AN EXPERIMENTAL ELECTRON MICROSCOPIC STUDY OF AFFERENT CONNECTIONS TO THE PRIMATE MOTOR AND SOMATIC SENSORY CORTICES

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[Plates 1–12]

CONTENTS

An experimental electron microscope (e.m.) study has been made of the termination of the afferent connections to the primate sensori-motor cortex. Following large, stereotaxically placed thalamic lesions, degeneration in the motor and somatic sensory cortices was studied at survival periods of 4 and 5 days. Degenerating thalamo-cortical terminals had asymmetric membrane specializations. In the motor cortex 89.5% made synapses on to dendritic spines, 9% on to dendritic shafts and 1.5% on to cell somata; in the somatic sensory area 89% made synapses on to spines, 11% on to dendritic shafts and one example contacted a cell soma and a spine. A considerable number of the spines receiving synapses from degenerating thalamo-cortical terminals were traced to their parent dendrites and these were of the pyramidal type whereas the dendritic shafts and cell somata contacted by degenerating thalamo-cortical terminals were mostly of the large stellate type. Most of the thalamo-cortical degeneration in both cortical areas occurred in a dense band in the upper two thirds of layer IV and

the lower half of layer III but a number of degenerating terminals were found deep to this; in the motor cortex a second, less dense, band of degeneration was present in the lower part of layer V and top of layer VI. Degenerating thalamo-cortical terminals making synapses on to dendritic shafts and cell somata were scattered through the deep half of the cortex and not concentrated in the dense band of degeneration and so formed a greater proportion of the degeneration in the deep layers, particularly in the motor cortex. Sections cut parallel to the pial surface in layer IV of the motor cortex showed a statistically significant association between the degenerating thalamo-cortical axon terminals and the bundles of apical dendrites present at this level.

Degeneration of commissural fibres was studied after removal of the contralateral sensori-motor cortex. Degenerating terminals had asymmetric membrane specializations. In the motor cortex 96% made synapses on to dendritic spines, 3% contacted dendritic shafts and one example made an axosomatic synapse; in area 3*b*, 97% made synapses on to dendritic spines and 3% contacted dendritic shafts. A number of the spines receiving synapses from degenerating commissural axon terminals were traced to their parent dendrites and these were of the pyramidal type. The cell soma and the majority of the dendritic shafts receiving synapses from commissural terminals were of the large stellate type although some of the dendritic shafts were probably those of small stellate cells. In the motor cortex degenerating commissural axon terminals were found in all cortical layers but were relatively more dense in layer I, the upper part of layer III, the upper part of layer V and the lowest part of layer V with layer VI; in the somatic sensory cortex most degenerating commissural terminals were found in the superficial half of the cortex.

Following lesions of the primary somatic sensory cortex (SI) or of area 6 of the premotor cortex, degenerating terminals making asymmetric synapses were found in the motor cortex. Of the terminals of association fibres from SI, 82% made synapses on to dendritic spines and 18% on to dendritic shafts; of those fibres from area 6, 76% made synapses on to dendritic spines and 24% on to dendritic shafts. For both these association fibre connections, a proportion of the dendritic shafts contacted were clearly identifiable as those of large stellate cells. Terminals of both association connections occurred in all cortical layers with no obvious concentrations at any particular depth.

Introduction

Although the motor cortex has been extensively studied by physiologists and is an area of considerable clinical interest, most previous ultrastructural studies of the neocortex have been of sensory or parietal cortical areas (e.g. Colonnier & Rossignol 1969; Jones & Powell 1970*a–e*; Lund & Lund 1970; Peters & Kaiserman-Abramof 1970; Peters 1971; Garey & Powell 1971; Fisken, Garey & Powell 1975; Peters & Feldman 1976). This study has therefore concentrated on the ultrastructural features and sites of termination of the afferent connections to the motor cortex described by light microscopy from the thalamus (Walker 1938; Kievit & Kuypers 1977) and from ipsilateral and contralateral cortical areas (Jones & Powell 1969*a*; Pandya & Kuypers 1969; Pandya & Vignolo 1971). Because the motor and somatic sensory cortices are thought to be very different in character, the thalamo-cortical and commissural afferents to area 3*b* of the somatic sensory cortex have been studied to give a direct comparison of these afferent connections.

The thalamo-cortical projection to the motor cortex of the cat has previously been described (Strick & Sterling 1974), and a preliminary report of these findings has been published (Sloper 1973).

Material and methods

The observations were made on material from 21 young adult rhesus monkeys which had been operated upon under pentobarbitone anaesthesia using full aseptic precautions. In three animals large electrolytic stereotaxic lesions were placed in the ventrolateral and ventral posterior nuclei of the thalamus using a horizontal approach passing through the ipsilateral occipital pole; in four animals the contralateral sensori-motor cortex was removed by suction; in ten animals the ipsilateral primary somatic sensory cortex was removed by suction, the posterior wall of the central sulcus being undercut but left in position to protect the motor cortex from direct damage, and in four animals the premotor cortex of area 6 anterior to the precentral dimple and medial to the upper part of the arcuate sulcus was removed by suction. The correct placement of lesions was confirmed by examination of the fixed brains and for area 6 lesions light microscopy (l.m.) of Nissl stained sections was used to ensure that the lesions had not involved the anterior part of the motor cortex. After survival periods of 1–6 days the animals were again anaesthetized, cooled to between 25 and 30 °C and perfused with a mixture of 4% formaldehyde and 1% glutaraldehyde following a brief washout with buffered saline.

One millimetre thick slices were cut from the brains and care was taken to make them perpendicular both to the central sulcus and the pial surface; they were taken at various mediolateral positions along the sulcus. Blocks about 1 mm wide and running through the whole depth of the cortex were then taken from the motor cortex (area 4) and from area 3*b* of the somatic sensory cortex. The blocks were rinsed in 10% sucrose in phosphate buffer, post-fixed in 2% osmic acid in phosphate buffer and dehydrated through a graded series of alcohols, being block stained with uranyl acetate at the 70% alcohol stage.

One micrometre 'thick' sections were cut from the block face perpendicular to the pial surface and stained with a mixture of methylene blue and Azure II (Richardson, Jarrett & Finke 1960). Using the 'thick' section as a guide, a mesa with dimensions of approximately 1×0.5 mm was trimmed and ultrathin sections of known depth and orientation were cut, mounted on Formvar coated copper grids with a single 1×2 mm hole and were stained with alkaline lead citrate (Reynolds 1963) and uranyl acetate (5% solution in 50% ethanol). This procedure meant that the orientation and position of any ultrathin section in relation to the cortical laminae was always known and this was of great importance in this study. The cortex was routinely studied systematically through its depth and this required three mesas per block to cover the depth of the motor cortex and two in the thinner somatic sensory cortex. Extensive use was also made of long series of up to a hundred small serial sections approximately 100 μm square taken from selected regions of a block.

Sections were also cut parallel to the pial surface of the brain and to do this a thick section was first cut from the long face of a block which was then turned and cut parallel to the pia. The depth of any section then cut could be determined by taking further thick sections from the block perpendicular to the surface and the top edge of these thick sections, when compared to the original thick section, corresponded to the depth at which the sections cut parallel to the pia had been taken. It was thus possible to cut sections parallel to the pia at an accurately known depth in the cortex.

The distributions of neurons and degenerating axon terminals in relation to the laminae of the cortex were plotted using the mapping technique described by Alksne, Blackstad, Walberg & White (1966) in which the microscope stage coordinates are recorded for the corners of the

section and each degenerating axon terminal; these are then plotted out on graph paper. The maps of individual sections were collated by comparison of the thick sections of the individual mesas used with the thick section of the entire block. The positions of the cortical laminae were determined from these thick sections and transferred to the maps so that a composite map showing the distribution of degenerating axon terminals through the depth of the cortex could be constructed.

Results

Following the placement of lesions in the thalamus, the contralateral sensori-motor cortex and the ipsilateral primary somatic sensory cortex (SI) and premotor cortex (area 6), typical degenerating axon terminals were found in the sensori-motor cortex of the monkey. These terminals showed swelling of synaptic vesicles, cytoplasmic darkening and progressive disruption of their internal structure with engulfment by glia as described previously in various sites (e.g. Colonnier 1964; Jones & Powell 1970*d*; Pinching & Powell 1972); the features of the process of degeneration in the axon terminals studied here are described in detail elsewhere (Sloper & Powell 1978*b*). No structure was identified as a degenerating axon terminal unless it showed clear evidence of degenerative change and also had an unequivocal postsynaptic specialization. The whole depth of the cortex was studied systematically and all degenerating

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Description of plate 1

Figures 1–7. Degenerating motor thalamo-cortical terminals making synapses on to spines.

Figure 1. An early degenerating thalamo-cortical terminal (dt) in the motor cortex making an *en passage* synapse on to a spine (sp) containing a spine apparatus (s). (Magn. × 29000.)

Figure 2. An early degenerating thalamo-cortical terminal in the motor cortex making a synapse on to a spine. Note the glycogen and prominent neurofilaments in the terminal. (Magn. × 19500.)

Figure 3. A large early degenerating motor thalamo-cortical terminal making a synapse on to a spine. Note the irregularly swollen synaptic vesicles. (Magn. × 29000.)

Figure 4. A late degenerating thalamo-cortical terminal making a synapse on to a spine containing a spine apparatus in the motor cortex. Note the glial engulfment (G). (Magn. × 48000.)

Figure 5. A late degenerating motor thalamo-cortical axon terminal making a synapse on to a spine and engulfed by glia. (Magn. × 29000.)

Figure 6. An early degenerating motor thalamo-cortical terminal making *en passage* synapses on to two spines. (Magn. × 29000.)

Figure 7. A late degenerating motor thalamo-cortical terminal making synapses on to two spines and engulfed by glia. (Magn. × 29000.)

Description of plate 2

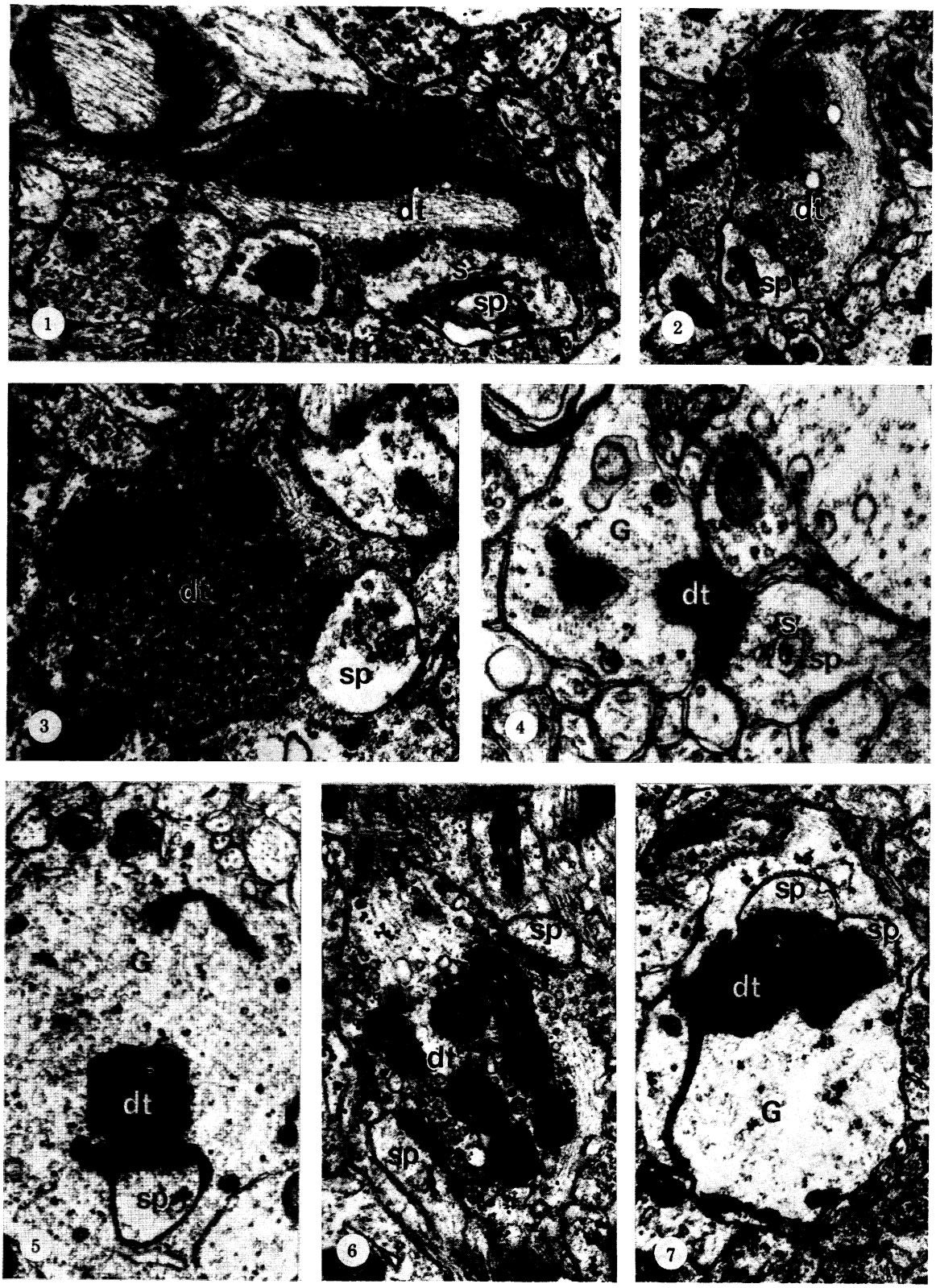
Figure 8. A degenerating thalamo-cortical terminal (dt) in the motor cortex making a synapse on to a spine (sp) which also receives a synapse from a normal axon terminal (t) and which is cut in continuity with its parent dendrite (d). Note the large diameter of the parent dendrite and the lack of other synapses on to it. (Magn. × 29000.)

