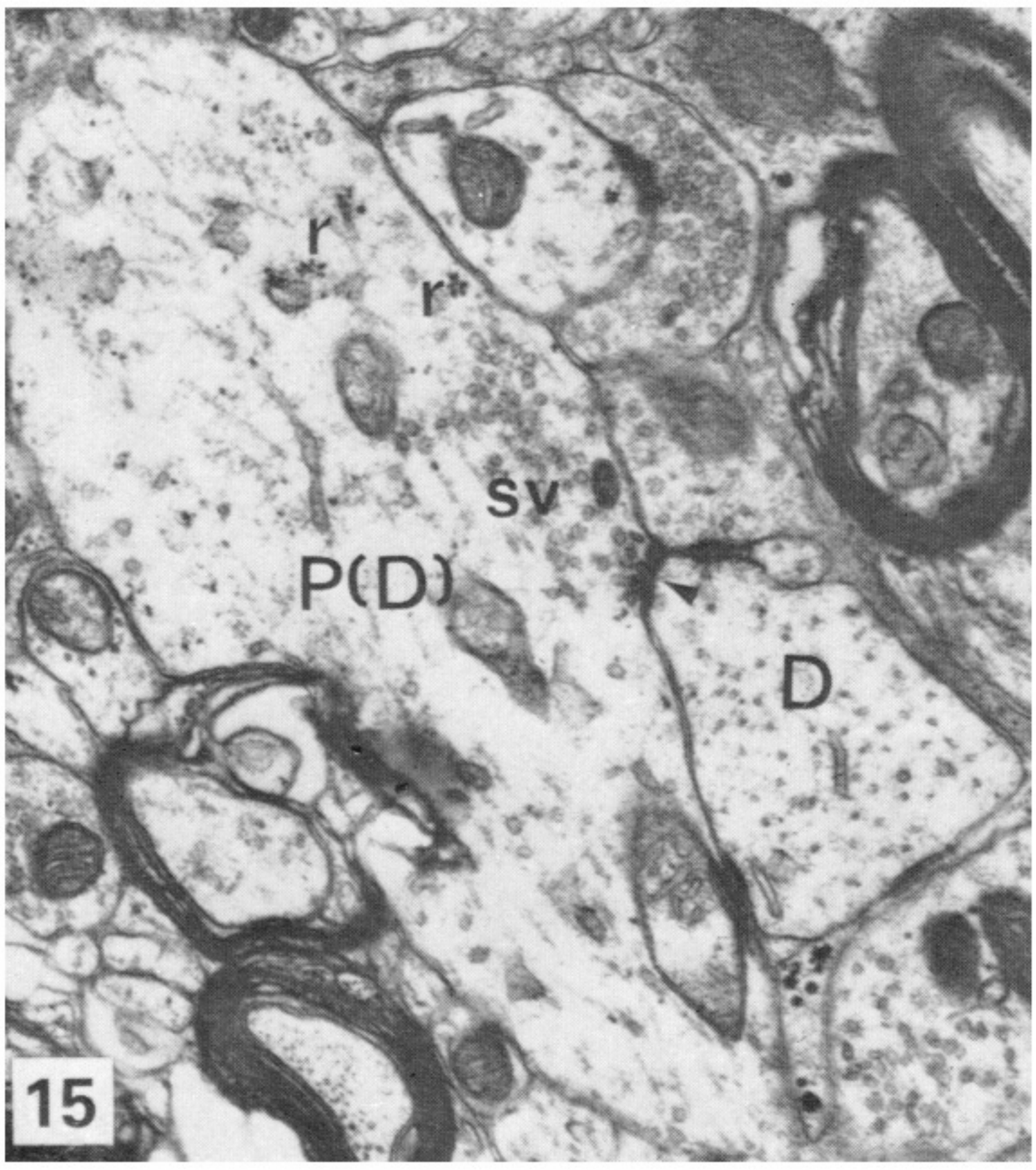


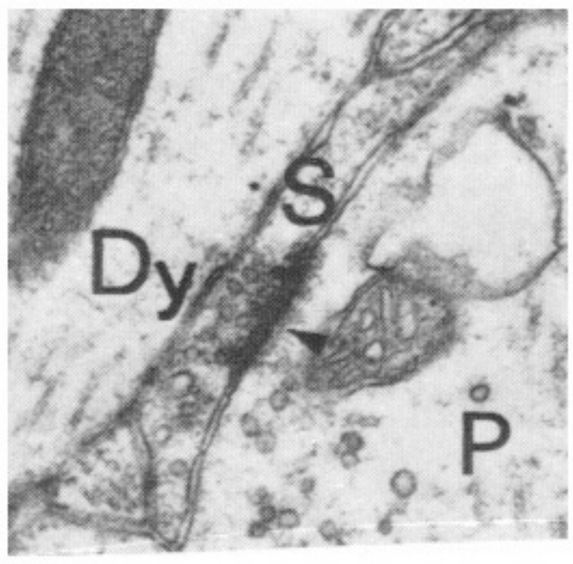
FIGURES 7–11. For description see opposite.

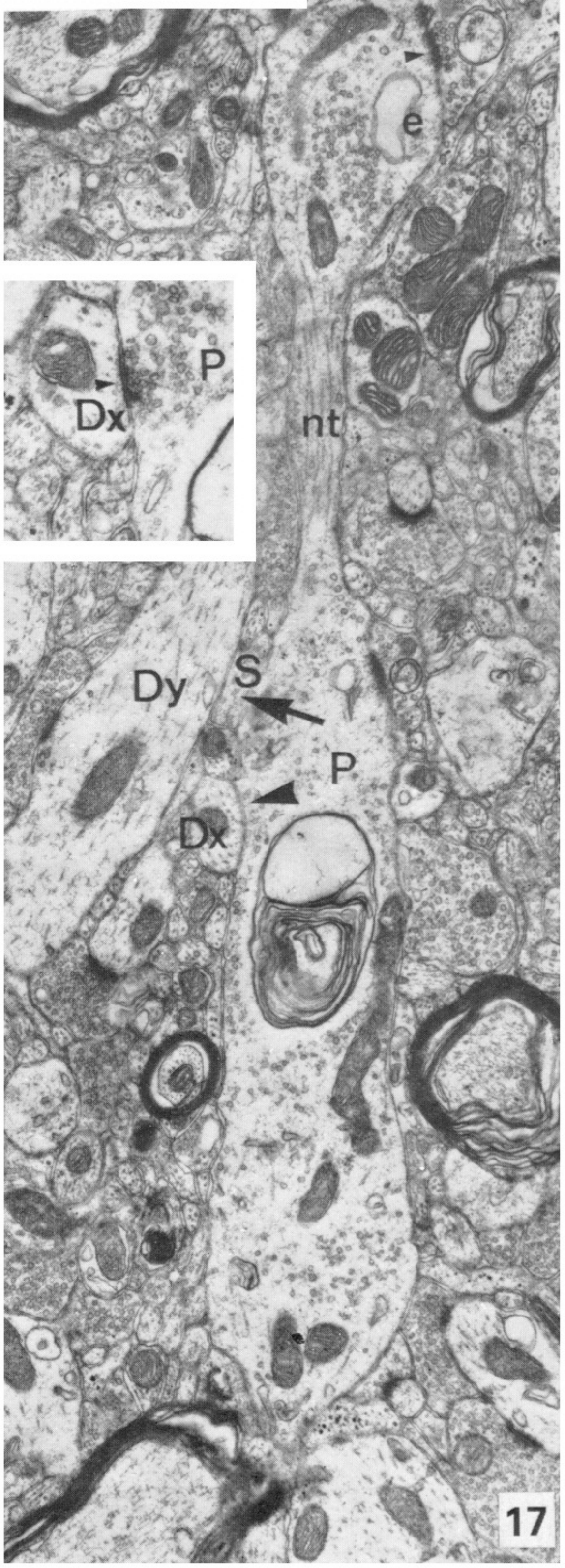


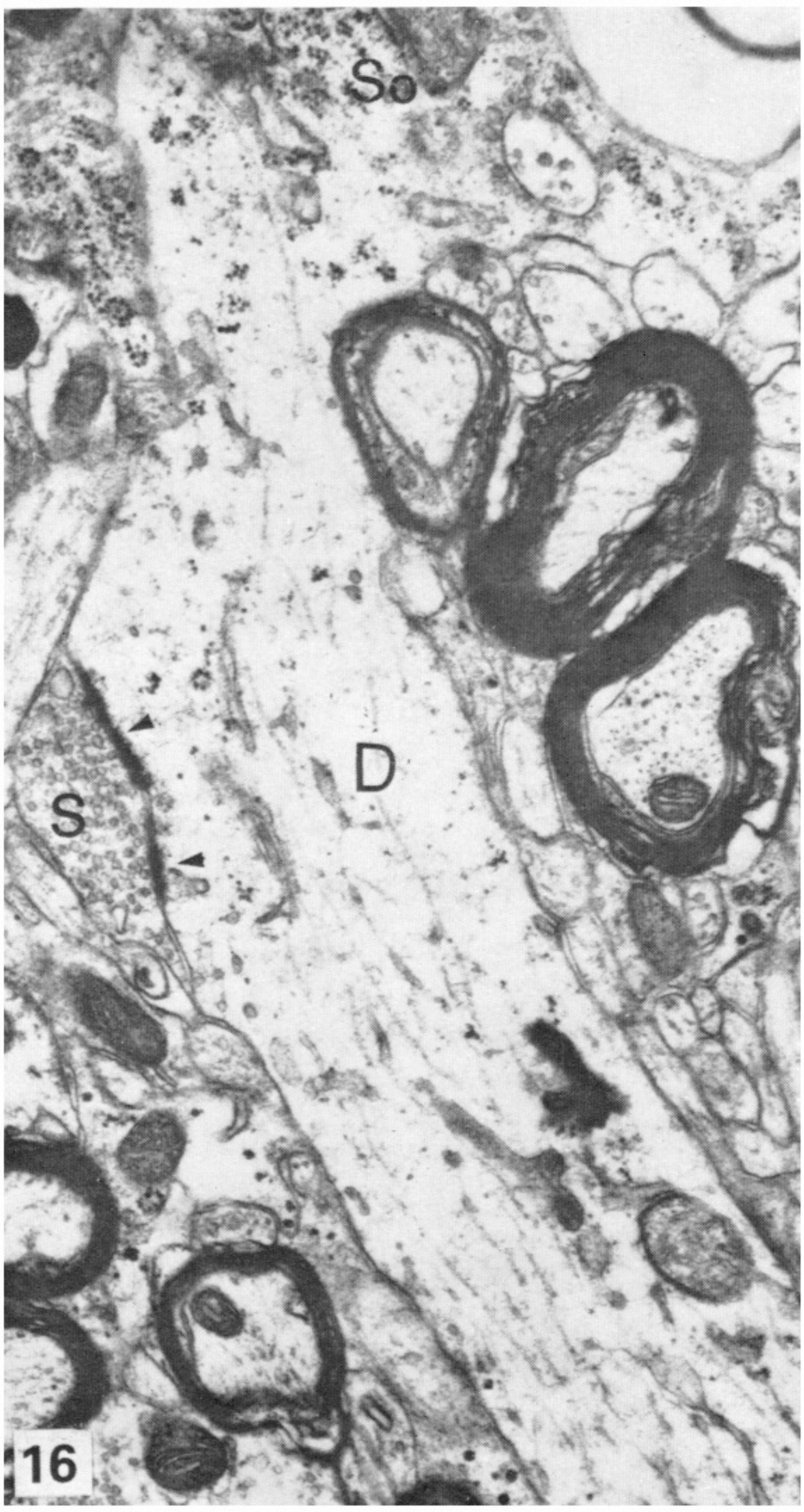


FIGURES 13 AND 14. For description see opposite.

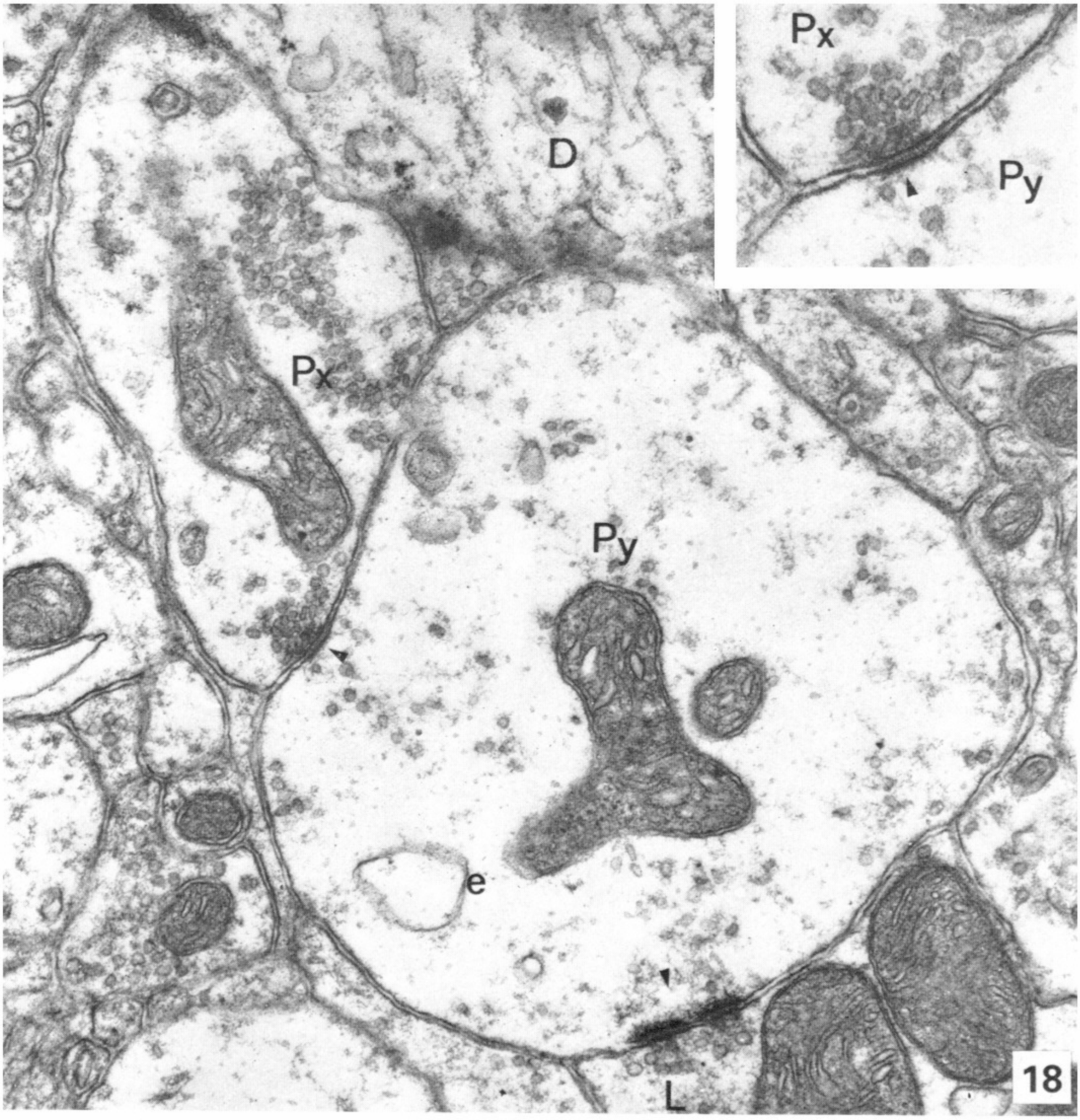


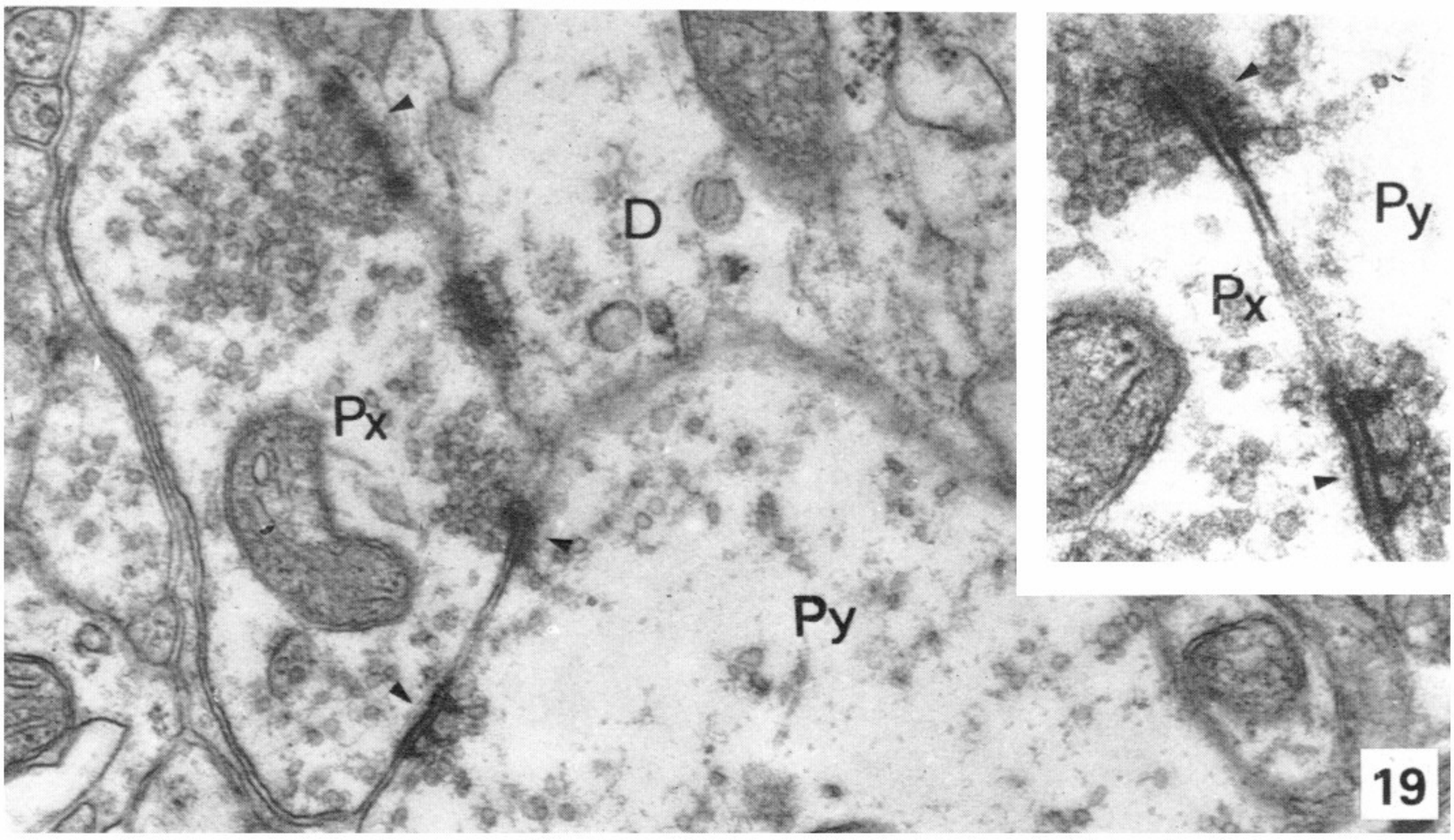




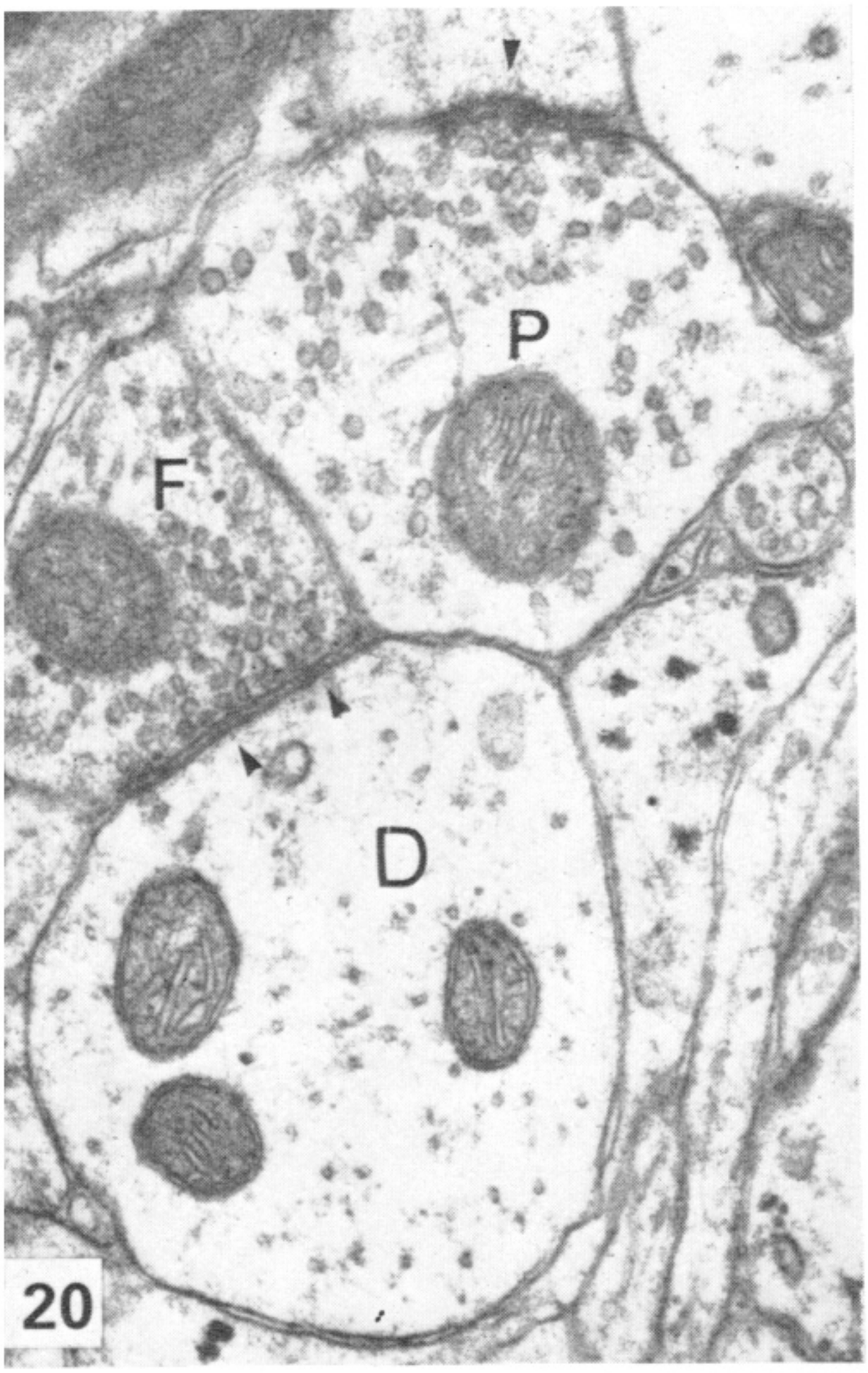


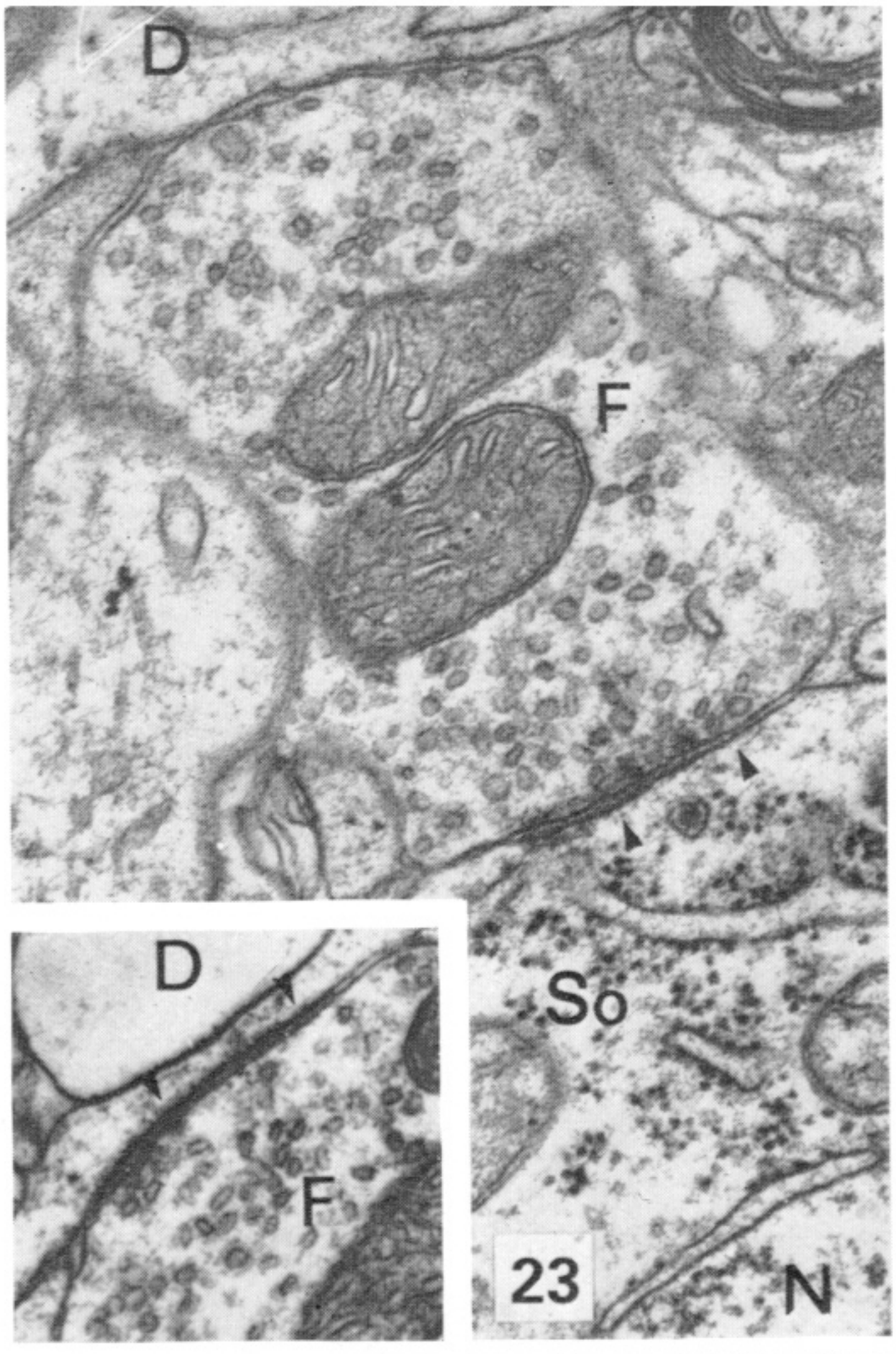
FIGURES 15–17. For description see p. 364.

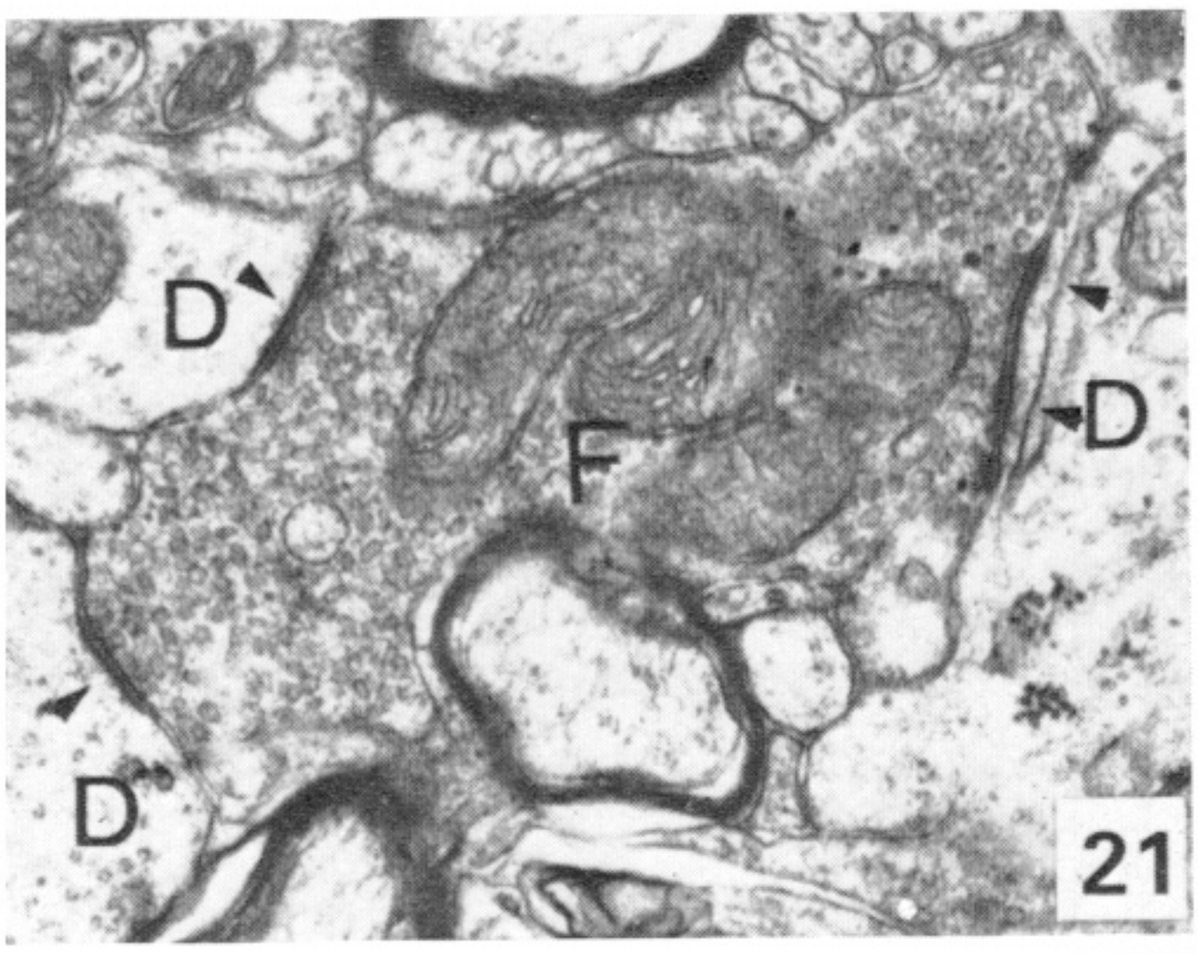


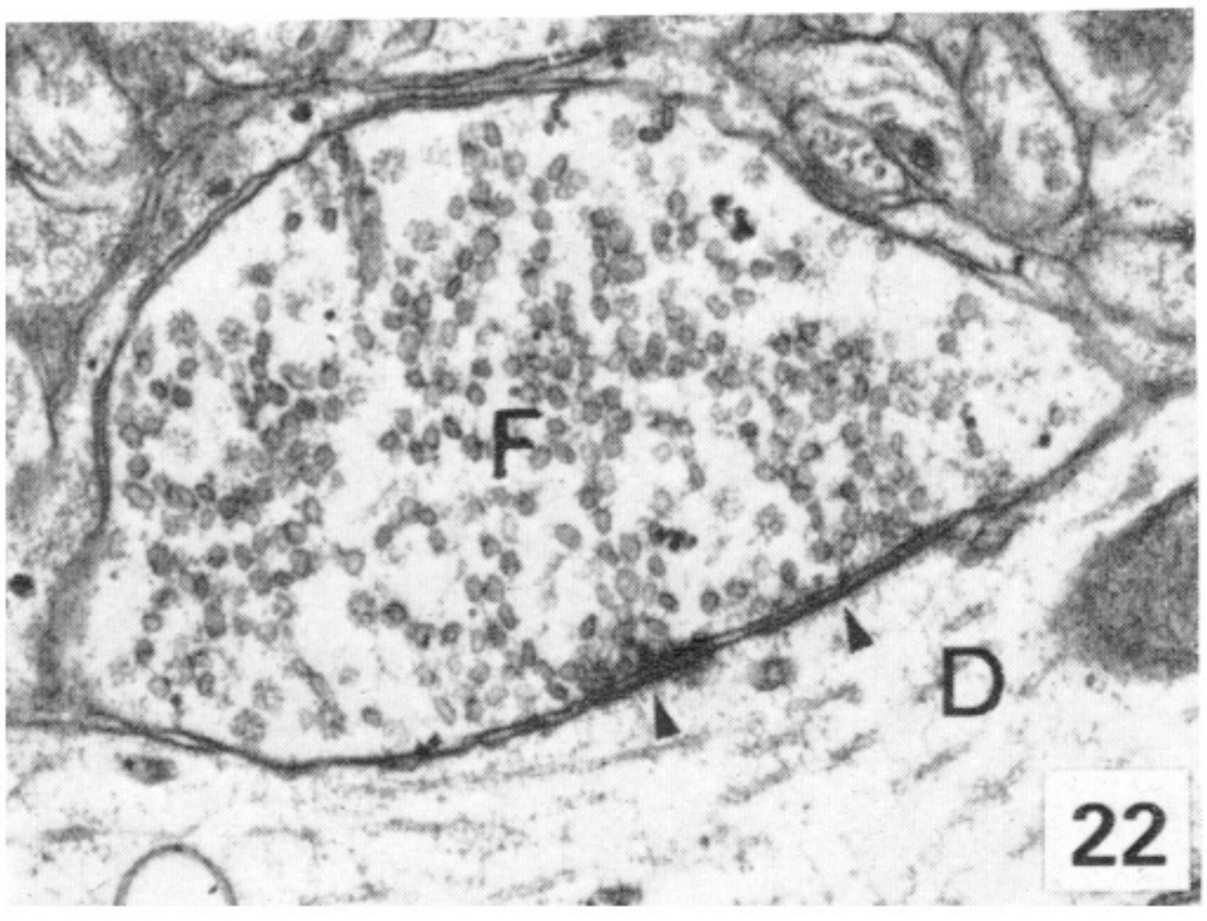


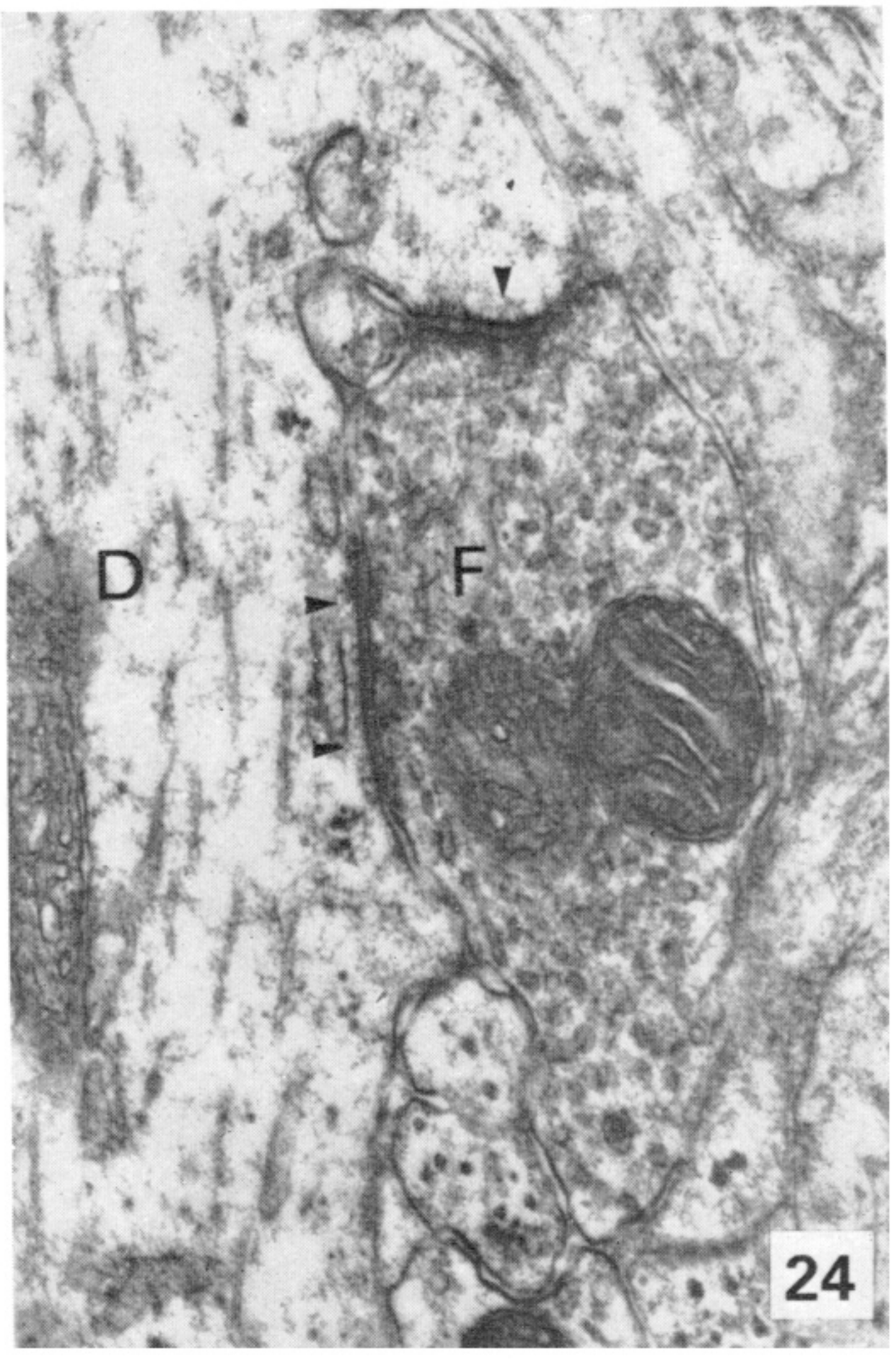
FIGURES 18 AND 19. For description see p. 365.