Figure 9. A degenerating thalamo-cortical terminal in the motor cortex making a synapse on to a spine which also receives an asymmetric synapse (arrowhead) from a normal axon terminal. (Magn. × 46000.)

Figure 10. A degenerating thalamo-cortical terminal in the motor cortex making a synapse on to a spine which also receives a symmetrical synapse (two arrowheads) from a normal axon terminal. (Magn. × 46000.)

Figure 11. A degenerating thalamo-cortical terminal in the motor cortex making a synapse on to a spine which contains a spine apparatus (s) and which is cut in continuity with its parent dendrite. Note the small diameter of the parent dendrite and the lack of synapses on its shaft. (Magn. × 29000.)

Figure 12. A degenerating thalamo-cortical terminal in the motor cortex which makes a synapse both with a spine and the shaft of a dendrite. (Magn. × 29000.)



FIGURES 1–7. For description see opposite.

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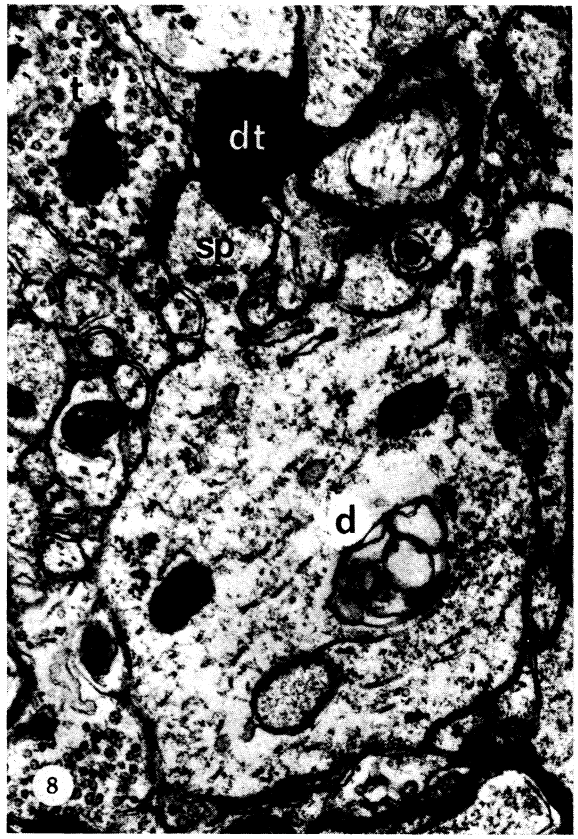
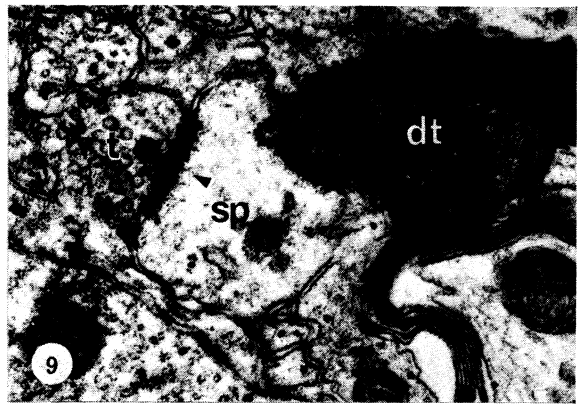
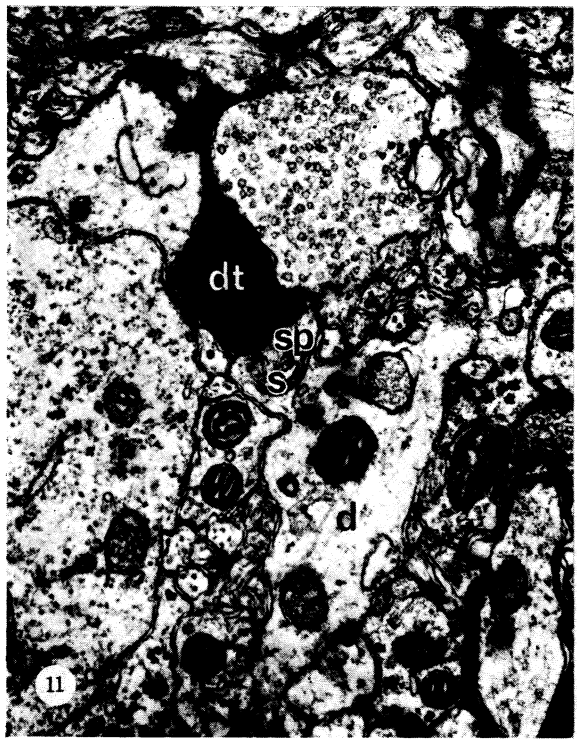
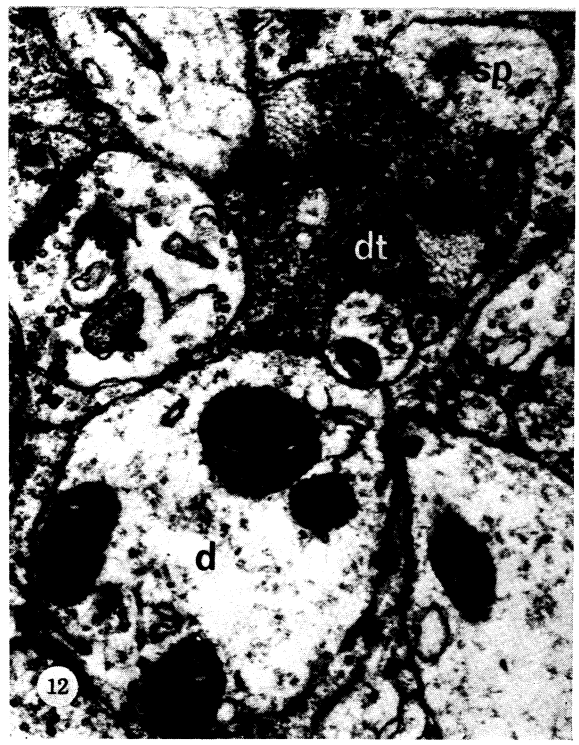
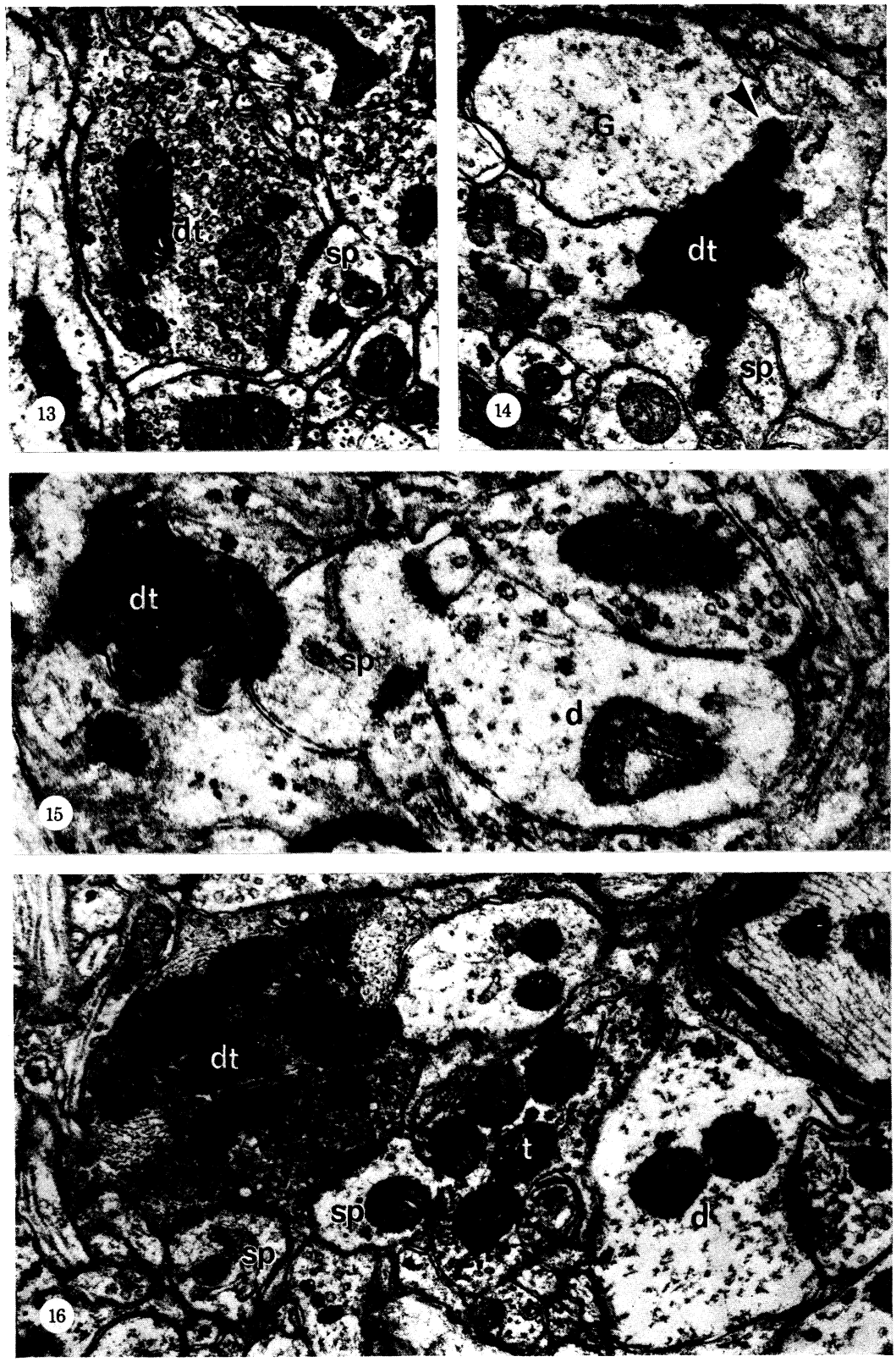




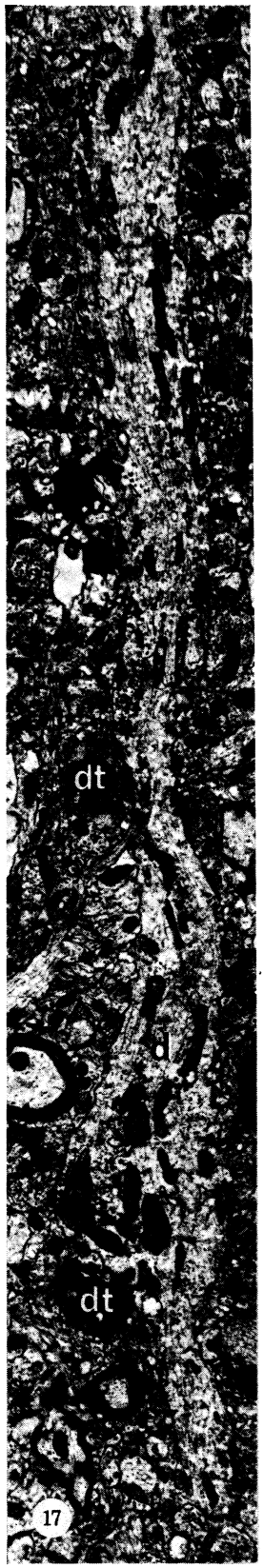


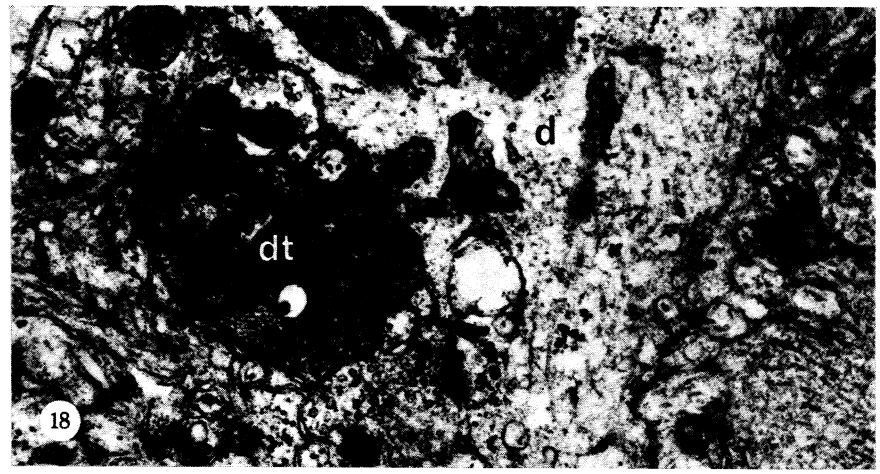


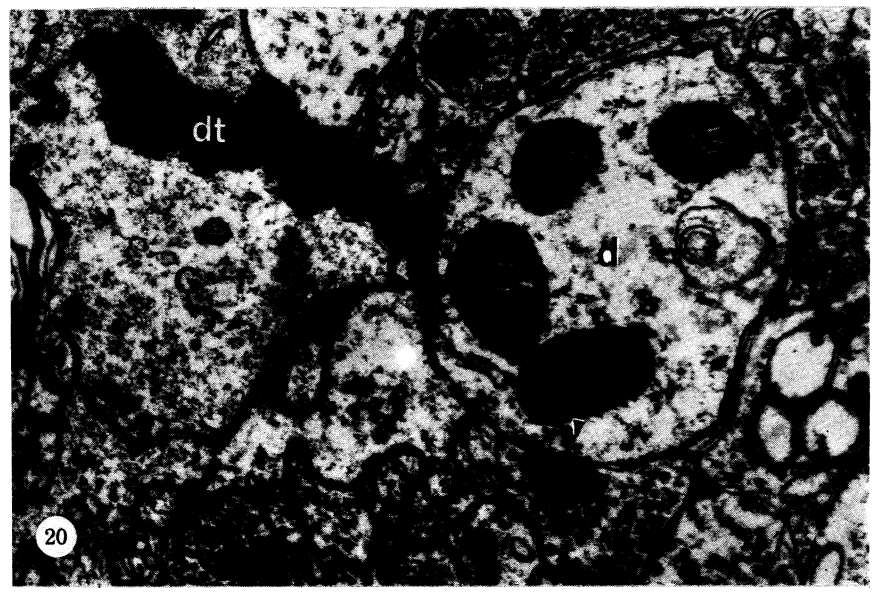
FIGURES 8–12. For description see page 202.



FIGURES 13–16. For description see page 203.







FIGURES 17–20. For description see opposite.

terminals recorded, so that an unbiased sample of terminals was obtained; this allowed valid quantitative comparisons to be made between the different connections.

Thalamo-cortical afferents

Following large thalamic lesions, dense degeneration was found in both motor cortex and area 3*b* of the somatic sensory cortex. After a survival period of four days much of the degeneration seen was at an early to medium stage (figures 1–3, plate 1) and after 5 days medium and late stages of degeneration predominated (figures 4 and 5). Extensive sampling and mapping were therefore done at the later survival period.

Degenerating thalamo-cortical terminals were found to have asymmetric membrane specializations and of 553 studied in the motor cortex 486 (88%) made synapses on to a single identifiable profile, 40 (7.2%) on to two postsynaptic profiles and 6 (1.1%) on to three post-synaptic profiles in a single section; in the remaining small proportion the postsynaptic profile could not be clearly identified. Of those terminals making synapses on to a single identifiable postsynaptic profile, 89.5% made synapses on to dendritic spines (figures 1–5), 9% on to dendritic shafts and 1.5% directly on to cell somata (table 1). Degenerating terminals making synapses on to more than one profile in a single section contacted two or three spines (figures 6 and 7), a spine and one or two dendritic shafts (figure 12, plate 2) and in one case two spines and a cell soma. Spines were also found which received synapses from both a degenerating thalamo-cortical terminal and a normal asymmetric or symmetrical axon terminal (figures 8–10).

Description of plate 3

Figures 13–16. Degenerating thalamo-cortical terminals making synapses on to spines in the somatic sensory cortex.

Figure 13. An early degenerating thalmo-cortical axon terminal (dt) making a synapse on to a spine (sp) in area 3*b* of the somatic sensory cortex. Note the irregularly swollen vesicles and the glycogen in the axon terminal. (Magn. × 29000).

Figure 14. A late degenerating thalamo-cortical terminal making a synapse on to a spine in area 3*b* of the somatic sensory cortex. Note its engulfment by glia (G) and the coated pit being formed (arrowhead). (Magn. × 29000.)

Figure 15. A degenerating thalamo-cortical axon terminal which makes a synapse on to a spine cut in continuity with its parent dendrite (d) in the somatic sensory cortex. (Magn. × 48000.)

Figure 16. A degenerating thalamo-cortical terminal which makes a synapse on to two spines in the somatic sensory cortex. One of these spines also receives a symmetrical synapse from a normal axon terminal (t) containing flattened vesicles and this terminal also makes a synapse on to a dendrite. (Magn. × 32000.)

Description of plate 4

Figures 17–20. Motor thalamo-cortical terminals contacting dendritic shafts.

Figure 17. A large dendrite (d) in layer IV of the motor cortex which receives synapses from two degenerating thalamo-cortical terminals (dt). Note the large number of other synapses received by the dendrite and the high concentration of organelles within it. The dendrite was traced in continuity with a typical large stellate cell soma which itself received a synapse from a degenerating thalamo-cortical terminal. (Magn. × 8400.)

Figure 18. Higher magnification of the lower degenerating thalamo-cortical terminal of figure 17. (Magn. × 29000.)

Figure 19. A degenerating thalmo-cortical axon terminal which makes a synapse on to the shaft of a dendrite. Note the large number of other synapses received by the dendrite, one of which is clearly asymmetric (arrowhead), and the high concentration of organelles in its cytoplasm. (Magn. × 29000.)

Figure 20. A late degenerating thalamo-cortical axon terminal which makes a synapse on to the shaft of a dendrite. Note the other asymmetric synapse received by the dendrite (arrowhead) and the glial engulfment (G). (Magn. × 29000.)

In the somatic sensory cortex, of 223 degenerating terminals 183 (84%) made synapses on to a single identifiable postsynaptic profile and 26 (12%) on to two profiles. Of those making synapses on to a single identifiable profile 89% contacted dendritic spines (figures 13 and 14, plate 3) and 11% contacted dendritic shafts (table 1); one made a synapse on to a cell soma and a spine. Examples were found where a single degenerating terminal made synapses on to two spines (figure 16) or a spine and a dendritic shaft in a single section and some spines received synapses from both a degenerating terminal and a normal asymmetric or symmetrical terminal (figure 16).

TABLE 1. PROPORTIONS OF THE DIFFERENT TYPES OF POSTSYNAPTIC PROFILE RECEIVING SYNAPSES FROM DEGENERATING AXON TERMINALS

(Figures represent proportions of degenerating axon terminals making synapses on to each type of postsynaptic site as a percentage of the total number of single identifiable postsynaptic profiles.)

connection	spine	dendrite	soma
thalamo-cortical			
motor	89.5	9	1.5
area 3*b*	89	11	–
commissural			
motor	96	3	<1
area 3*b*	97	3	–
association			
SI → motor	82	18	–
area 6 → motor	76	24	–

In fortunate single sections and by extensive use of serial sections, 32 spines receiving synapses from degenerating thalamo-cortical terminals were traced to their parent dendrites in the motor cortex and 7 were traced in the somatic sensory cortex. Most of these parent dendrites were of small or medium size, between 0.2 and 1.0 μm in diameter and rarely received other synapses (figures 11 and 15). They were not varicose in shape and contained few organelles although they contained a number of microtubules. A few of the dendrites were larger, around 2 μm in diameter, had a regular outline and contained more organelles (figure 8) with a considerable number of relatively evenly spaced microtubules. Some of these larger dendrites were orientated obliquely in relation to the cortical surface, but in two examples found in sections cut parallel to the cortical surface in layer IV of the motor cortex the parent dendrites of such spines appeared to be the apical dendrites of deep pyramidal cells cut in transverse section.

The majority of the 44 dendritic shafts receiving synapses from degenerating thalamo-cortical terminals in the motor cortex (figures 17–20, plate 4) and the 20 from the somatic sensory cortex (figures 21–23, plate 5) received a high density of other synapses, with a proportion of these being asymmetric; a few dendrites were found receiving two degenerating terminals. Most of these dendrites were 0.5–2.0 μm in diameter, contained abundant mitochondria and ribosomes and, when cut in longitudinal section, were frequently varicose in outline and ran in a straight line for considerable lengths; these features identify them as arising from large stellate cells and one dendrite receiving synapses from two degenerating thalamo-cortical axon terminals was traced in continuity with a large stellate cell soma (figure 17). A similar dendrite received synapses from two degenerating thalamo-cortical terminals and made a gap junction (Sloper & Powell 1978*a*). In the motor cortex two degenerating thalamo-cortical terminals made synapses on to the shafts of fairly large dendrites, each of which also had a spine

receiving a synapse from a normal axon terminal; only one other synapse was present on the shaft of either dendrite and so they were probably pyramidal in origin. In area 3*b* one degenerating terminal made a synapse on to the shaft of a very large (diameter 6 μm) vertically orientated dendrite at the base of a side branch (figures 22 and 23); this dendrite received only two other synapses in spite of its large size and had the typical appearance of a pyramidal apical dendrite.

Seven cell somata received synapses from degenerating thalamo-cortical axon terminals in the motor cortex and one in the somatic sensory cortex. All received numerous asymmetric and symmetrical synapses, had abundant cytoplasm containing a high concentration of mitochondria, ribosomes and clusters of rough endoplasmic reticulum (figures 24–26, plate 6) and were typical of large stellate cells. Histograms of the size distribution of these cells and of the numbers of synapses on to them are shown in figure 27.

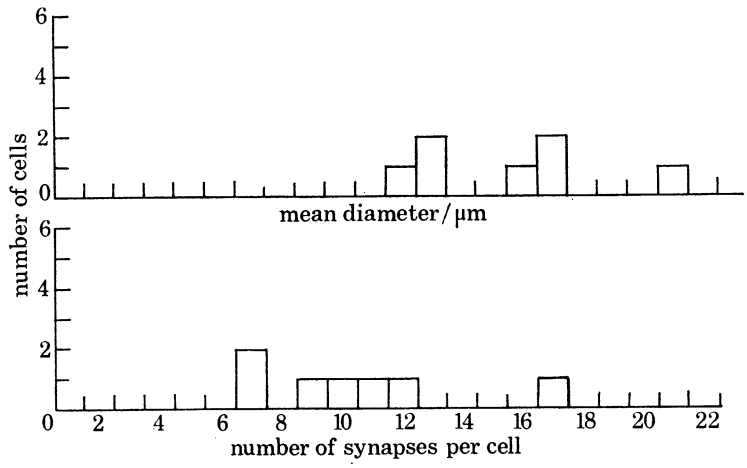


FIGURE 27. Histograms showing the distributions of the mean cell diameters and numbers of synapses received per cell profile for all those cell somata found to receive axo-somatic synapses from degenerating thalamo-cortical terminals in the motor cortex. These distributions correspond to those of the large stellate cell population defined in normal material (see text).

Degenerating thalamo-cortical axon terminals were found in all layers of the cortex both in the motor cortex and area 3*b* but there were striking differences in the density of degenerating terminals in the different laminae. In the motor cortex a few degenerating terminals were present in layers I and II and in the upper half of layer III; there was a very dense band of degenerating terminals occupying the lower half of layer III and the upper two thirds of layer IV; some degenerating terminals were present in the lower third of layer IV and the upper two thirds of layer V, and there was a moderately dense band in the lowest part of layer V and the top of layer IV with a few below this level (figure 28). The relation of the degeneration to the laminae of the motor cortex was also studied with the light microscope using the Wiitanen technique (1969); this confirmed that the dense band of degeneration was in the lower half of layer III and the upper two thirds of layer IV and also the presence of a second much less dense band of degeneration in the boundary region between layers V and VI.

Electron microscope study of area 3*b* of the somatic sensory cortex also showed a very dense band of degenerating thalamo-cortical axon terminals in the lower half of layer III and the upper two thirds of layer IV. Above this level were a few scattered degenerating terminals and

below it there were rather more, but there did not appear to be a second concentration of degenerating terminals at the boundary of layers V and VI (figure 29). Sections of the somatic sensory cortex, when stained by the Wiitanen method, showed a dense band of finely granular degeneration in the lower half of layer III and the upper two thirds of layer IV in area 3*b*, but there was no band of degeneration in the deep laminae.