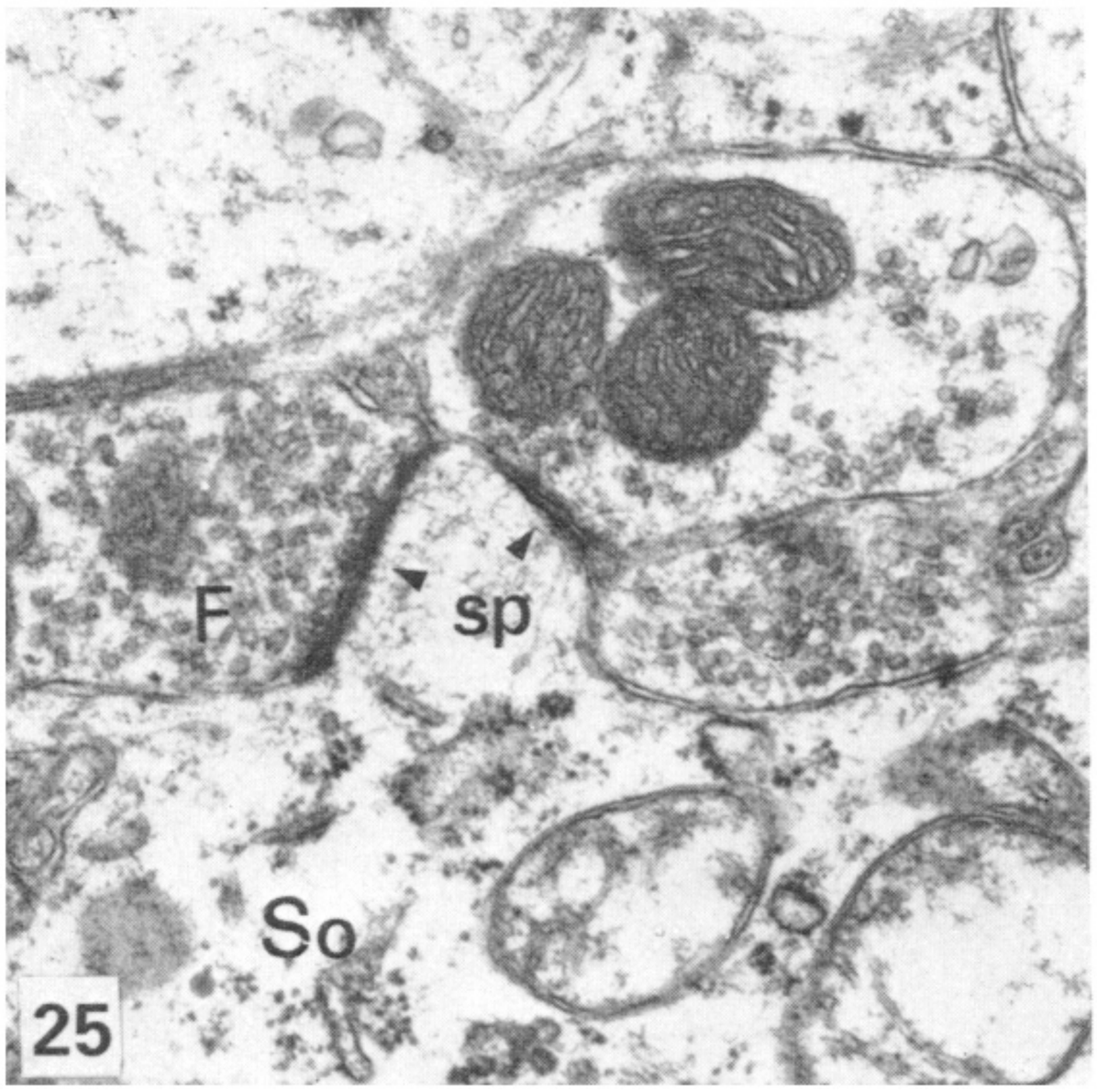


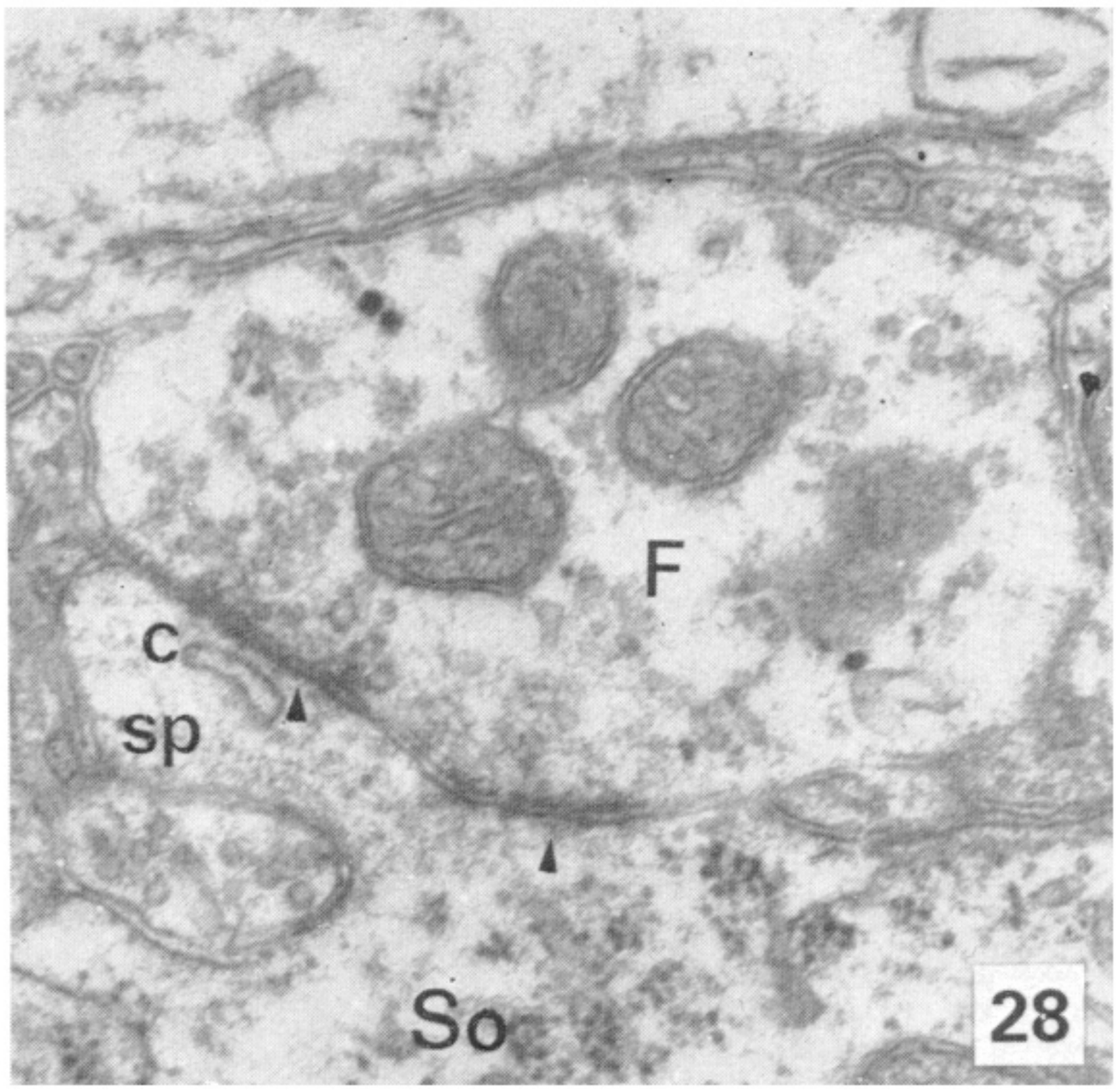


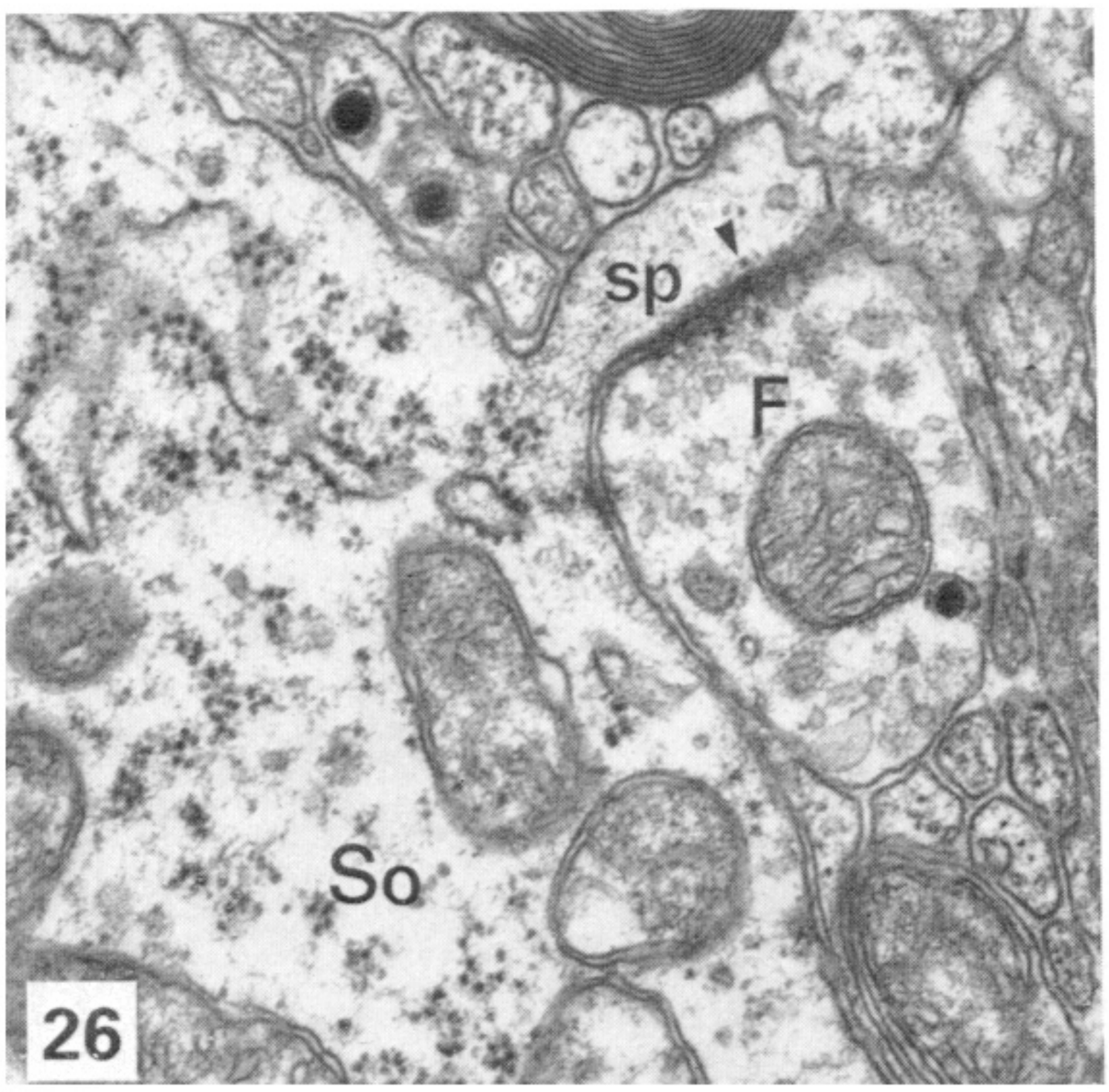


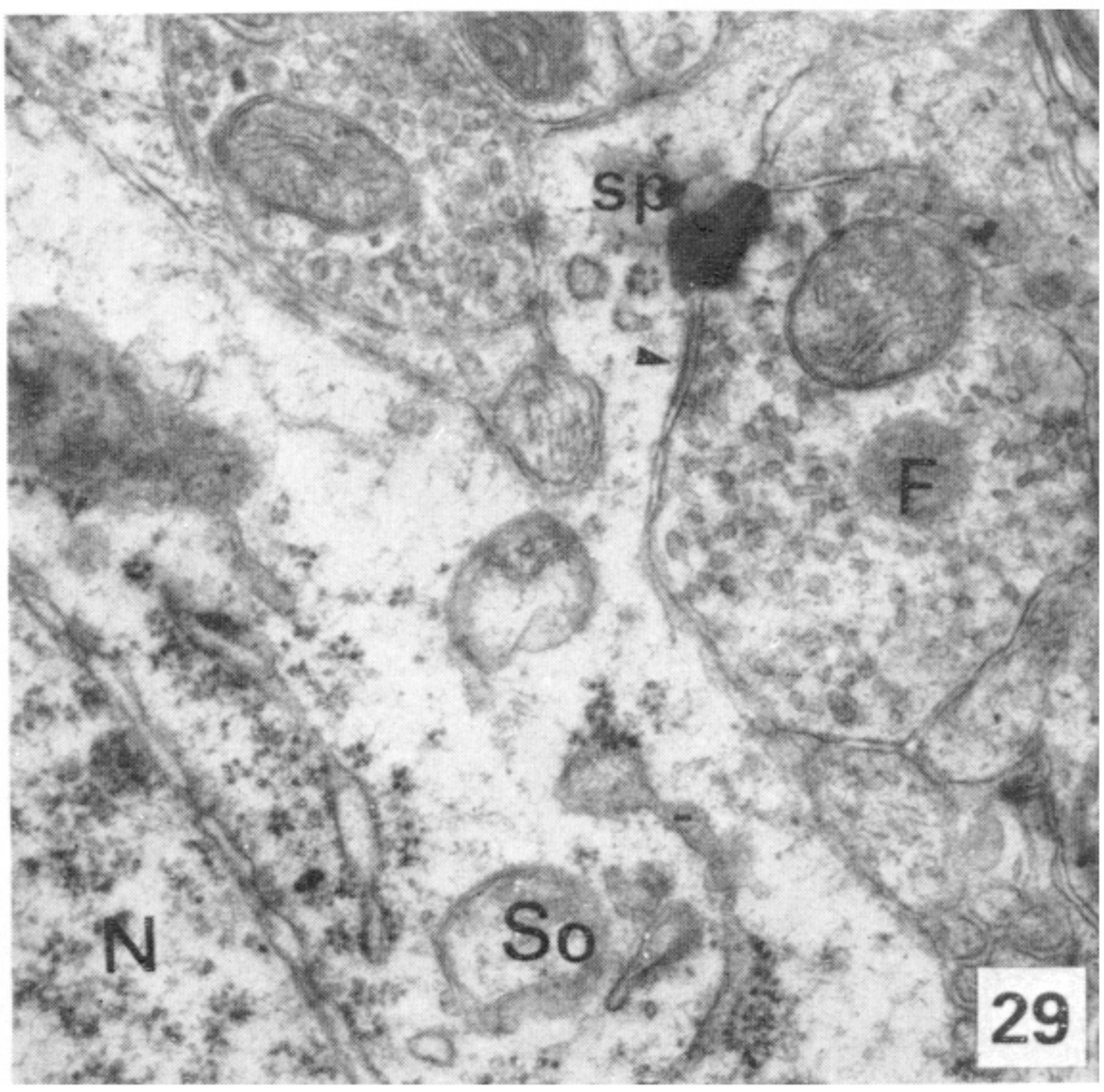


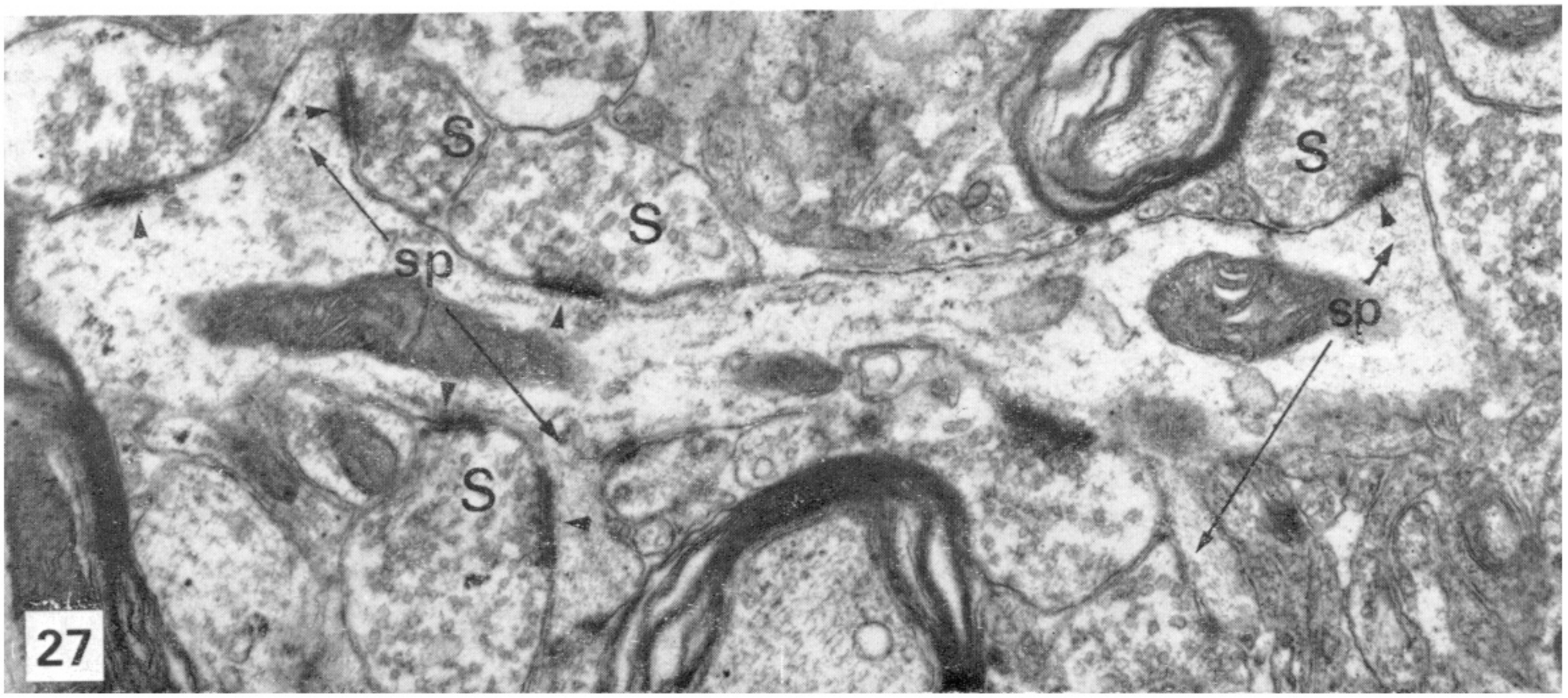
FIGURES 20–24. For description see opposite.



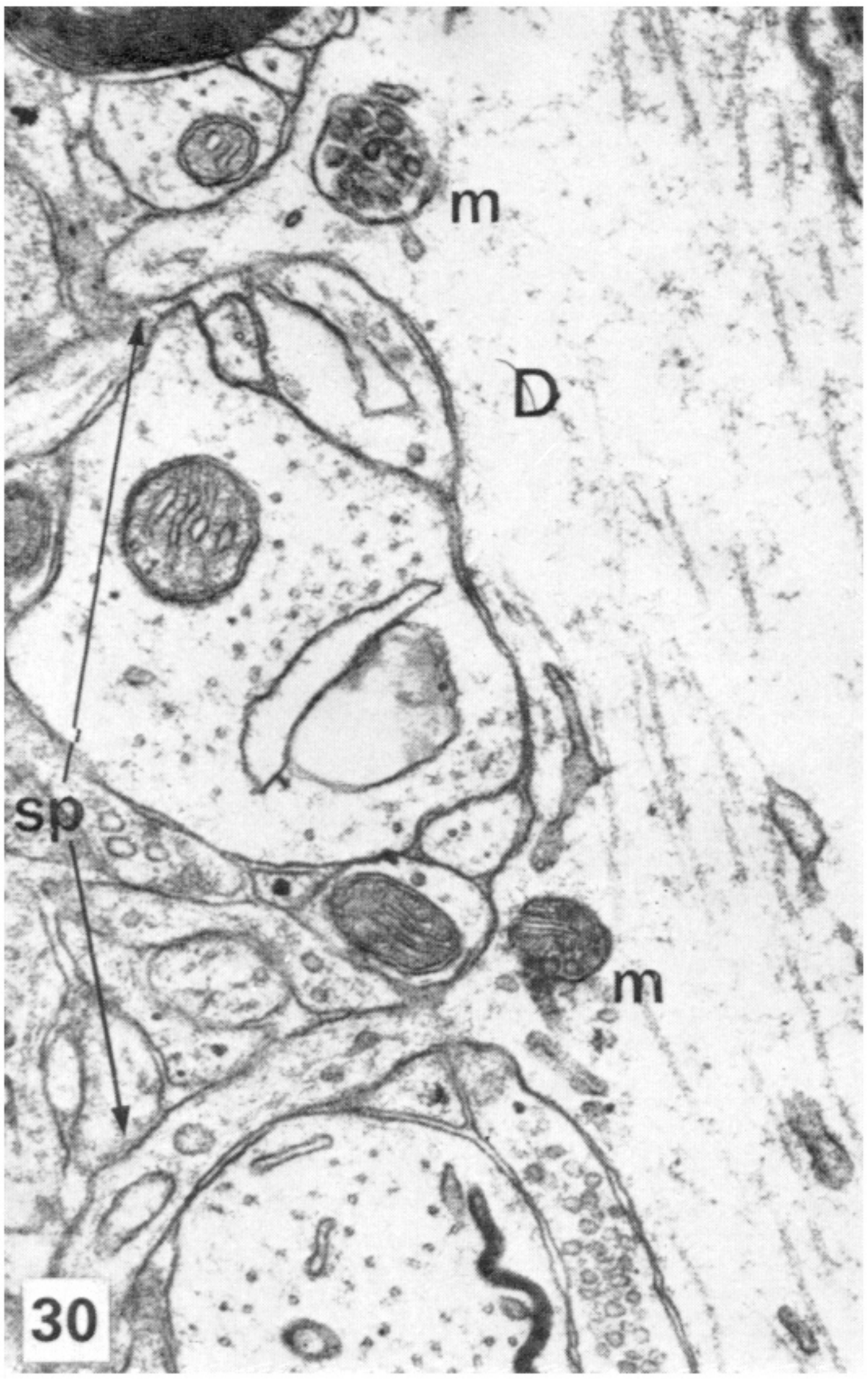


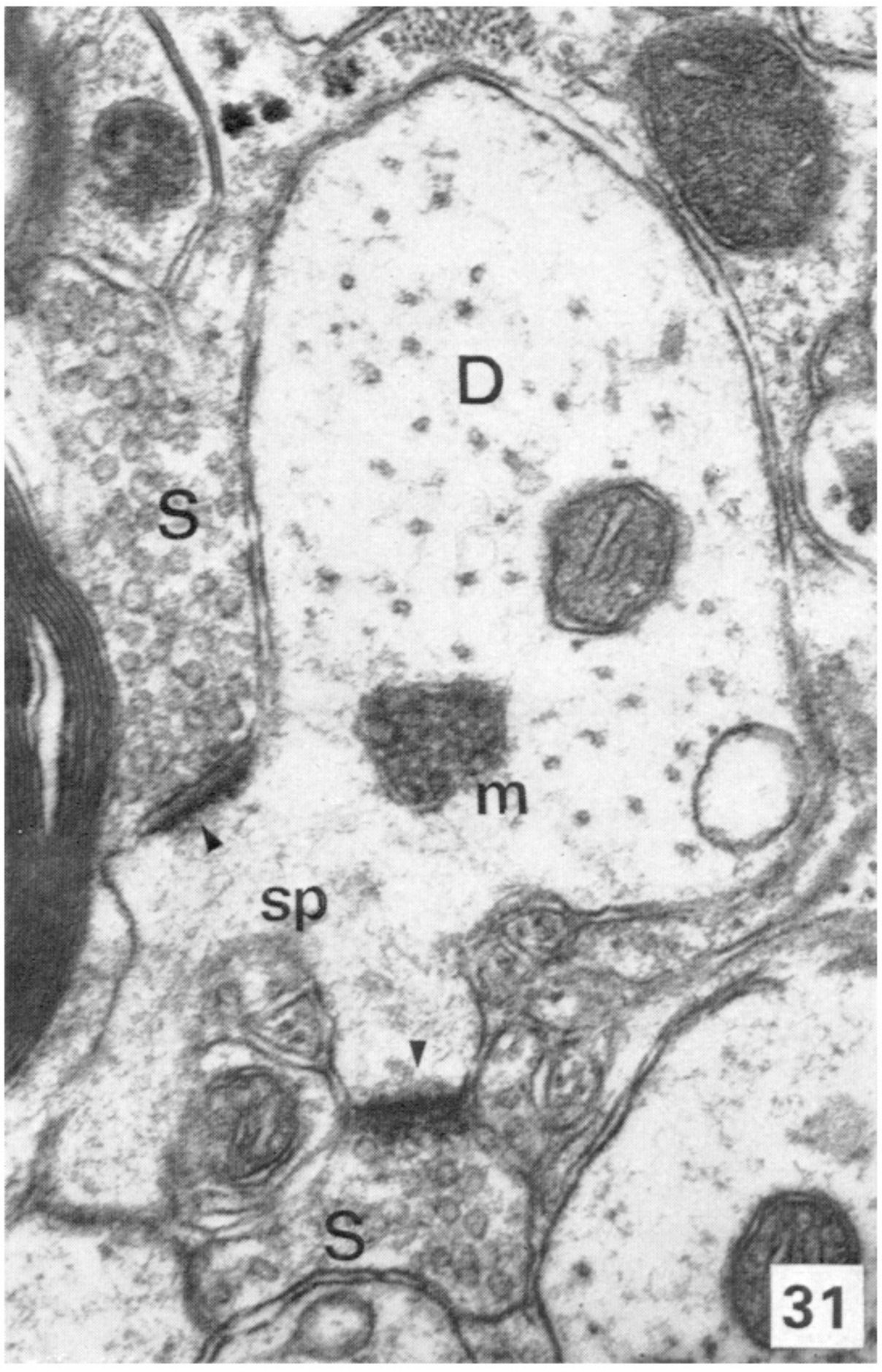


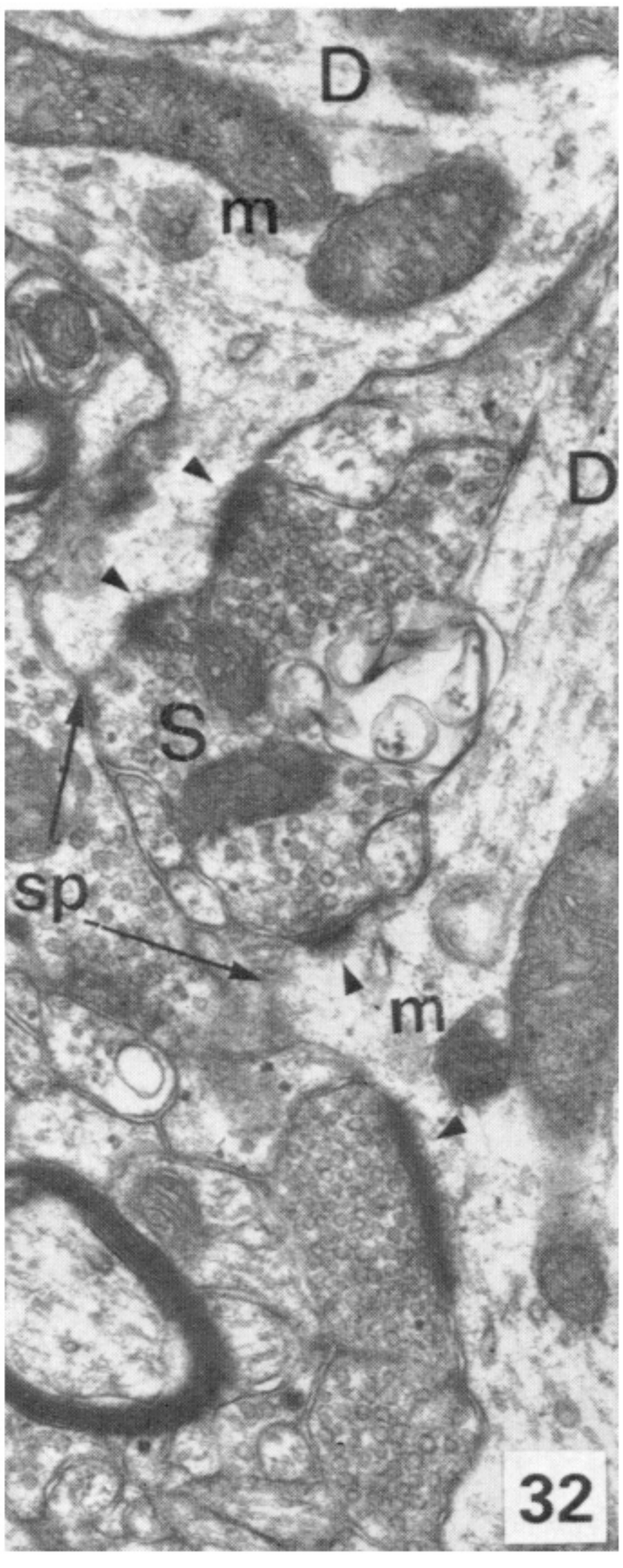


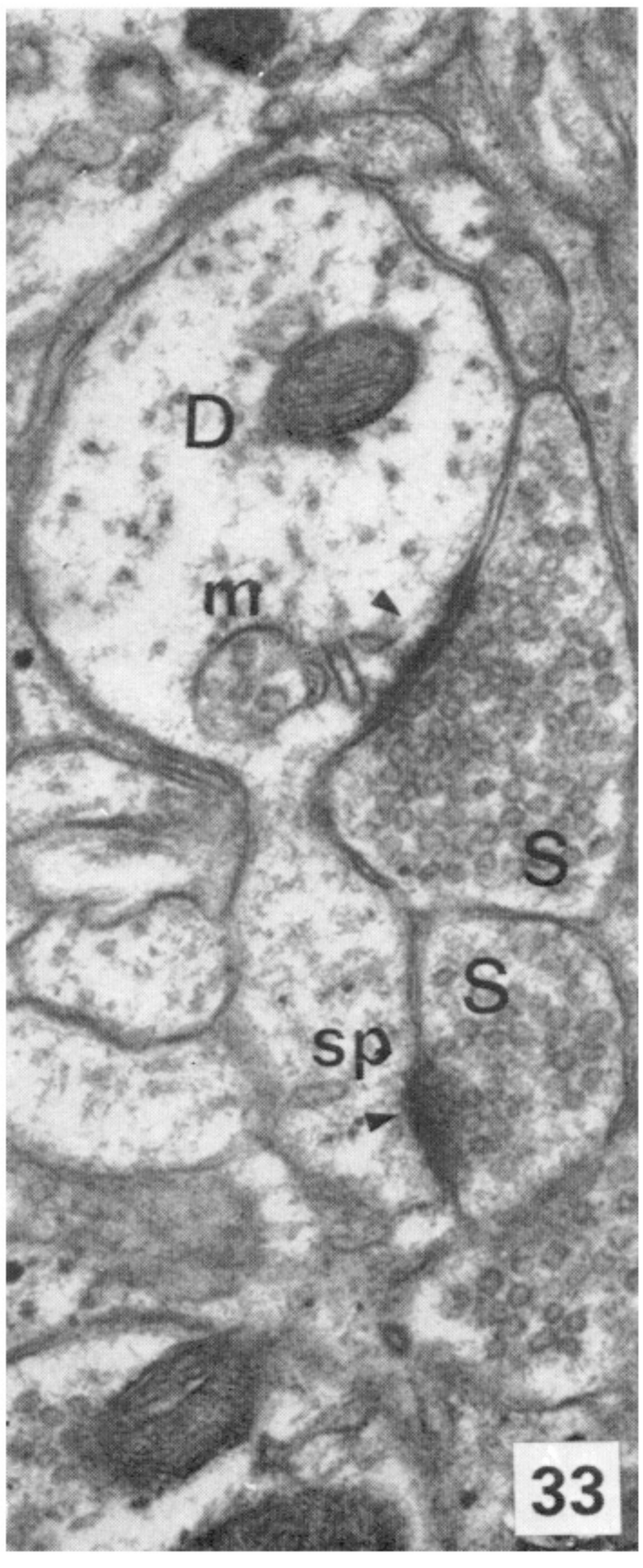


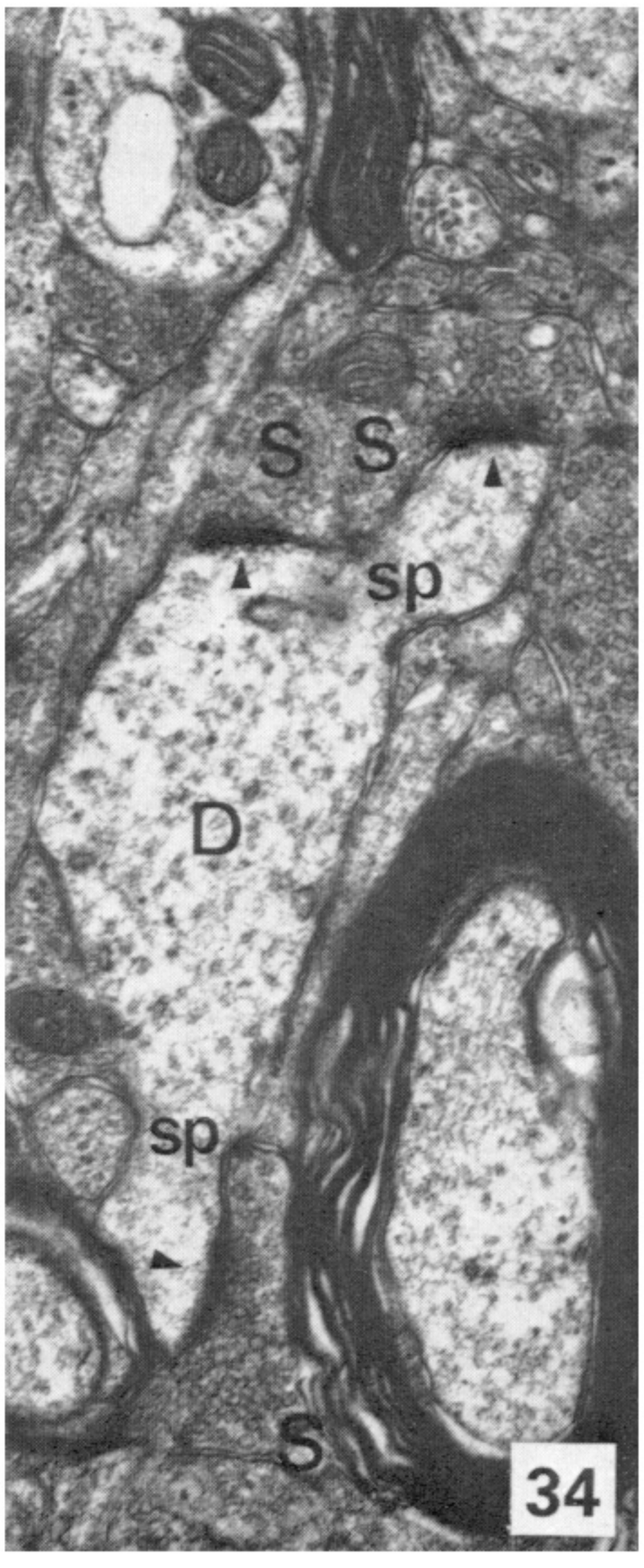
FIGURES 25–29. For description see opposite.



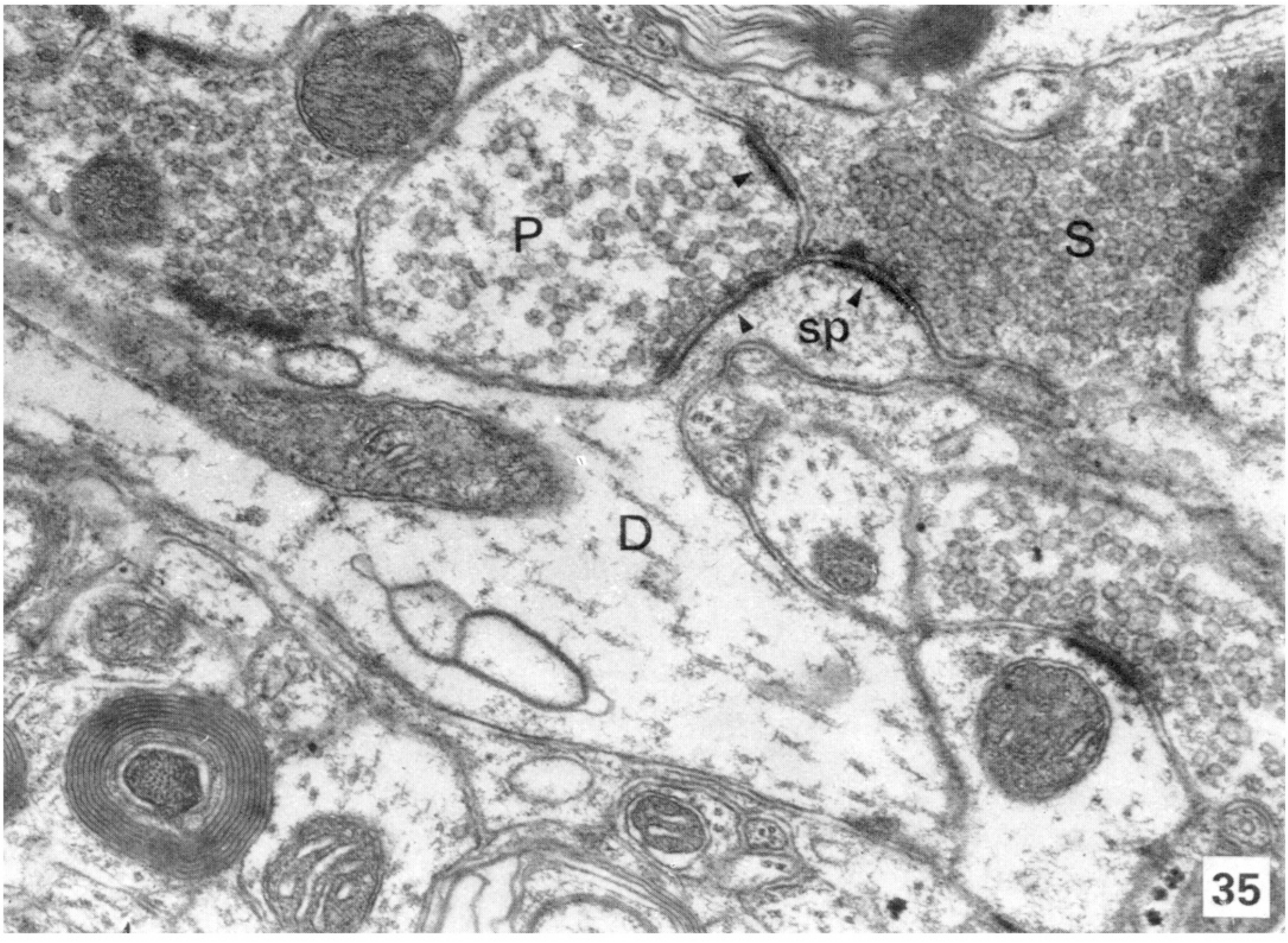


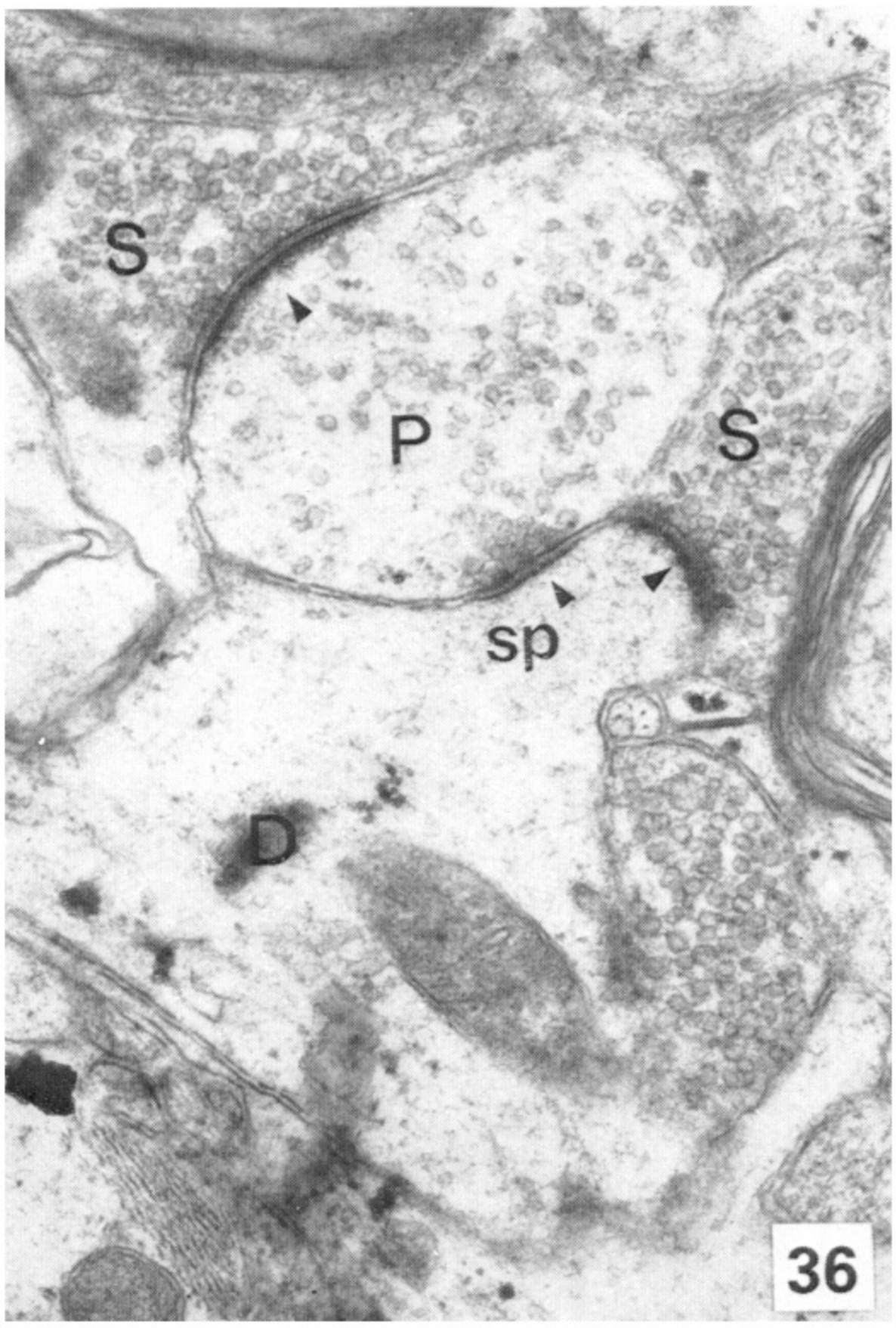


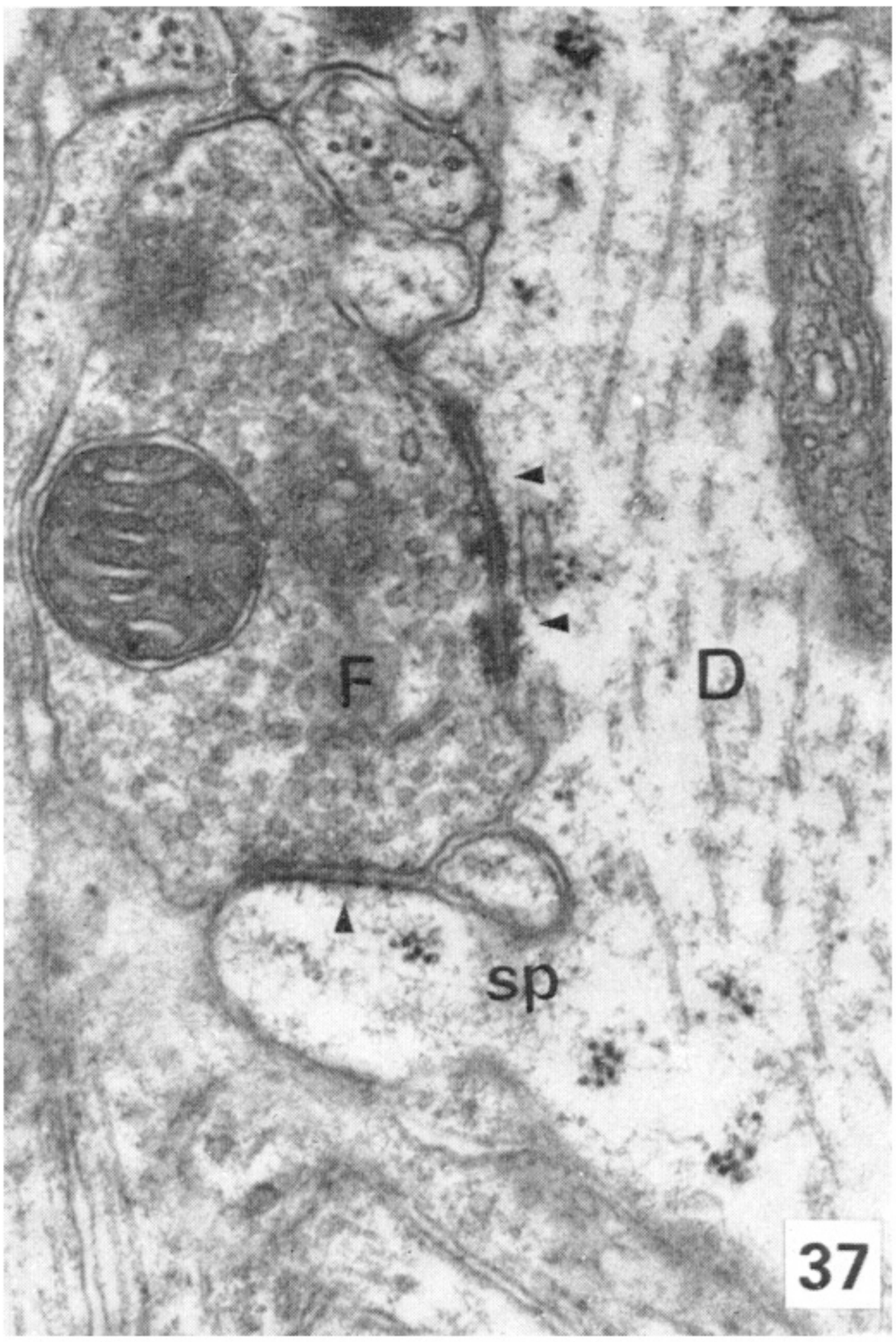




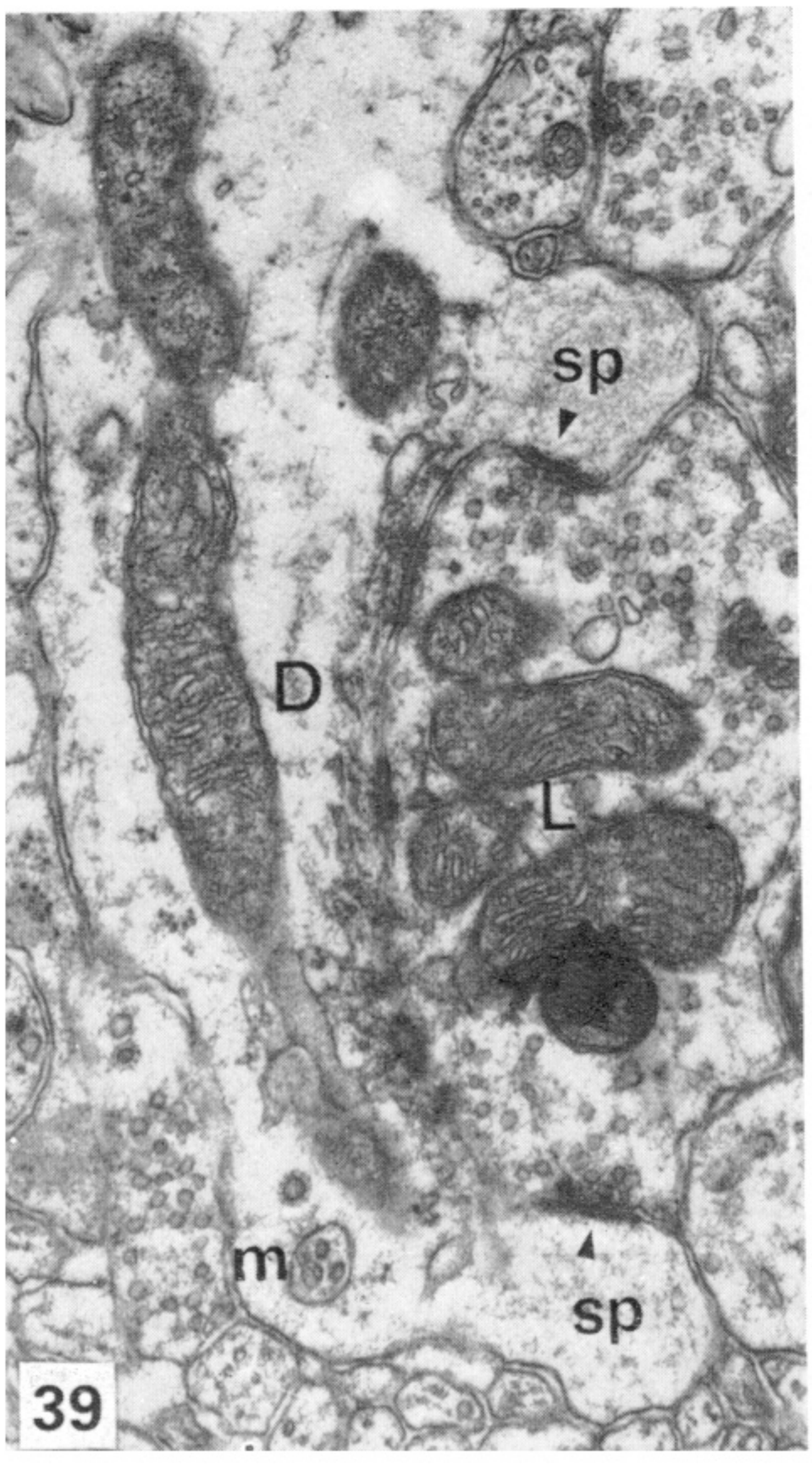
FIGURES 30–34. For description see p. 368.