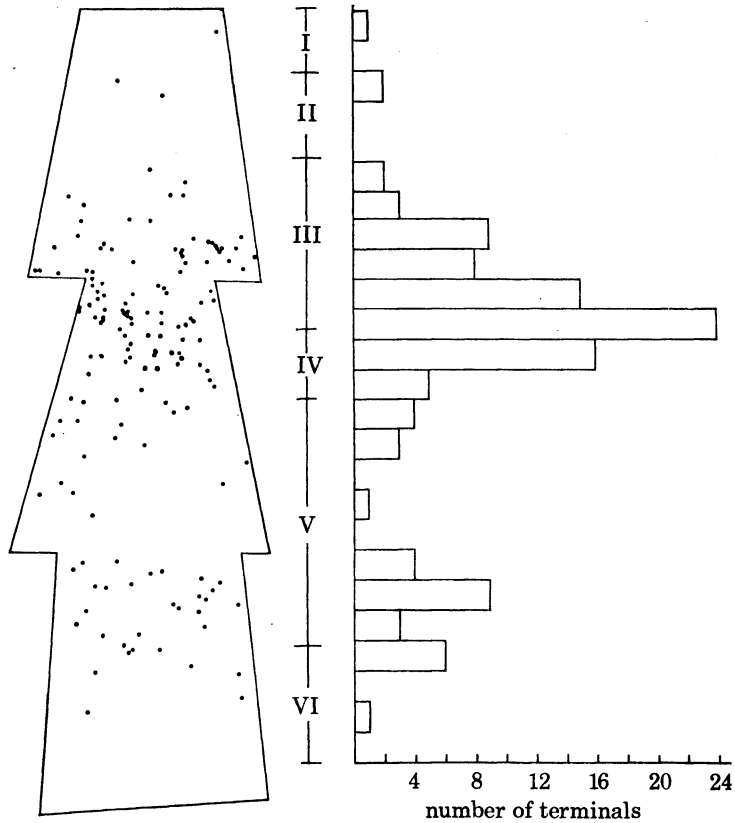


FIGURE 28. A map and histogram showing the depth distribution of degenerating thalamo-cortical axon terminals in the motor cortex, a single section having been mapped at each of the three levels. Note that the dense band of degeneration is in the upper two thirds of layer IV and the lower half of layer III and that there is a second smaller concentration of degeneration in the deep part of layer V. The histograms were prepared from a constant width strip running through the whole depth of the cortex for all maps.

In e.m. maps of degeneration the nature of the postsynaptic profile or profiles was recorded for each degenerating thalamo-cortical terminal (figures 30 and 31). Those degenerating terminals classed as ending on spines are those ending on one or more spines but not those ending on a spine plus a dendrite or cell soma; those classed as ending on dendritic shafts or cell somata similarly exclude those ending on more than one type of profile. The degenerating terminals in the dense band in layers III and IV make synapses mostly on to dendritic spines and the distribution of degenerating terminals contacting spines corresponds approximately to the overall distribution of degenerating terminals. However, those degenerating terminals making synapses on to dendritic shafts do not follow this overall pattern but are fairly evenly spread through the deeper layers of the cortex, occurring mainly below the dense band of degeneration in layers III and IV, this being better shown in the motor cortex where the deep laminae are thicker. The two cell somata receiving synapses from degenerating thalamo-cortical

terminals belong to the same type of neuron as the majority of the dendritic shafts and appear to occur within the same distribution. The difference between the distribution of degenerating thalamo-cortical axon terminals making synapses on to spines and those making synapses on to dendrites and somata was tested statistically by comparing the mean depths of the two distributions. This showed a significant difference between the two distributions in the motor cortex (Student's t test, $t = 2.697$, $P < 0.01$); although the mean depths were different in the somatic

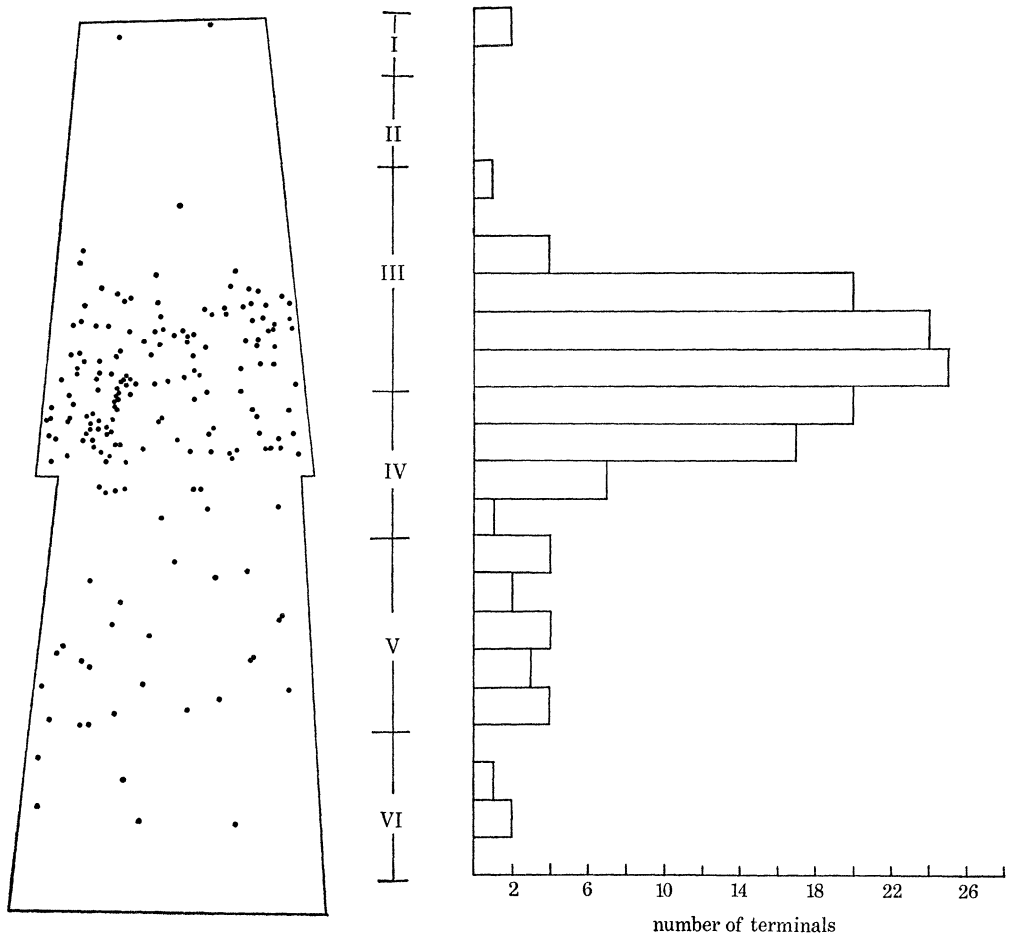


FIGURE 29. A map and histogram showing the depth distribution of degenerating thalamo-cortical axon terminals in area 3*b* of the somatic sensory cortex, a single section having been mapped at each of two levels. Note that, as in the motor cortex, the dense band of degeneration is in the upper two thirds of layer IV and the lower half of layer III but although degeneration is present in layer V it does not appear to form a separate band as in the motor cortex.

sensory cortex, this was not statistically significant. This difference in the distribution of degenerating terminals ending on spines and dendrites or somata means that the proportions ending on the different post-synaptic sites vary greatly between different laminae. If the histograms (figures 30 and 31) are divided immediately below the dense bands of degeneration (below bin 12) and the proportions making synapses on to each site above and below this level are calculated, it is found that in the motor cortex 5% of the degenerating terminals contact dendrites or somata within and above the dense band whereas 29% do so below it and in the somatic sensory cortex 9% contact dendrites within and above the dense band and 18% below it.

In sections taken parallel to the pial surface of the motor cortex the apical dendrites of deep pyramidal cells occur in groups as they pass through layer IV and the lower part of layer III. Qualitative examination of sections of experimental material cut at this level and corresponding to the dense band of degeneration in layers III and IV showed that many of the degenerating terminals occurred close to or within the bundles of apical dendrites (figure 32, plate 7) and all but a few of them made synapses on to dendritic spines. Three maps were made at the level

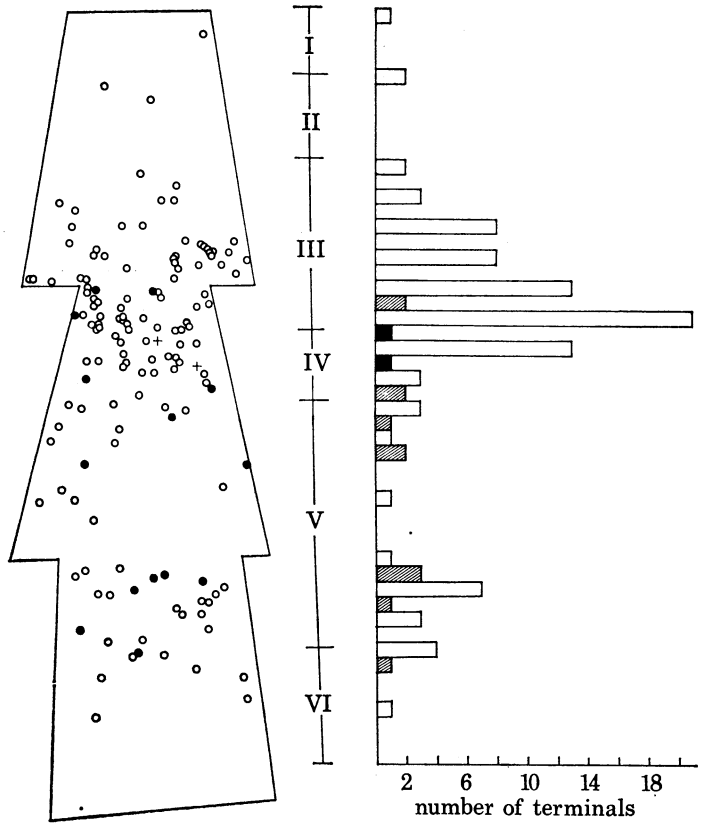


FIGURE 30. A map and histogram of the same sections of the motor cortex as figure 28 but showing the depth distributions of the different types of postsynaptic profile contacted by degenerating thalamo-cortical axon terminals. Note that whereas most of those contacting spines (○ and □) are in the dense band of degeneration in layers III and IV, those contacting dendrites (● and ▨) and cell somata (+ and ■) are spread through the deeper layers of the cortex. Those degenerating terminals contacting more than one type of postsynaptic profile or unidentified postsynaptic profiles are not shown in this map.

of the boundary of layers III and IV from two brains and the positions of all the degenerating terminals and apical dendrites were plotted (e.g. figure 33). This confirms the impression that the degenerating terminals frequently occur in relation to the apical dendrites and measurement of all the maps showed that about three quarters of the degenerating thalamo-cortical terminals occurred within 10–15 μm of an apical dendrite. The maps were analysed statistically by superimposing a grid of squares randomly on to each map and noting the numbers of apical dendrites and degenerating terminals in each square. If the position of degenerating thalamo-cortical terminals is independent of that of apical dendrites, then the proportion of squares containing degenerating terminals should be the same whatever the number of apical dendrites in the

FIGURE 21. A degenerating thalamo-cortical axon terminal (dt) which makes an *en passage* synapse on to a dendrite (d) in the somatic sensory cortex. Note the large size of the dendrite and the other synapses it receives, one of which is clearly of the asymmetric type (arrowhead). (Magn. × 29000.)

FIGURE 22. A degenerating thalamo-cortical terminal which makes a synapse on to a very large vertically running dendrite at the base of a side branch in layer IV of the somatic sensory cortex. This dendrite is probably the apical dendrite of a pyramidal cell in layer V. (Magn. × 8400.)

FIGURE 23. Higher magnification of the degenerating thalamo-cortical terminal of figure 22. Note the glial engulfment (G). (Magn × 29000.)

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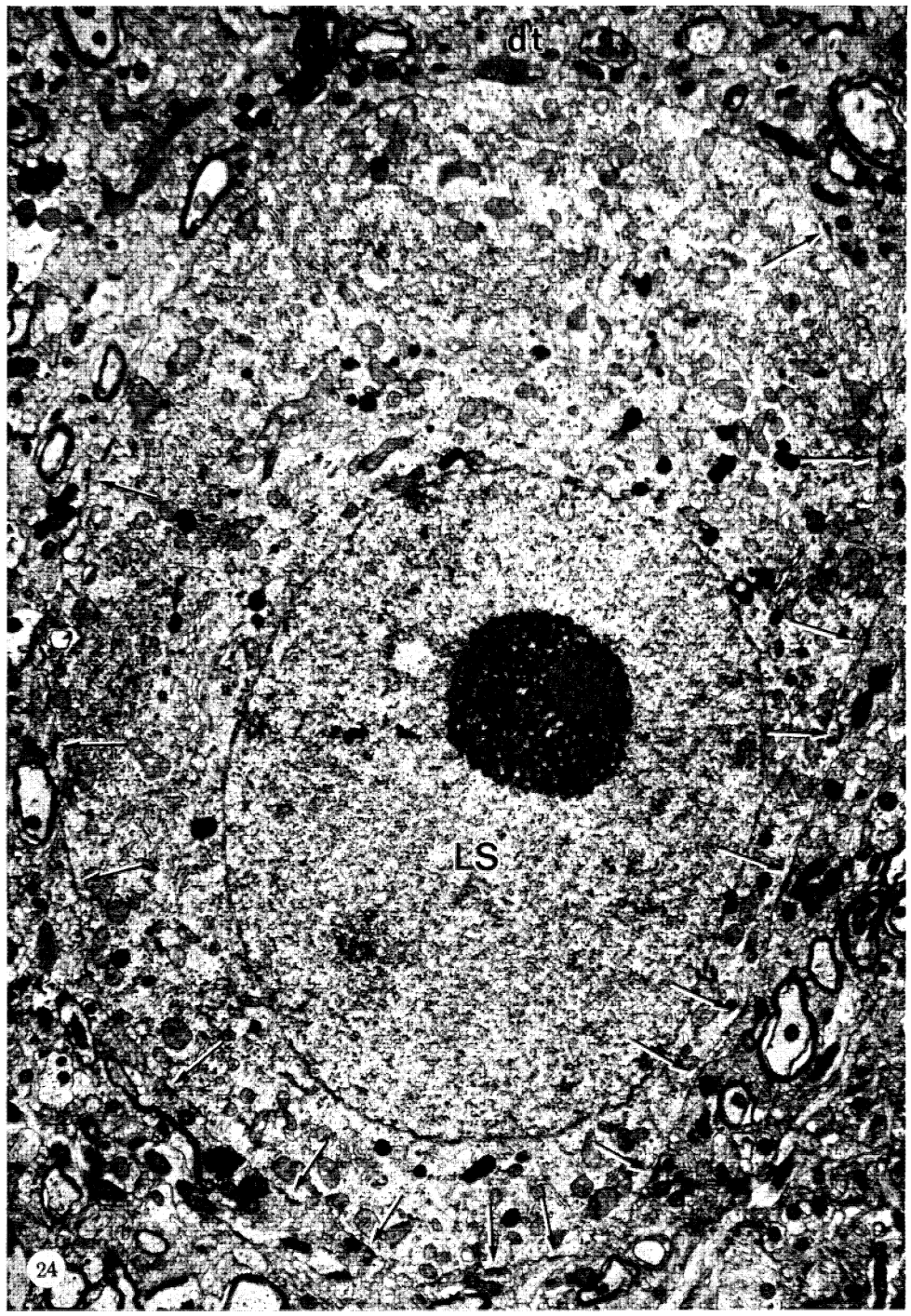


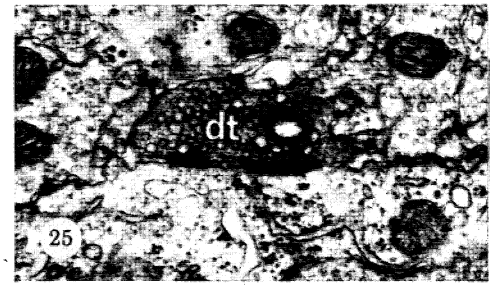


FIGURE 24. A degenerating thalamo-cortical axon terminal (dt) which makes an axo-somatic synapse on to a large stellate cell (LS) in layer IV of the motor cortex. Note the large number of other synapses received by the cell soma (arrows) and its abundant cytoplasm full of organelles. (Magn. × 8400.)

FIGURE 25. Higher magnification of the degenerating thalamo-cortical terminal of figure 24. (Magn. × 29000.)

FIGURE 26. A degenerating thalamo-cortical axon terminal making an axo-somatic synapse on to part of a large stellate cell soma (c). This large stellate cell received 8 normal axo-somatic synapses in the same section. (Magn. × 29000.)

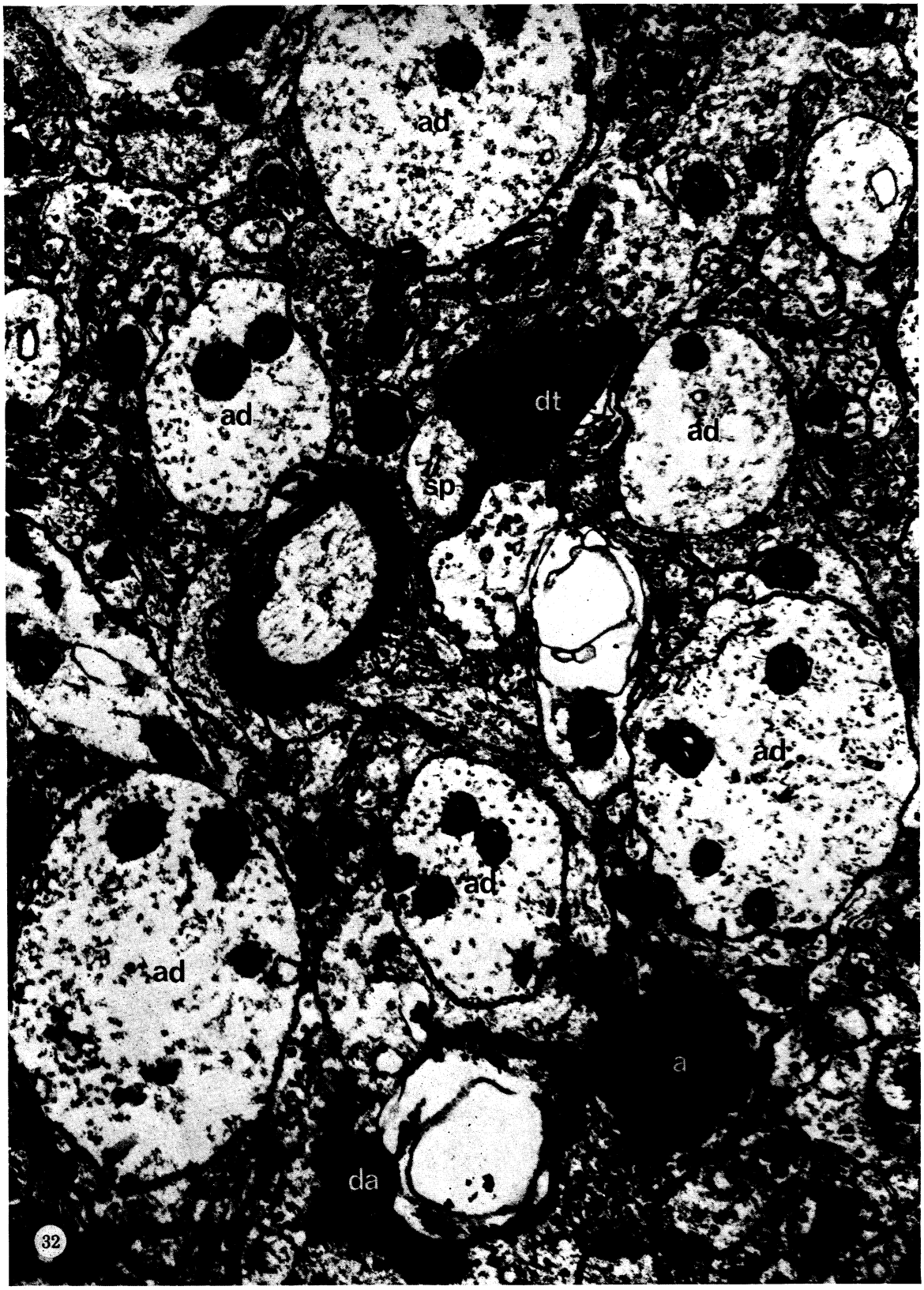
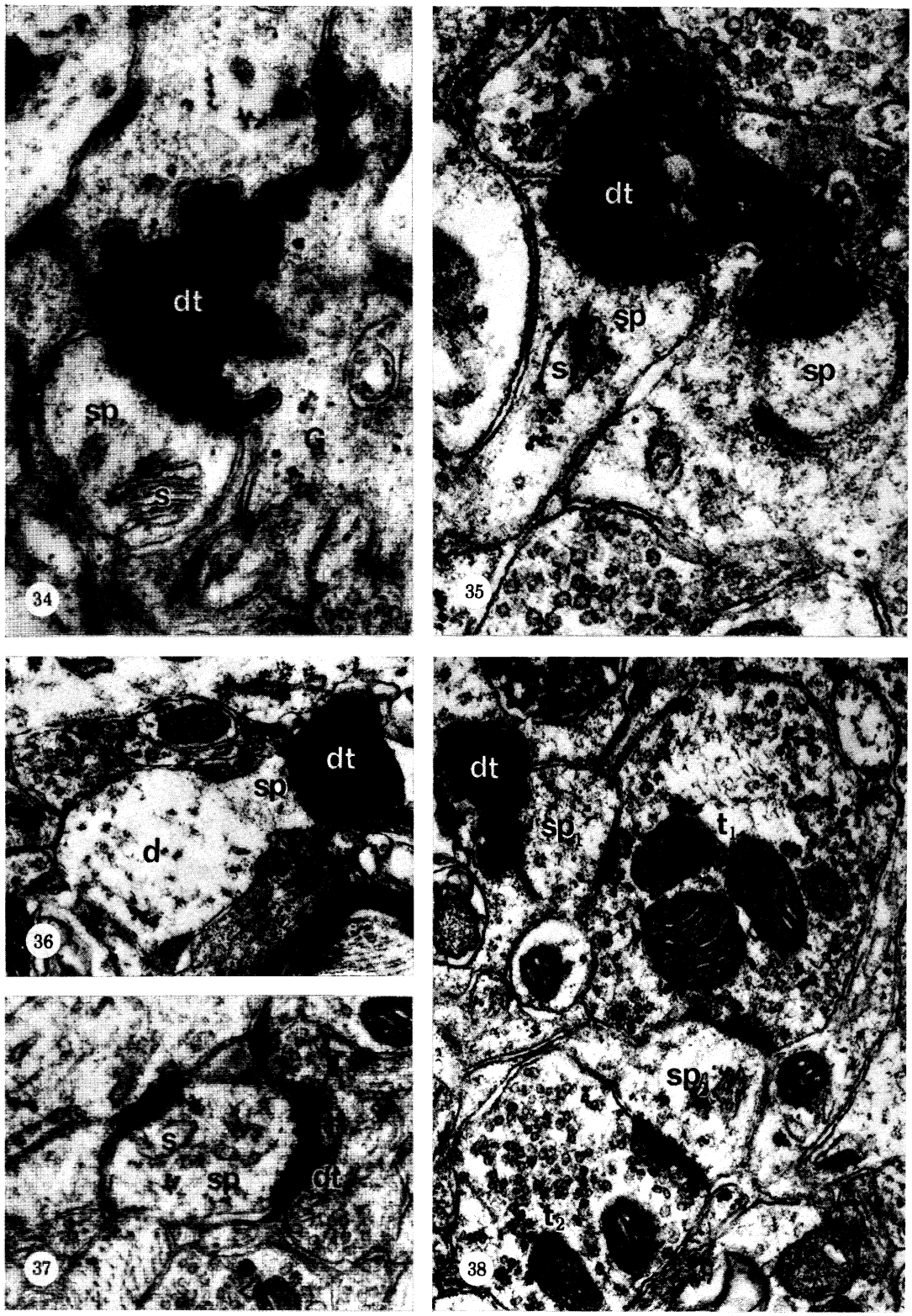


FIGURE 32. A section of layer IV of the motor cortex taken parallel to the pial surface showing a bundle of apical dendrites (ad) cut in transverse section, together with a degenerating thalamo-cortical axon terminal (dt) which makes a synapse on to a spine (sp), a degenerating myelinated axon (a) running vertically with the bundle of apical dendrites and a degenerating preterminal axon (da). (Magn. × 29000.)



FIGURES 34–38. For description see opposite.

square. The results are shown in table 2 for the map illustrated, tables 3 and 4 for the other two maps, and the overall results are shown in table 5. From these tables it can be seen that the proportion of the squares containing degeneration increases with the number of apical dendrites in a square and that overall a square containing one or more apical dendrites is about twice as likely to contain a degenerating terminal as a square with no apical dendrites. These

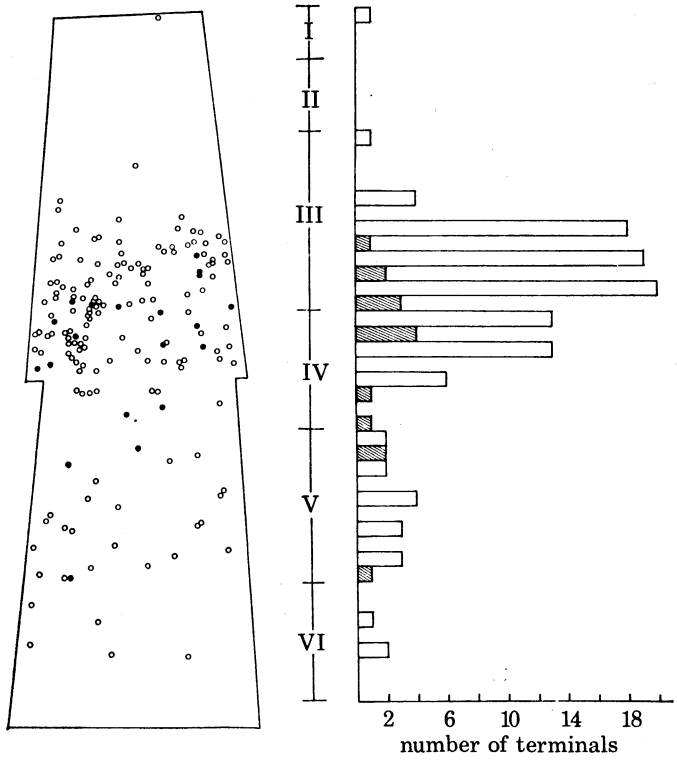


FIGURE 31. Map and histogram of the same sections of the somatic sensory cortex as in figure 29 but showing the depth distributions of the different types of postsynaptic profile contacted by degenerating thalamocortical axon terminals. Although not as obvious as in the motor cortex there appears to be some tendency for those terminals contacting dendrites (• and ▨) to be deeper in the cortex than those contacting spines (○ and □).