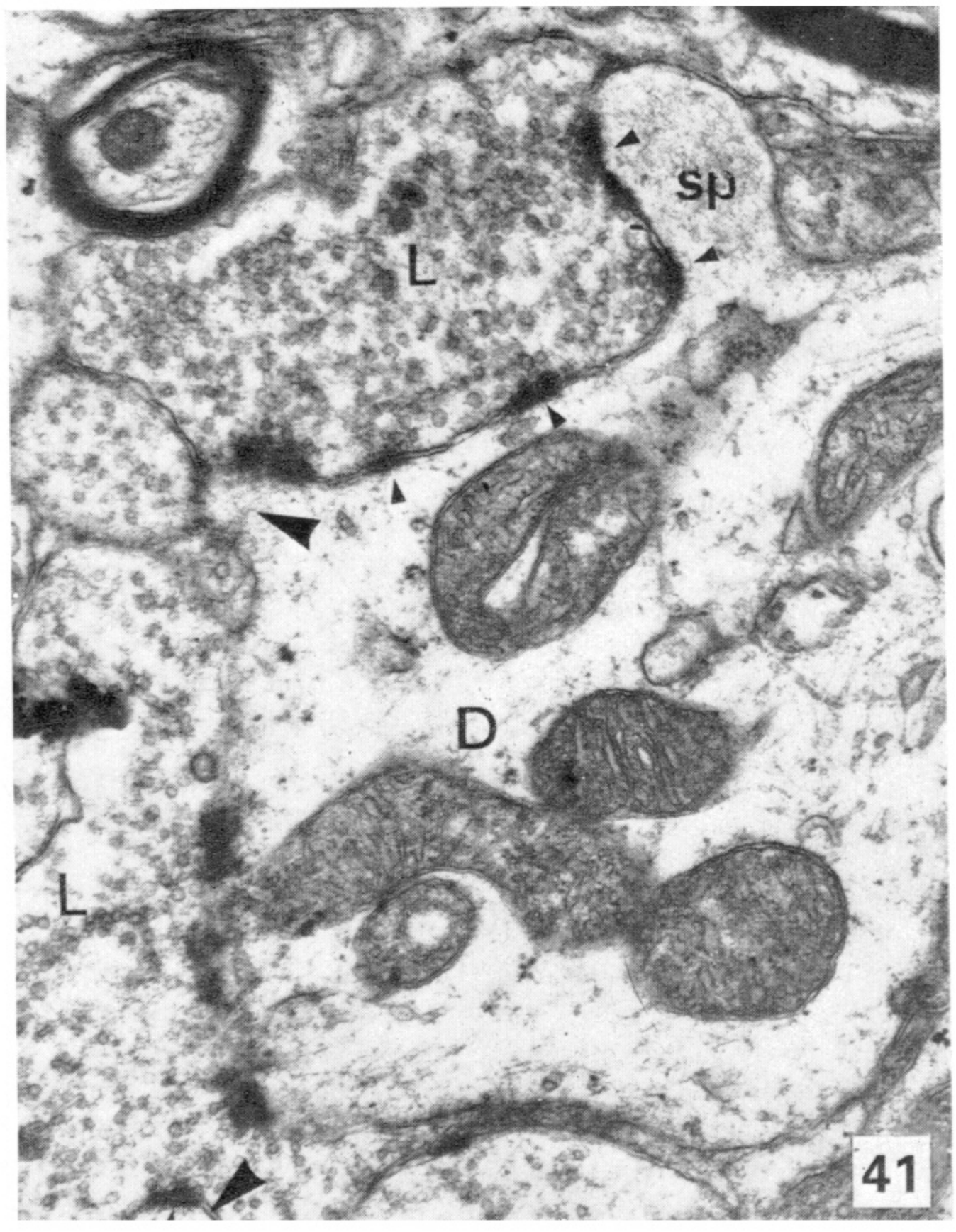


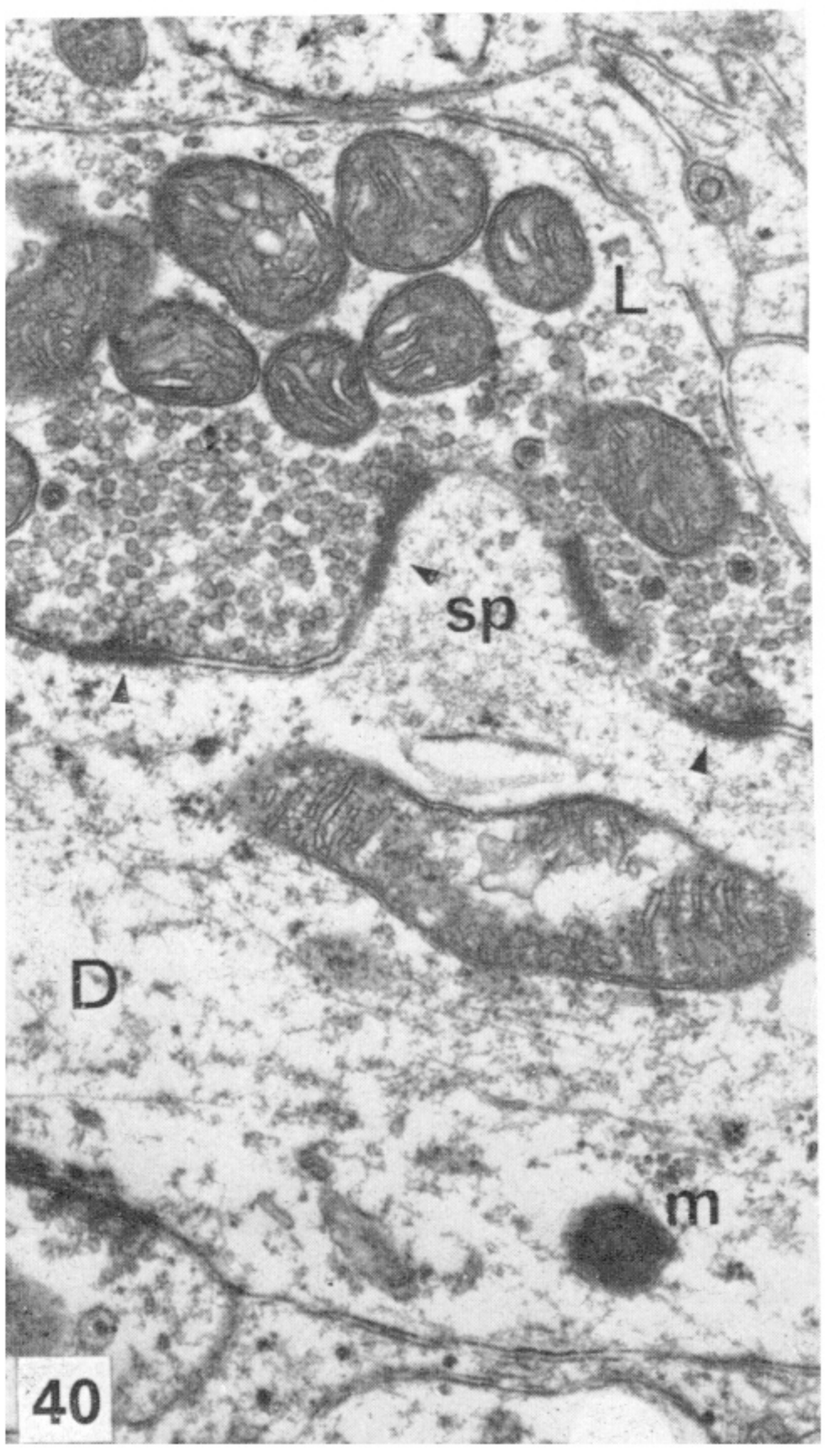


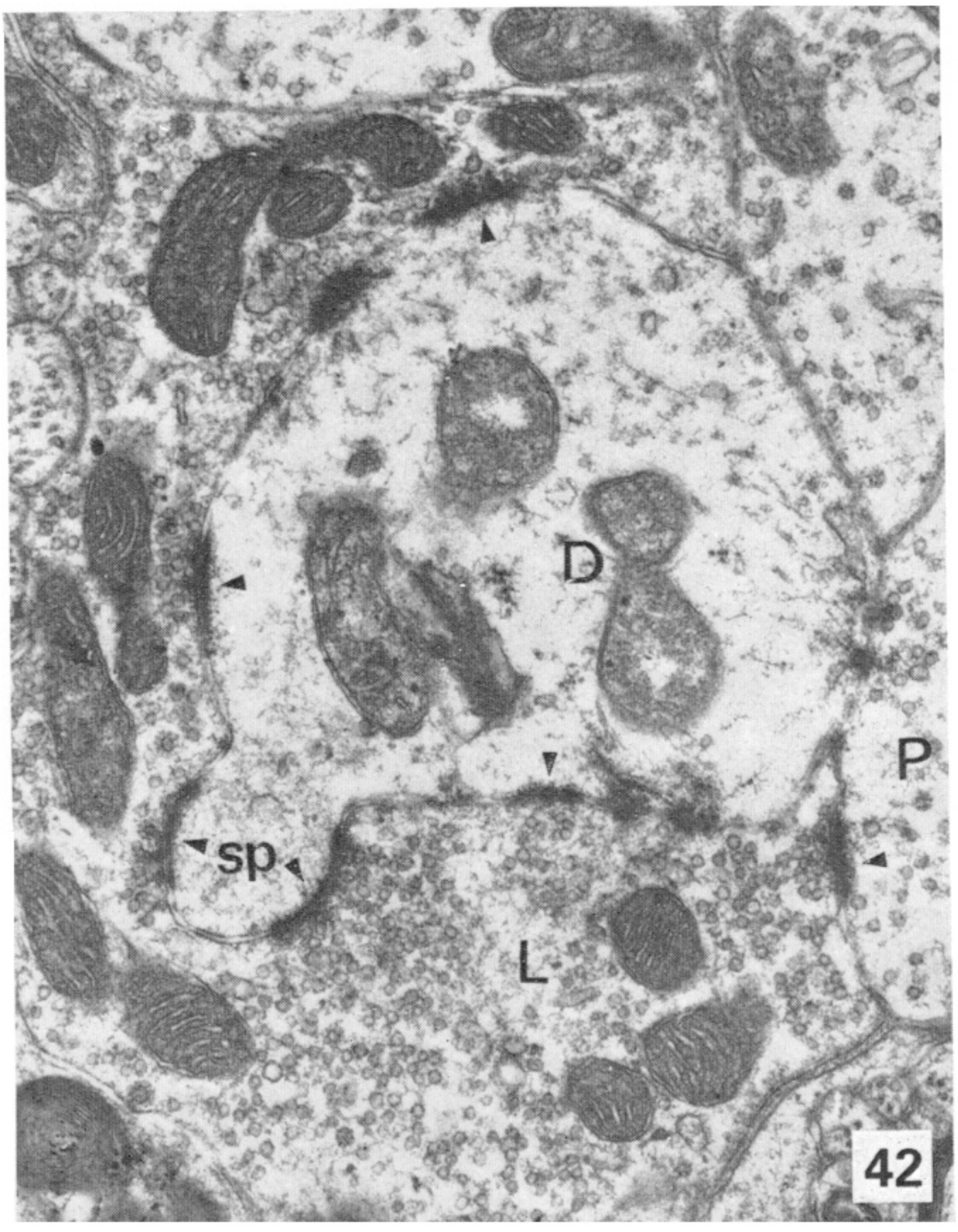


FIGURES 35–37. For description see p. 369.

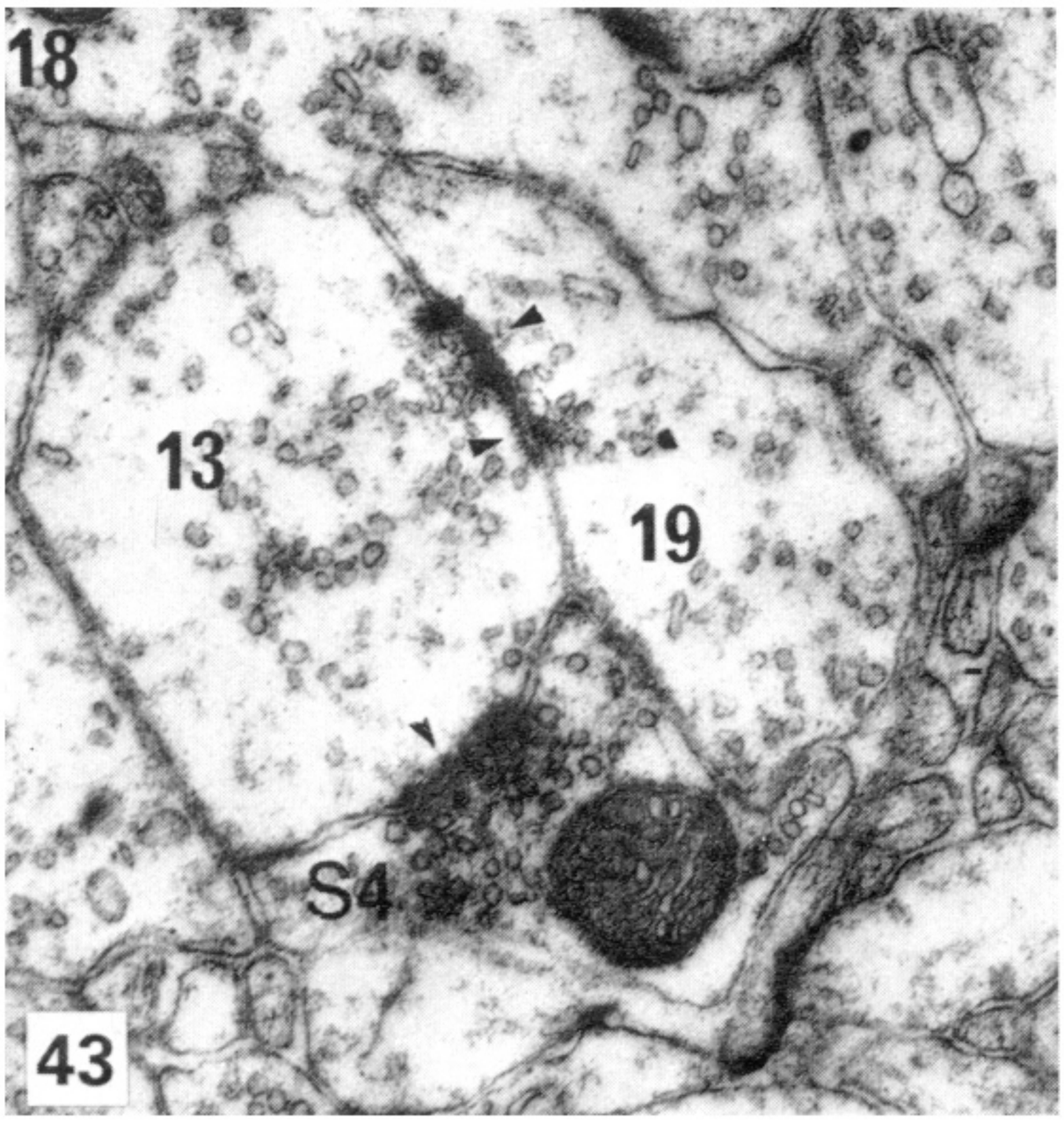


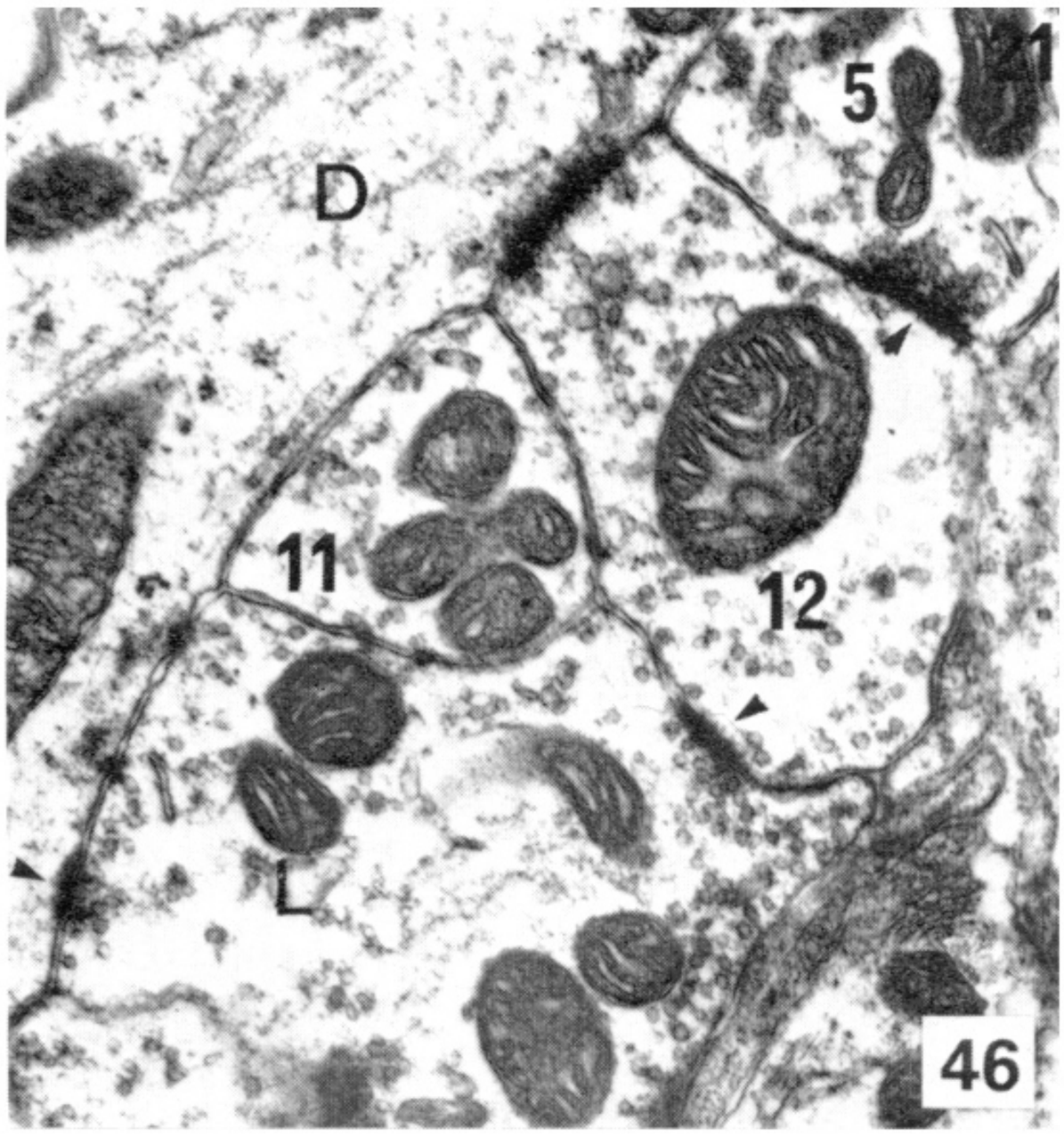


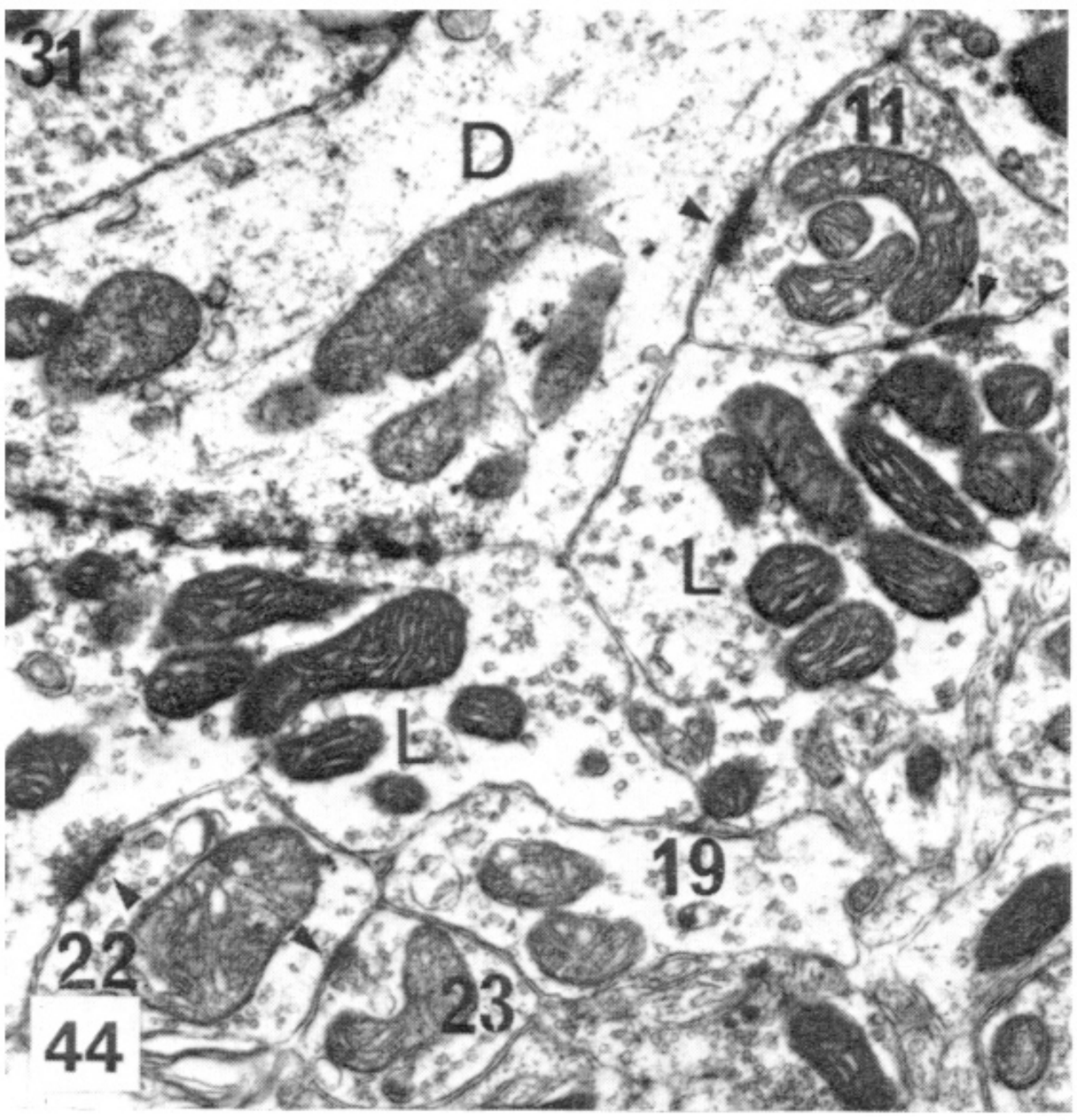


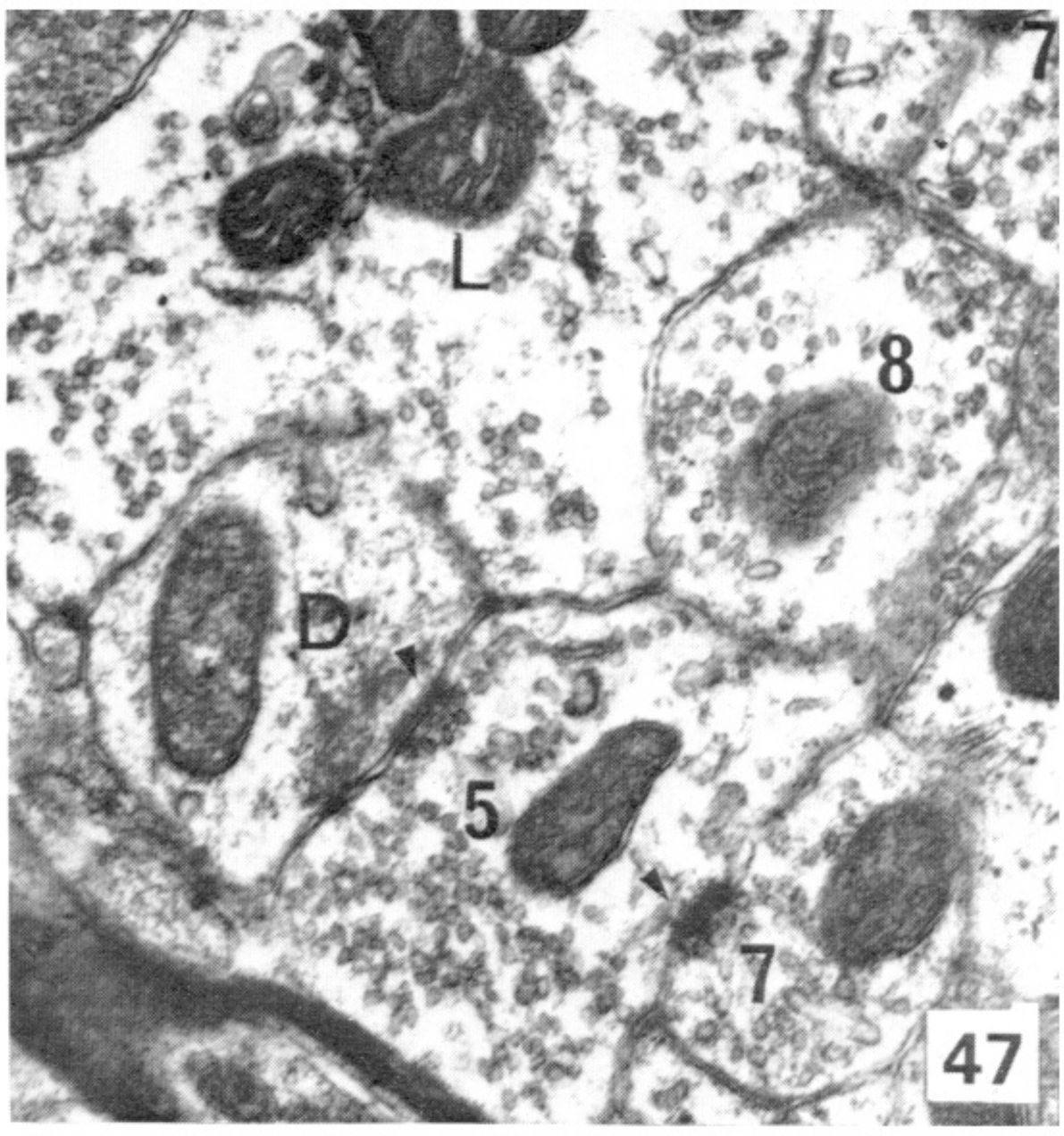


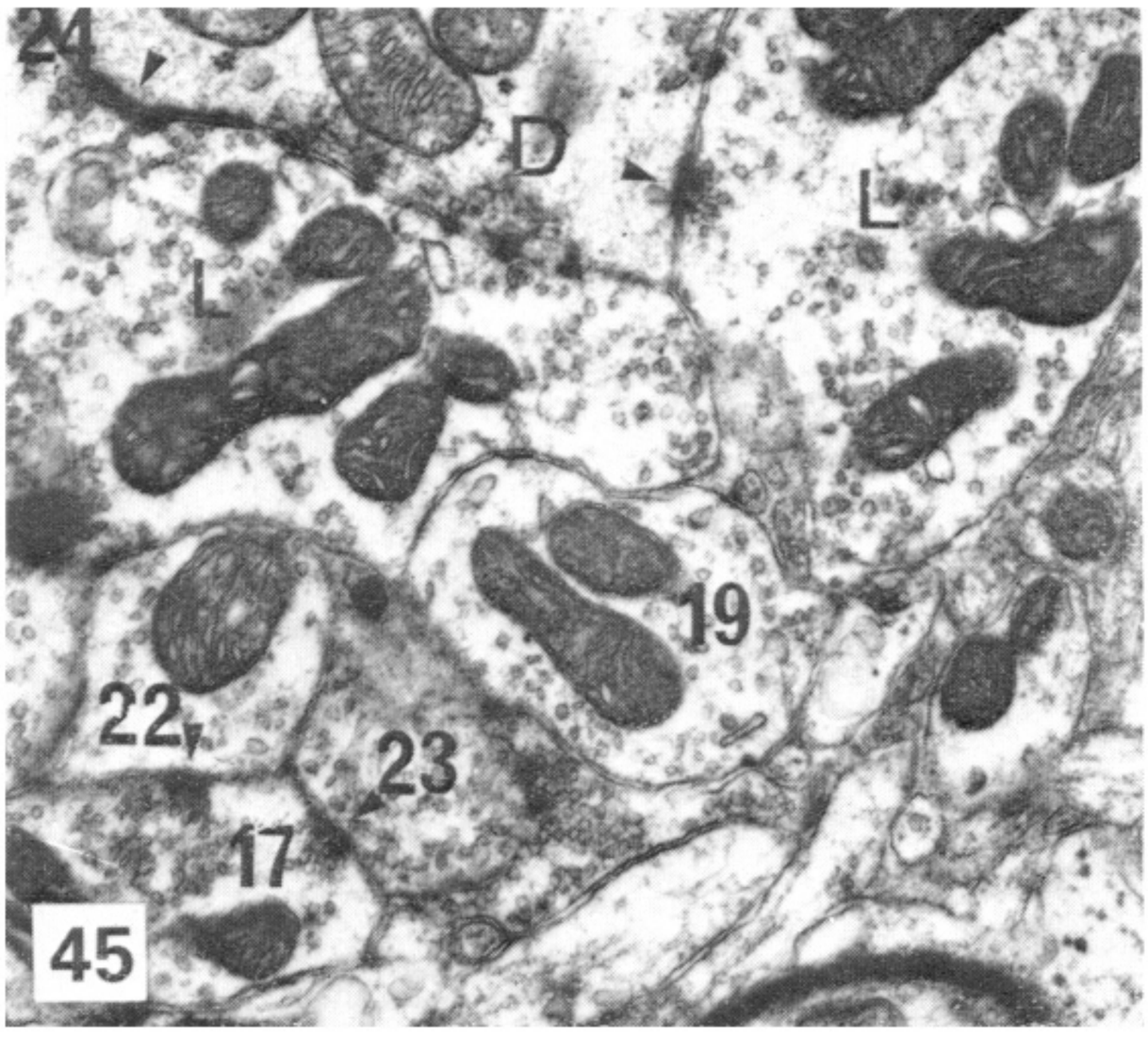
FIGURES 39–42. For description see opposite.

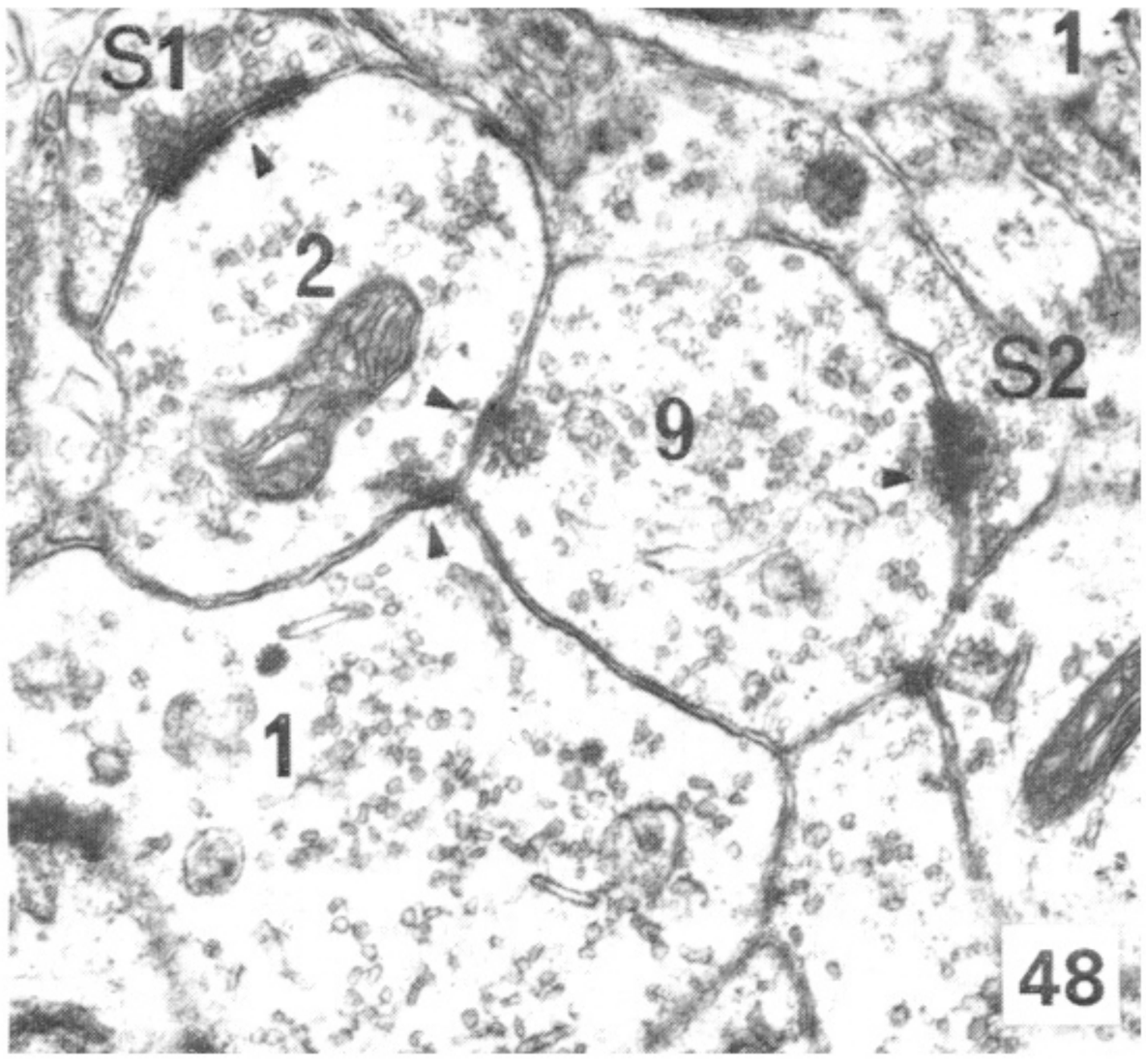




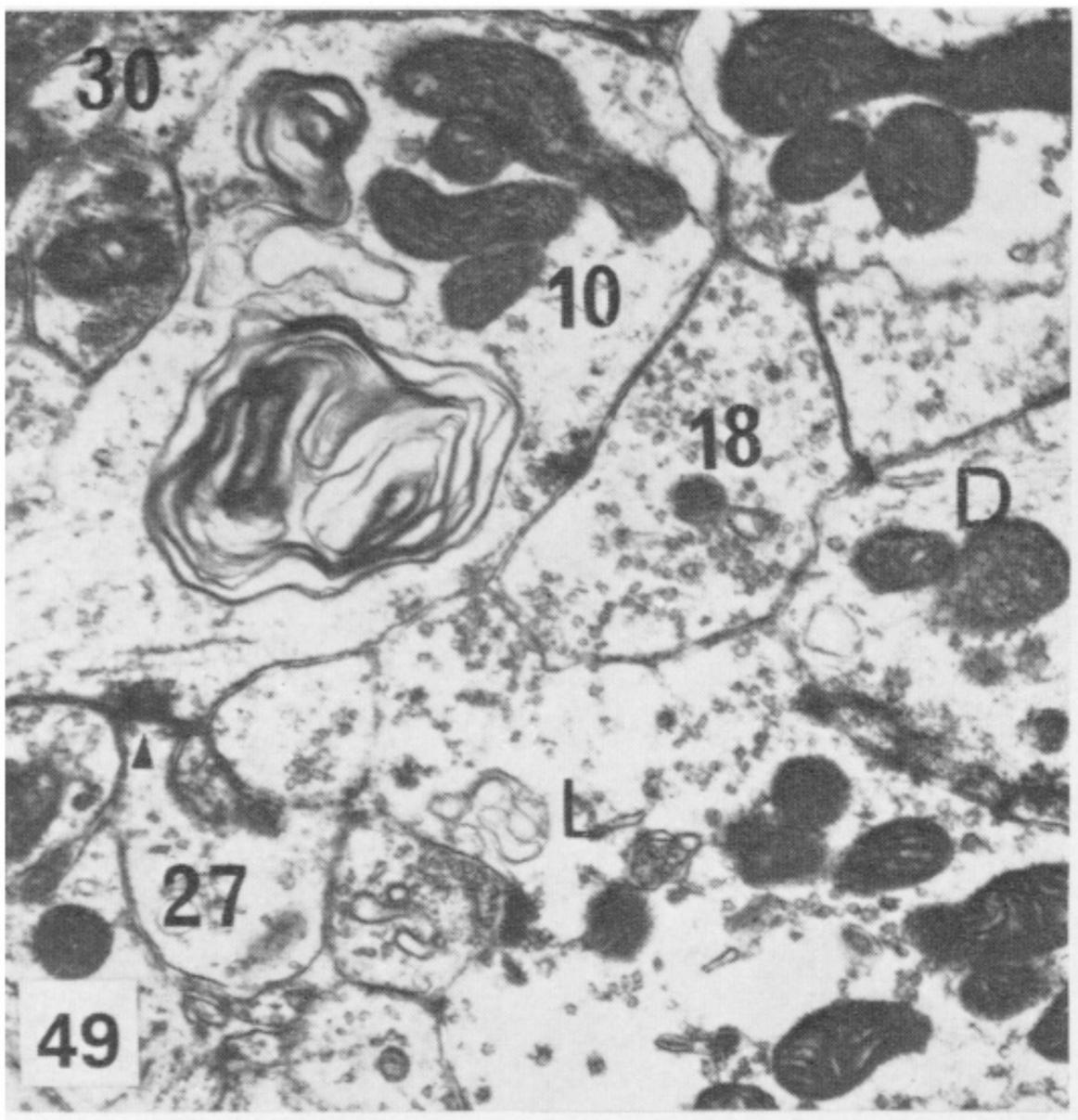


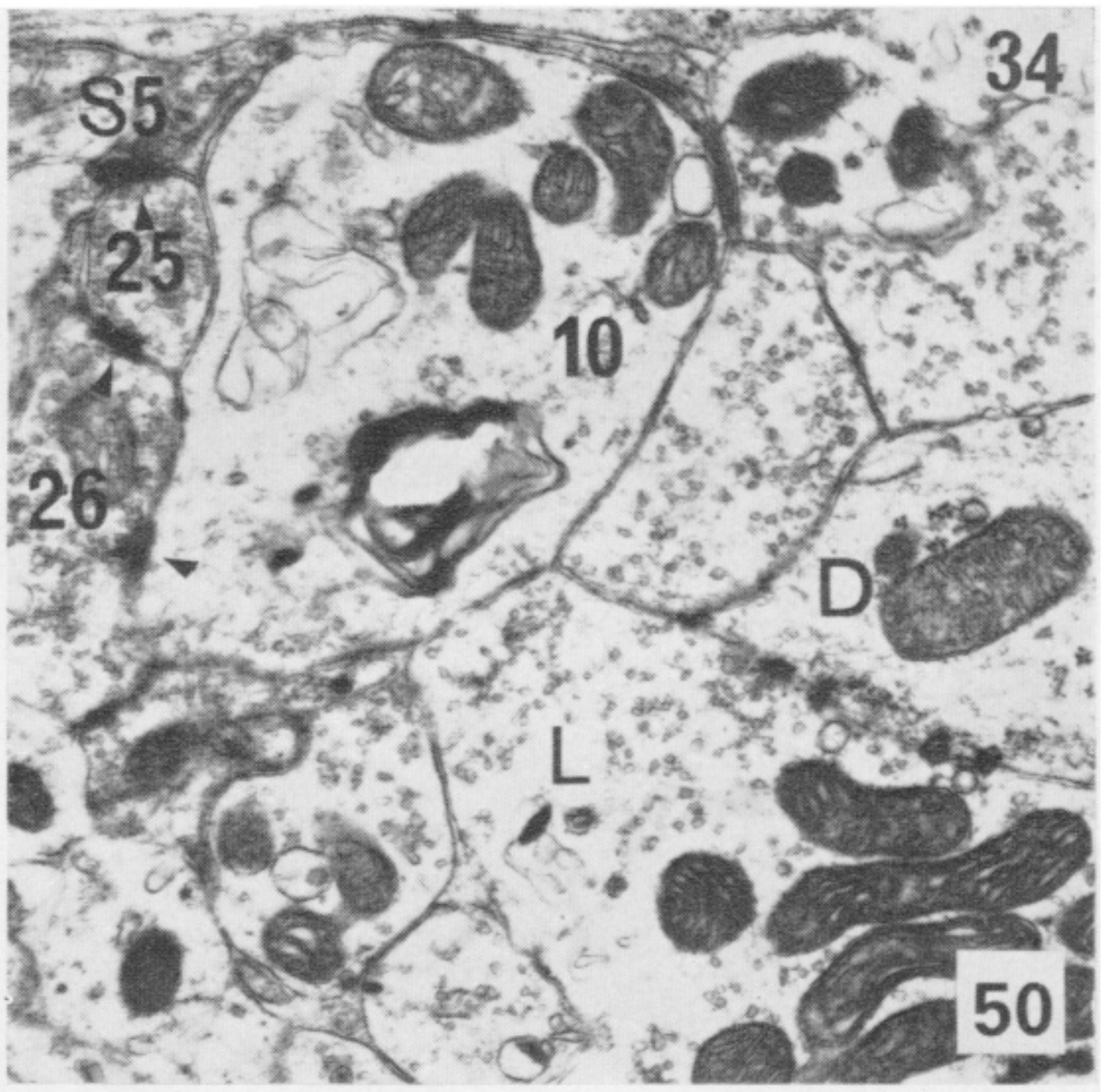


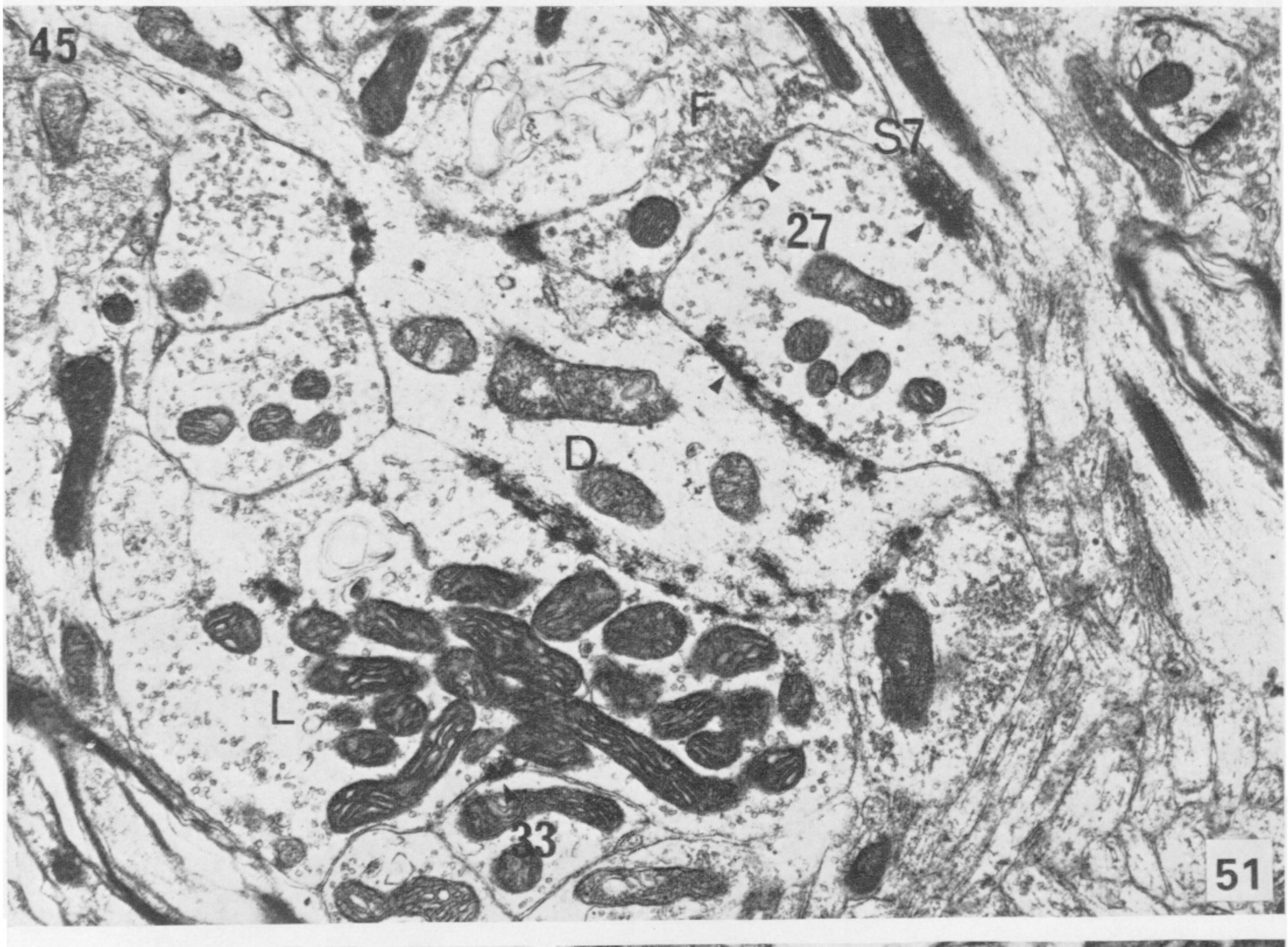


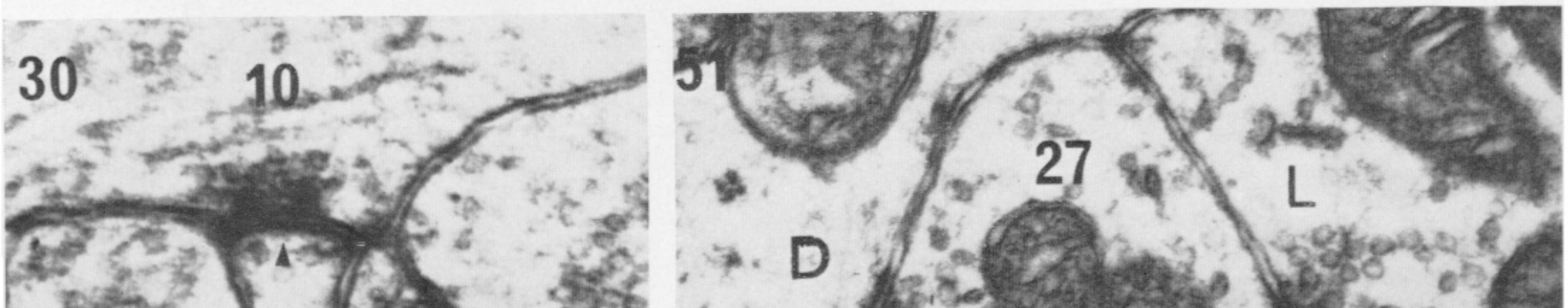


FIGURES 43–48. For description see opposite.