DESCRIPTION OF PLATE 8

FIGURE 34. A degenerating commissural axon terminal (dt) making a synapse on to a spine (sp) containing a spine apparatus (s) in the motor cortex and engulfed by glia (G). (Magn. × 53000.)

FIGURE 35. A degenerating commissural axon terminal making synapses on to two spines in the motor cortex, one of which contains a spine apparatus. (Magn. × 67000.)

FIGURE 36. A degenerating commissural axon terminal which makes a synapse on to a sessile spine cut in continuity with its parent dendrite (d) in the motor cortex. Note the flocculent cytoplasm in the spine which contained a small spine apparatus in a serial section and the lack of synapses on the shaft of the parent dendrite. (Magn. × 36000.)

FIGURE 37. A degenerating commissural axon terminal which makes two synapses on to a spine containing a spine apparatus in the motor cortex. Continuity between the two parts of the degenerating axon terminal was demonstrated in serial sections. (Magn. × 36000.)

FIGURE 38. A degenerating commissural axon terminal making a synapse on to a spine (sp_1) in layer V of the motor cortex, which receives a symmetrical synapse from a normal axon terminal (t_1). This normal terminal also makes a synapse on to a second spine (sp_2) which itself receives an asymmetric synapse from a further normal axon terminal (t_2). (Magn. × 36000.)

TABLES 2–5. THE INCIDENCE OF DEGENERATING THALAMO-CORTICAL TERMINALS IN MAP SQUARES CONTAINING DIFFERENT NUMBERS OF APICAL DENDRITES IN TANGENTIAL SECTIONS OF THE MOTOR CORTEX

(Figures in parentheses represent percentages based upon less than ten squares.)

TABLE 2 (MAP 1)

number of apical dendrites per square	number of squares with degeneration	number of squares without degeneration	total	squares showing degeneration (percent)
0	6	57	63	9.5
1	16	42	58	28.0
2	13	31	44	34.0
3	3	14	17	18.0
4	4	7	11	36.0
5	2	3	5	(40.0)
6	0	2	2	—
≥1	38	99	137	28.0
≥2	22	57	79	28.0

TABLE 3 (MAP 2)

0	13	174	187	7.1
1	23	148	171	13.5
2	12	61	73	16.4
3	4	17	21	19.0
4	1	4	5	(20.0)
5	0	1	1	—
≥1	40	231	271	14.0
≥2	17	83	100	17.0

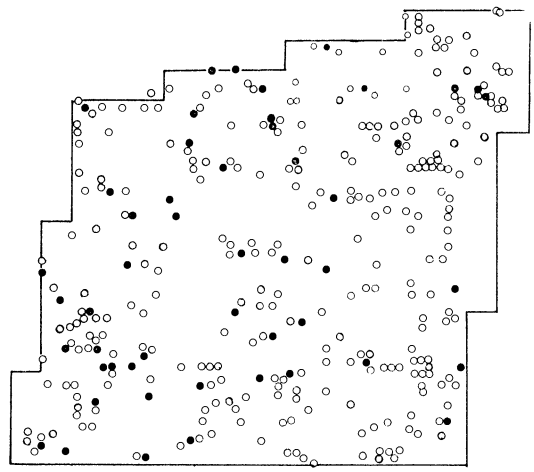


FIGURE 33. A map of layer IV of the motor cortex cut parallel to the pia showing the position of apical dendrites (○, cut transversely) and degenerating thalamo-cortical axon terminals (•). Note that the apical dendrites tend to occur in groups and that the degenerating thalamo-cortical axon terminals frequently occur in association with the apical dendrites.

TABLE 4 (MAP 3)

number of apical dendrites per square	number of squares with degeneration	number of squares without degeneration	total	squares showing degeneration (percent)
0	18	68	86	21
1	9	56	65	14
2	13	33	46	28
3	8	16	24	33
4	6	5	11	55
5	0	1	1	—
6	0	1	1	—
7	0	1	1	—
$\geqslant 1$	36	113	149	24
$\geqslant 2$	27	57	84	32

TABLE 5 (POOLED RESULTS OF MAPS 1–3)

0	37	299	336	11
1	48	246	294	16
2	38	125	163	23
3	15	47	62	24
4	11	16	27	41
5	2	5	7	(29)
6	0	3	3	—
7	0	1	1	—
$\geqslant 1$	114	443	557	21
$\geqslant 2$	66	197	263	25

differences in the frequency of degeneration between those squares containing no apical dendrites and those containing one or more were tested statistically by using Student's t test. For maps 1 and 2 the differences in frequency of degeneration between squares with no apical dendrites and those with one or more are significant (map 1, $t = 2.88$, $P < 0.01$; map 2, $t = 2.655$, $P = 0.01$) and for these same maps the differences between squares containing no apical dendrites and those containing two or more are also significant (map 1, $t = 2.73$, $P < 0.01$; map 2, $t = 2.65$, $P < 0.01$). The differences for map 3 do not reach statistical significance. This map was from a deeper level in the cortex than the other two maps and may be below the optimal level for the association. When all three maps are pooled the differences are highly significant for both the comparison between squares with no apical dendrites and one or more apical dendrites ($t = 3.65$, $P < 0.001$) and between squares with no apical dendrites and those containing two or more ($t = 4.54$, $P < 0.0001$).

Commissural connections

As the commissural connections of both the somatic sensory and motor cortices are largely restricted to those parts of cortex corresponding to the trunk and proximal limbs (Jones & Powell 1969*b*; Pandya & Vignolo 1971) material for e.m. study of commissural connections was taken from the cortex containing the representation of the trunk. Following removal of the contralateral sensori-motor cortex, typical degenerating axons and axon terminals were found in both the motor cortex and area 3*b* of the somatic sensory cortex. At four days' survival the degeneration was fairly sparse with early forms predominating; at five days' survival more

degeneration was present with a greater proportion of medium and late forms; at six days' survival the degeneration was fairly dense and predominantly late in character (figures 34–47, plates 8–10). Extensive sampling and mapping were therefore done at the six day survival period.

In all cases where the synaptic membrane complex of degenerating commissural terminals could be clearly classified, it was of the asymmetric type in both motor and somatic sensory cortices. Of the 468 degenerating commissural terminals studied in the motor cortex, 84% made synapses on to a single identifiable postsynaptic profile and of these, 96% contacted a dendritic spine (figures 34, 36 and 37) and 3% a dendritic shaft, while one terminal was found to make a synapse on to a cell soma (table 1). Twenty-eight (6%) of the commissural terminals made synapses on to two postsynaptic profiles in a single section; 23 on two spines (figure 35), two on to a spine and the shaft of a varicose dendrite and three on to a spine and an unidentifiable process. In about 10% the postsynaptic process could not be identified. Examples were also found of spines receiving synapses from both a degenerating terminal and a normal asymmetric or symmetrical axon terminal (figure 38). In the somatic sensory cortex 183 degenerating commissural terminals were studied of which 158 (86%) made synapses on to a single identifiable postsynaptic profile. Of these, 97% contacted dendritic spines (figures 39 and 41) and 3% dendritic shafts (table 1). Fifteen (8.2%) terminals made synapses on to two spines (figure 40) and one contacted three spines in a single section (figure 42); examples were also found of both a normal and a degenerating terminal making synapses on to the same spine.

Ten spines receiving degenerating commissural terminals were traced to their parent dendrites in the motor cortex (figure 36) and six in the somatic sensory cortex (figure 42). All the parent

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Description of plate 9

Figure 39. Two adjacent degenerating commissural axon terminals (dt) in area 3*b* of the somatic sensory cortex, both of which make synapses on to spines (sp), one of which contains a spine apparatus (s). (Magn. × 32000.)

Figure 40. An early degenerating commissural axon terminal which makes synapses on to two spines in area 3*b* of the somatic sensory cortex, both of which contain a spine apparatus. Note the very irregular synaptic vesicles and the darkening of the axon terminal. (Magn. × 29000.)

Figure 41. A late degenerating commissural axon terminal making a synapse on to a spine in area 3*b* of the somatic sensory cortex and engulfed by glia (G). (Magn. × 32000.)

Figure 42. A degenerating commissural terminal in area 3*b* of the somatic sensory cortex which makes synapses on to three spines, one of which is cut in continuity with its parent dendrite and contains a spine apparatus. Note the small size of the parent dendrite, the lack of synapses on it and the contrasting appearance of the flocculent cytoplasm in the spine and the clear cytoplasm with neurotubules in the dendritic shaft. (Magn. × 53000.)

Description of plate 10

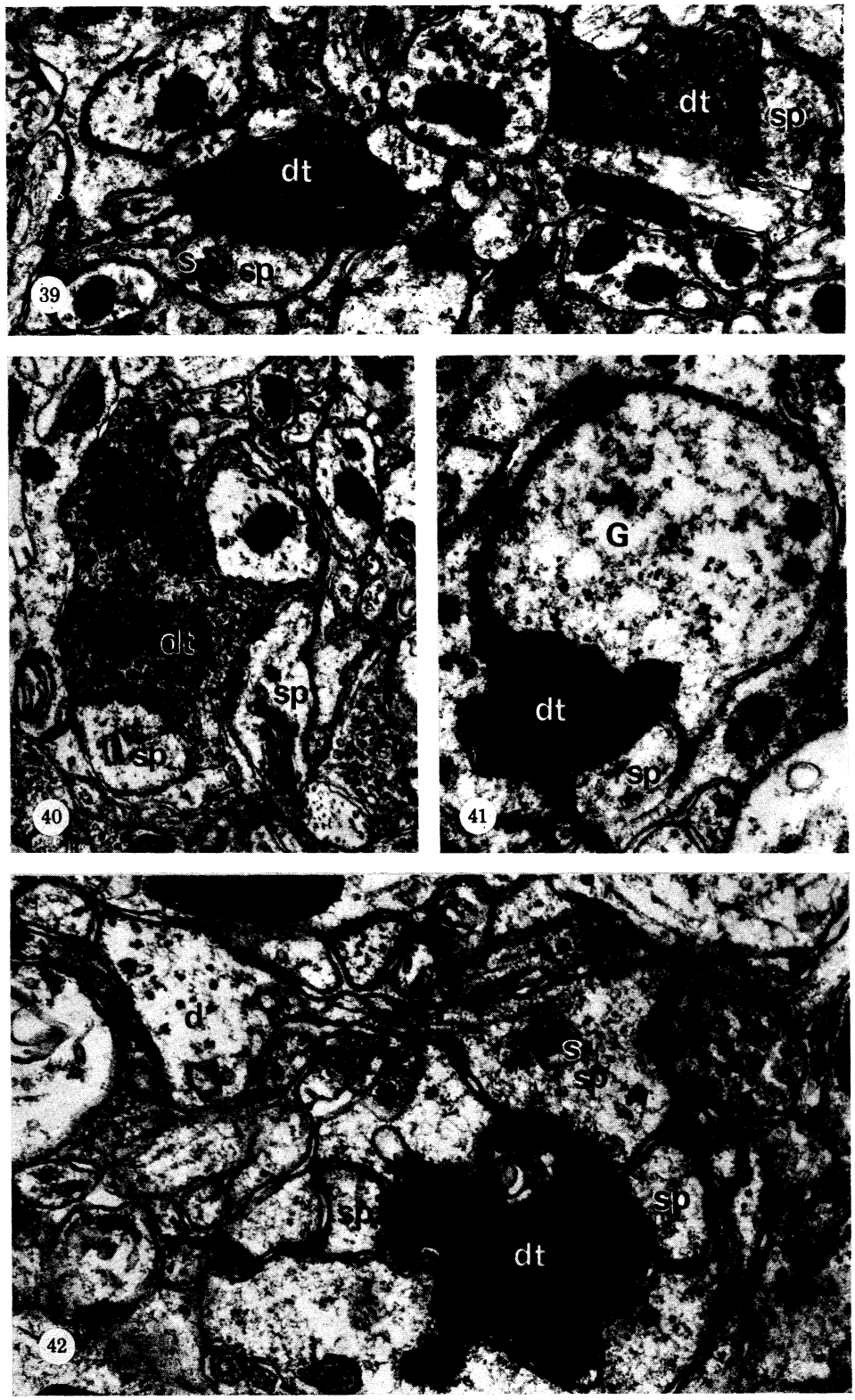
Figure 43. A degenerating commissural axon terminal (dt) making a synapse on to the shaft of a dendrite (d) in the motor cortex. Note the moderately varicose shape of the dendrite, the large number of other synapses upon it and the high concentration of organelles within it. (Magn. × 18000.)

Figure 44. A degenerating commissural axon terminal which makes a synapse on to the shaft of a dendrite in the motor cortex. Note the other synapse received by the dendrite and the high concentration of organelles it contains. (Magn. × 39000.)

Figure 45. A degenerating commissural terminal in the motor cortex making a synapse on to the shaft of a dendrite which receives another asymmetric synapse from a normal axon terminal (t). (Magn. × 29000.)

Figure 46. A degenerating commissural axon terminal which makes a synapse on to a large stellate cell soma (LS) in layer IV of the motor cortex. Note the other synapses received by the cell soma (arrows), and its abundant cytoplasm full of organelles. (Magn. × 8400.)

Figure 47. The degenerating commissural terminal of figure 46 at a greater magnification. (Magn. × 29000.)



FIGURES 39–42 For description see opposite.

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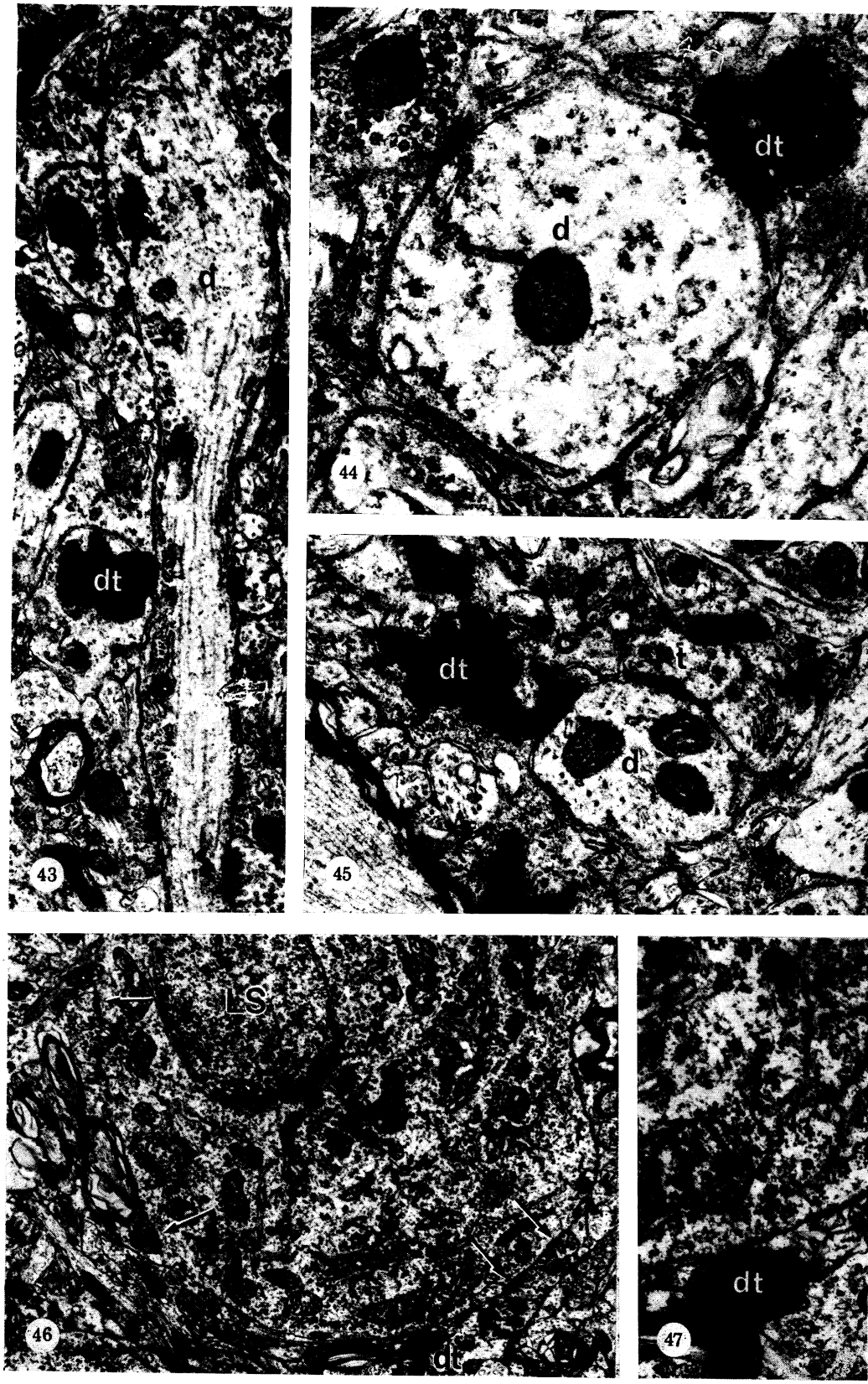
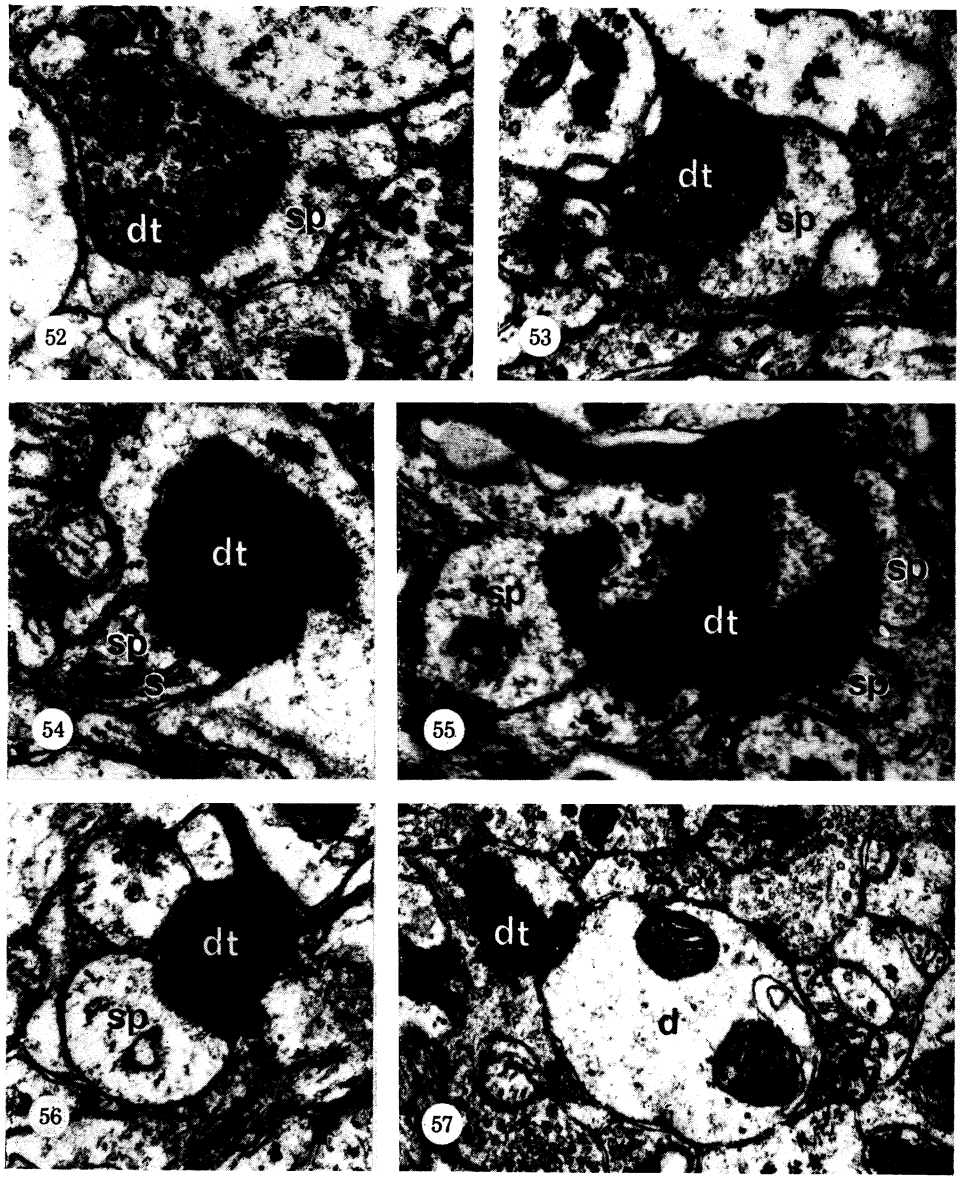


FIGURES 43–47. For description see page 212.



FIGURES 52–57. For description see page 213.

FIGURES 58–62. For description see opposite.

dendrites in both areas were of small or medium size, between 0.3 and 1.2 μm diameter and were in general smaller than the parent dendrites of spines receiving synapses from degenerating thalamo-cortical terminals. The shafts of these parent dendrites rarely received other synapses and contained few organelles and they were generally of approximately constant width when cut longitudinally. They therefore had the features of pyramidal cell dendrites and one dendrite was found in the somatic sensory cortex which had one spine receiving a synapse from a degenerating commissural terminal and a second spine receiving one from a normal asymmetric terminal.

Of the dendritic shafts receiving synapses from degenerating commissural terminals in both areas of cortex the majority could be identified as those of large stellate cells (figures 43–45). They were of similar diameter to the comparable dendritic shafts receiving synapses from degenerating thalamo-cortical terminals but no very large examples were found. The markedly varicose shape and lack of organelles of some of the others suggest that they belong to small stellate cells (Sloper, Hiorns & Powell 1979). One degenerating commissural terminal from the motor cortex made a synapse on to the shaft of a small dendrite which had a spine but received no other synapse. The cell soma found to receive a synapse from a degenerating commissural terminal in the motor cortex was in the upper part of layer V and was that of a large stellate cell (figures 46 and 47).

Degenerating commissural axon terminals were found in all layers of the cortex in both the motor and somatic sensory areas. The distribution of these degenerating terminals was mapped as for the thalamo-cortical projection (figures 48 and 49) and the degeneration is comparatively more dense in layer I, the upper part of layer III, the upper part of layer V and the

Description of plate 11

Figure 52. An early degenerating association axon terminal (dt) making a synapse on to a spine (sp) in the motor cortex following an SI lesion. (Magn. × 38000.)

Figure 53. An early degenerating SI association axon terminal making a synapse on to a spine in the motor cortex. (Magn. × 41000.)

Figure 54. A late degenerating SI association terminal making a synapse on to a spine containing a spine apparatus (s) in the motor cortex. (Magn. × 38000.)

Figure 55. A late degenerating SI association terminal in the motor cortex making synapses on to three spines. (Magn. × 35000).

Figure 56. A late degenerating SI association axon terminal making a synapse on to a spine in the motor cortex. (Magn. × 39000.)

Figure 57. A late degenerating SI association axon terminal making a synapse on to the shaft of a dendrite in the motor cortex. Note the normal asymmetric synapse received by the dendrite. (Magn. × 29000.)

Description of plate 12

Figure 58. A degenerating association axon terminal (dt) which makes a synapse on to the shaft of a large dendrite (d) in the motor cortex following a lesion of SI. Note the large size of the dendrite, the large number of synapses it receives and the high concentration of organelles in its cytoplasm. (Magn. × 18000.)

Figure 59. A higher magnification of the degenerating SI association terminal of figure 58. (Magn. × 53000.)

Figure 60. A degenerating association axon terminal making a synapse on to a spine (sp) in the motor cortex following a lesion of area 6 and engulfed by glia (G). (Magn. × 29000.)

Figure 61. A degenerating association axon terminal from area 6 making a synapse on to a spine in the motor cortex and engulfed by glia. (Magn. × 29000.)