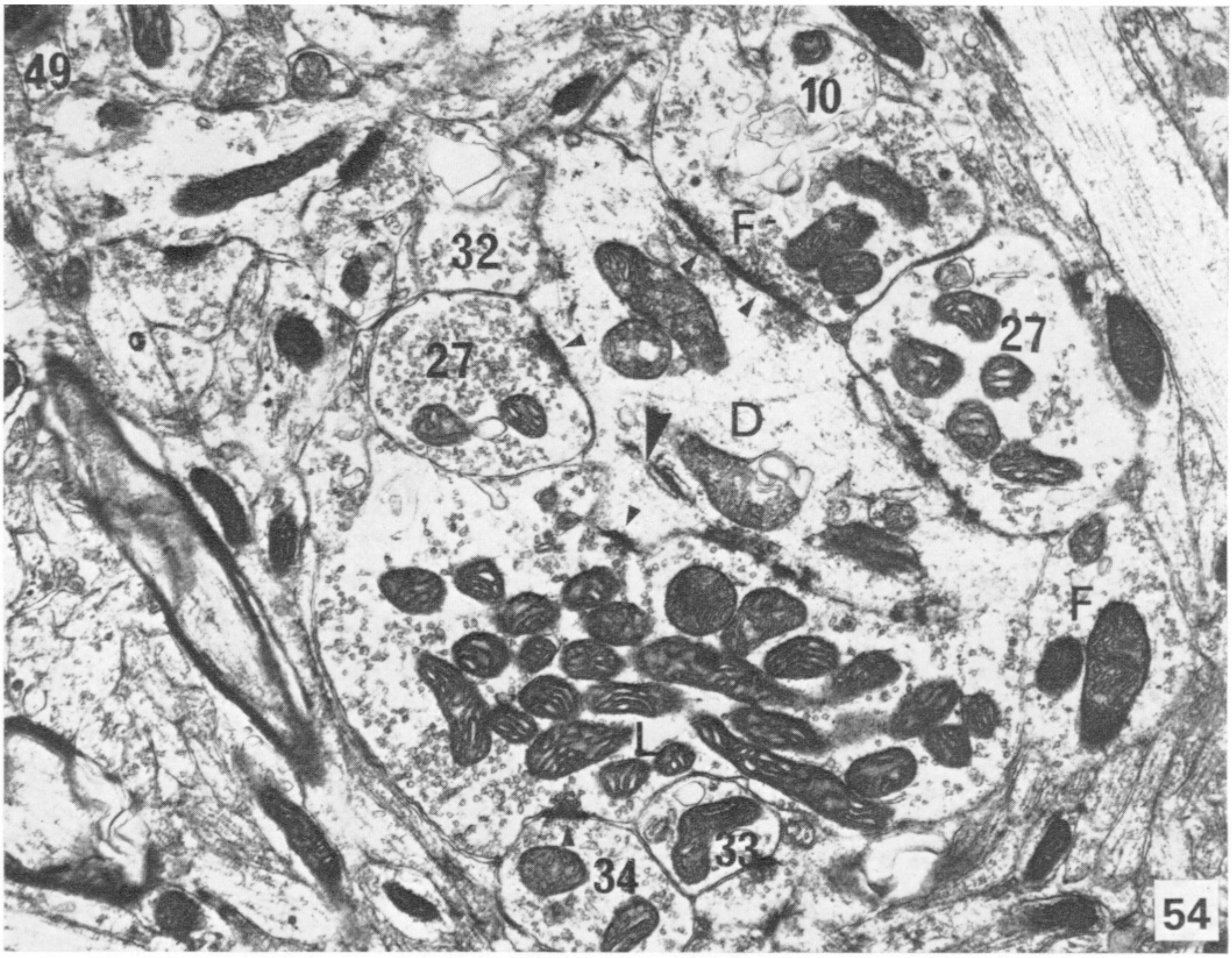


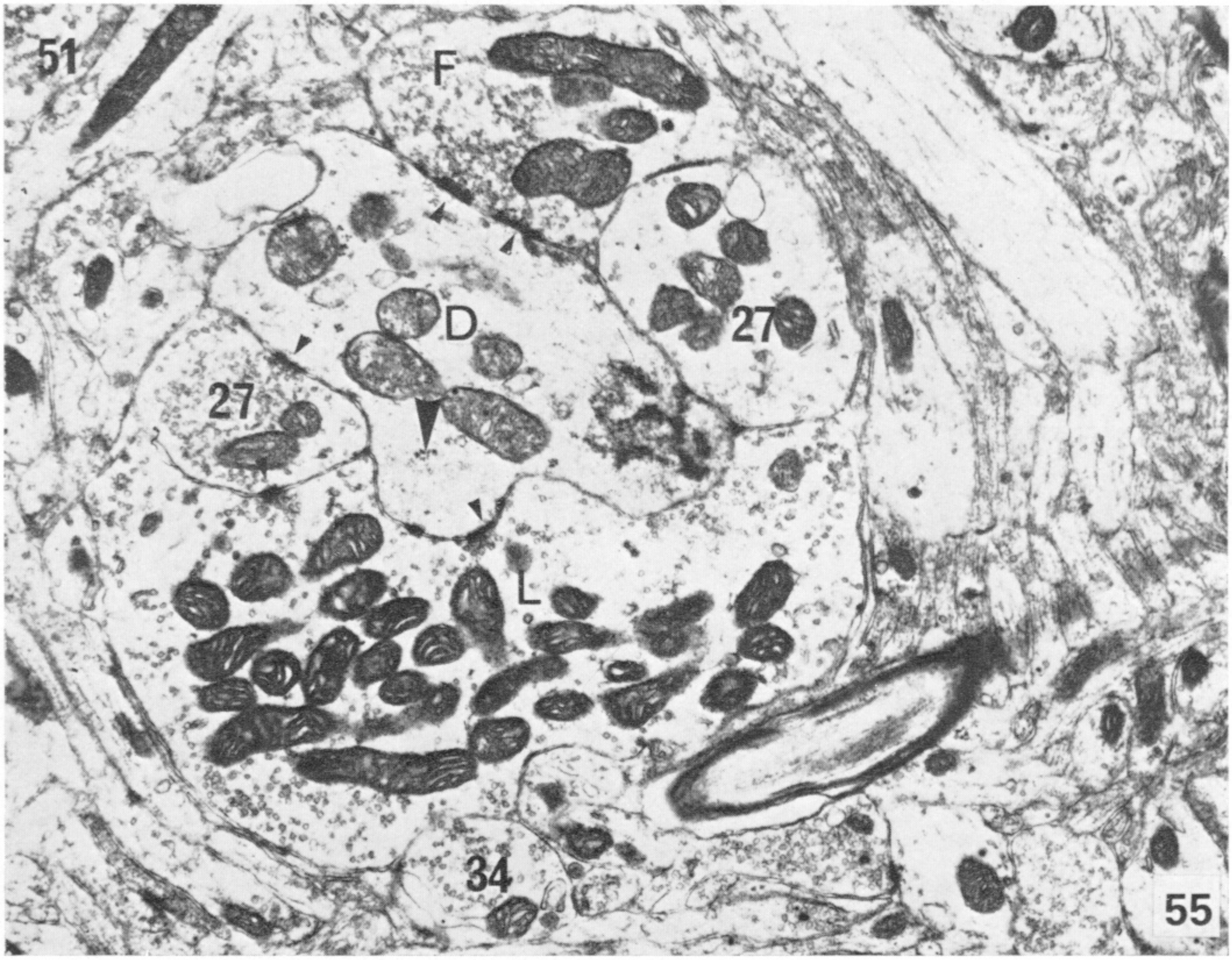




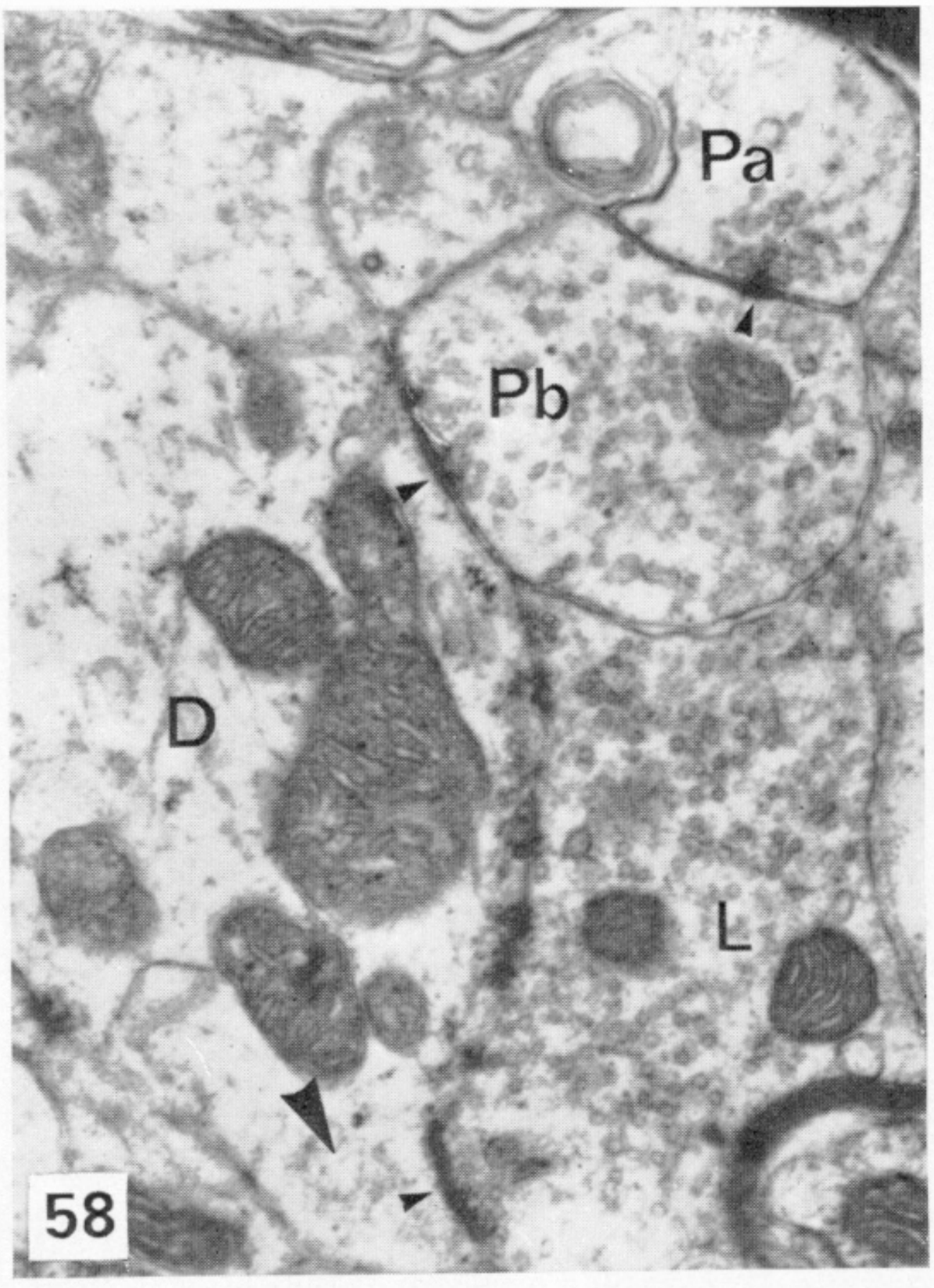


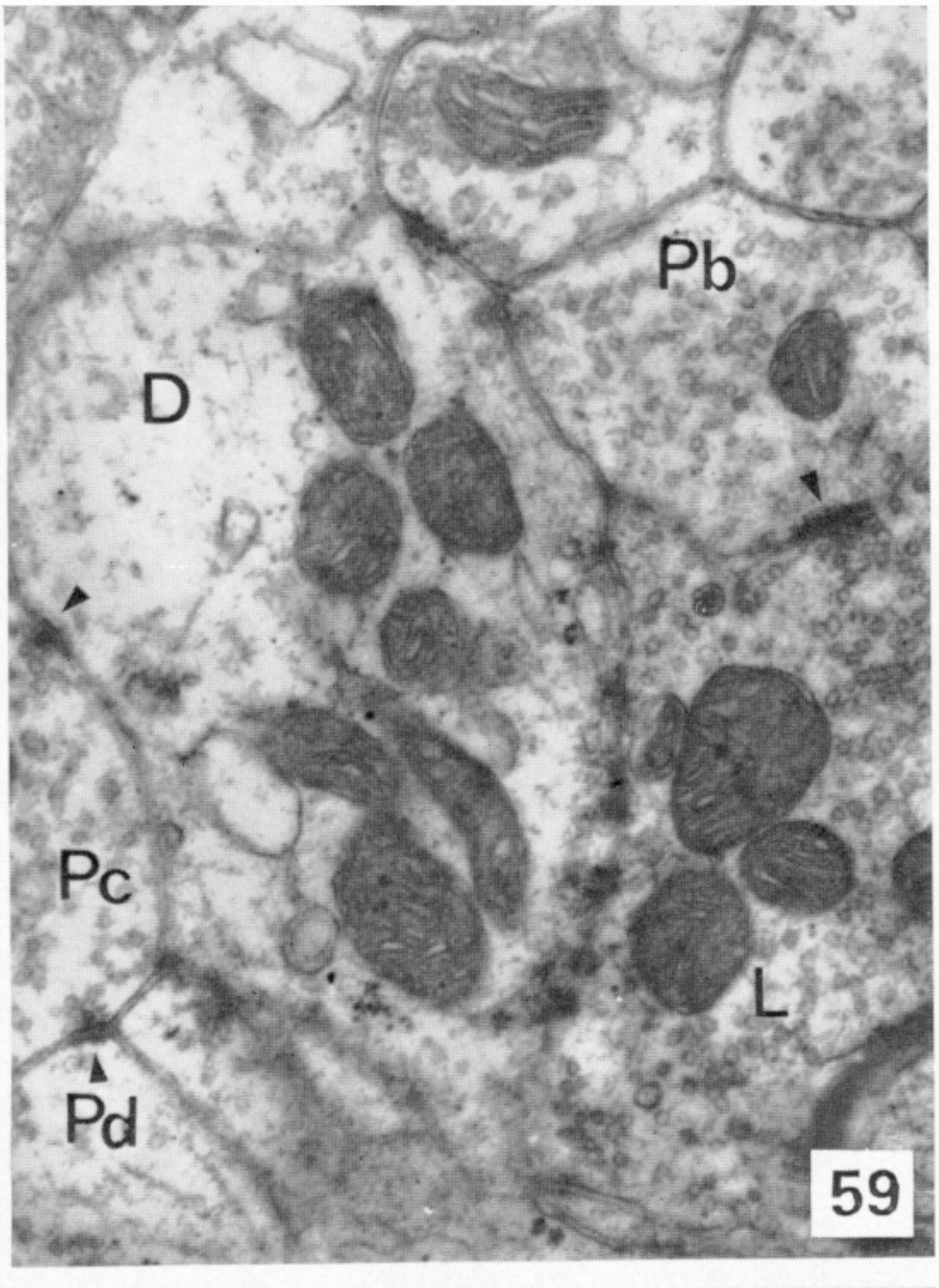
FIGURES 49–53. For description see p. 372.

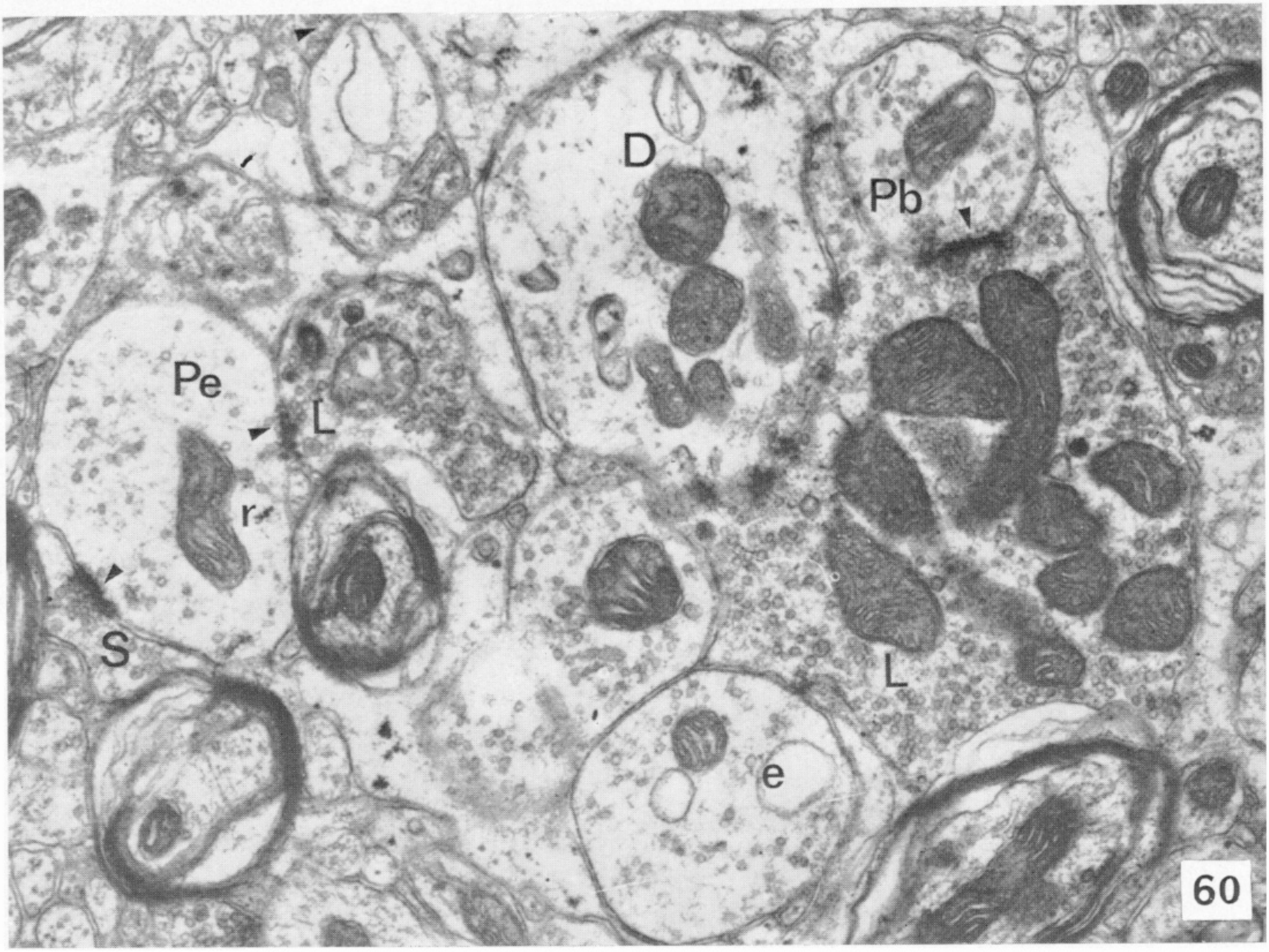




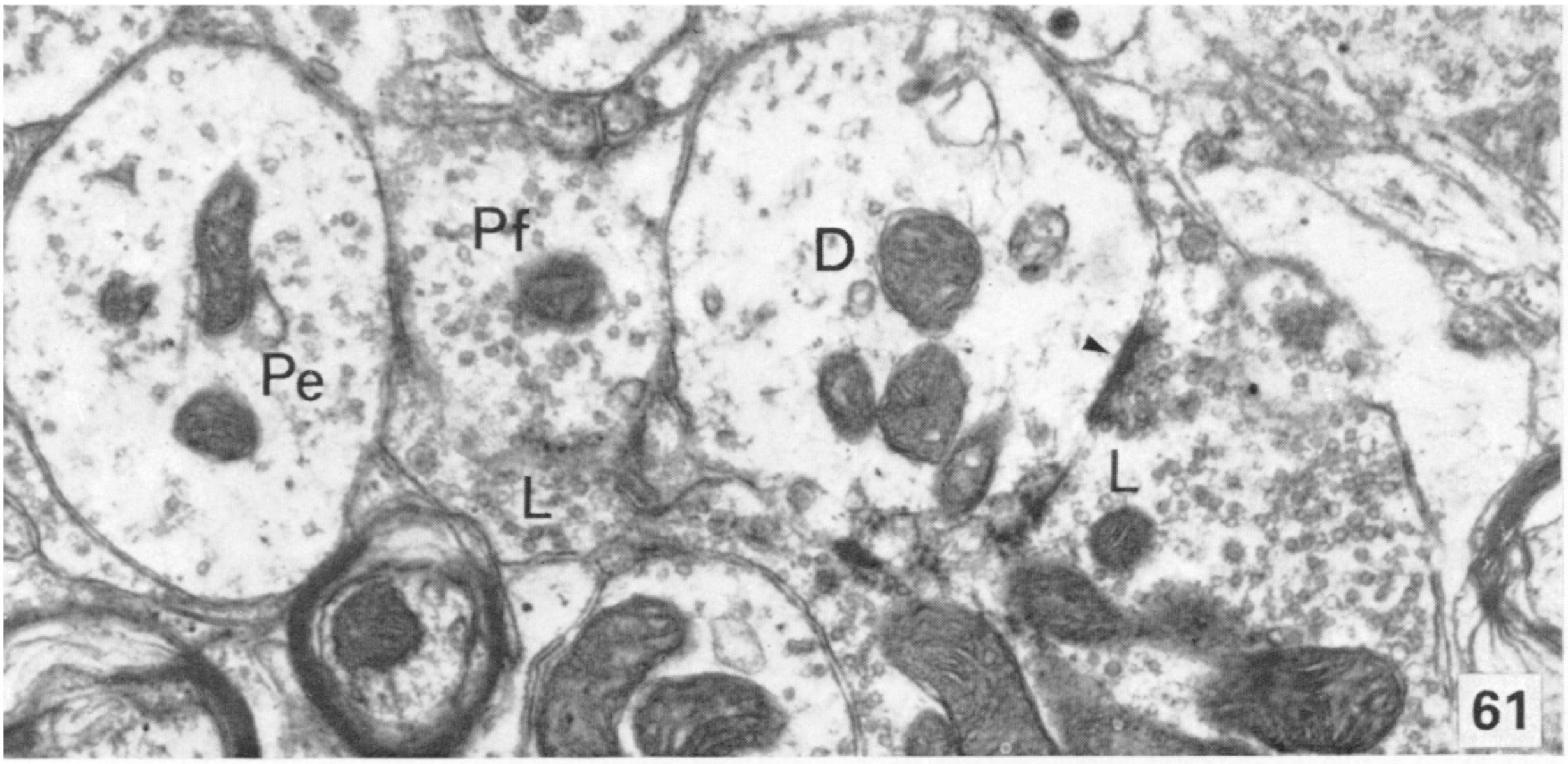
FIGURES 54 AND 55. For description see p. 373.

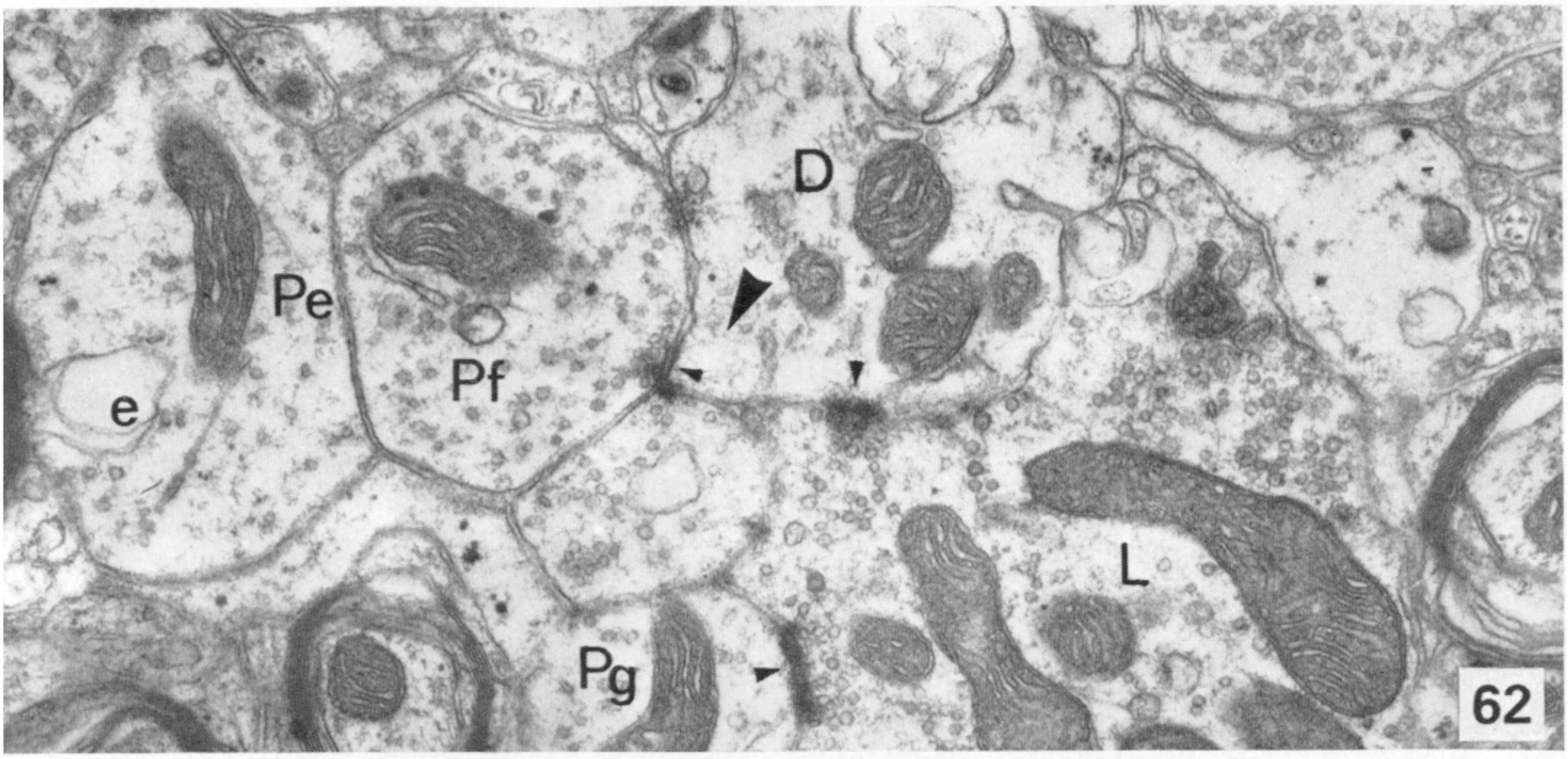


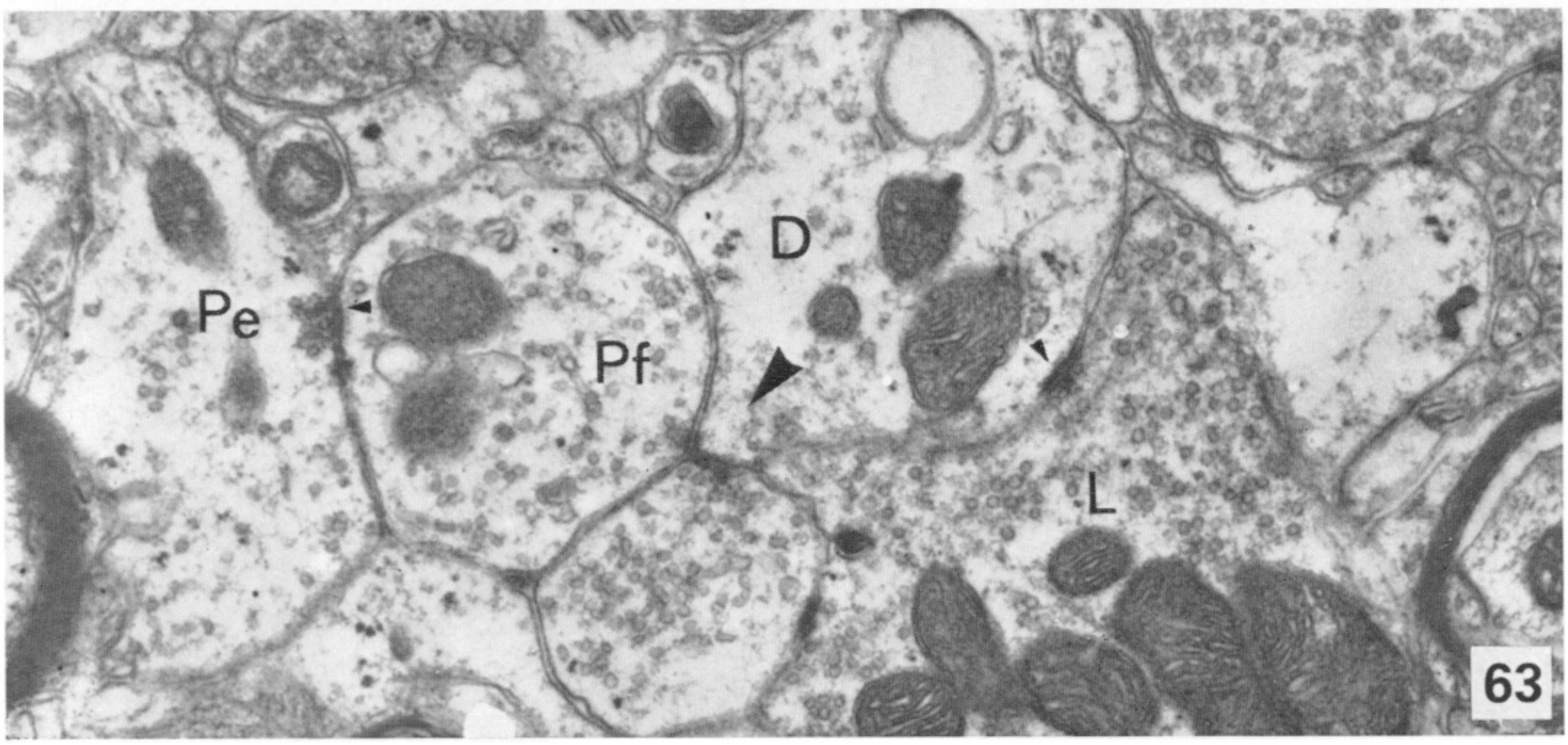




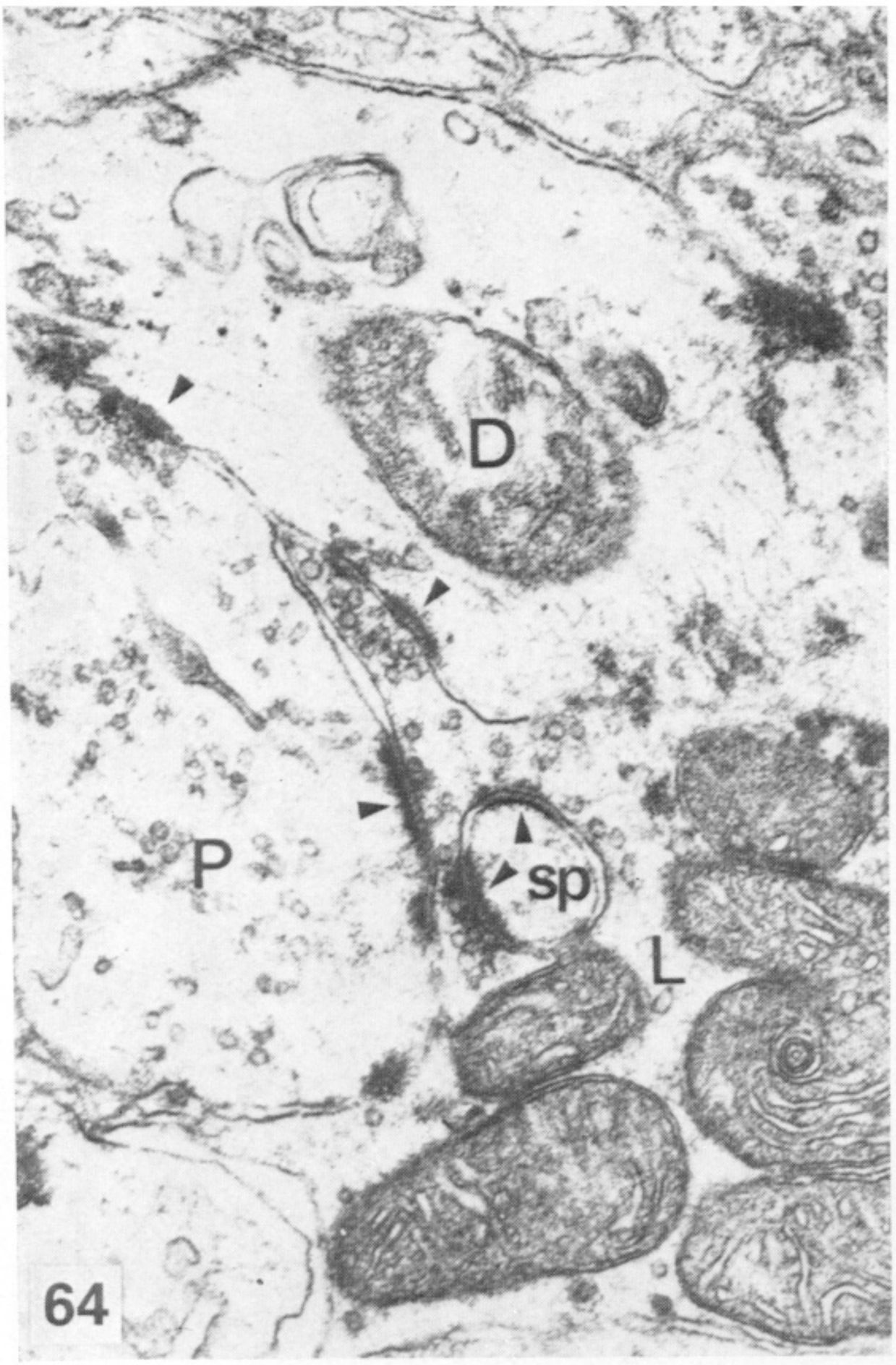
FIGURES 58–60. For description see opposite.

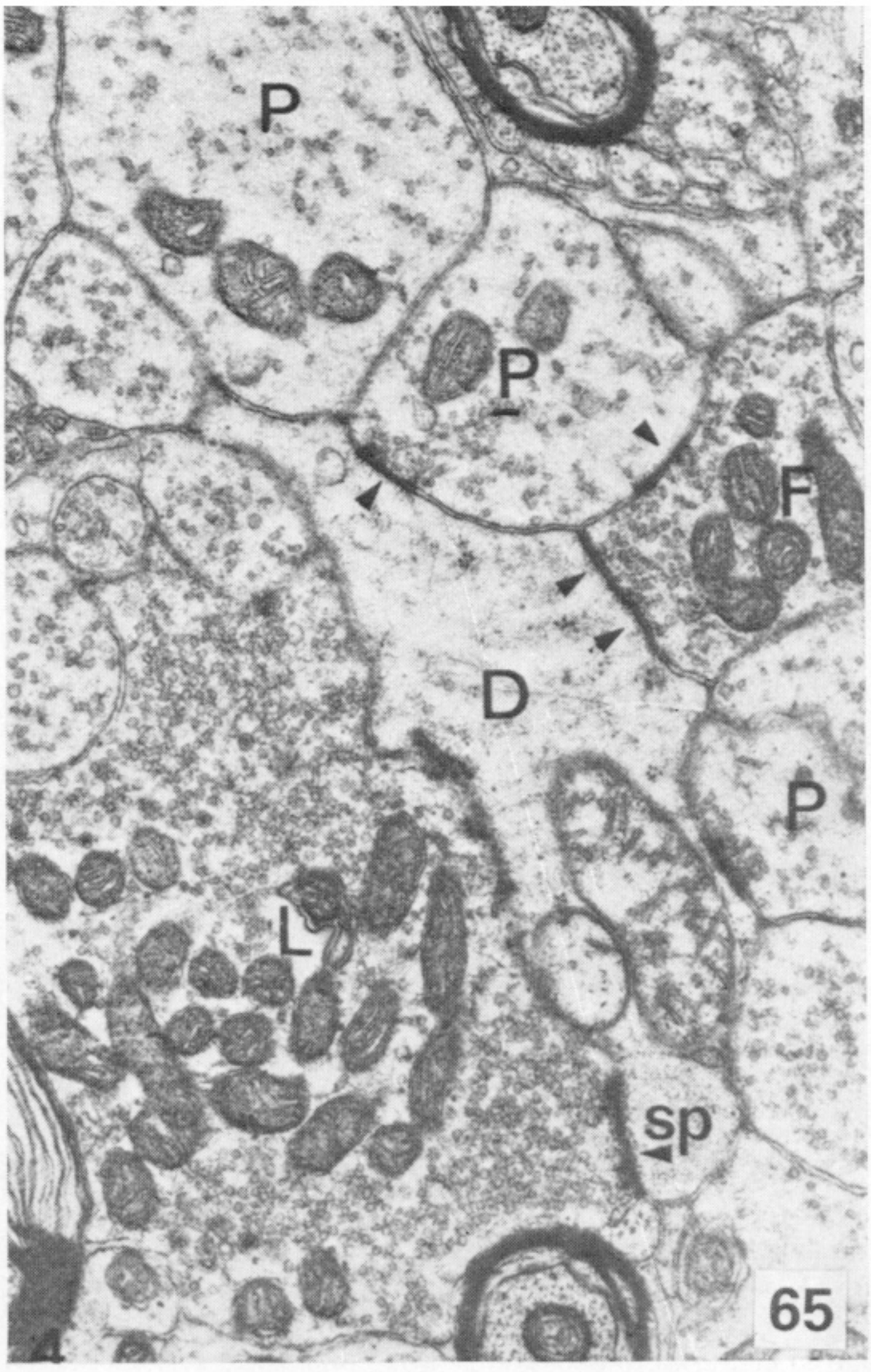


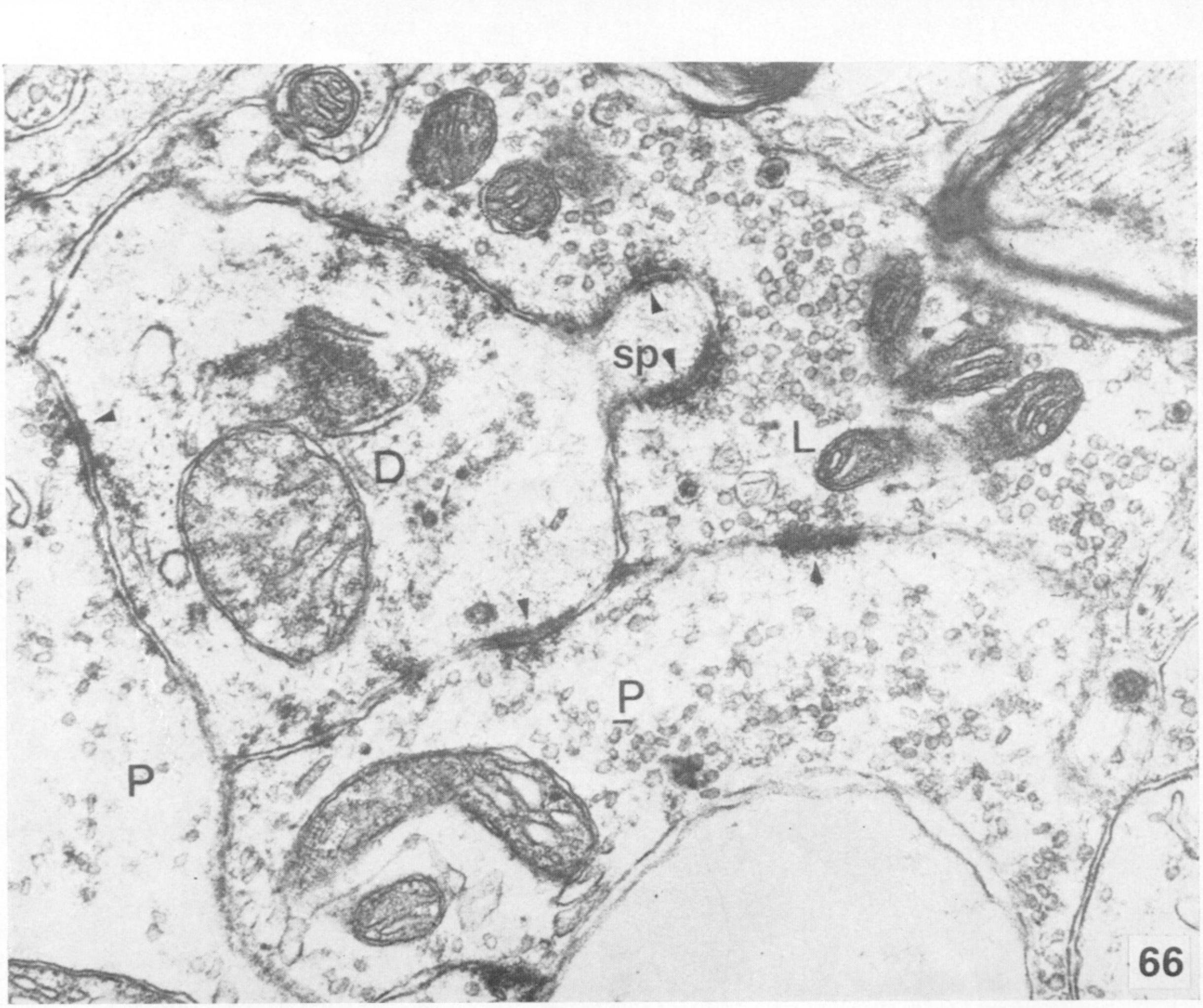




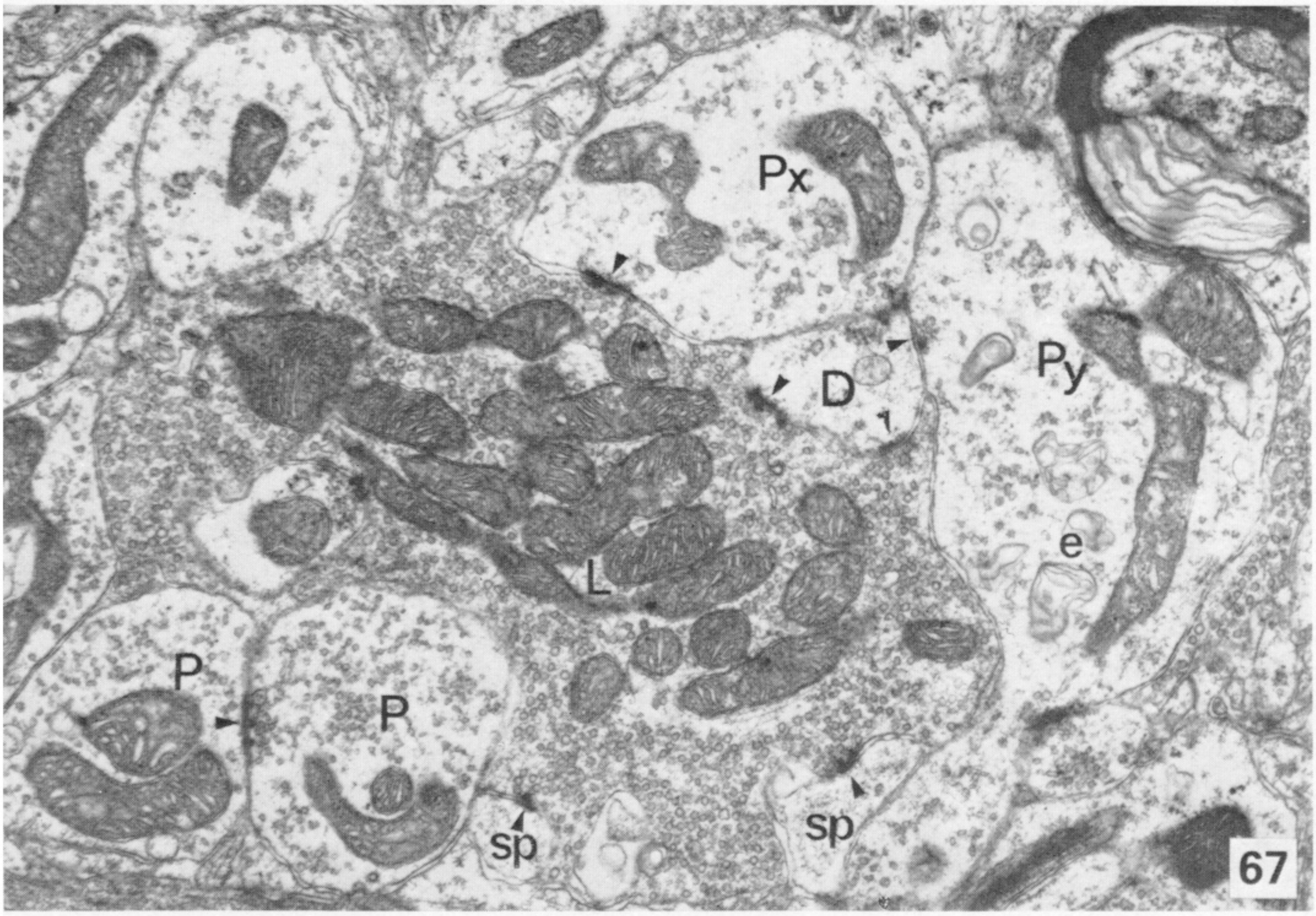
FIGURES 61–63. For description see opposite.

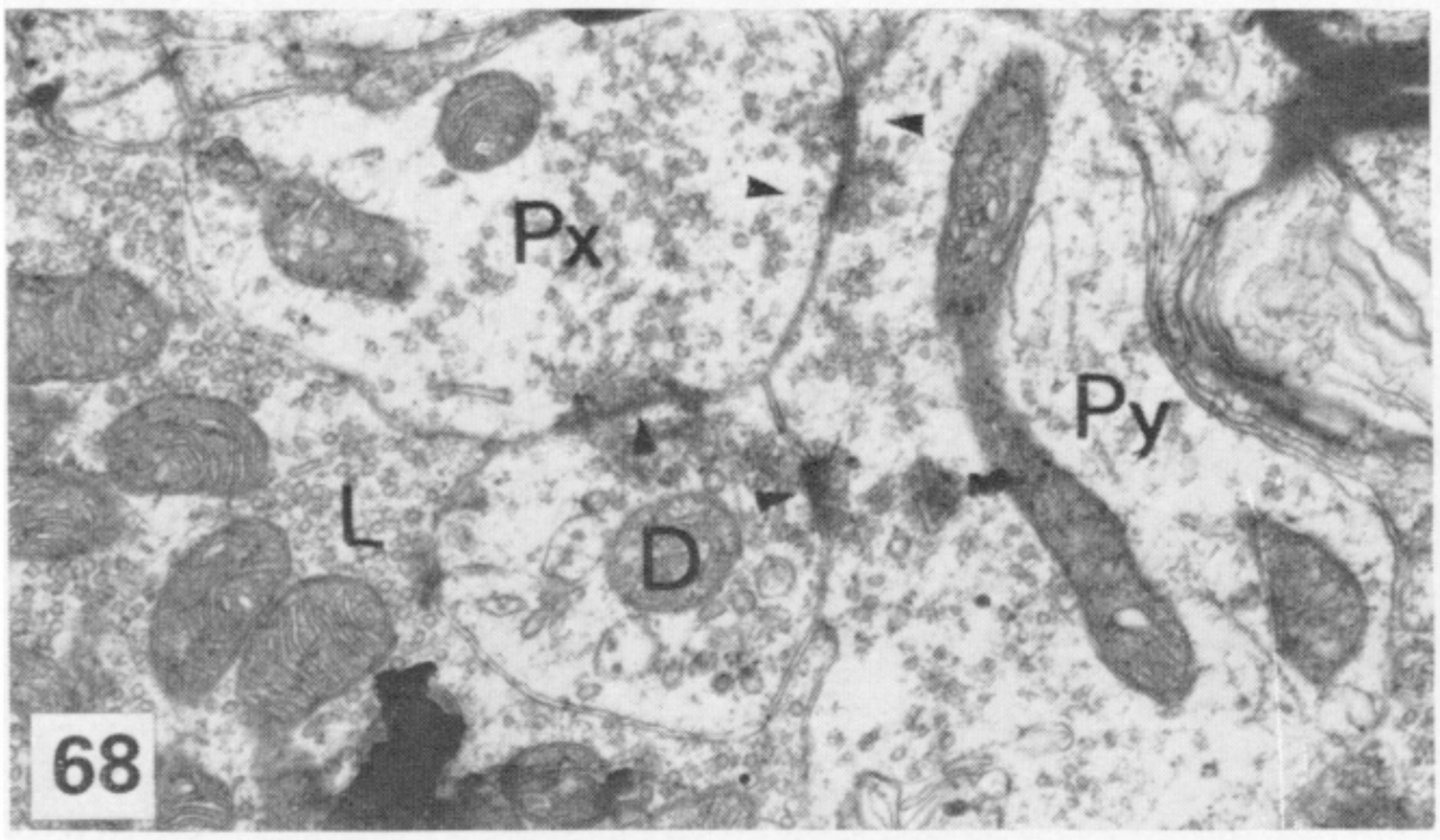


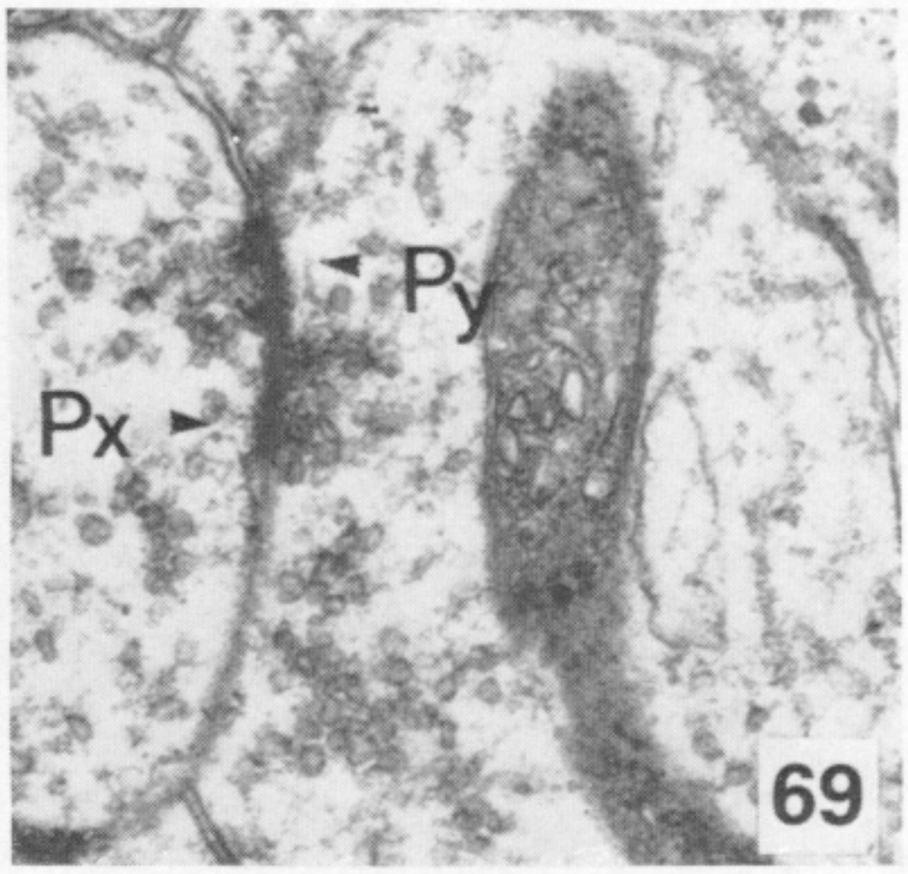


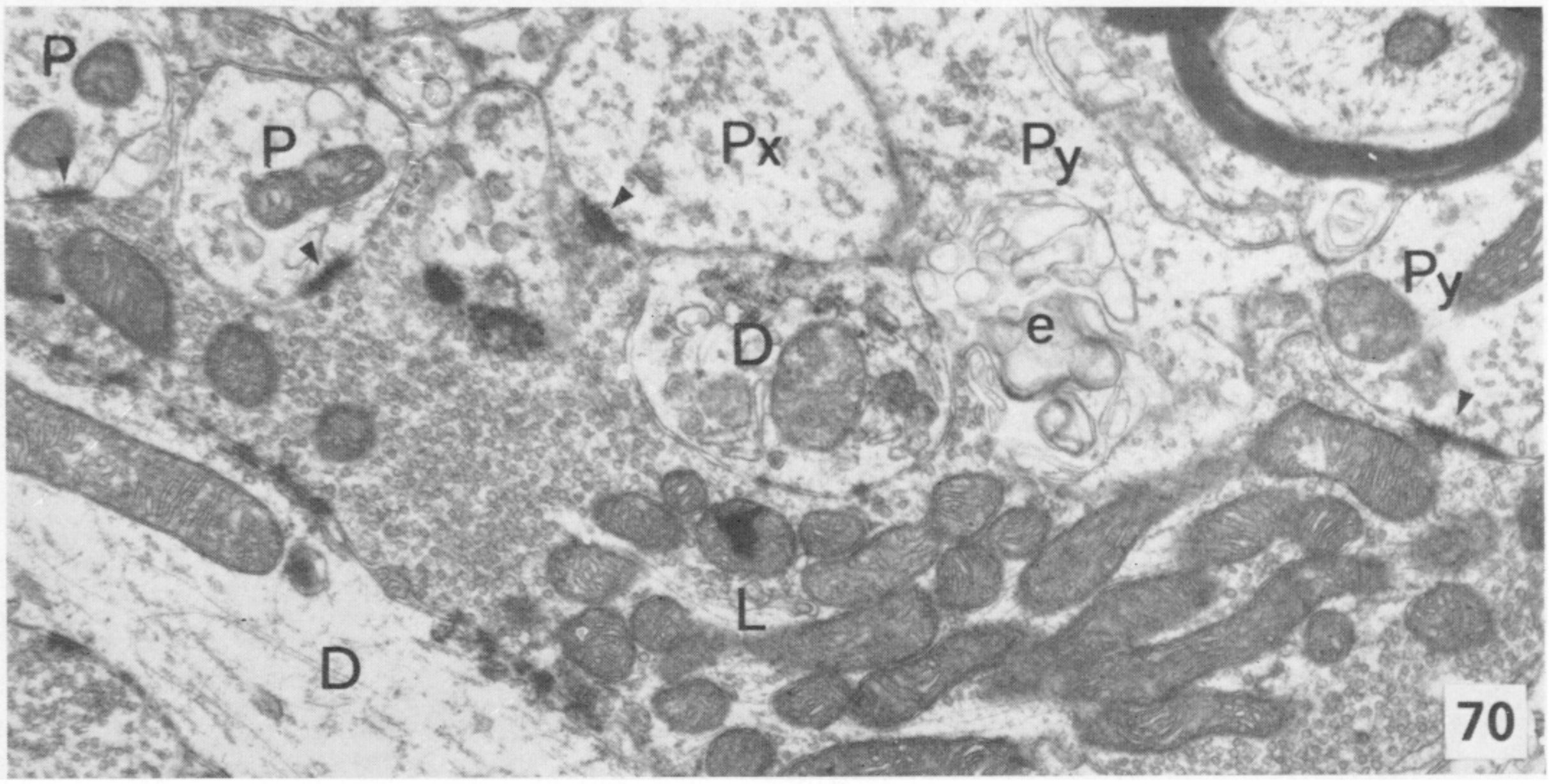


FIGURES 64–66. For description see p. 380.

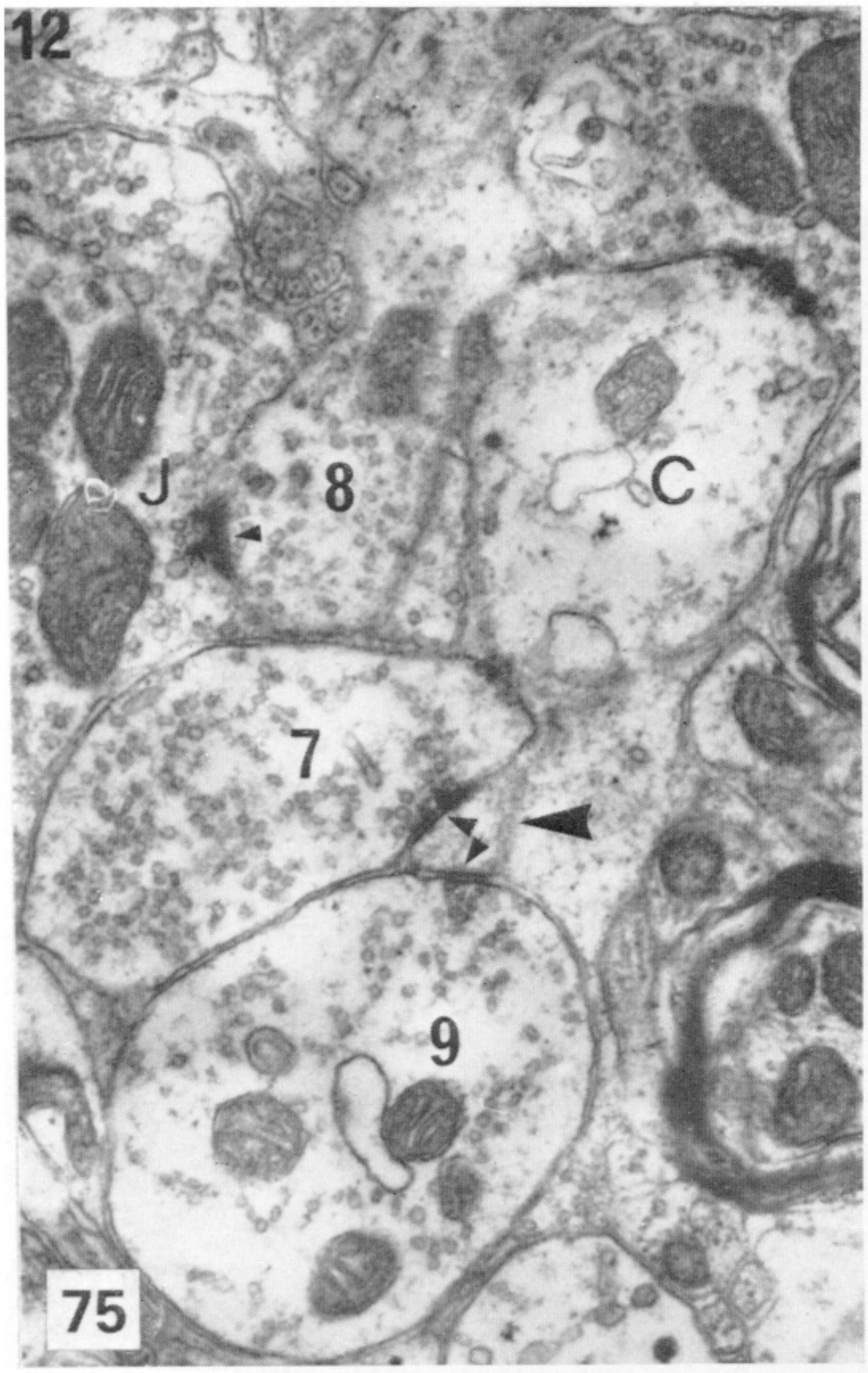


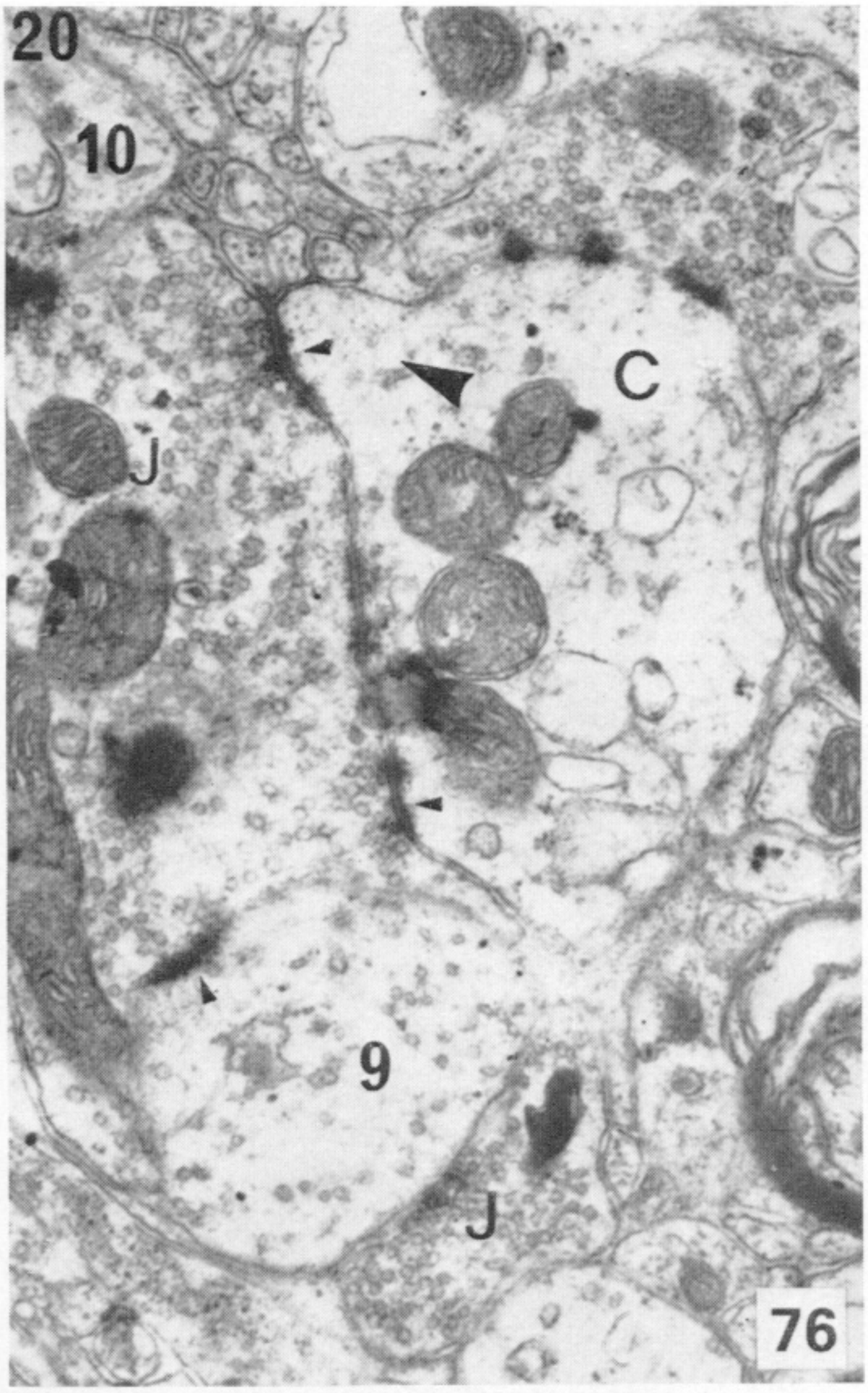


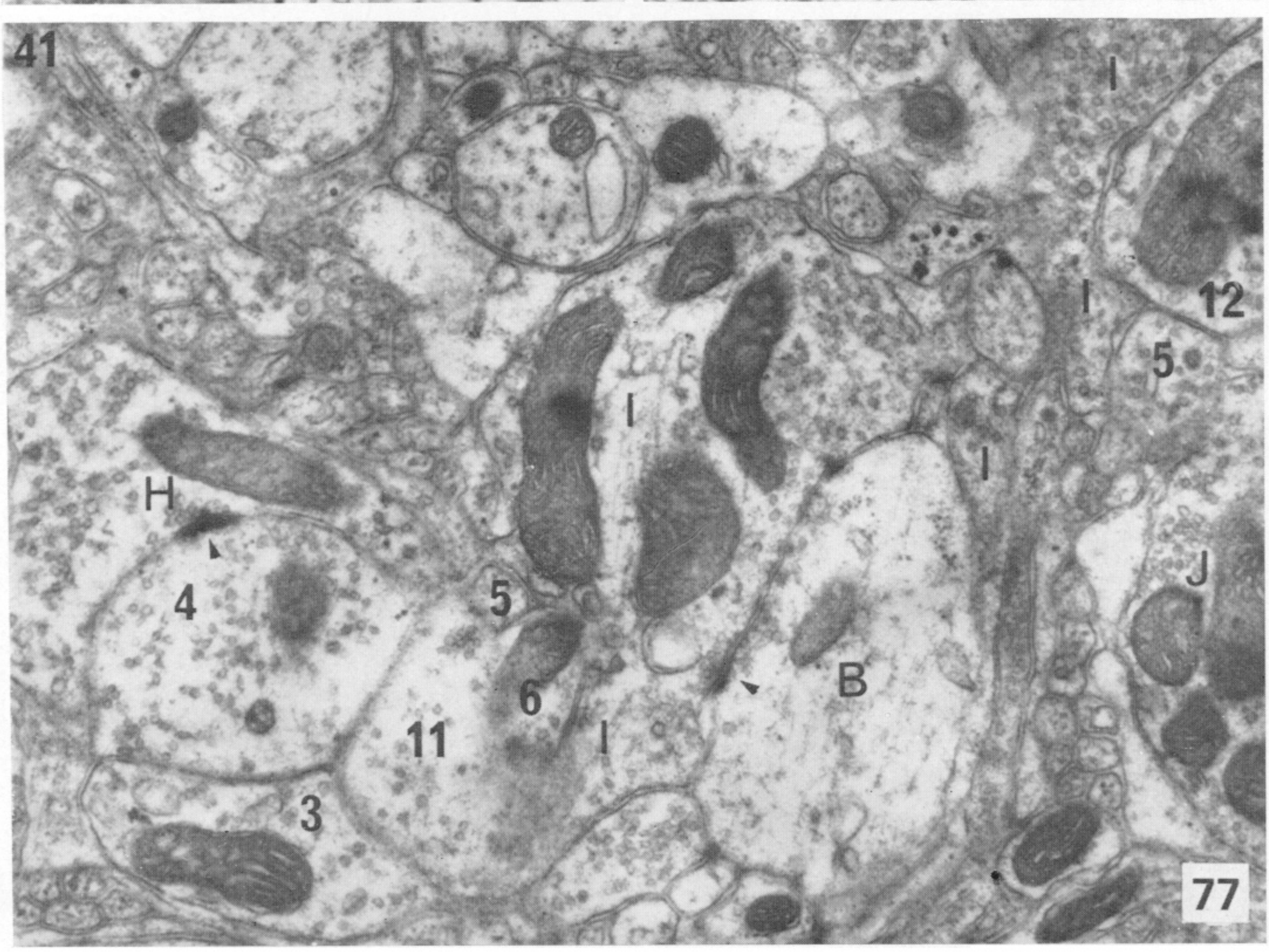




FIGURES 67–70. For description see p. 381.







FIGURES 75–77. For description see opposite.

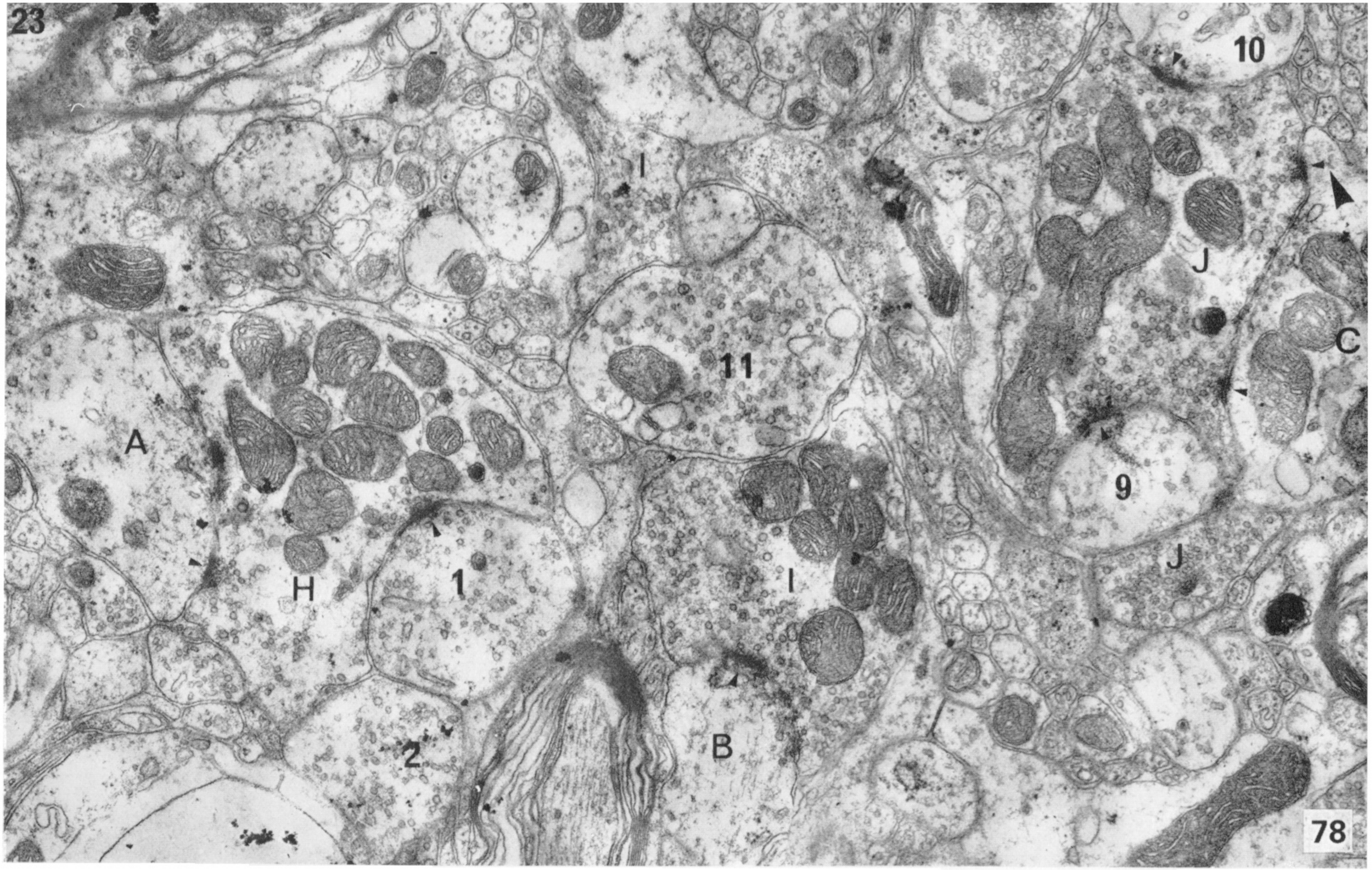
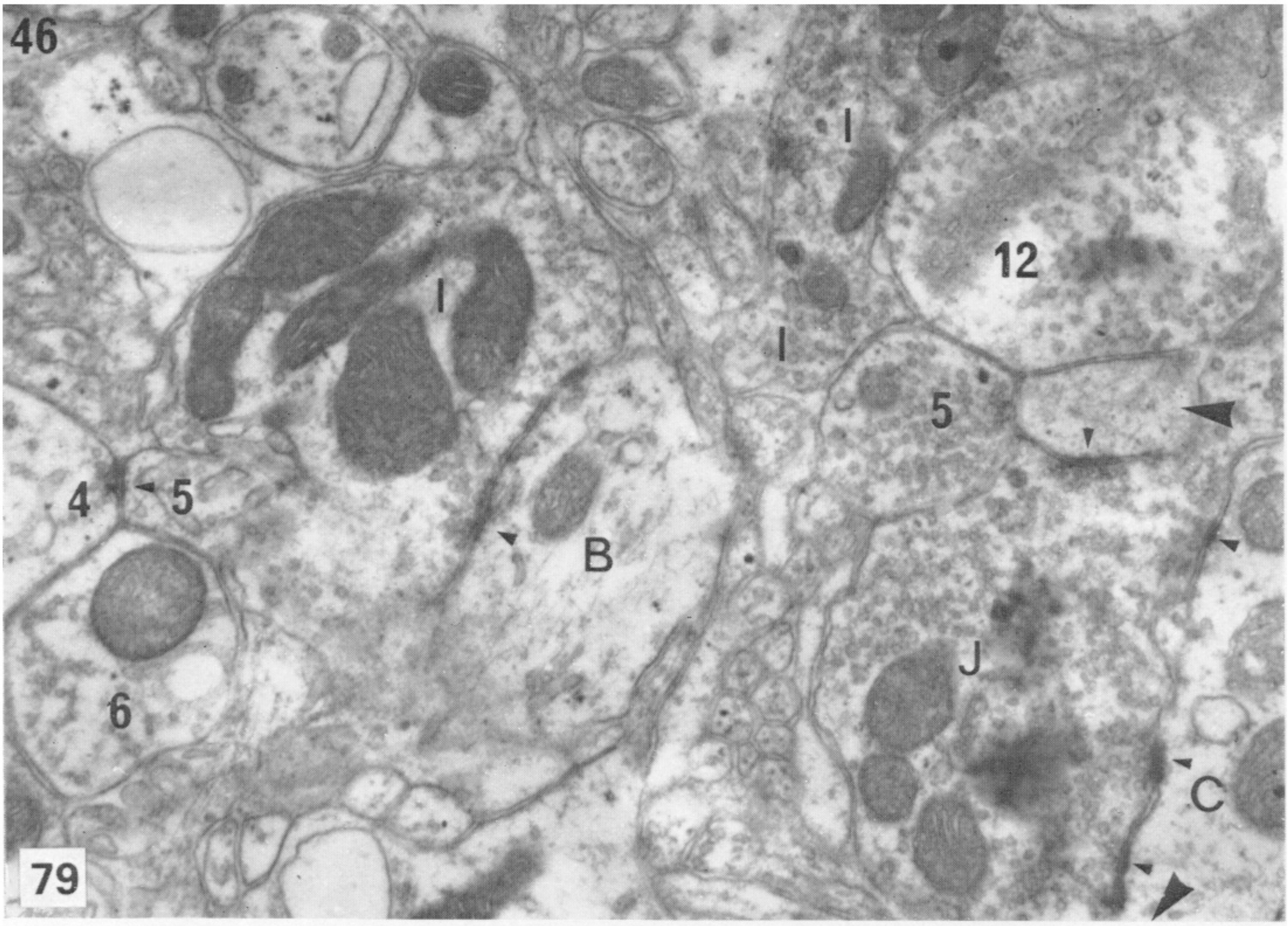
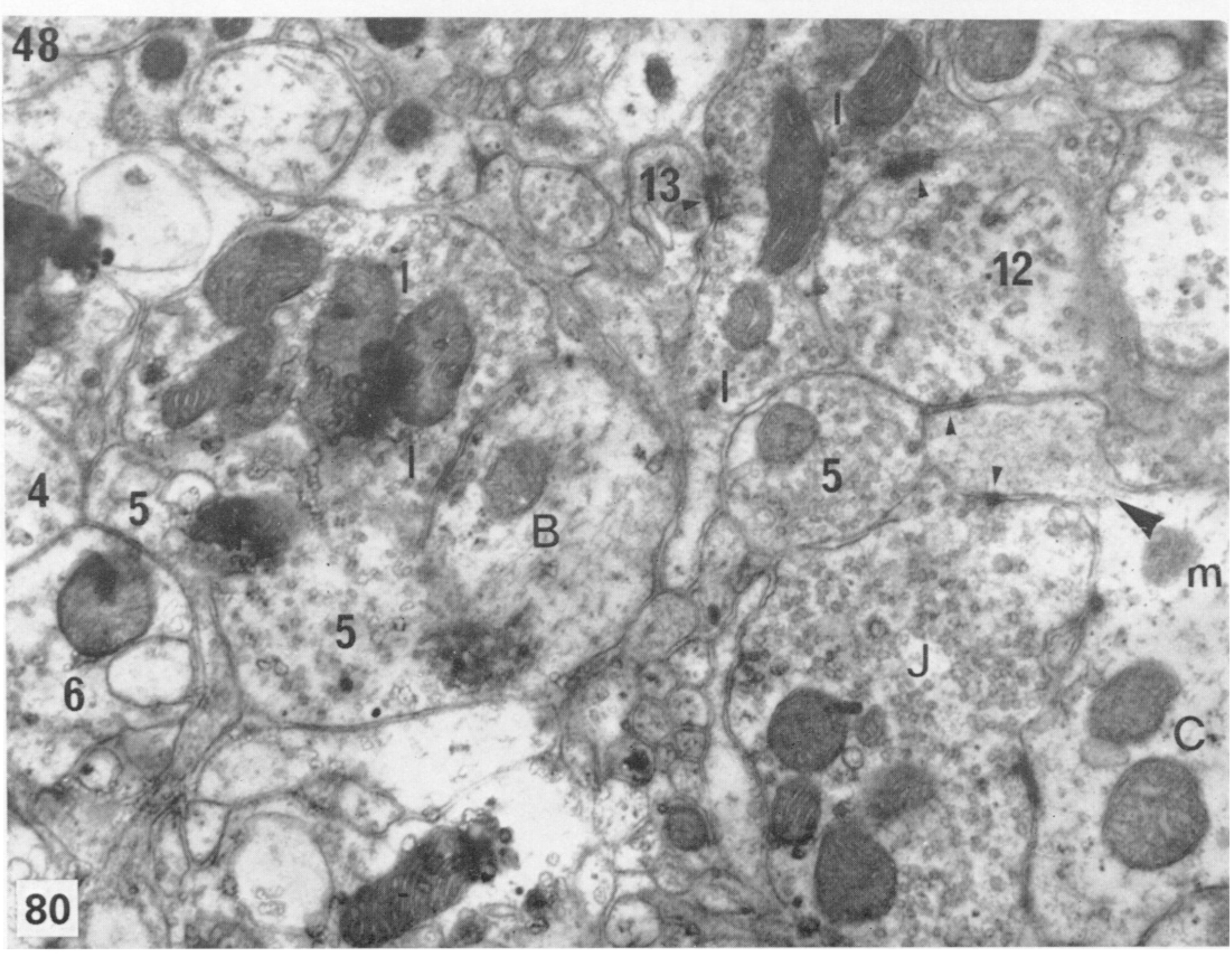
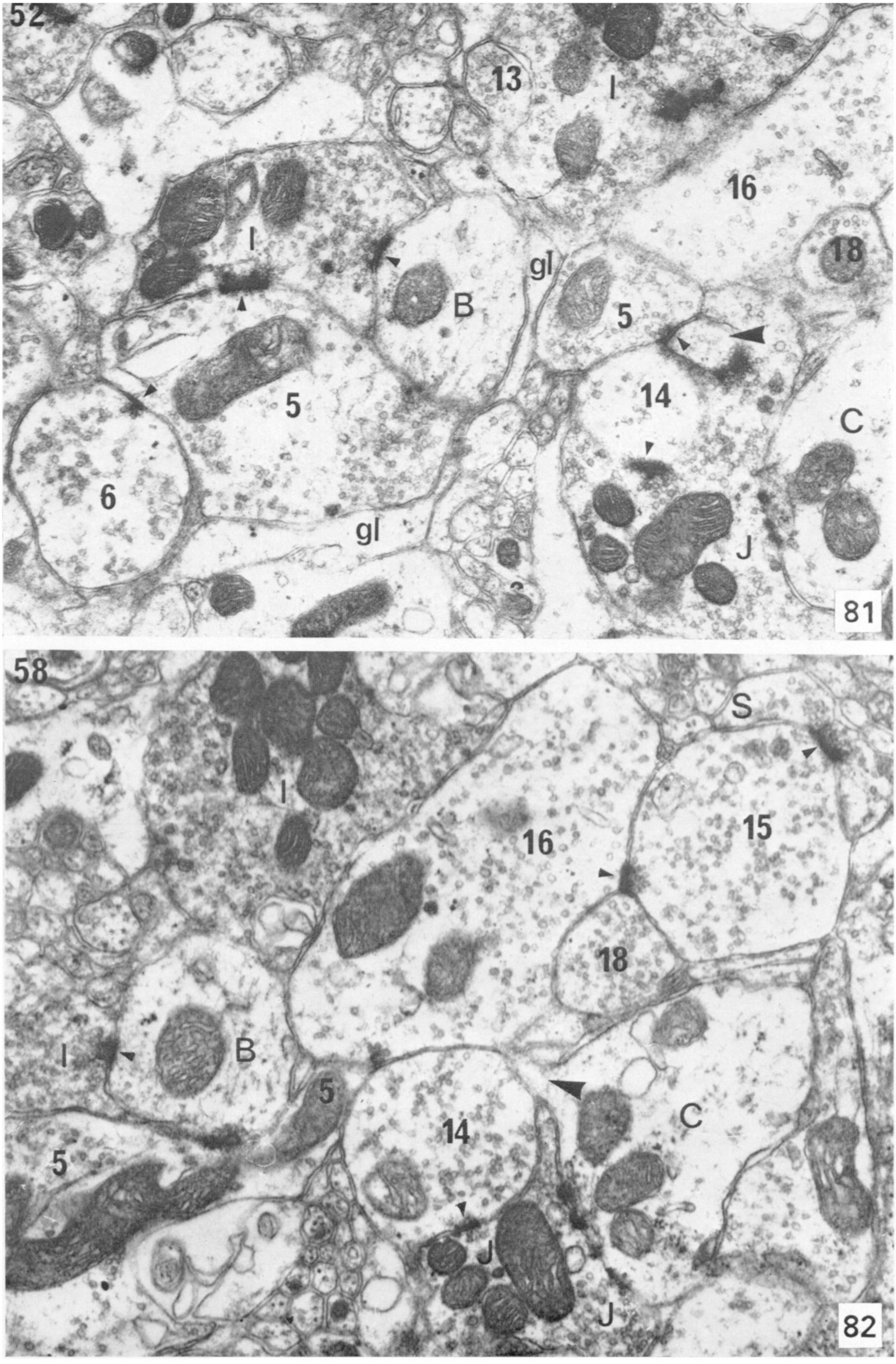


FIGURE 78. For description see opposite.

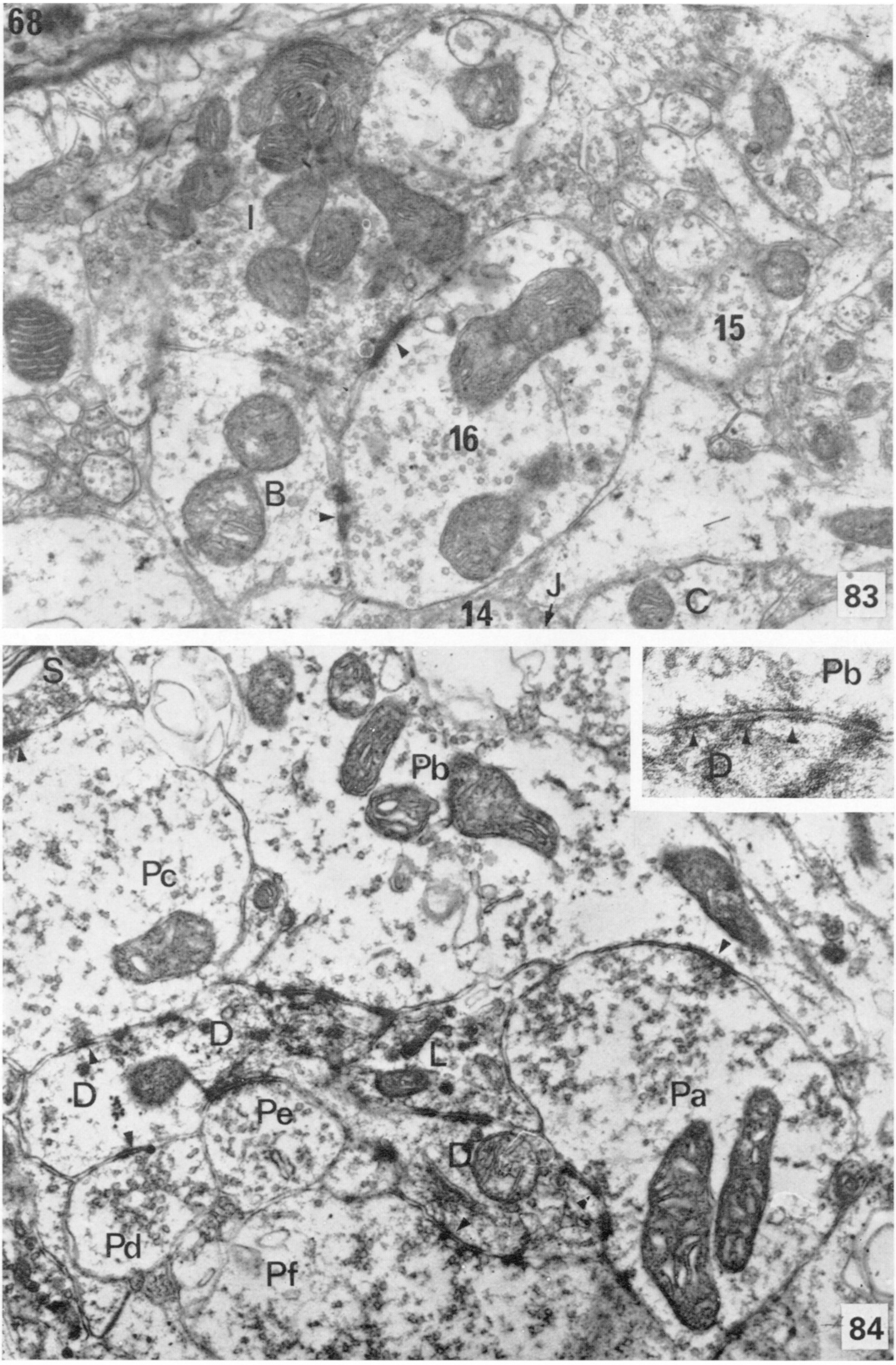




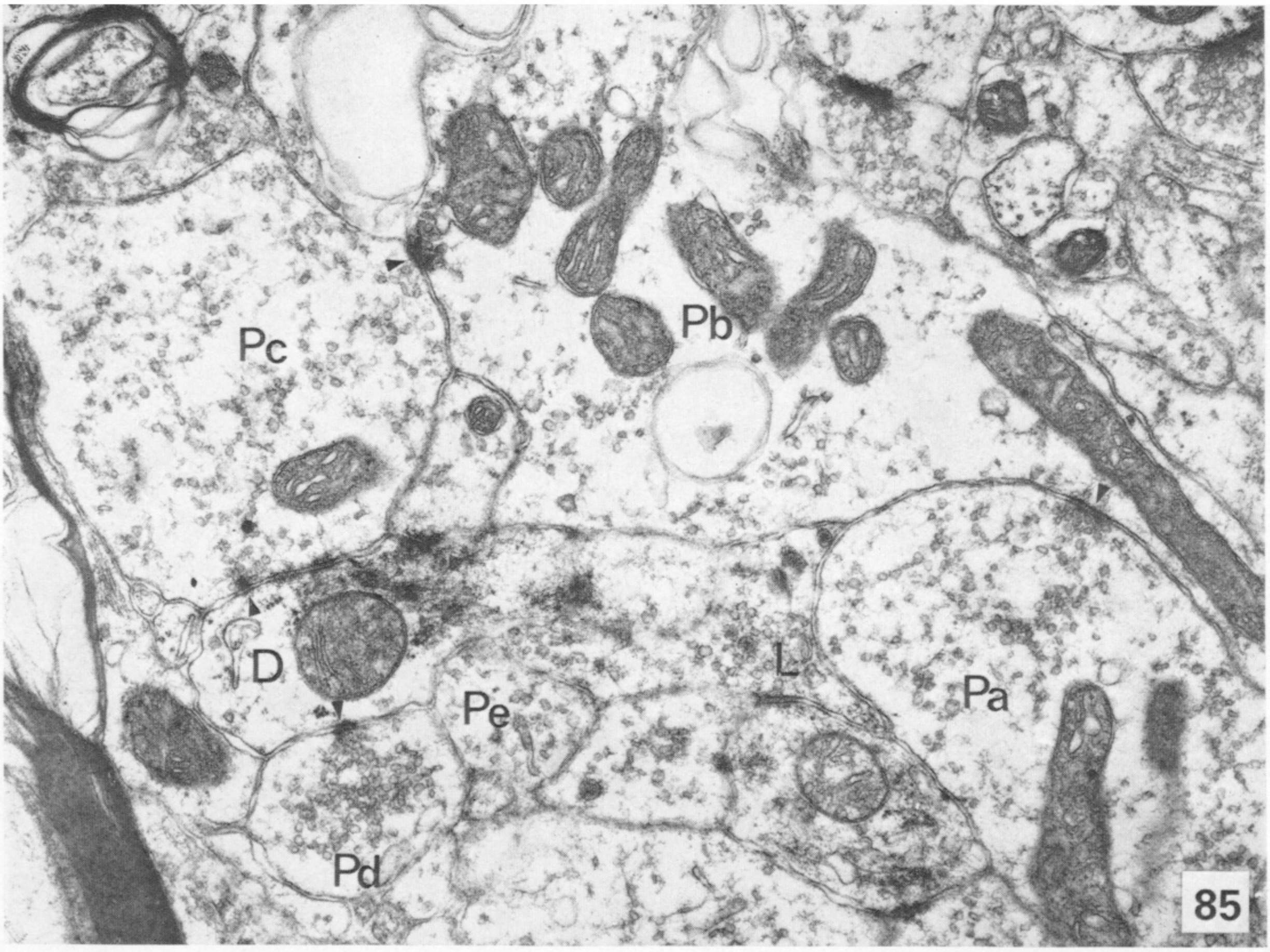
FIGURES 79 AND 80. For description see p. 384.

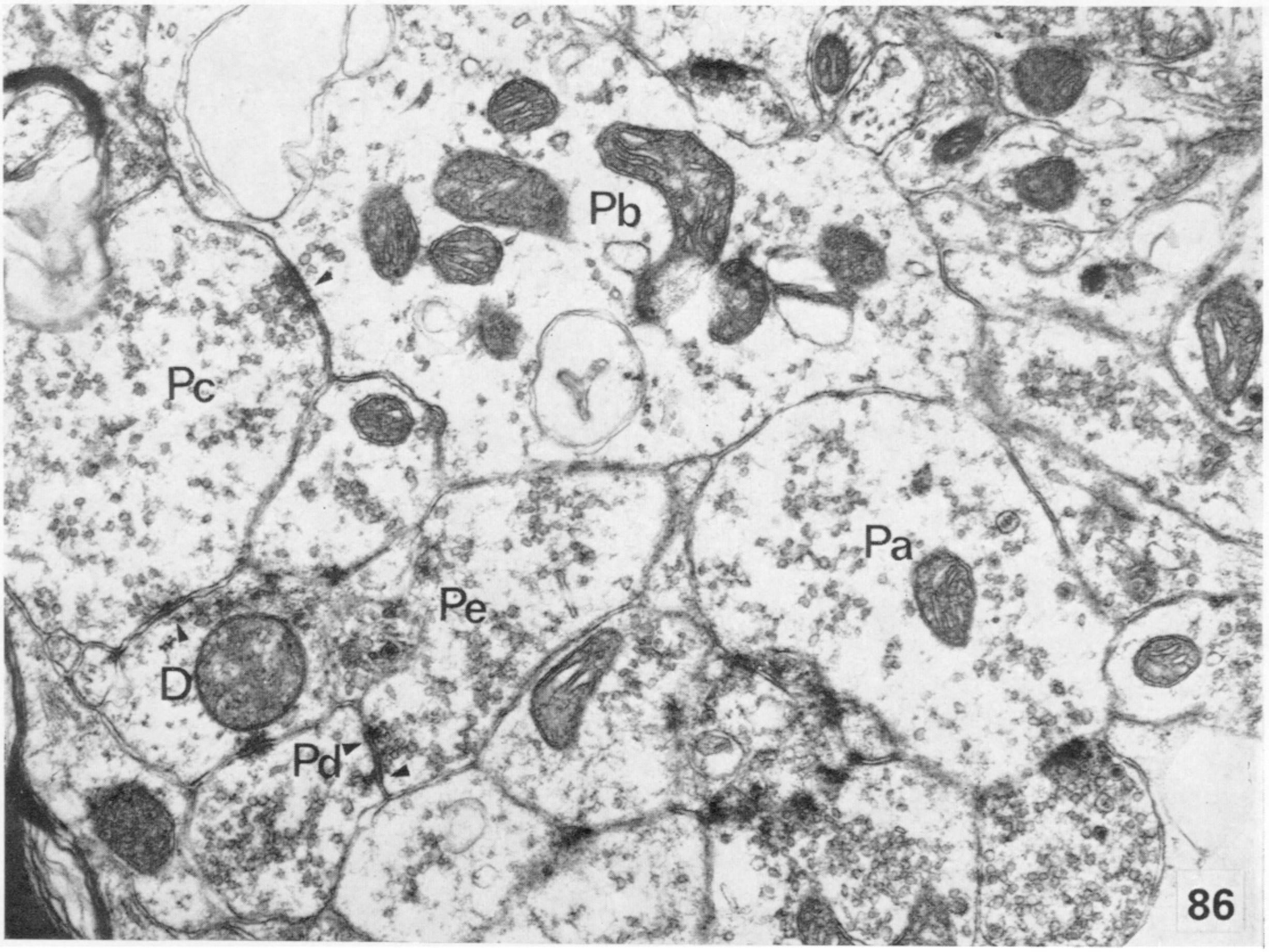


FIGURES 81 AND 82. For description see p. 385.

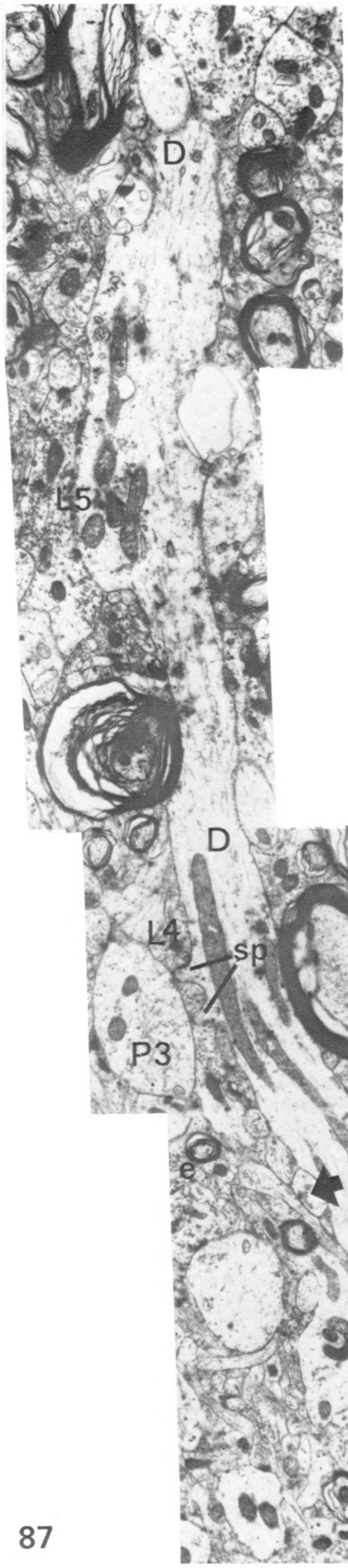


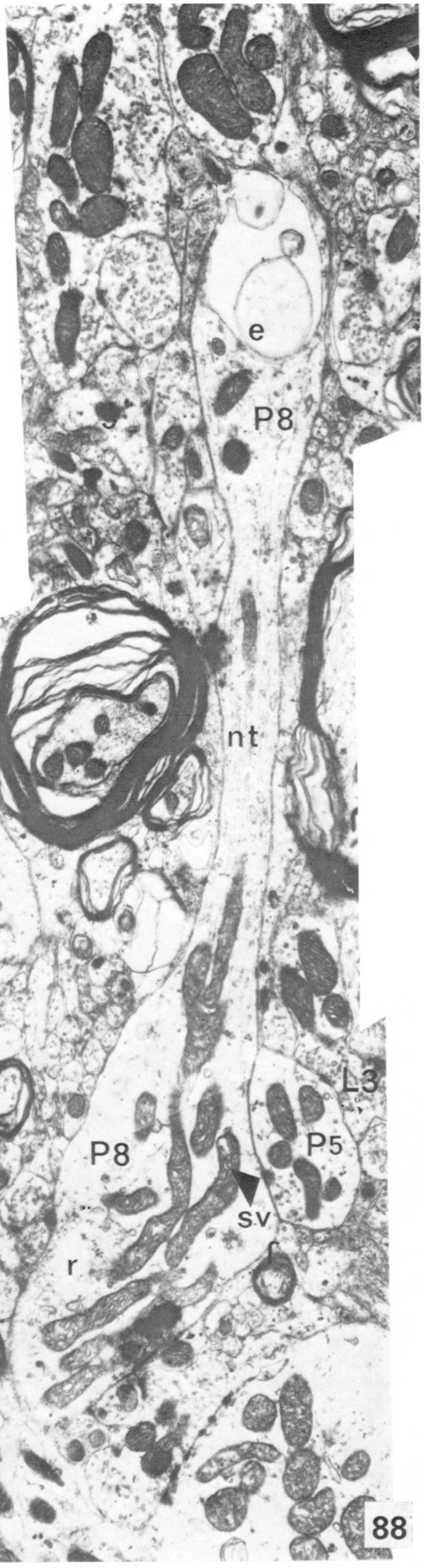
FIGURES 83 AND 84. For description see opposite.





FIGURES 85 AND 86. For description see opposite.





87

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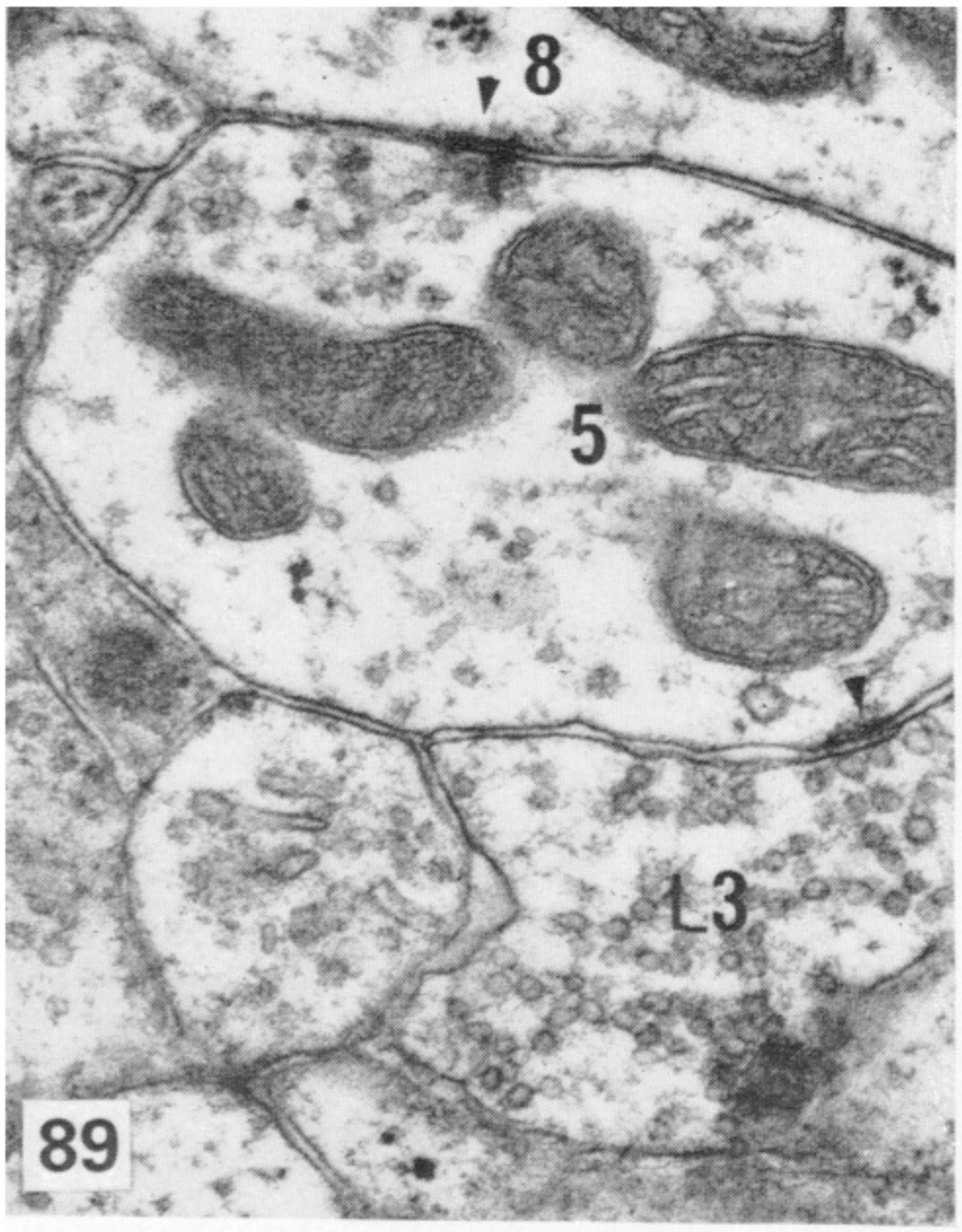
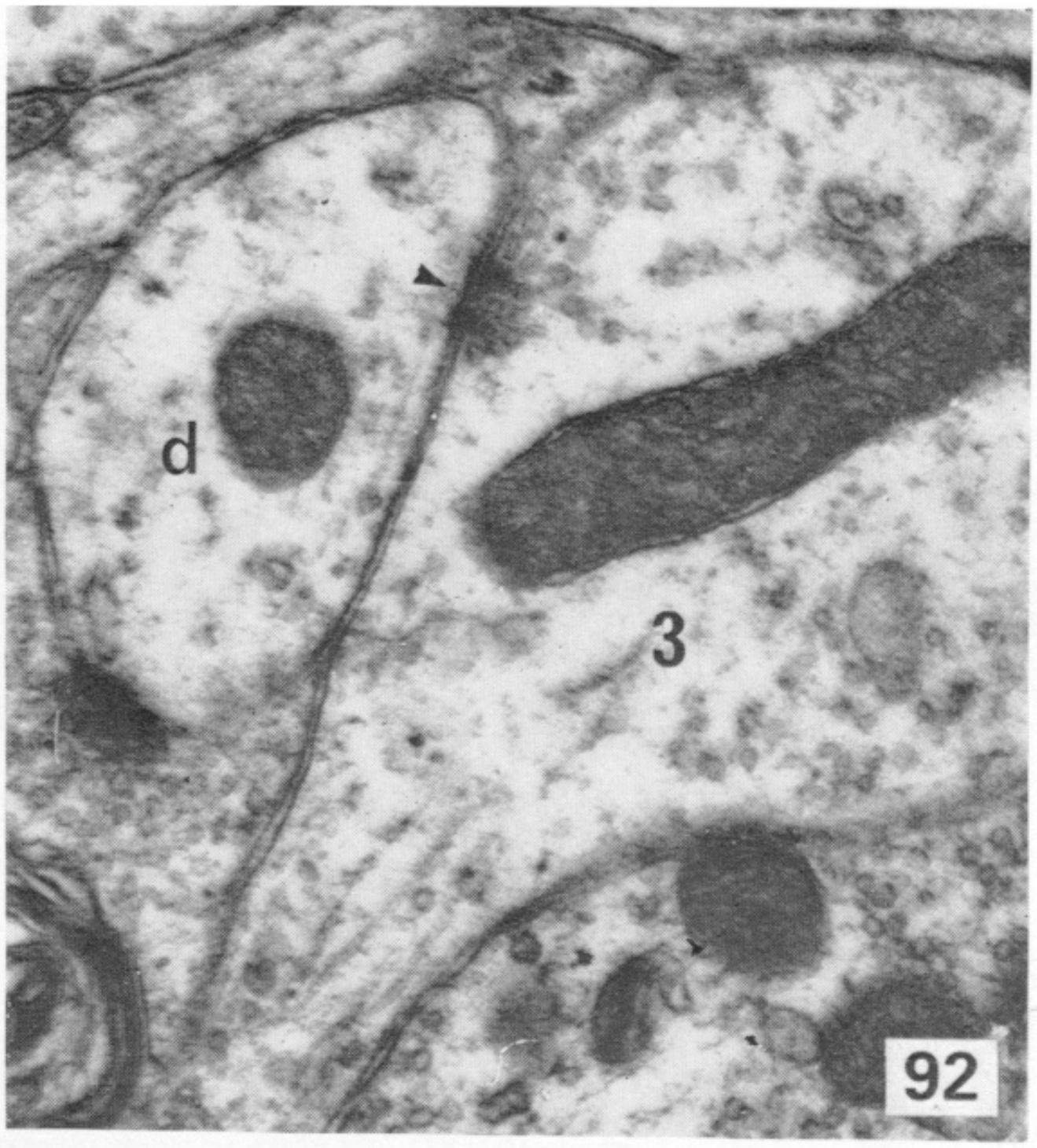
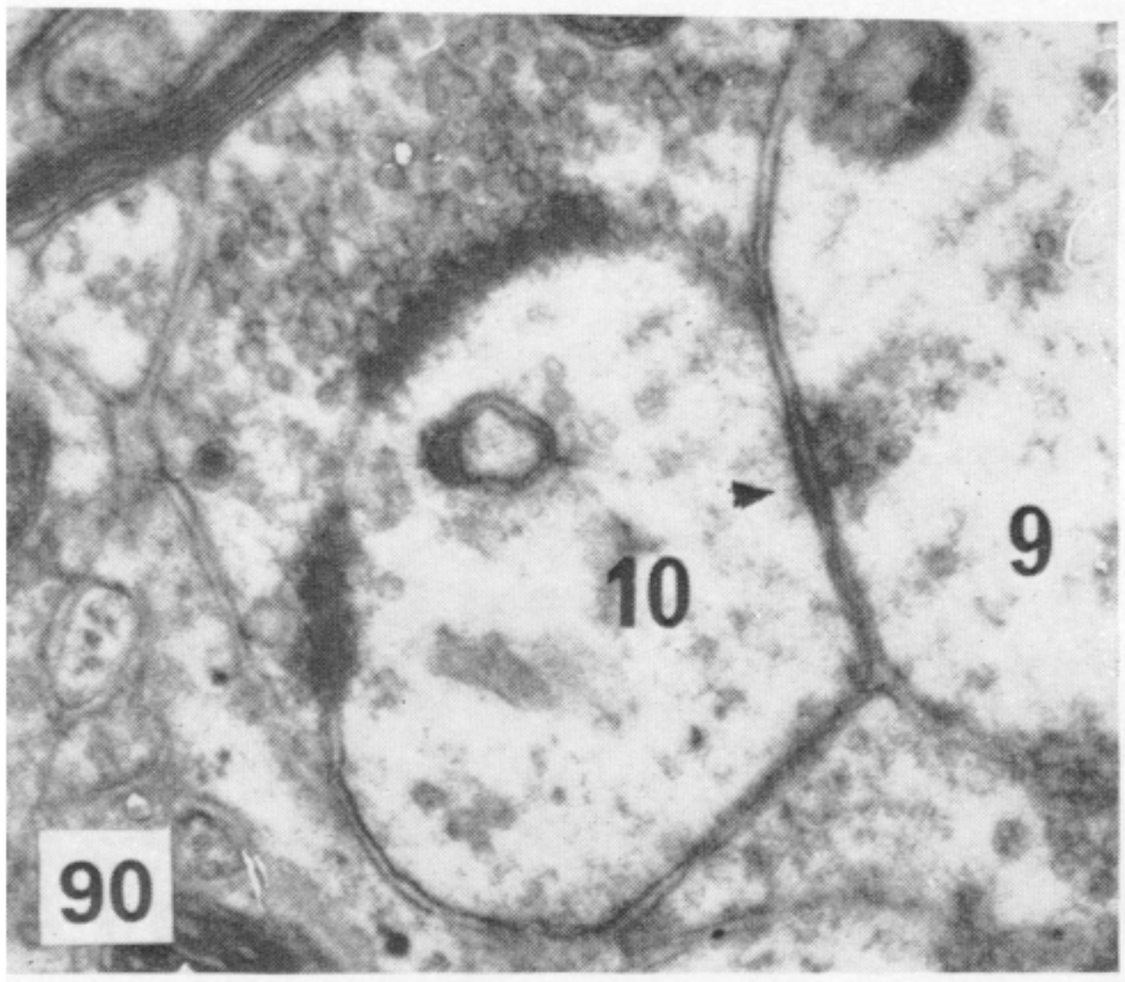
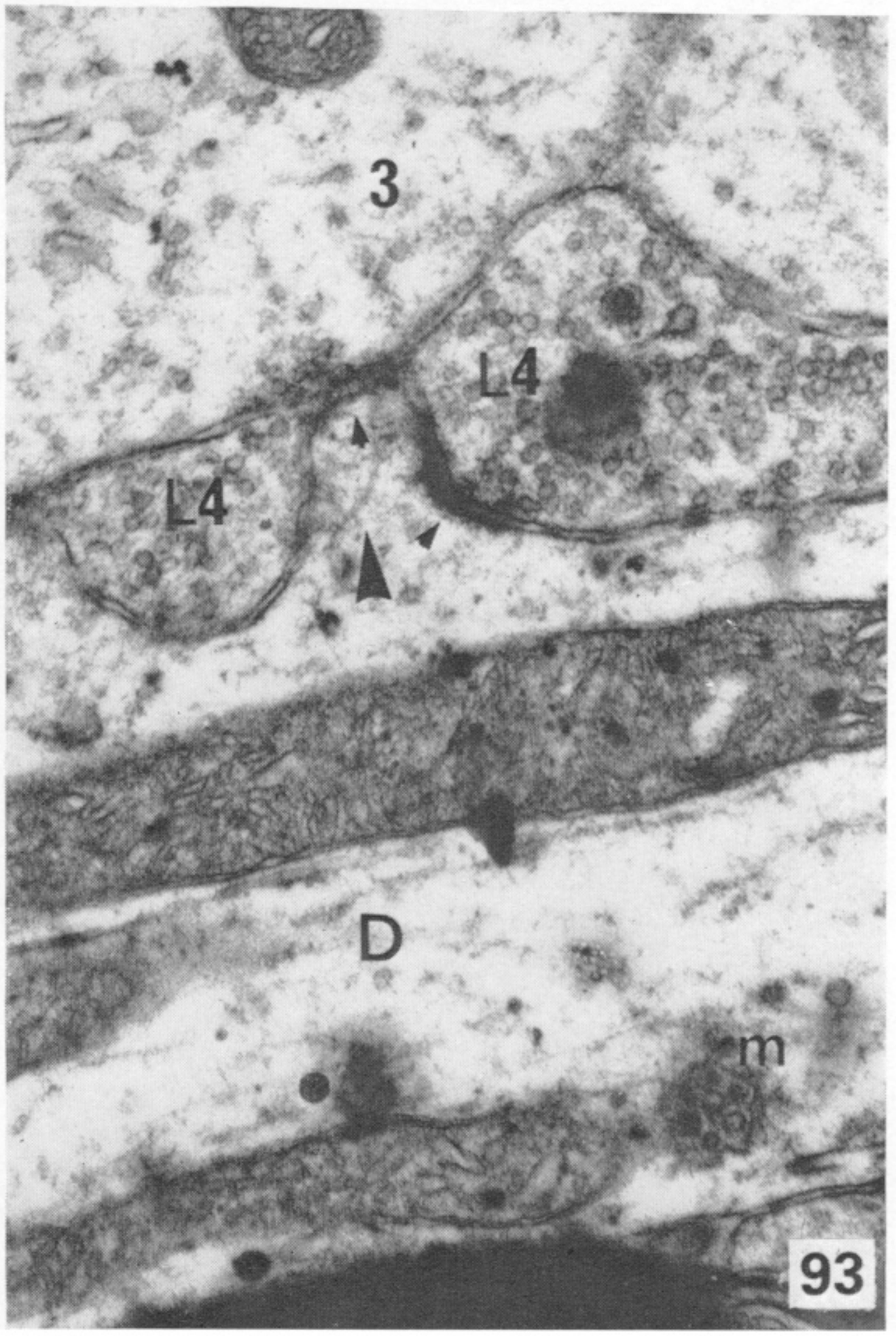
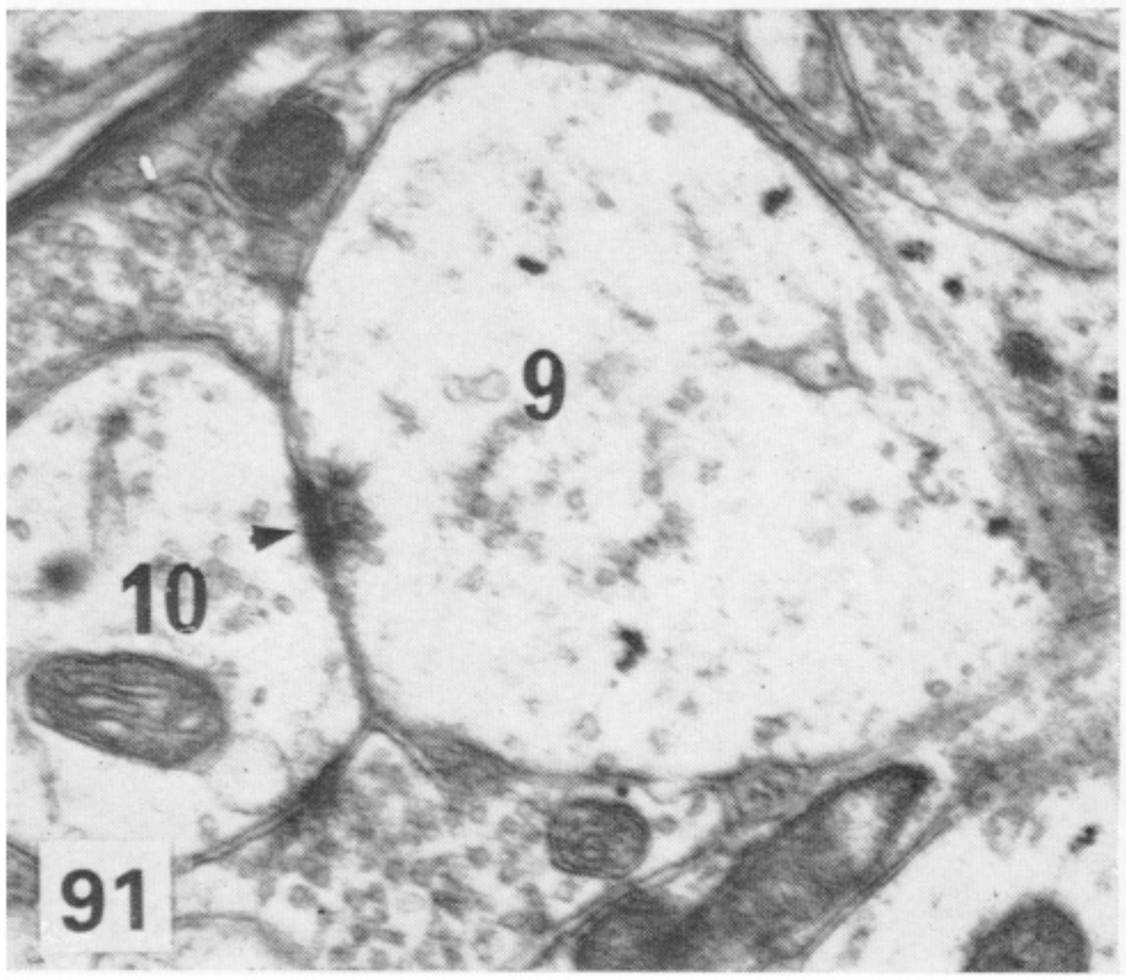
FIGURES 87 AND 88. For description see p. 388.



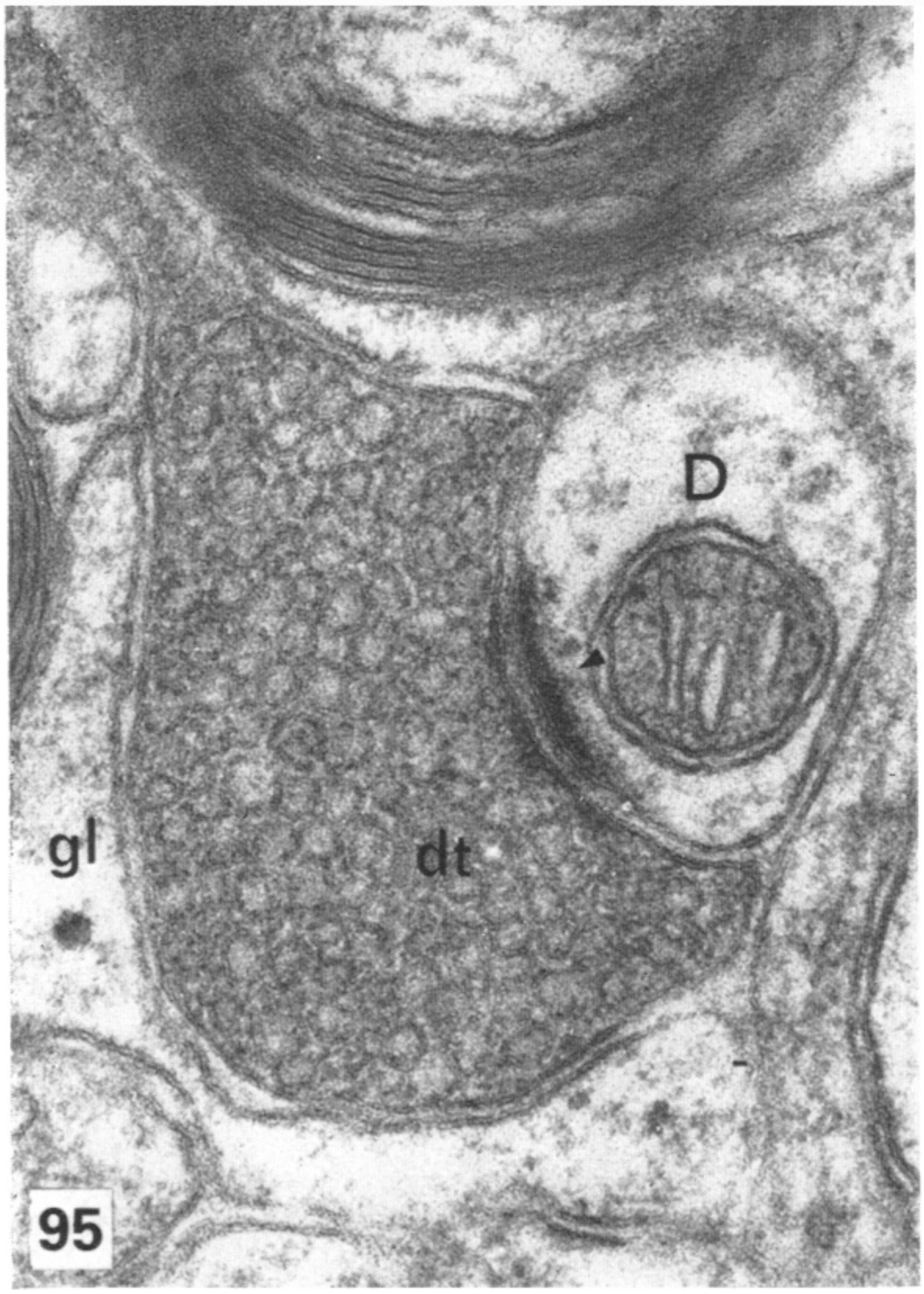


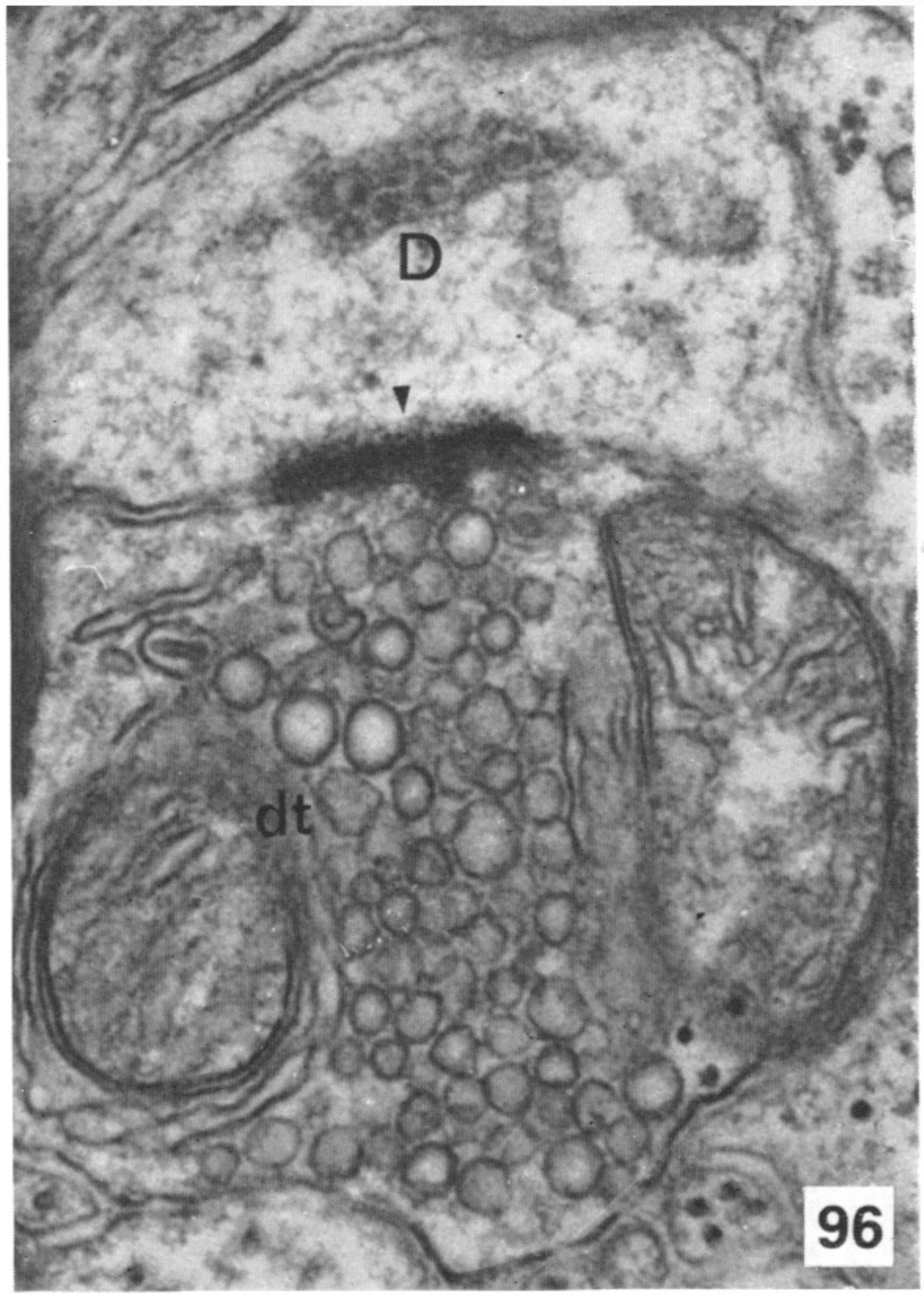


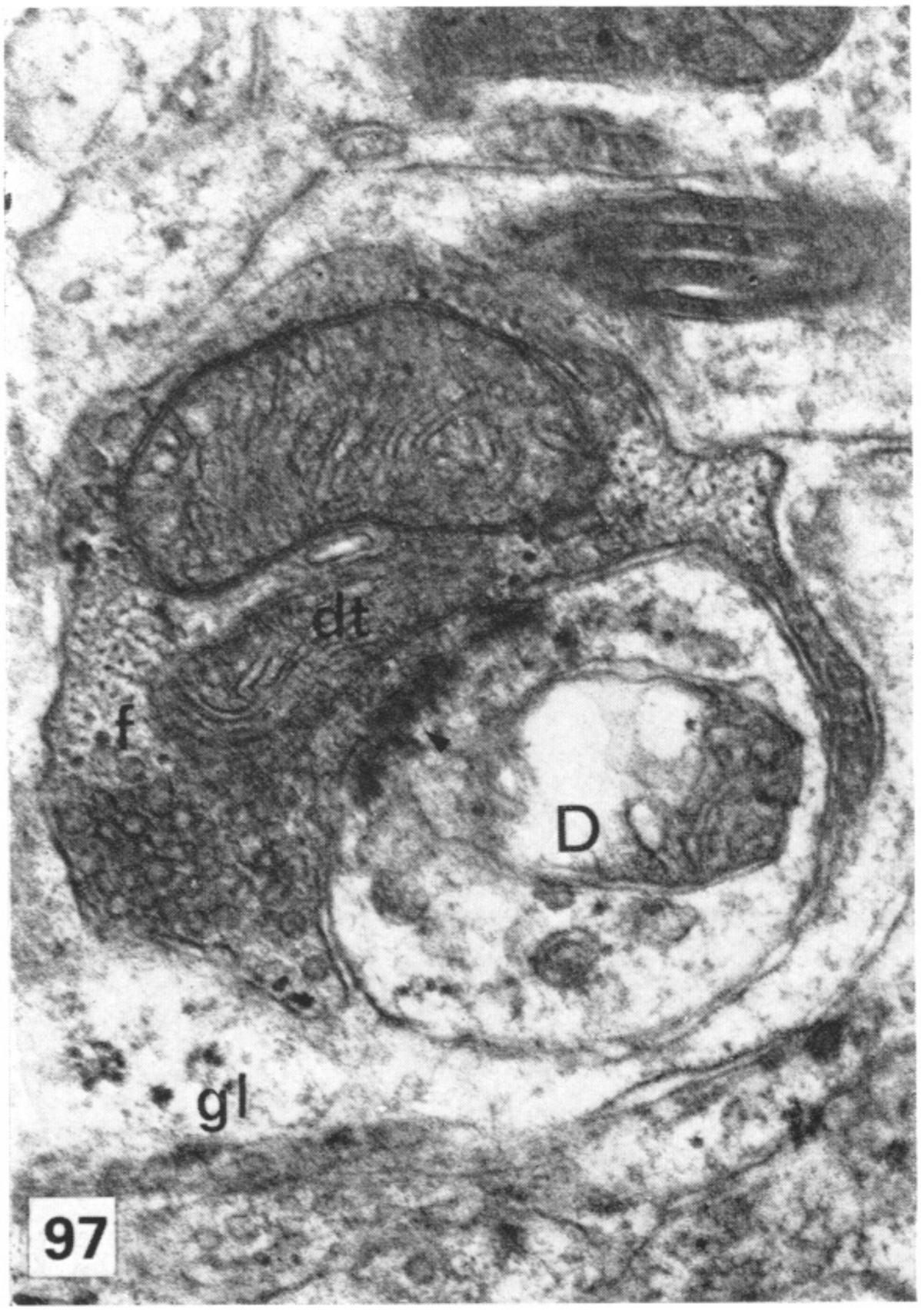


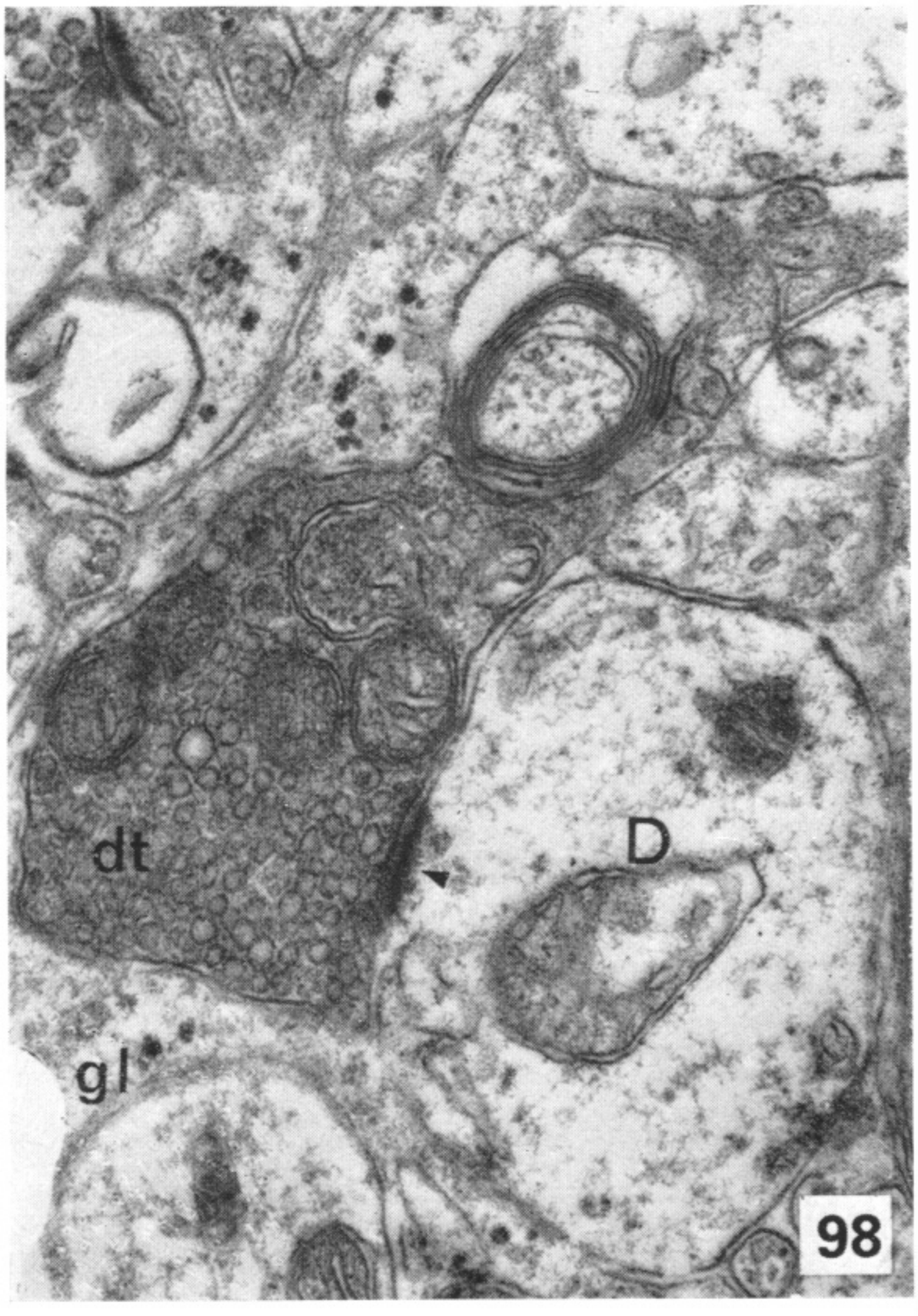


FIGURES 89–93. For description see p. 389.

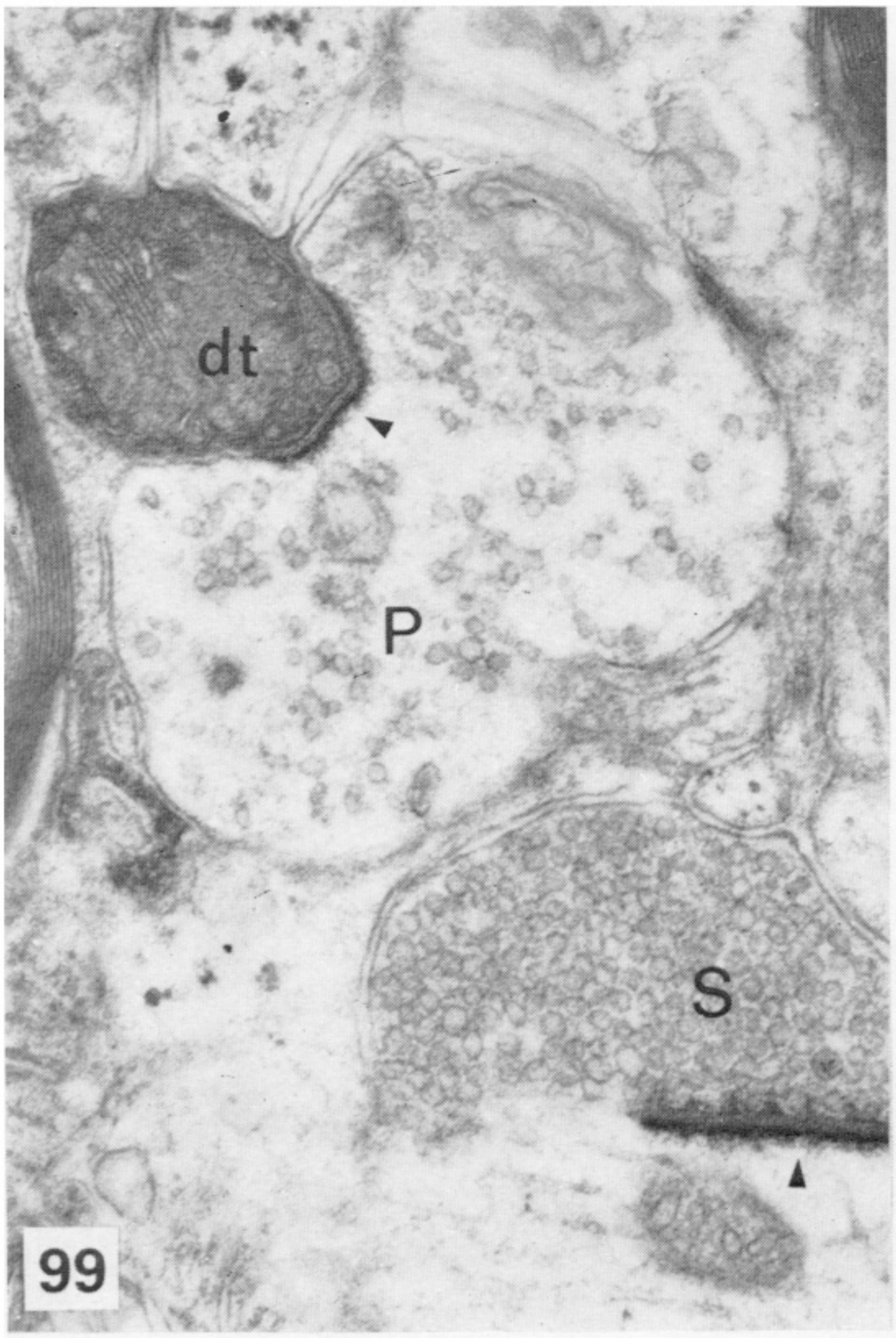


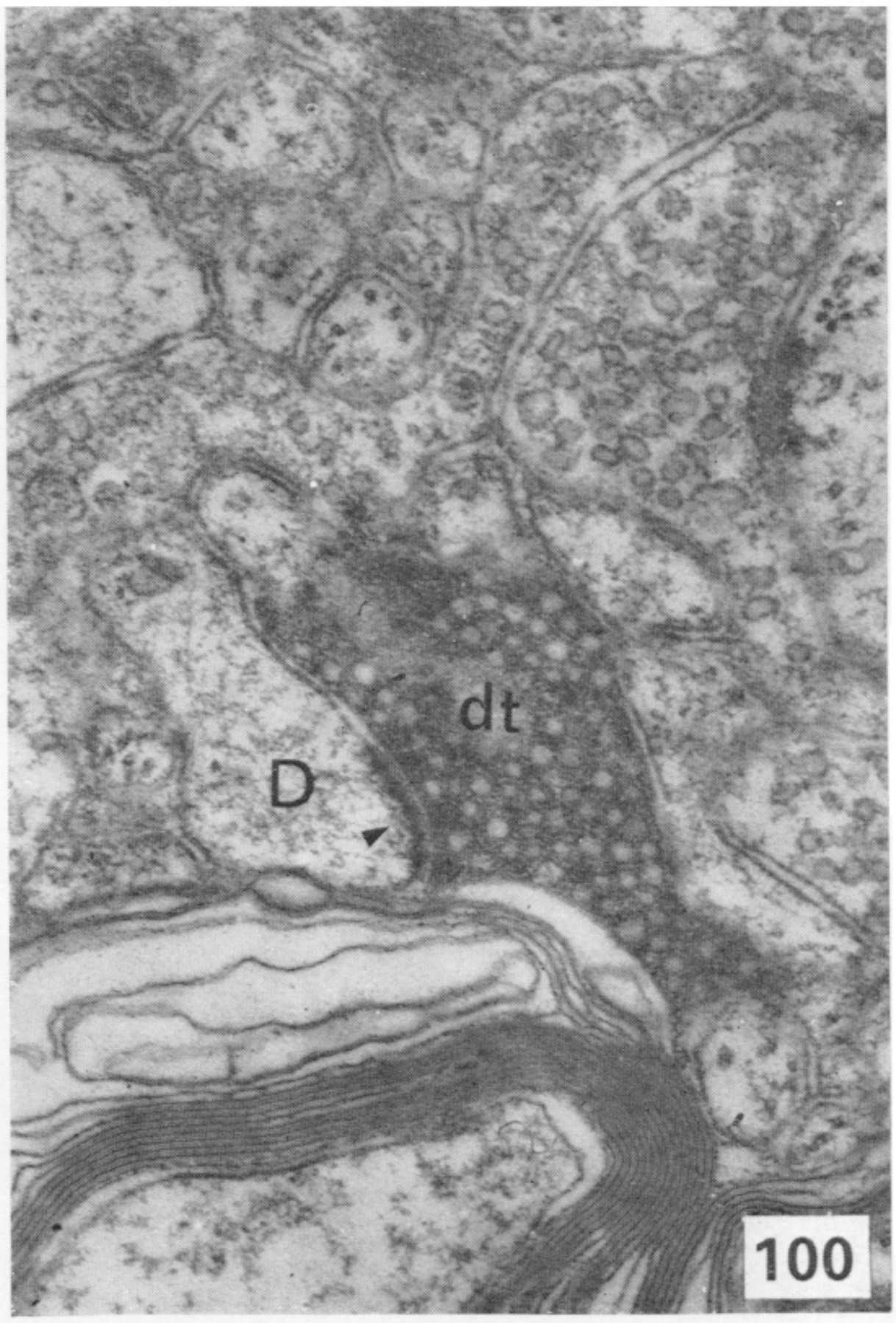


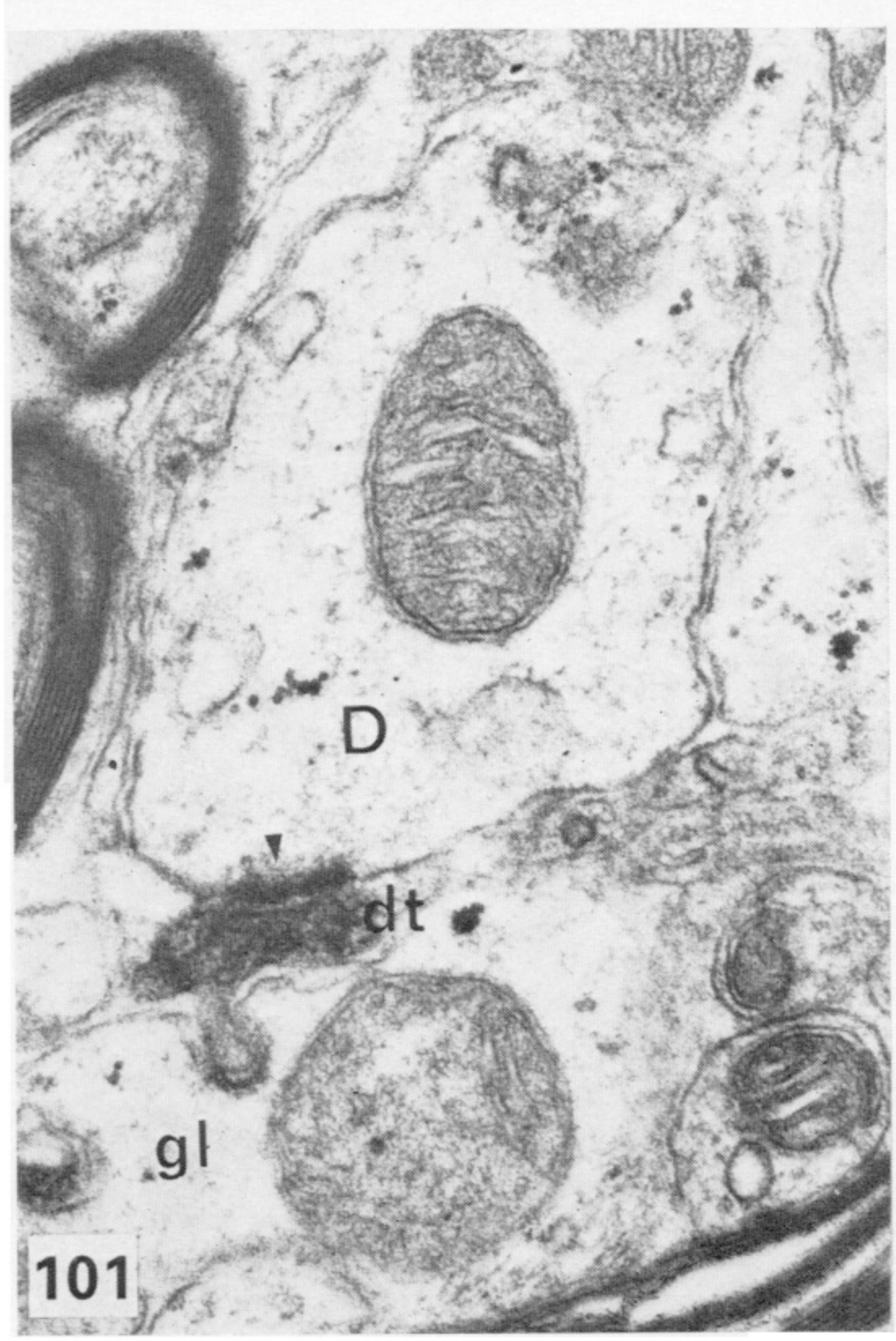


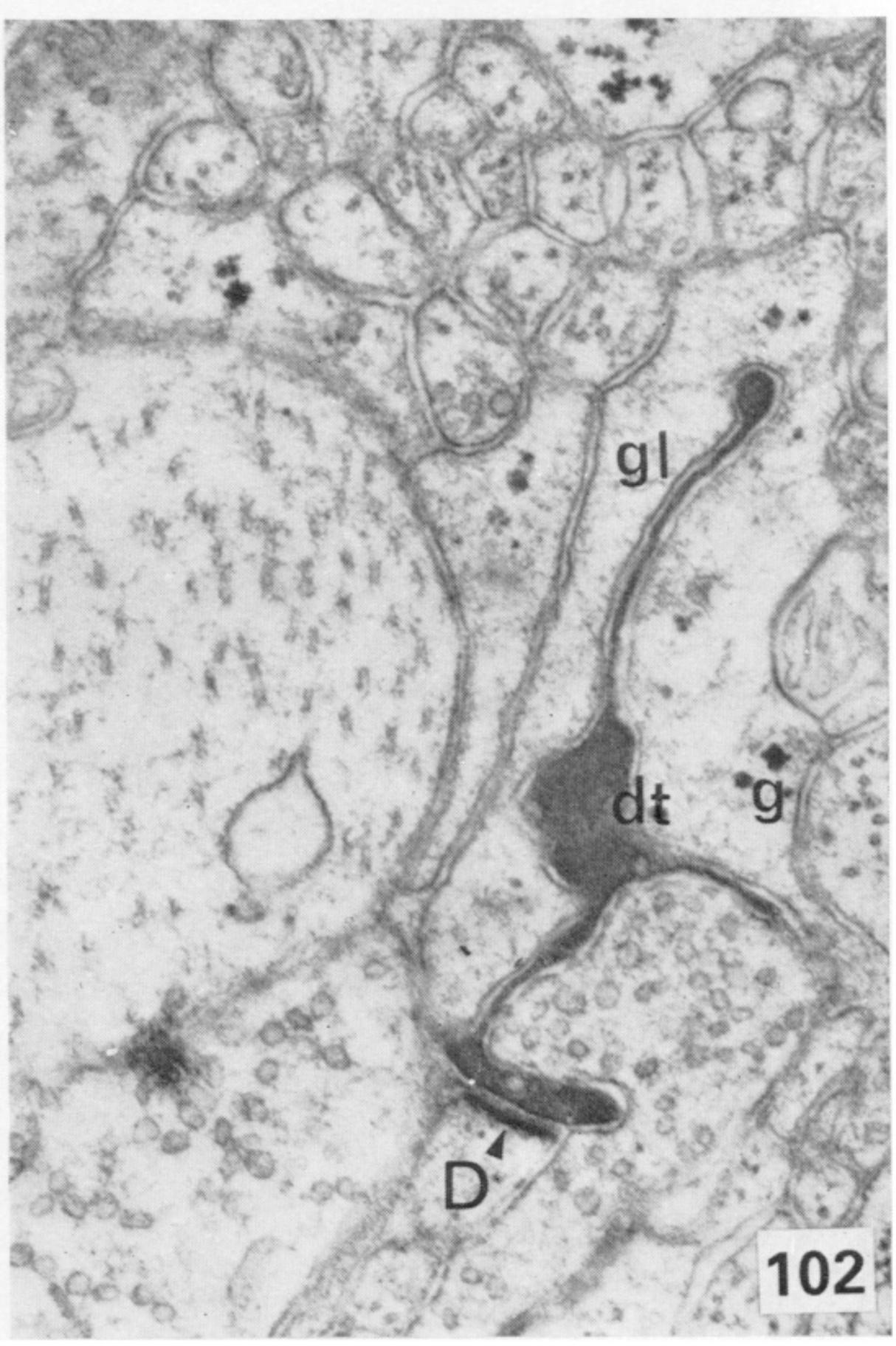


FIGURES 95–98. For description see opposite.

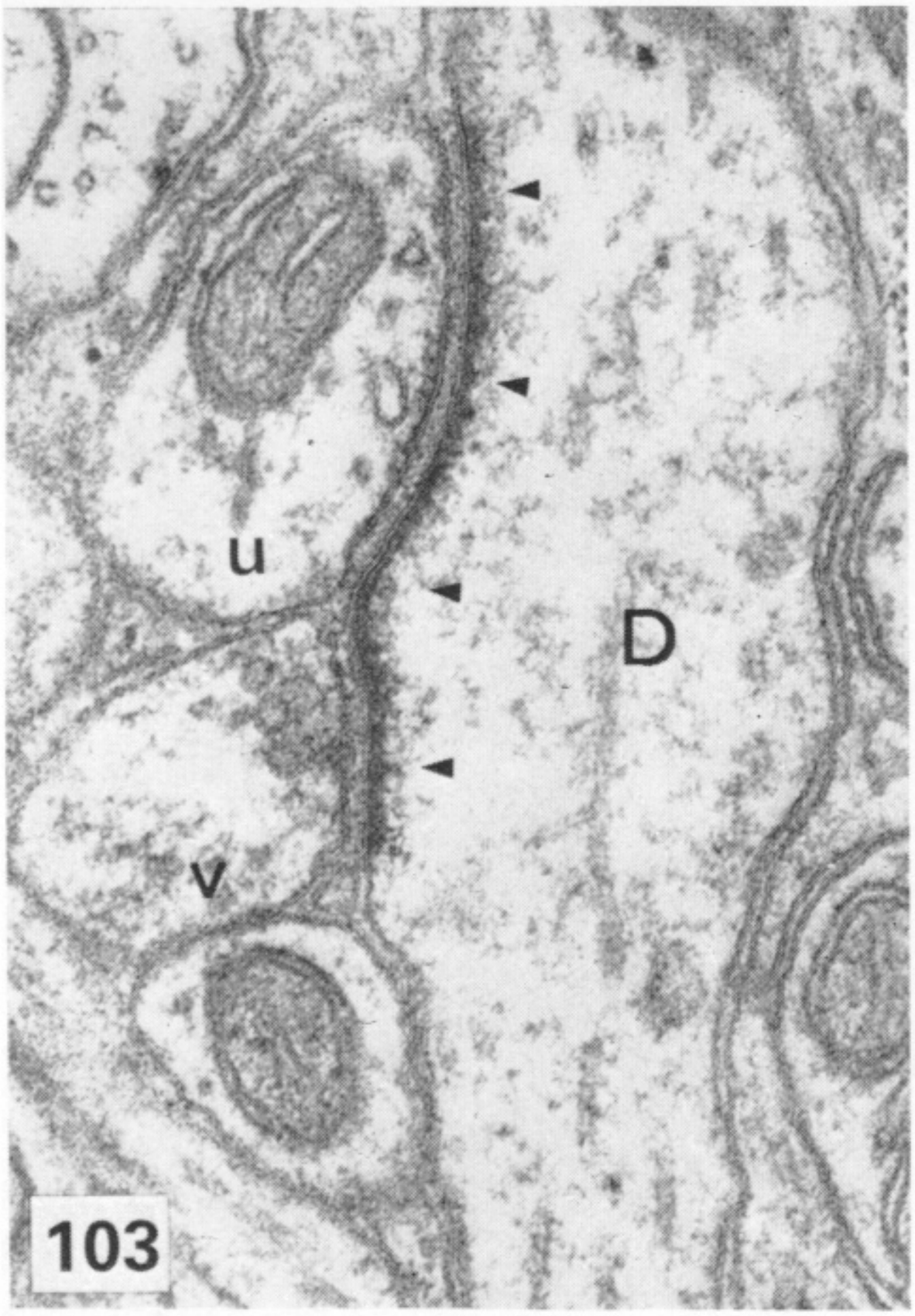




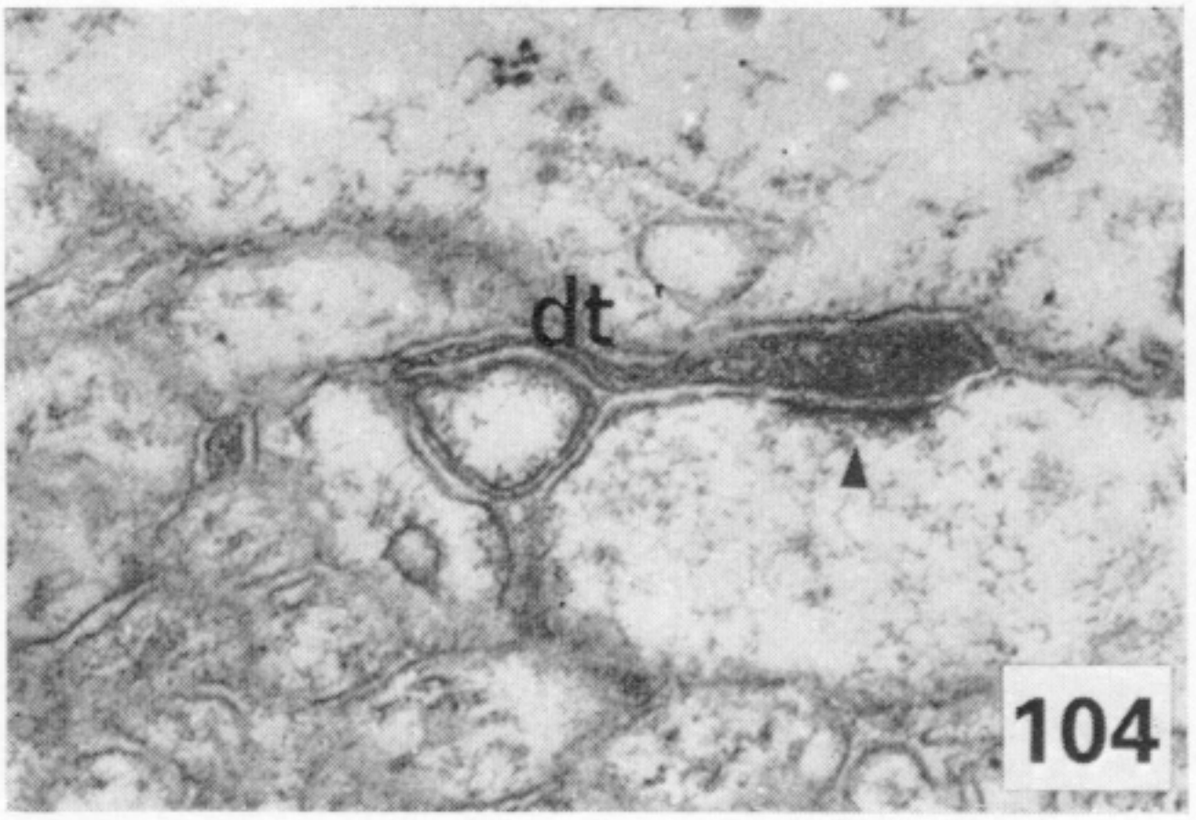




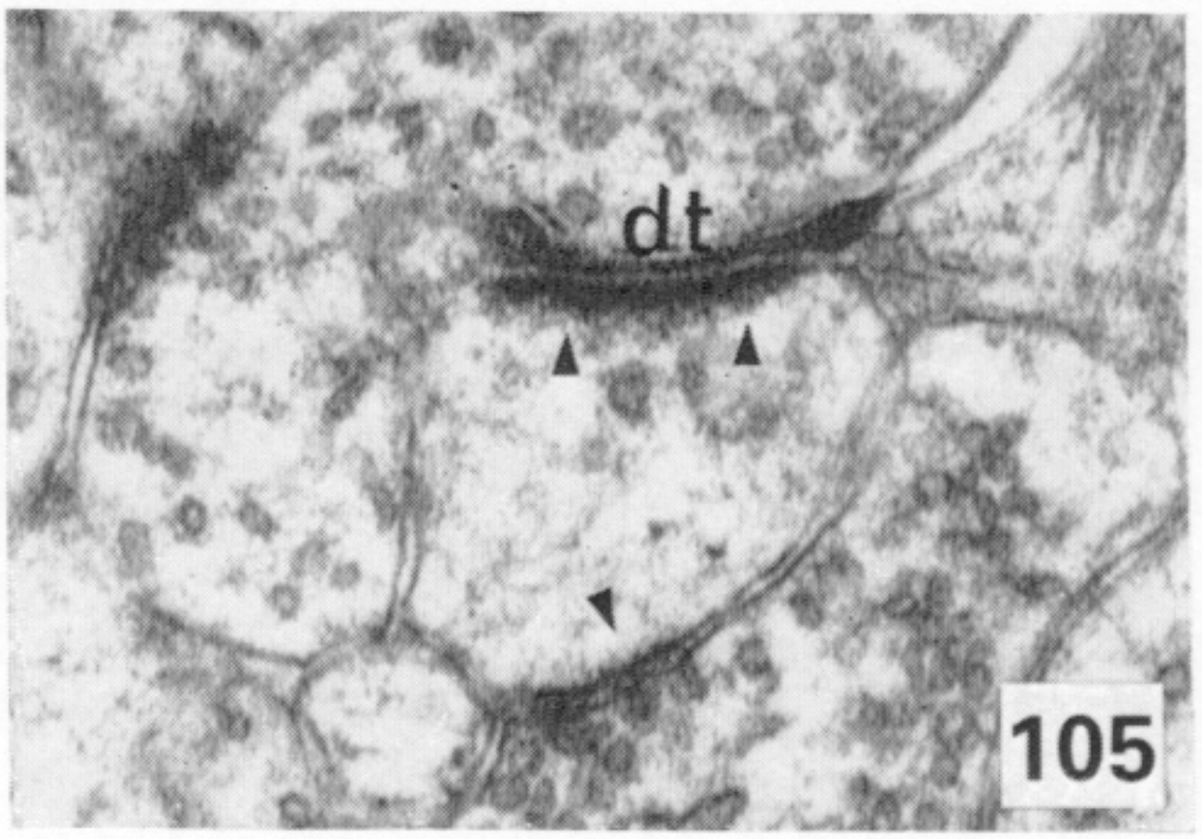
FIGURES 99–102. For description see opposite.



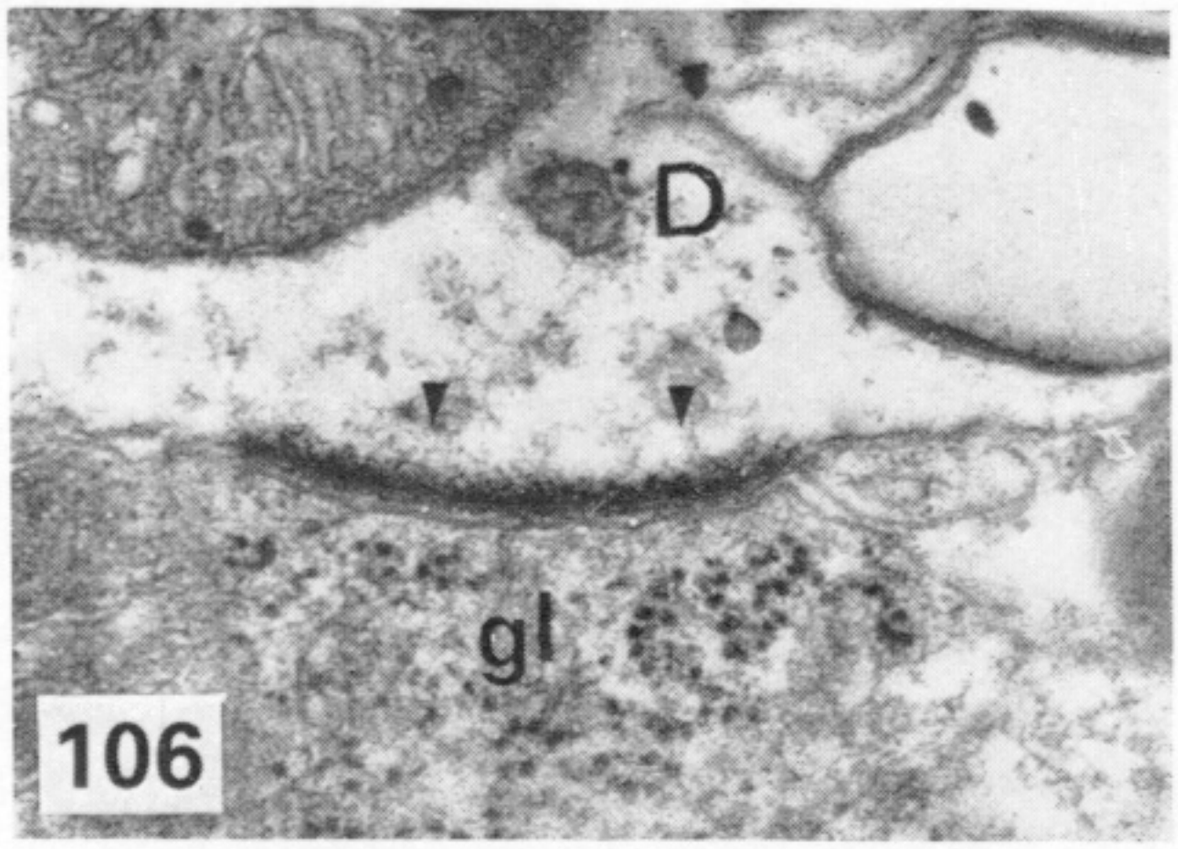
103



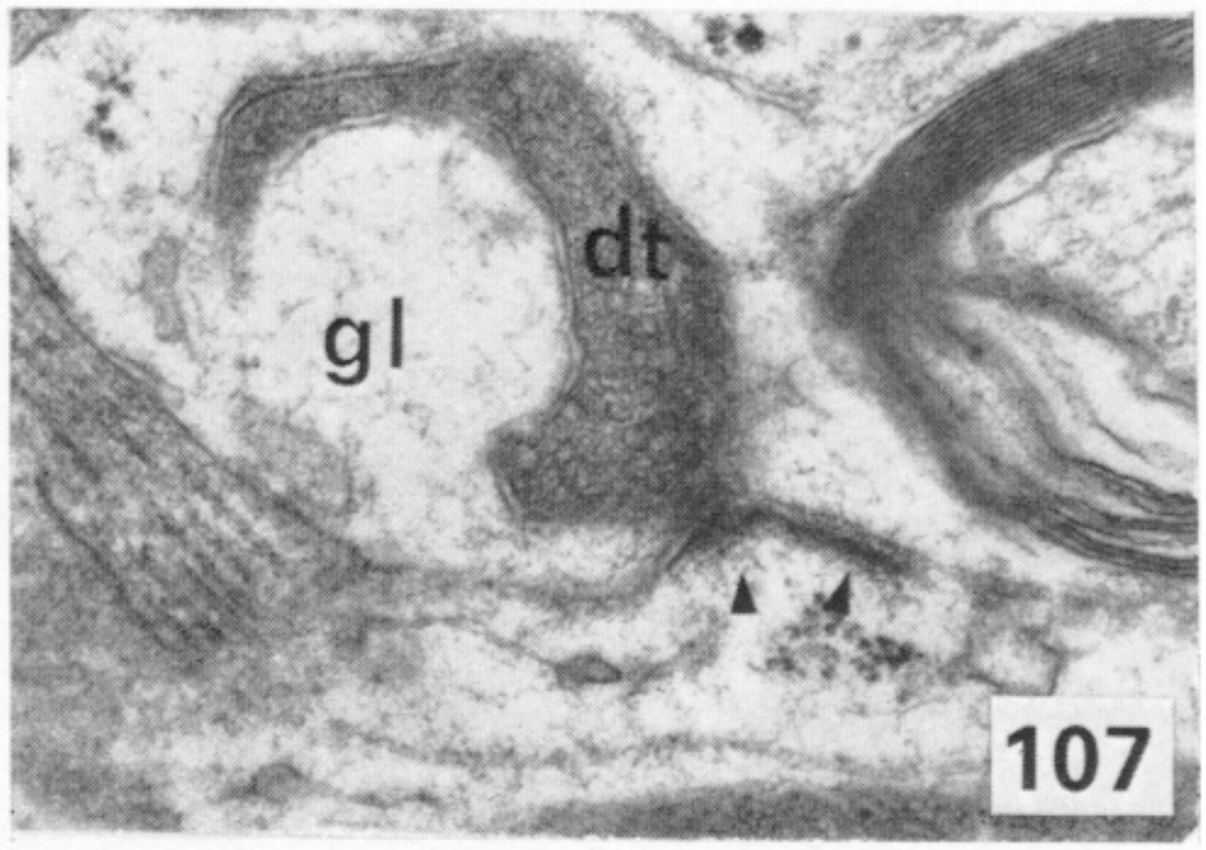
104



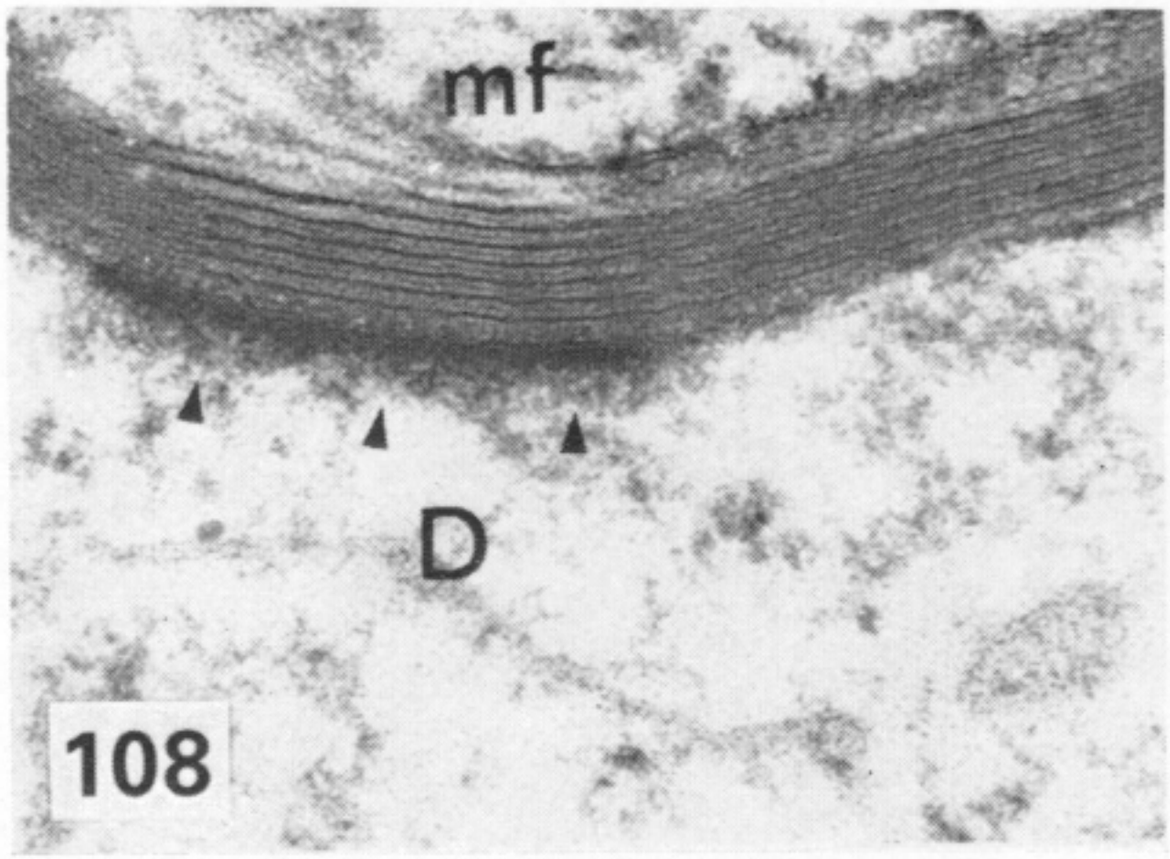
105



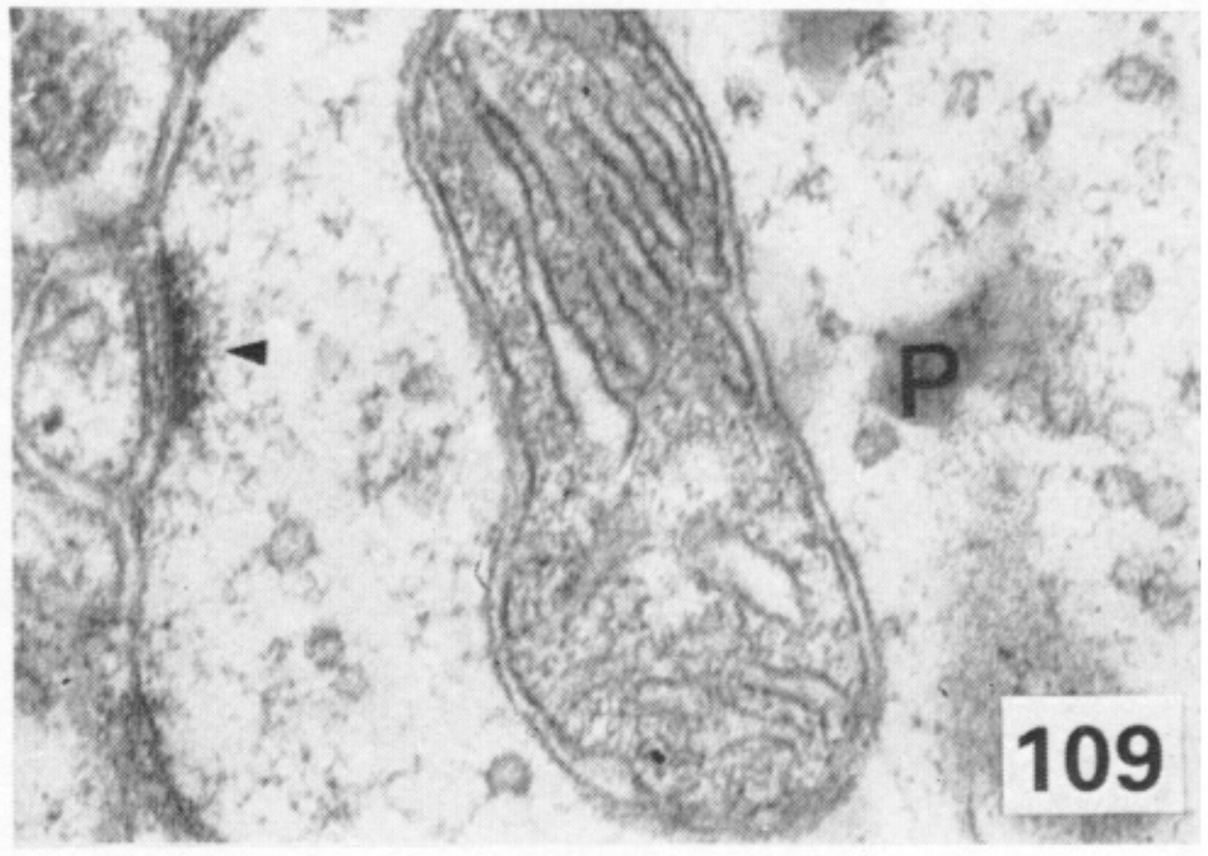
106



107

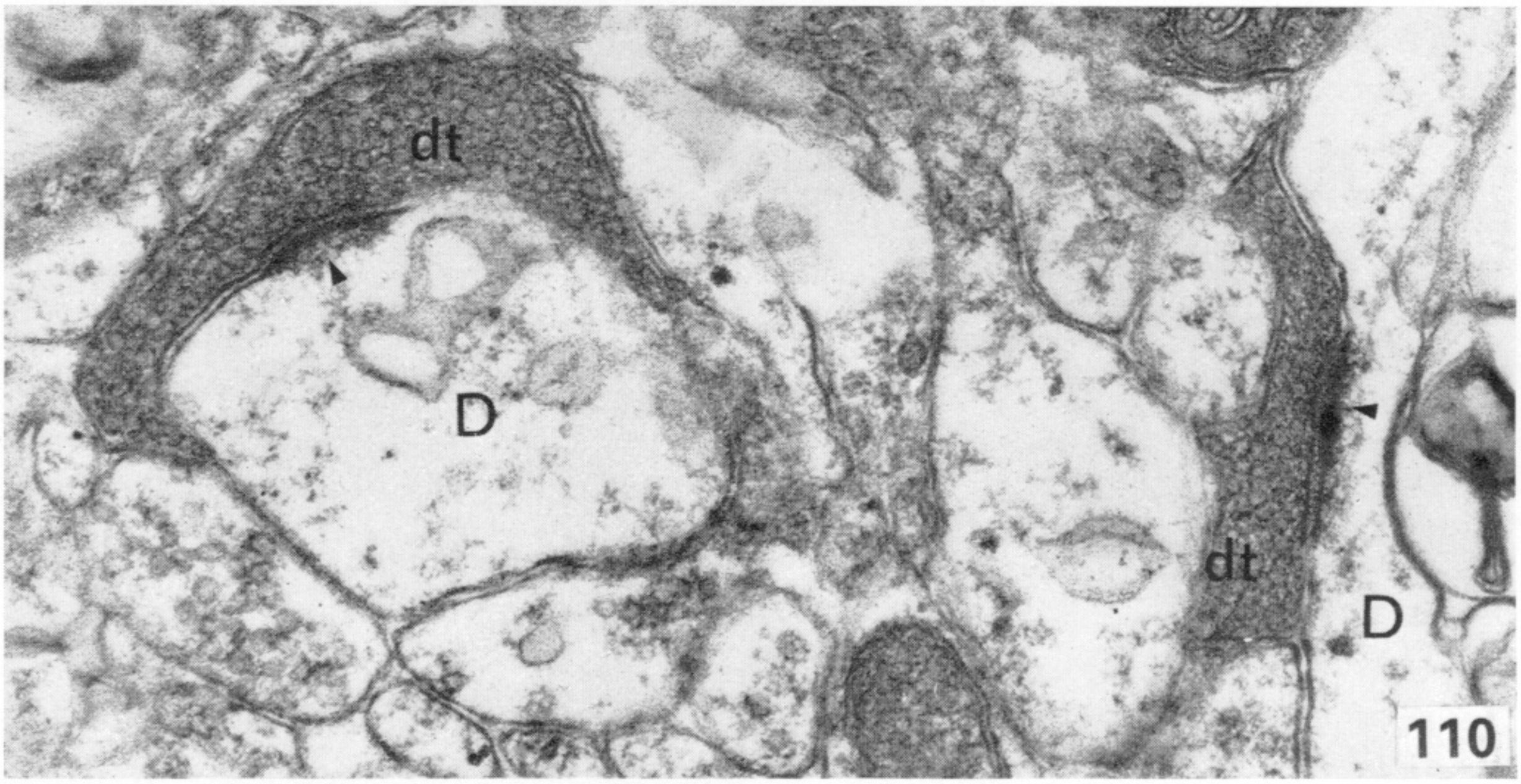


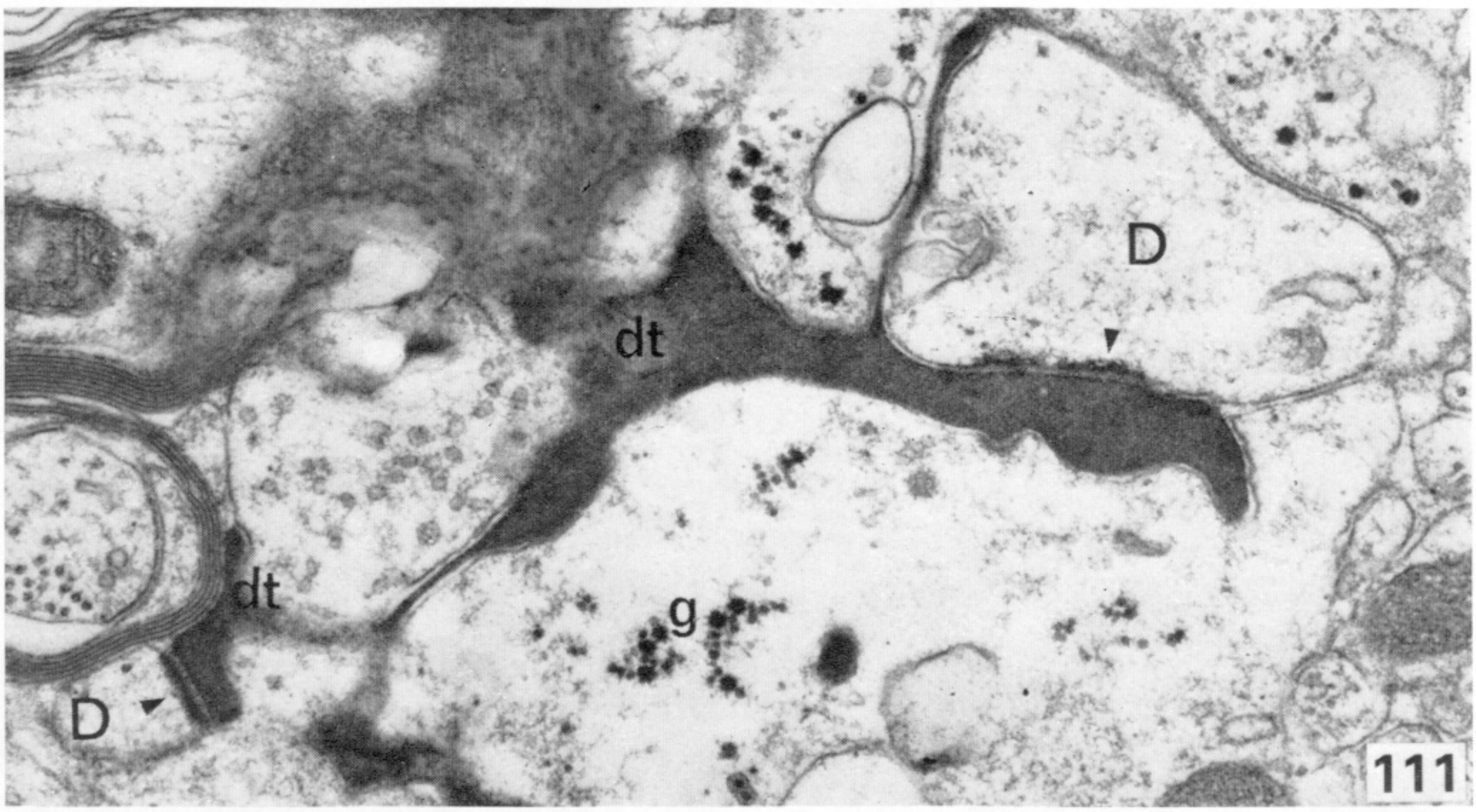
108

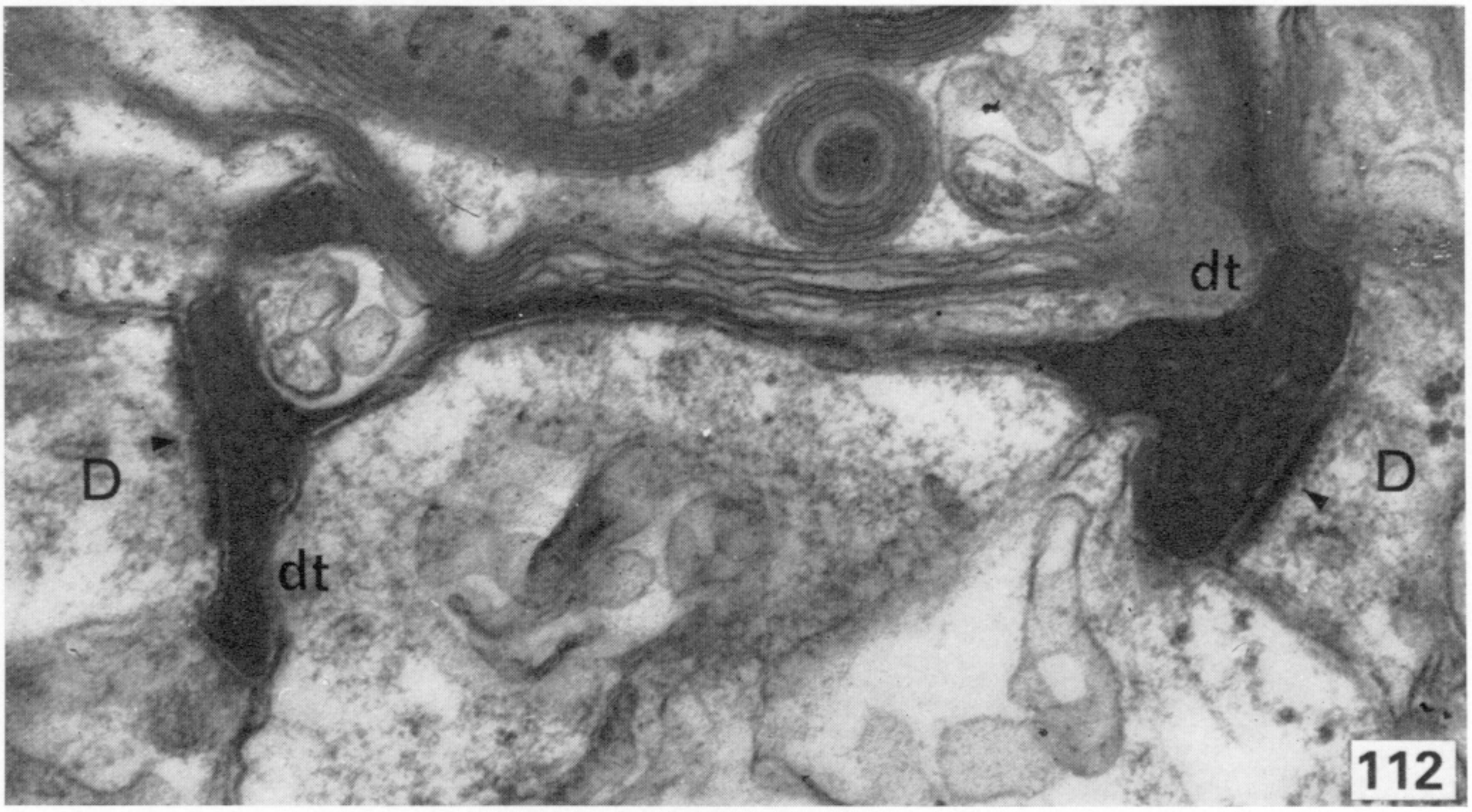


109

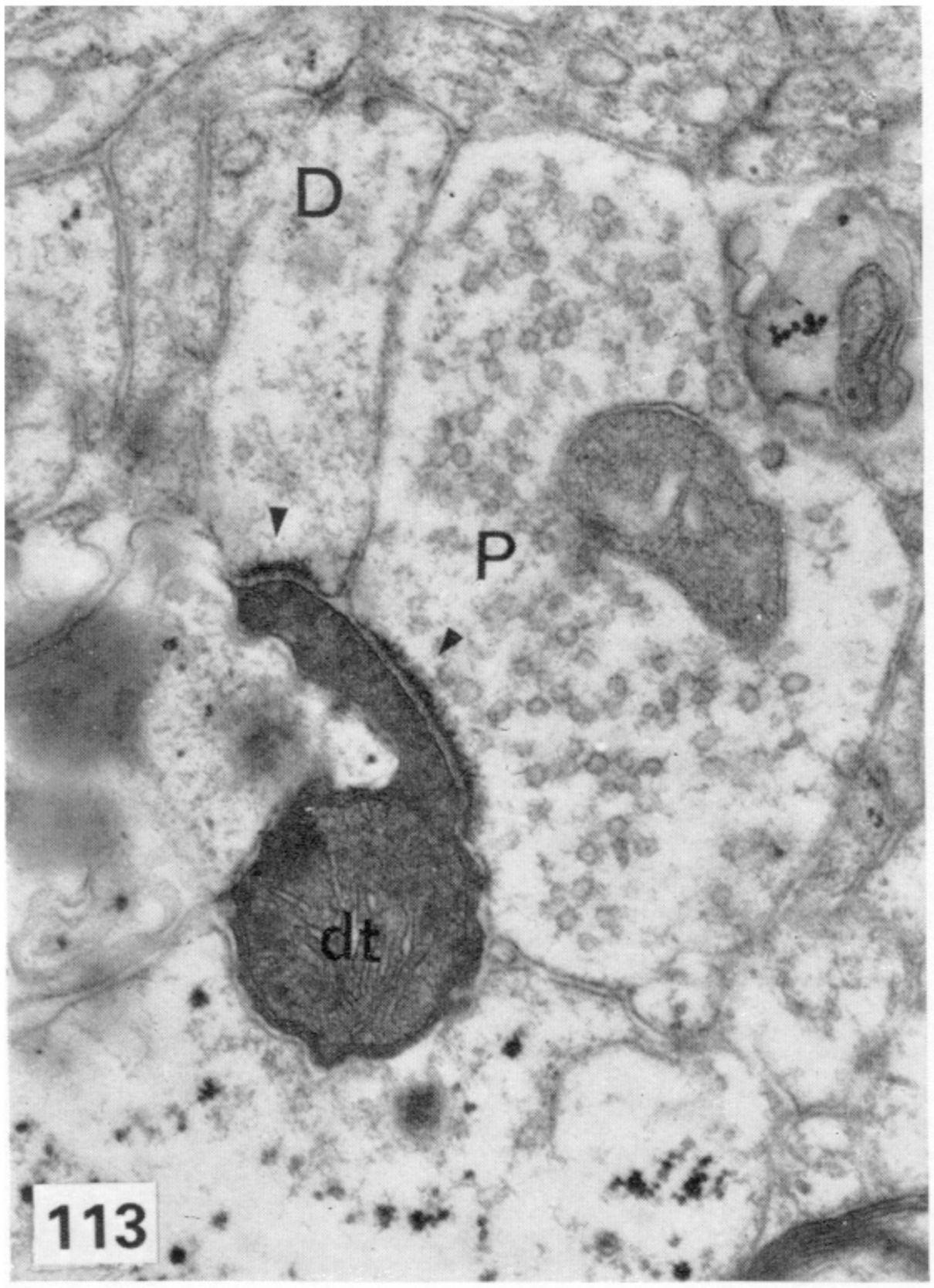
FIGURES 103–109. For description see p. 392.

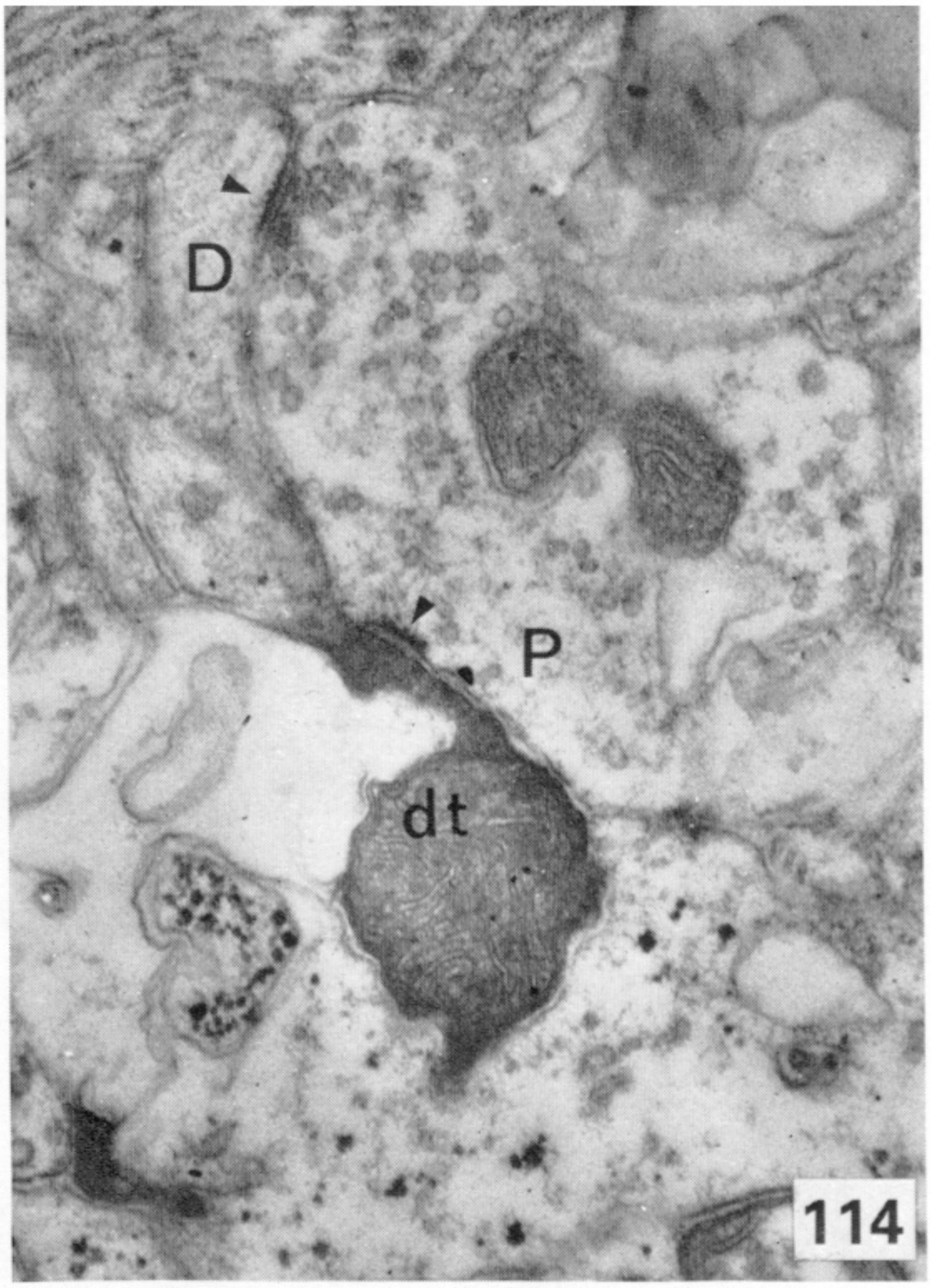


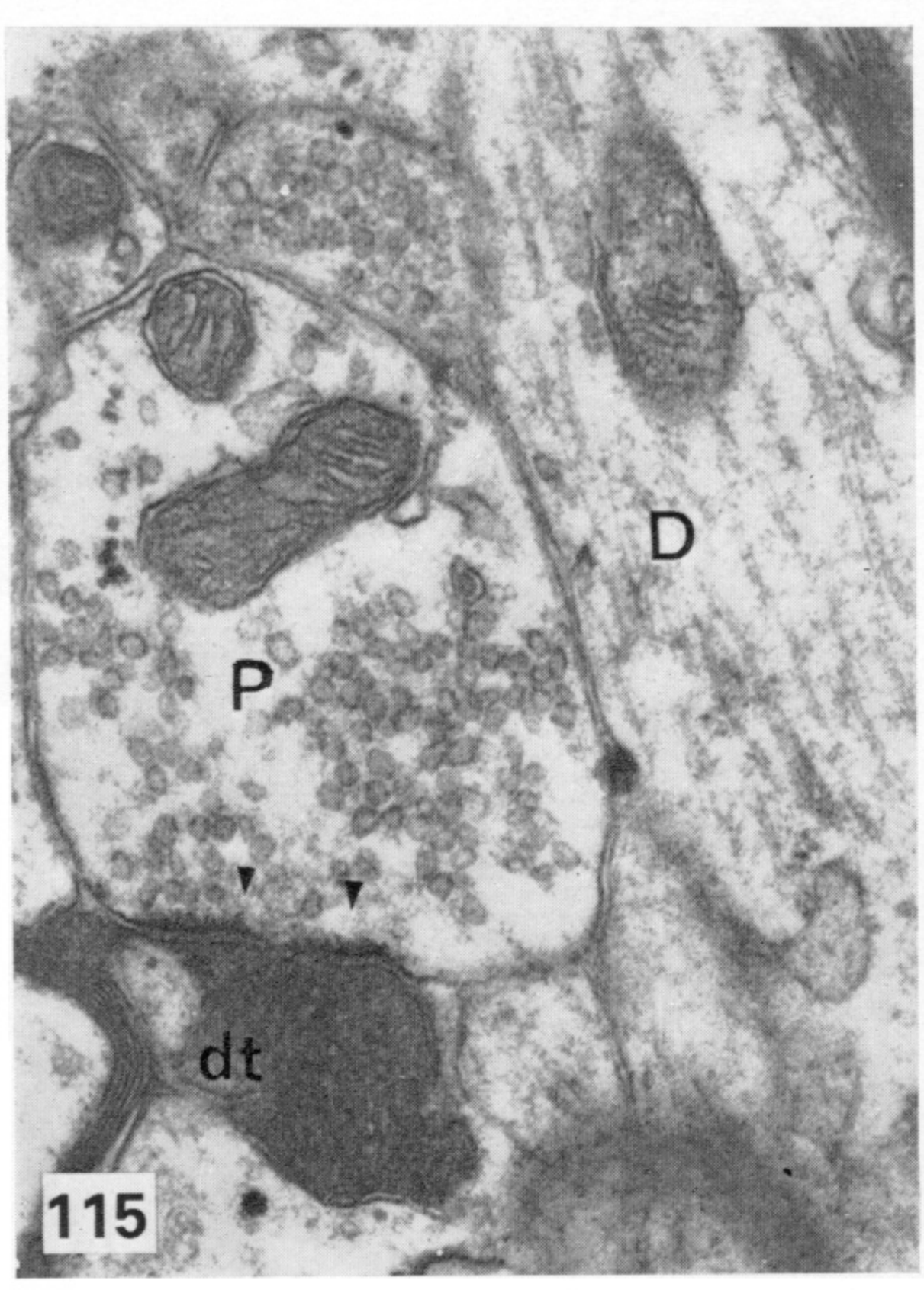


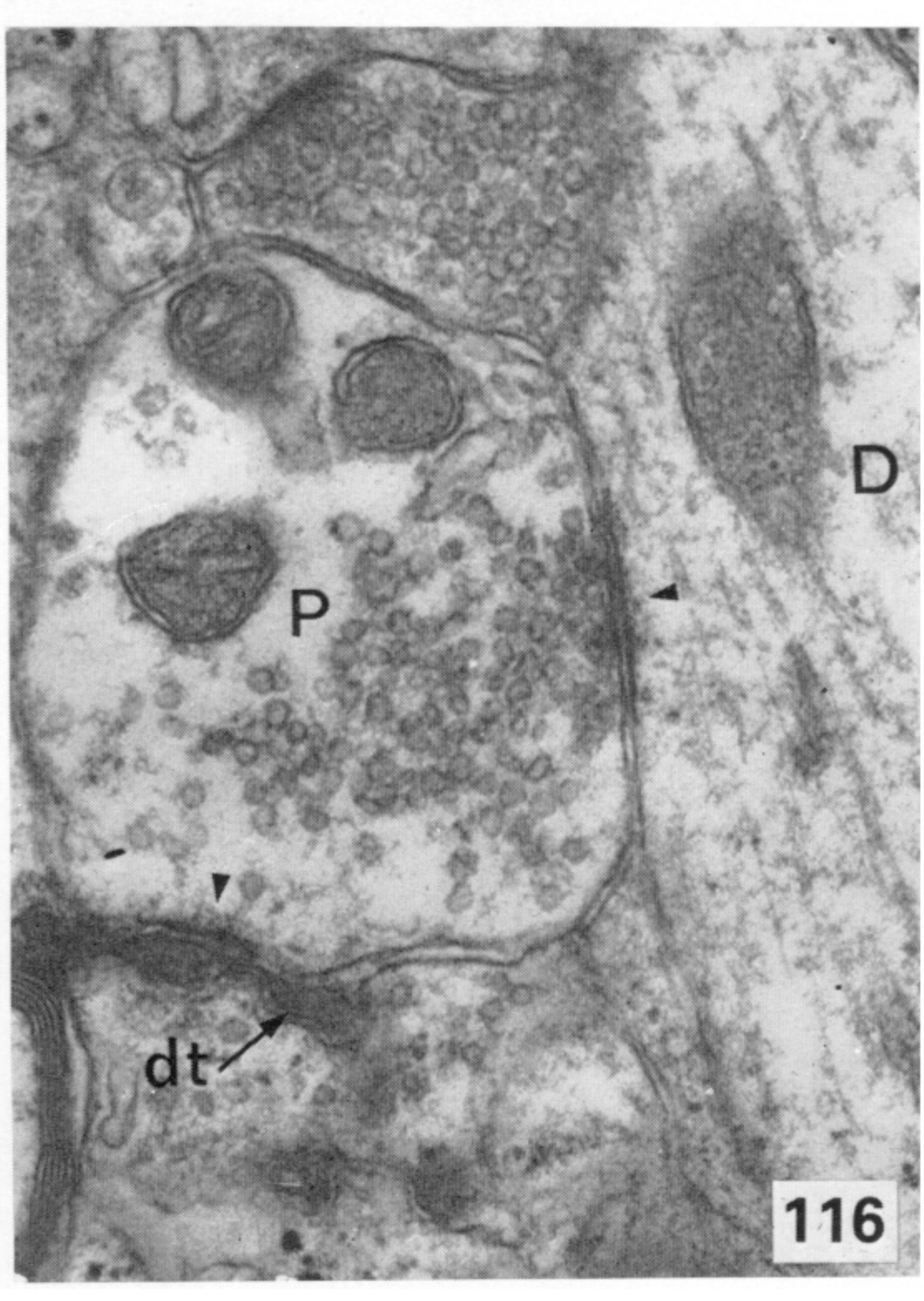


FIGURES 110–112. For description see p. 393.

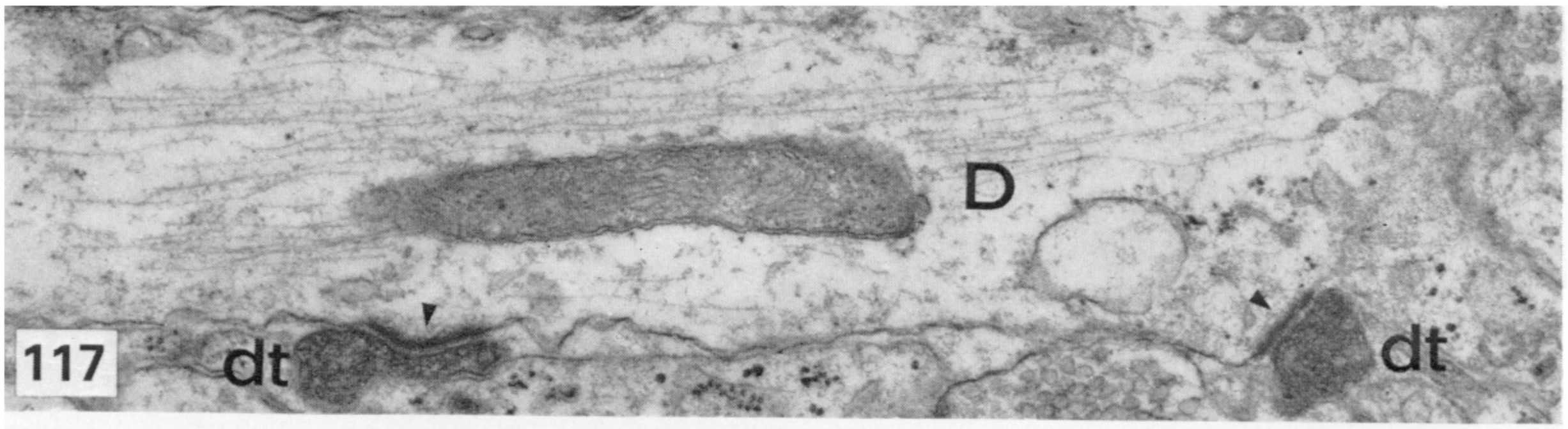


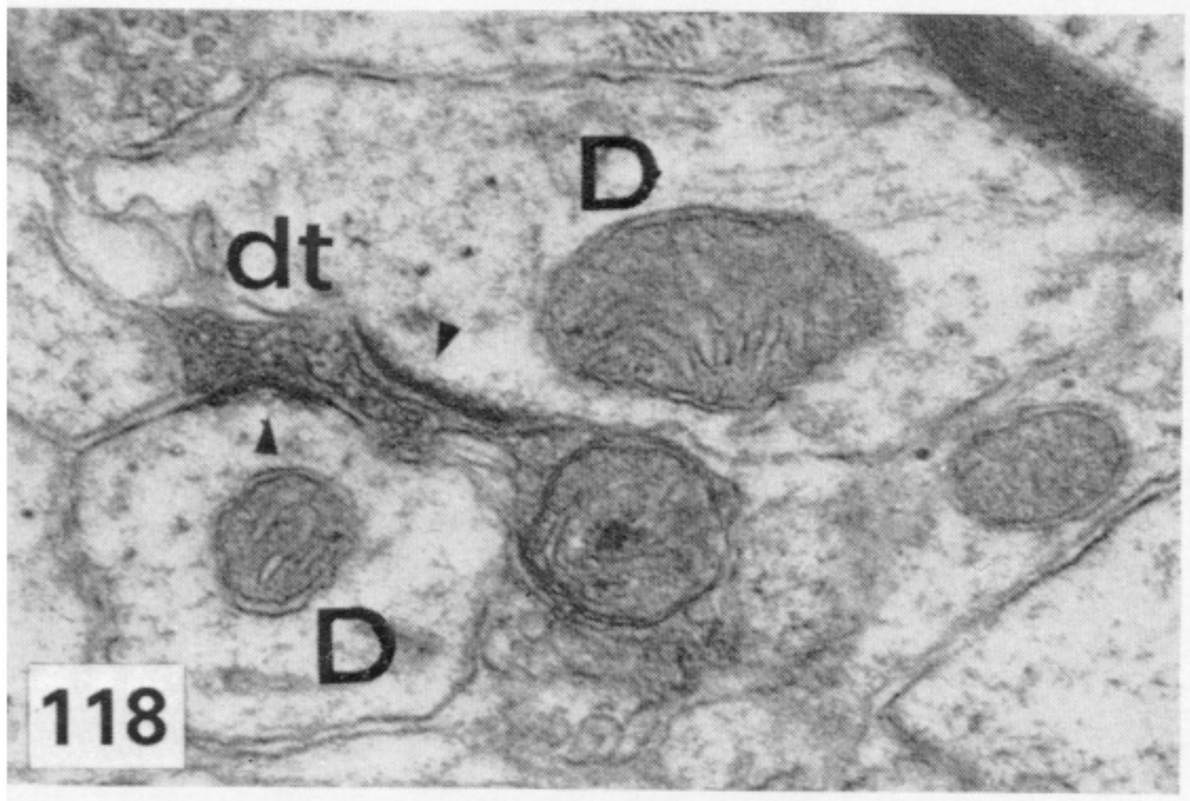


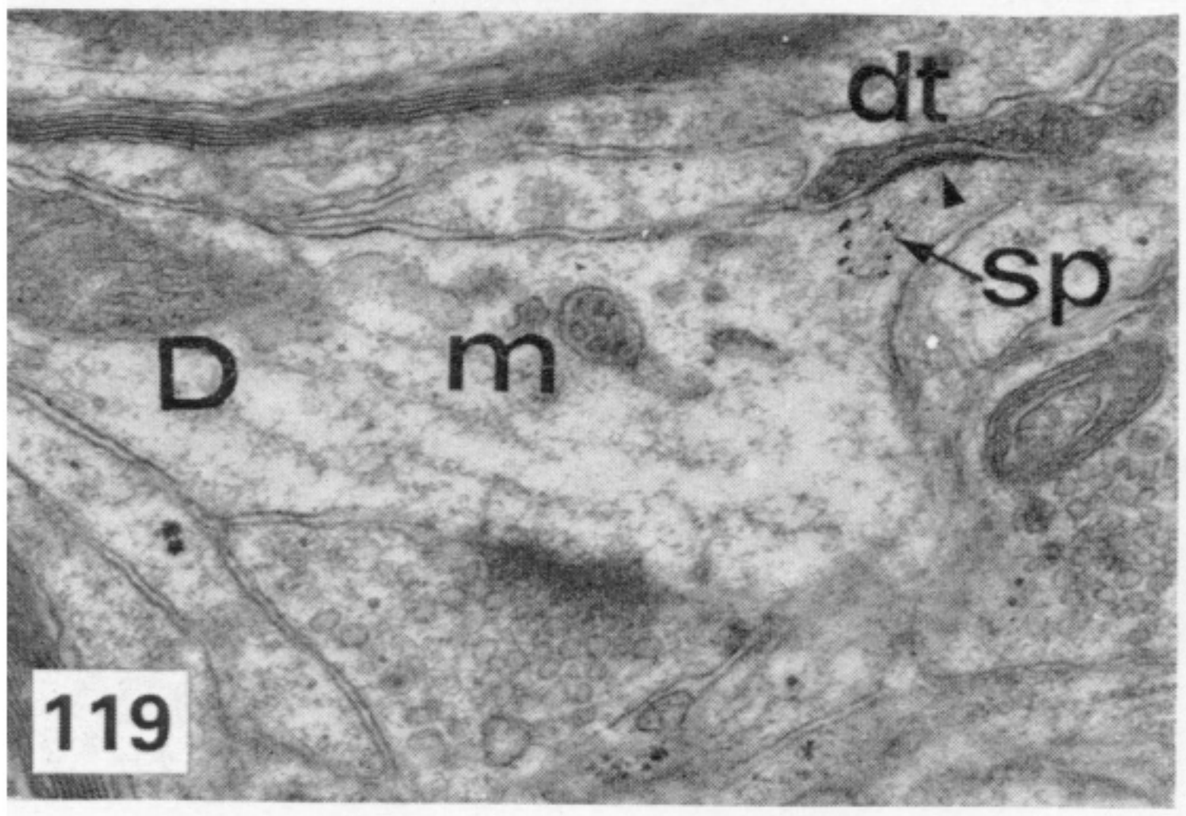


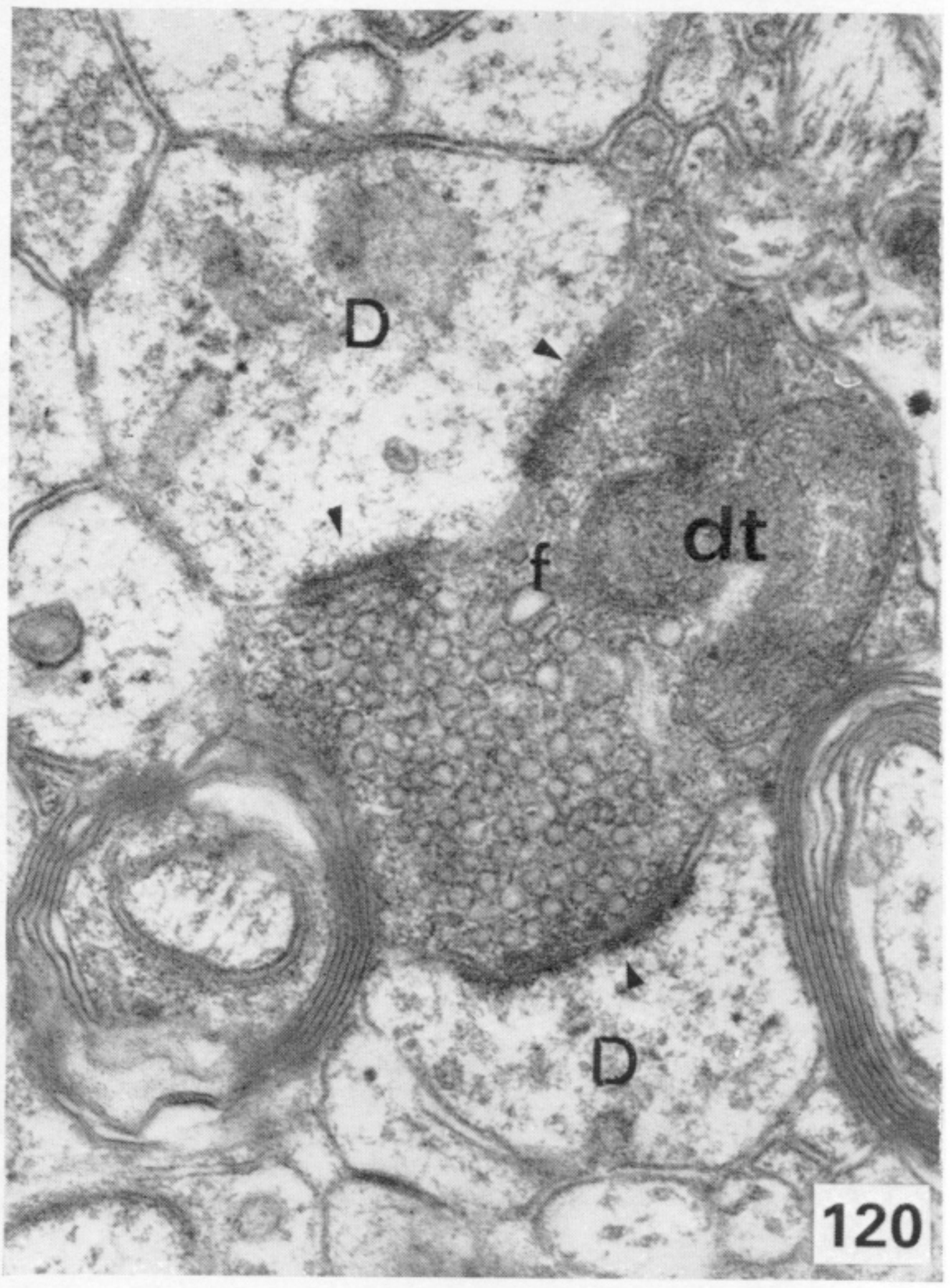


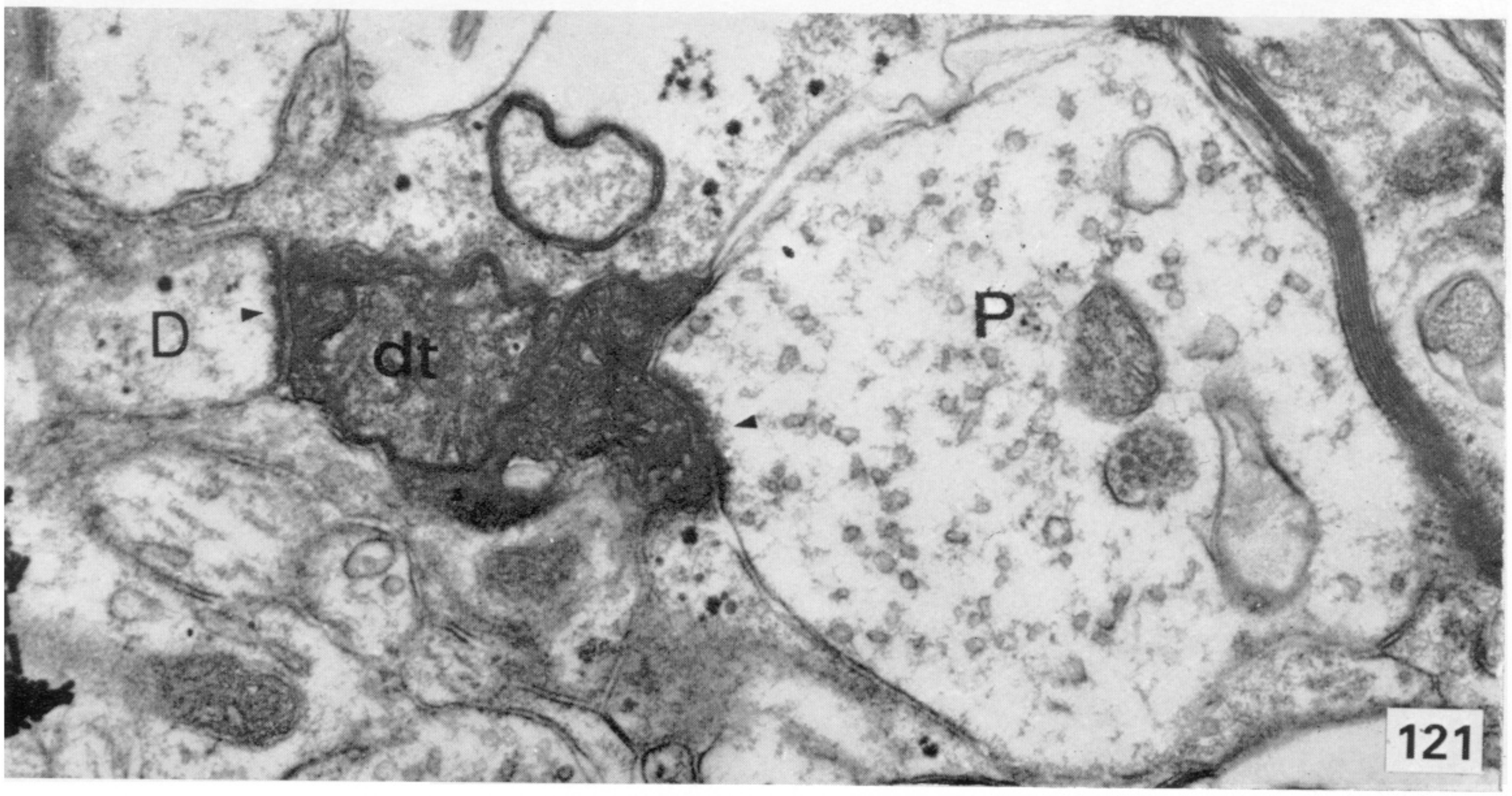
FIGURES 113–116. For description see opposite.



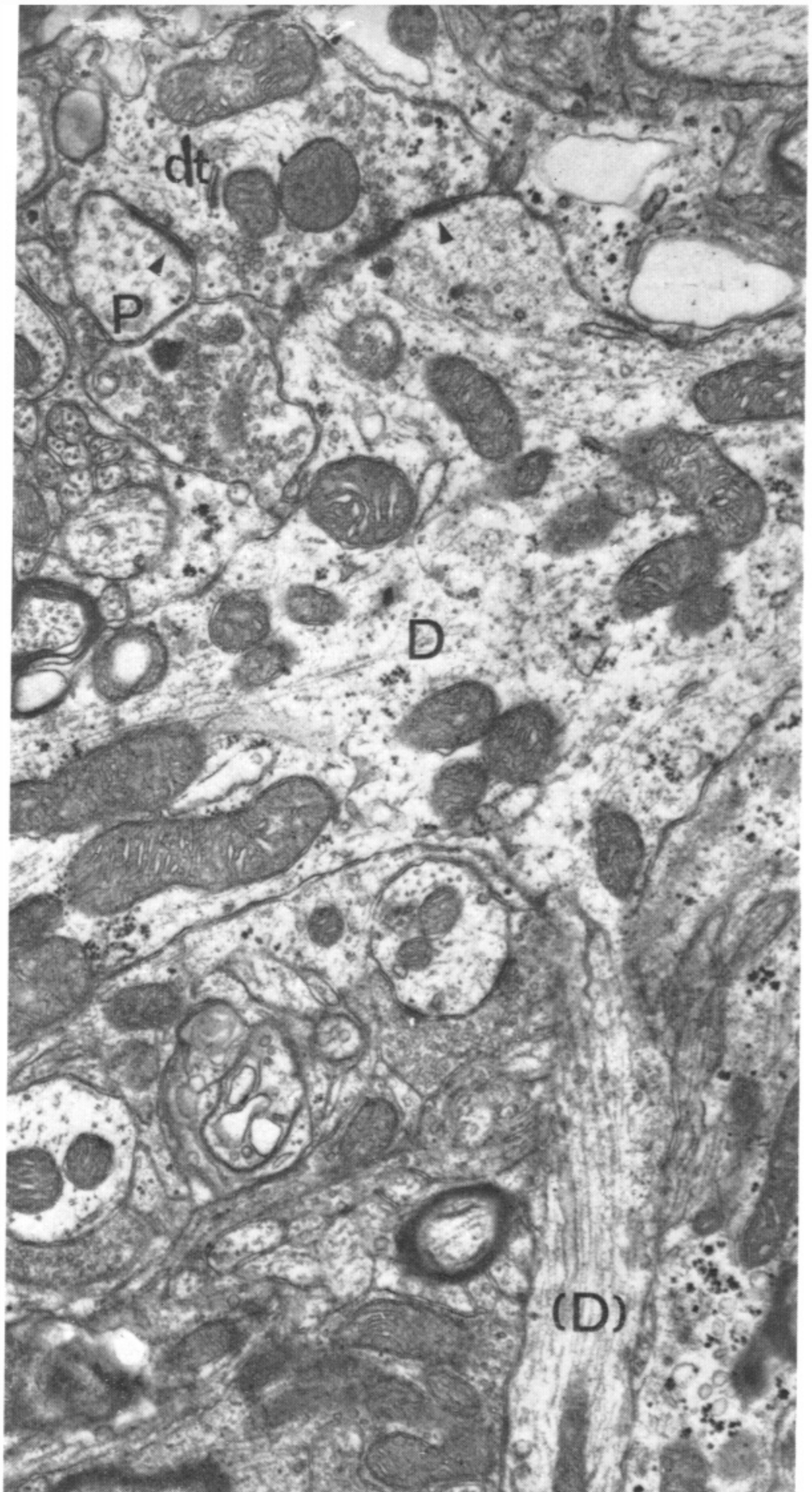


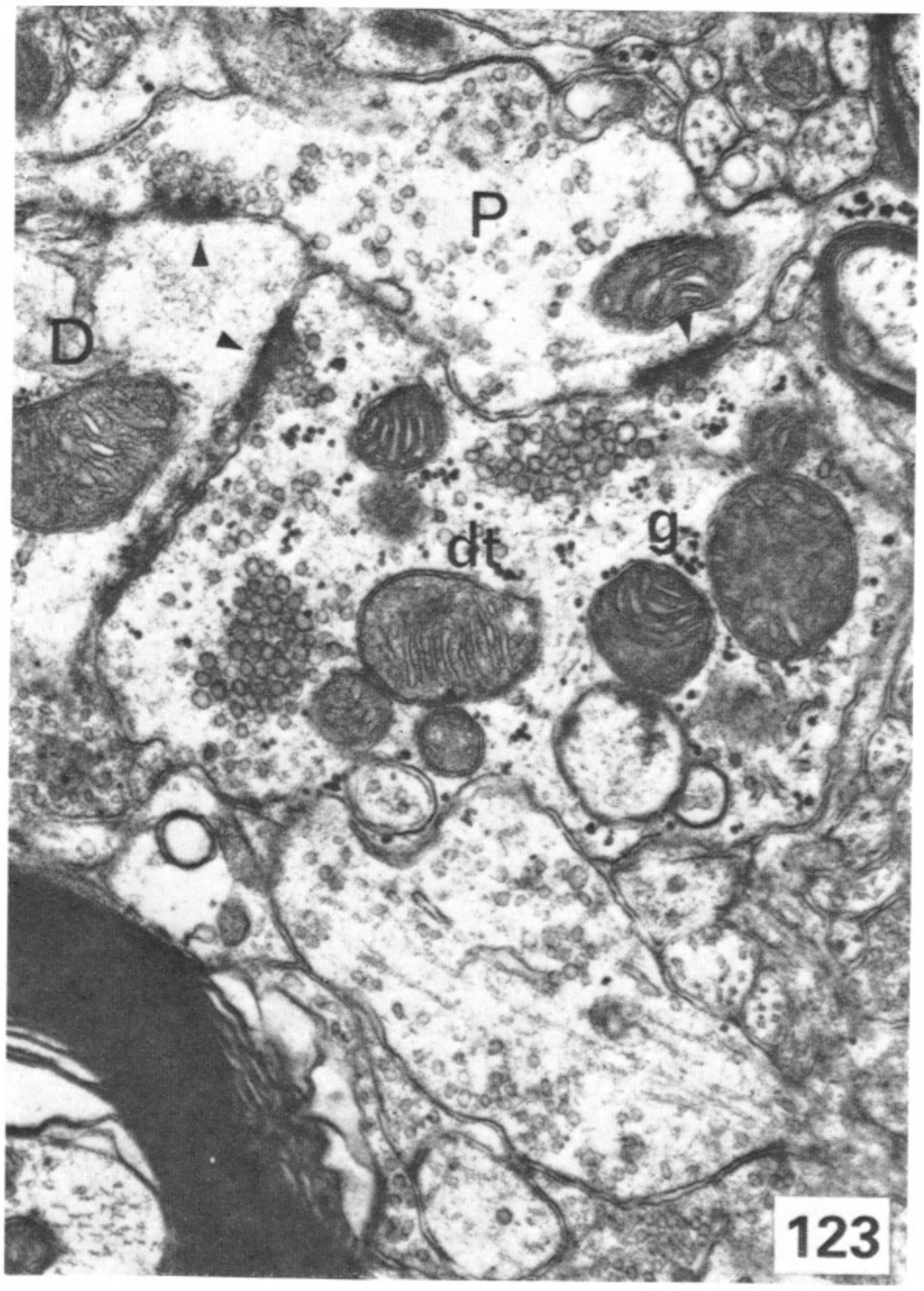


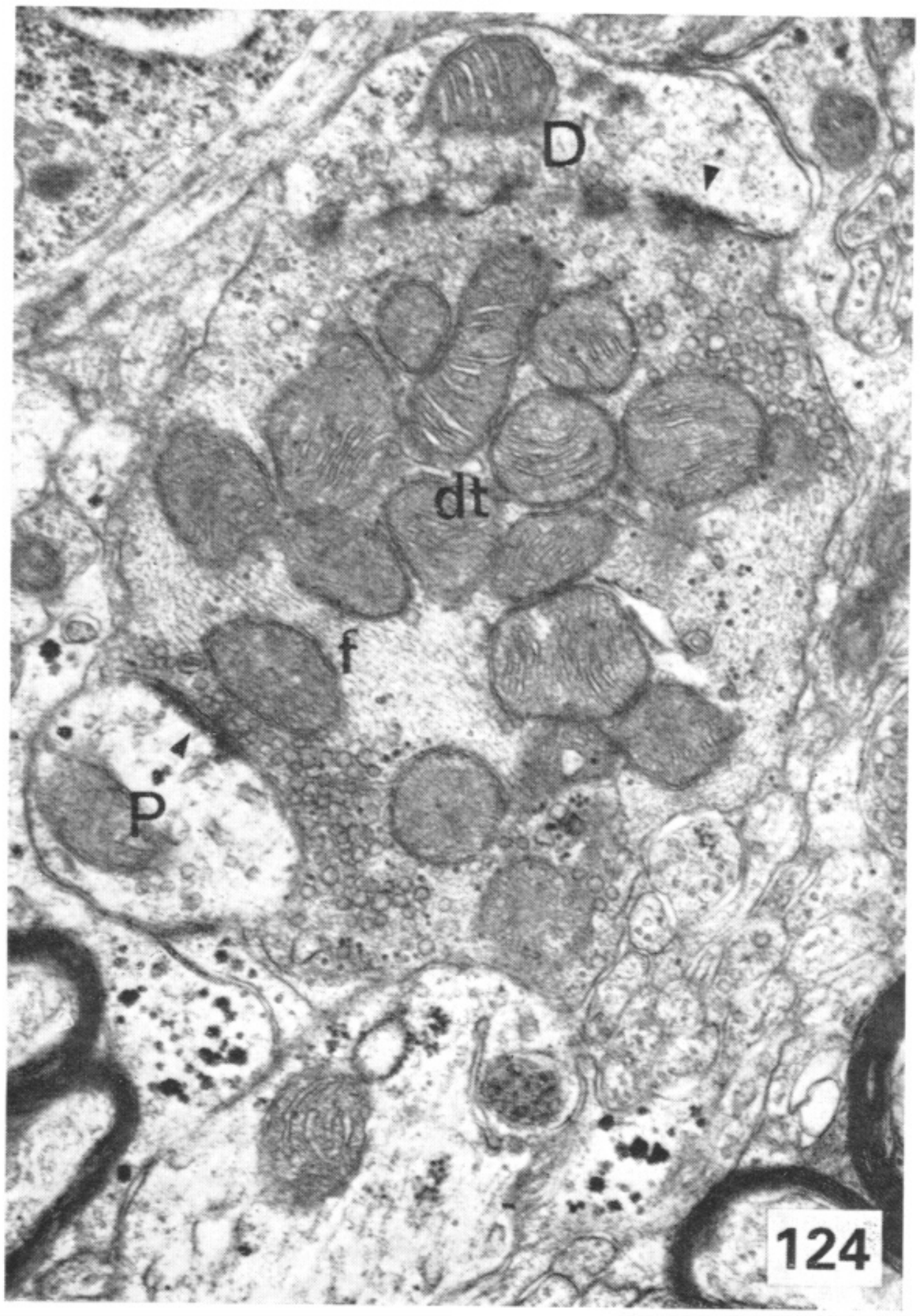




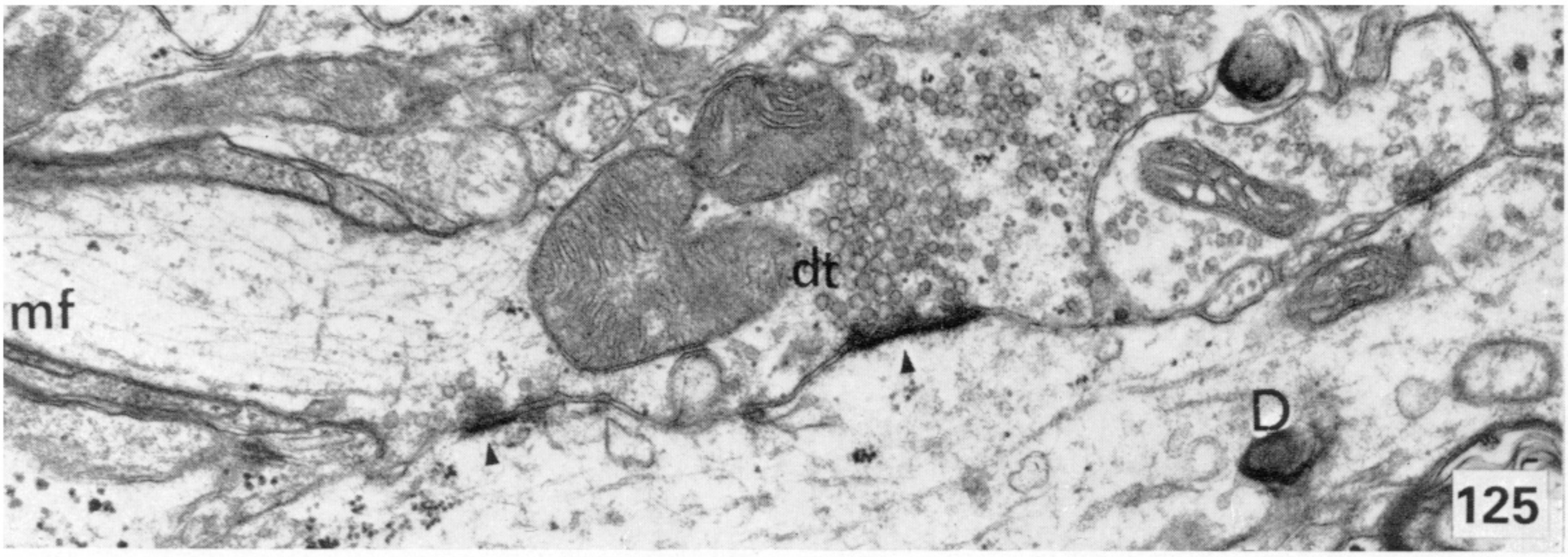
FIGURES 117–121. For description see opposite.

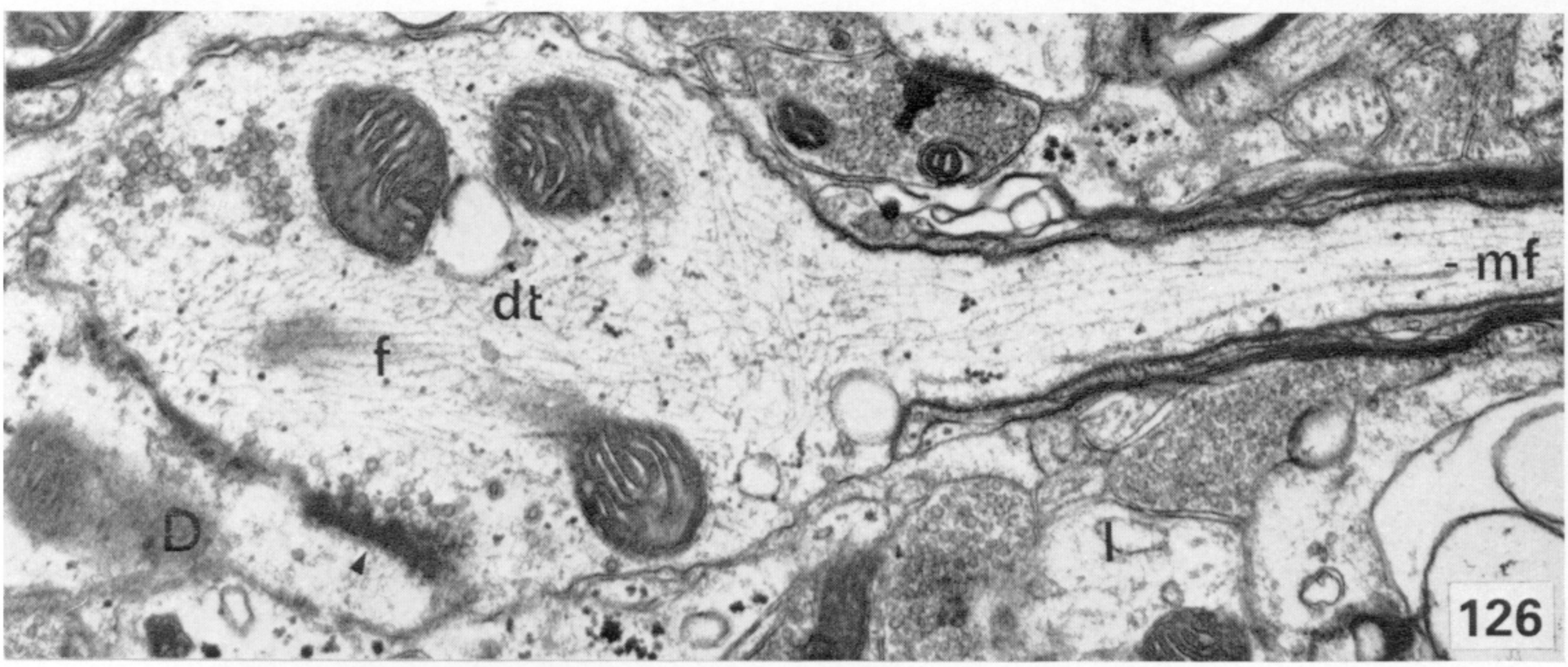


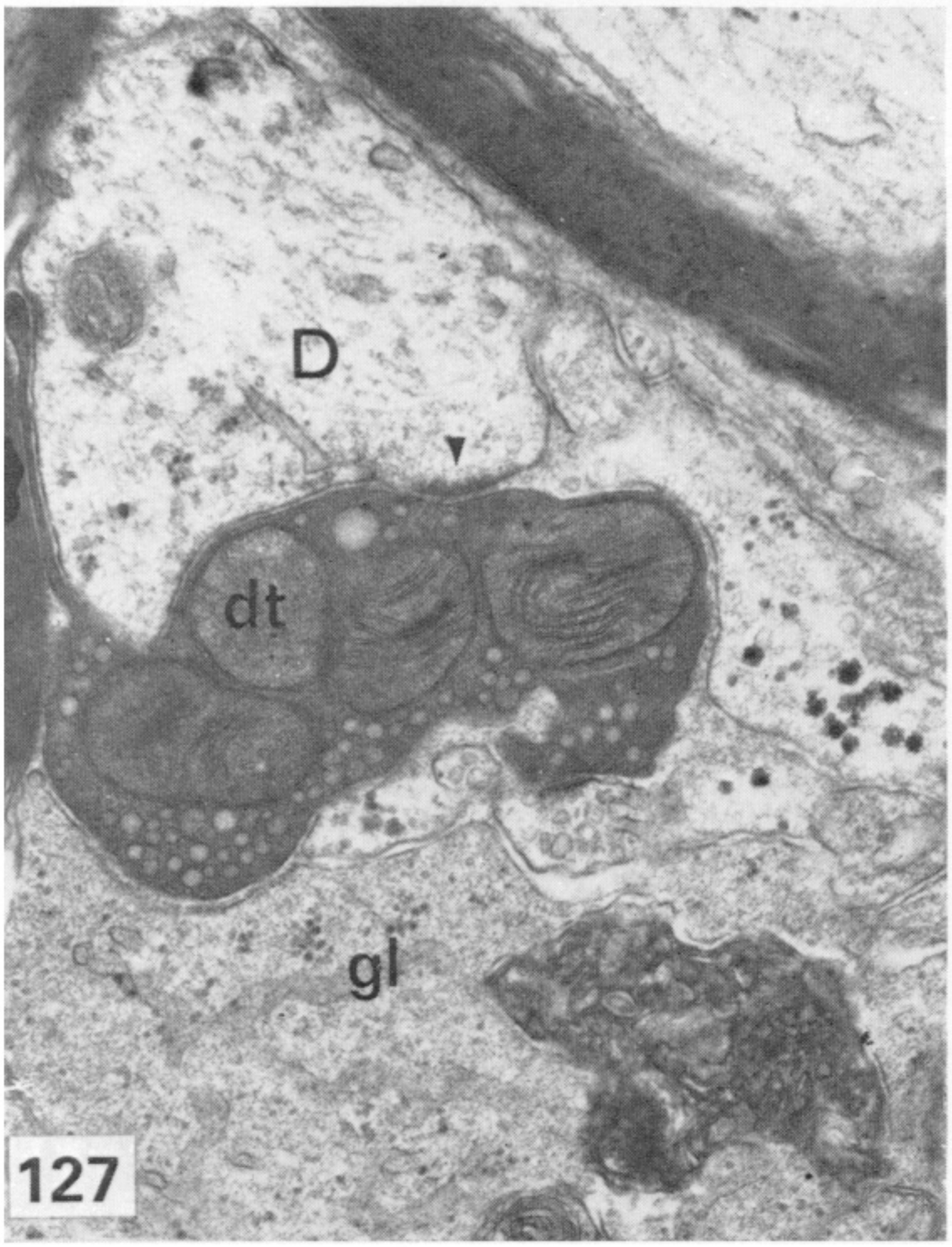


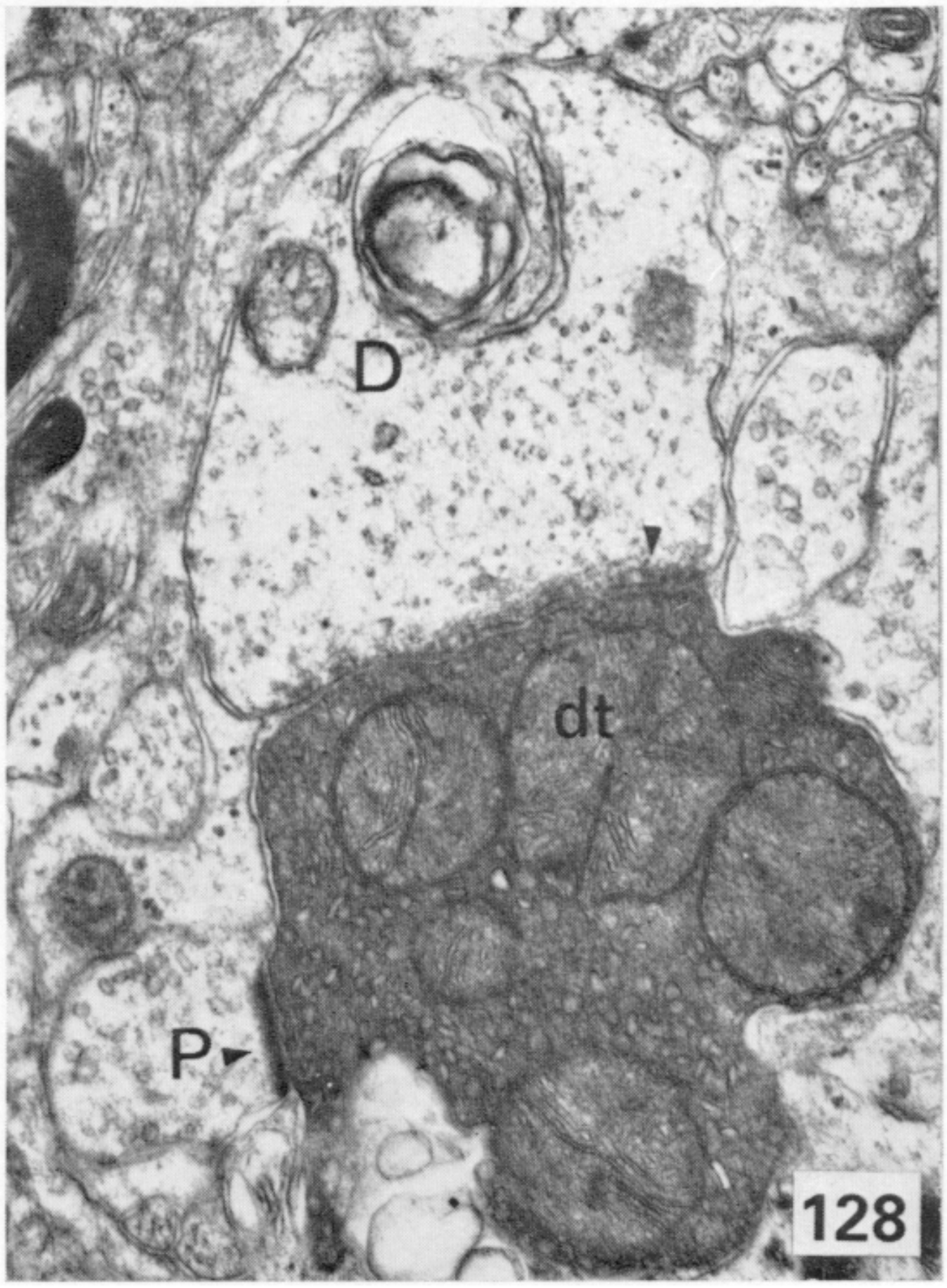


FIGURES 122–124. For description see opposite.









FIGURES 125–128. For description see opposite.