Figure 62. A rare example of an axon terminal making a synapse on to a dendritic shaft and showing neurofilamentous hypertrophy in the motor cortex following an area 6 lesion. Note the small cluster of vesicles still adjacent to the synaptic membrane complex (arrowhead). (Magn. × 18000.)

lowest part of layer V with layer VI, there being relatively clear bands in layer IV and the middle of layer V. In the somatic sensory cortex there is also degeneration in all the cortical layers but there is a dense concentration of degeneration in layers II and III which is much more pronounced to one side of the mapped area (figure 49). A further section taken of the same area of the superficial half of the cortex but further into the block showed that this patch

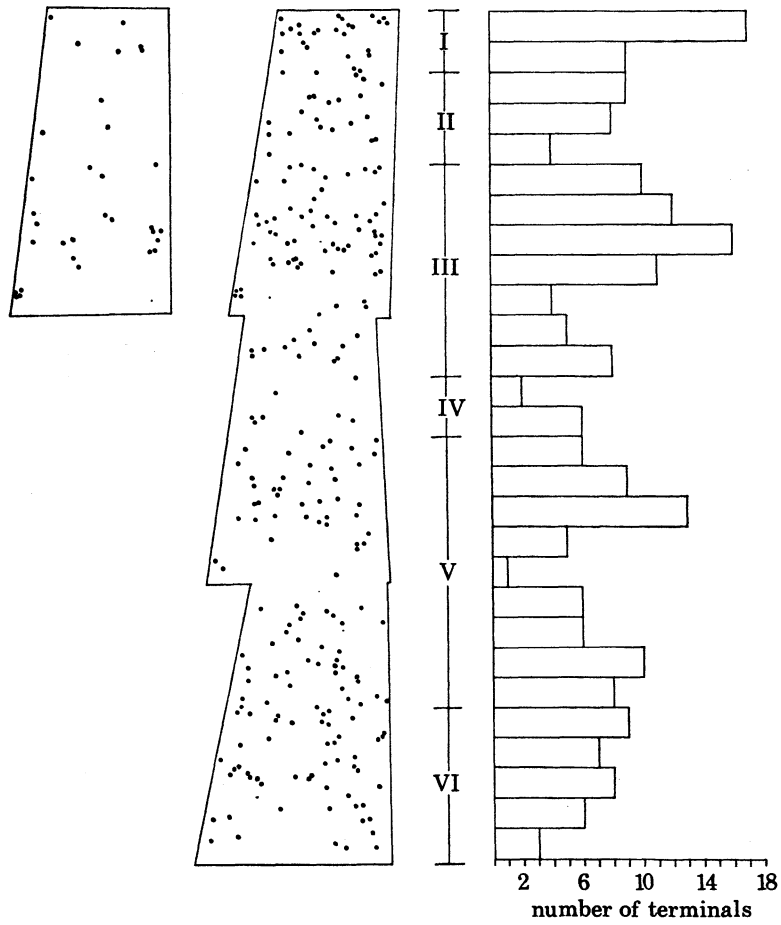


FIGURE 48. A map and histogram showing the depth distribution of degenerating commissural axon terminals in the motor cortex. The map at the top left is of a single section to show the density of degeneration present. The composite map shows three sections from the same block superimposed at each of three levels, making a total of nine sections. The histograms for all maps are derived from a constant width strip through the full depth of the cortex. Note the relative concentrations of degenerating terminals in layer I, the upper part of layer III, the upper part of layer V and in the lower part of layer V and upper part of layer VI, with relatively clear bands in layer IV and the middle of layer V.

of degeneration was still present but was markedly less dense, indicating that it was an isolated patch of dense degeneration. However at its most dense it did not involve more than a small percentage of the terminals in the area. Similar local differences in the density of degeneration have been seen by using the light microscope (Jones, Burton & Porter 1975; Shanks, Rockel & Powell 1975). The small proportion of degenerating commissural terminals making synapses on to dendritic shafts occurred at all levels in the cortex and there were no differences apparent in the proportions of the different types of postsynaptic process in the different laminae (figures 50 and 51).

Association connection from SI to the motor cortex

Following the removal of the ipsilateral primary somatic sensory cortex (SI, areas 3*b*, 1 and 2 of Brodmann), typical degenerating axon terminals were found in the motor cortex. A few early signs of degeneration were present at 1¼ days' survival and after 2 days unequivocal degenerating terminals showing marked cytoplasmic darkening and internal disruption were observed. More degeneration was present after 3 days and the peak density appeared to be at 4 or 5 days' survival, with a predominance of medium and late forms of degeneration. At 6 days most of the degeneration was of the late variety. Mapping was therefore done on 5-day survival material.

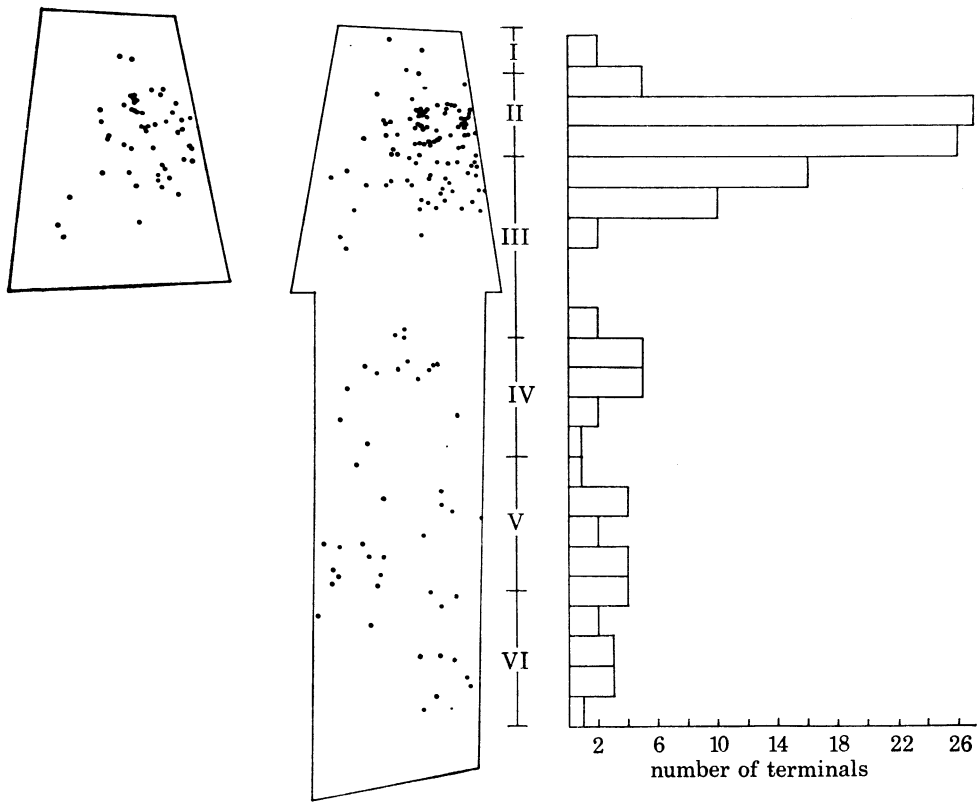


FIGURE 49. A map and histogram showing the depth distribution of degenerating commissural axon terminals in area 3*b* of the somatic sensory cortex. The map at the top left is of a single section to show the density of degeneration; the composite map consists of three superimposed sections of each of the superficial and deep parts of the cortex.

In all cases where the synaptic type was clearly identifiable degenerating axon terminals from SI had asymmetric membrane specializations. Of the 142 degenerating terminals studied, 119 (84%) made synapses on to a single identifiable postsynaptic profile. Of these 82% contacted dendritic spines (figures 52–54 and 56, plate 11) and 18% dendritic shafts. Seven (4.9%) of the terminals made synapses on to two profiles and one on to three spines in a single section (figure 55); of those contacting two profiles, 4 made synapses on to two spines and 3 on to a spine and a dendritic shaft, one of these dendrites being of the large stellate type and the other two having clearly varicose shapes. Three spines receiving synapses from degenerating terminals from SI were traced to their parent dendrites. These dendrites received few other

synapses, contained few organelles, did not have a varicose outline, and so were probably pyramidal. Of the 22 dendritic shafts found to receive degenerating terminals, almost all were of the large stellate type (figure 57; figures 58 and 59, plate 12) but the markedly varicose shape and lack of organelles of a few suggested that they were dendrites of small stellate cells.

Degenerating terminals from SI were found scattered through all the cortical laminae. They showed no marked differences in density between the different layers but more were present in the superficial half of the cortex (figure 63). The dendritic shafts receiving degenerating terminals were distributed through the depth of the cortex and there were no marked differences in the proportions of each type of postsynaptic profile contacted at different depths (figure 64).

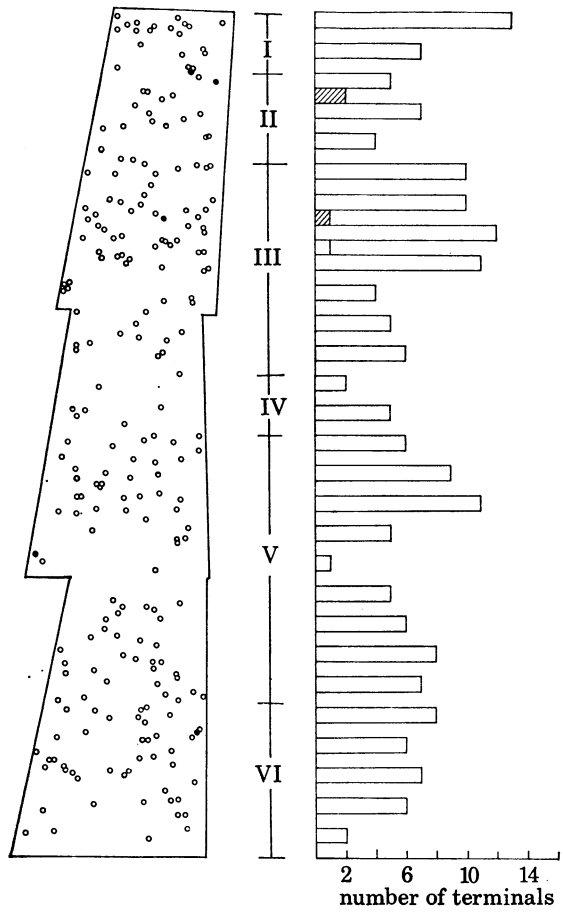


FIGURE 50. A map and histogram of the same sections of the motor cortex as figure 48 showing the depth distribution of the different types of postsynaptic profile receiving synapses from degenerating commissural axon terminals. The five dendrites (• and ▨) postsynaptic to commissural terminals are scattered through the depth of the cortex although those in the deep layers happen to come outside the constant width strip from which the histogram was compiled.

Association connection from area 6 to the motor cortex

Because of the necessary restriction of area 6 lesions to prevent damage to the motor cortex the degeneration found was sparse and so a detailed study could not be made. Degenerating terminals of medium and late stages were present in the motor cortex 4 and 5 days after area 6 lesions and, when classifiable, their postsynaptic thickenings were of the asymmetric type. Of 43 terminals found 38 (88%) made synapses on to a single identifiable postsynaptic process, 76%

on to spines (figures 60 and 61) and 24% on to dendritic shafts (figure 62). Two degenerating terminals made synapses on to two spines in a single section and one spine was found receiving a synapse from a degenerating terminal and a symmetrical synapse from a normal axon terminal. Two spines receiving synapses from degenerating association terminals from area 6 were traced to their parent dendrites, both of which were small, received few other synapses and did not have a varicose shape or contain many organelles, and so were probably pyramidal. Of the 9 dendritic shafts receiving synapses from axons arising in area 6, nearly all were of the large stellate type. Degenerating terminals were found scattered through all layers of the cortex with no obvious differences in density between different laminae.

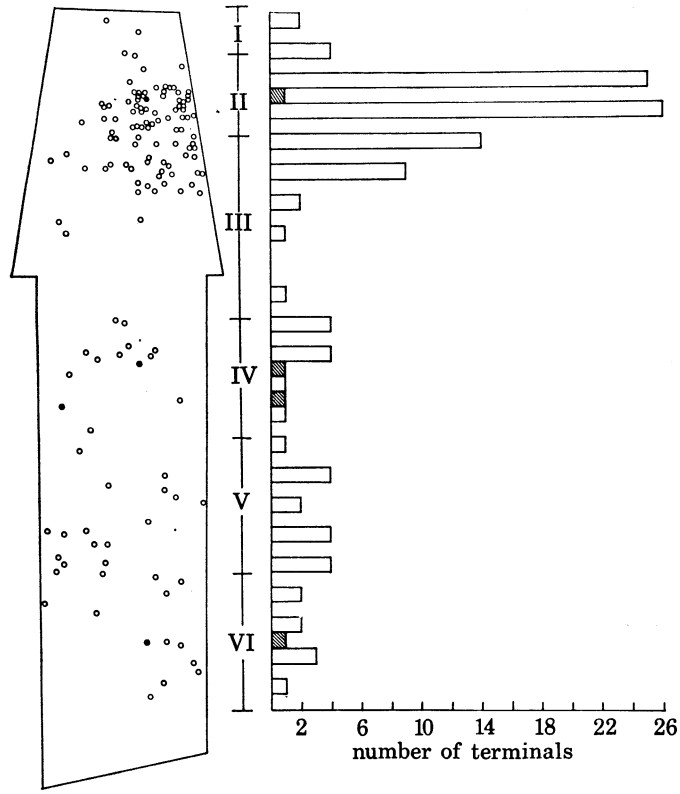


FIGURE 51. A map and histogram of the same section of the somatic sensory cortex as figure 49, showing the laminar distribution of the different kinds of postsynaptic profile receiving synapses from degenerating commissural axon terminals. The few dendrites (• and ▨) postsynaptic to commissural terminals are scattered through the depth of the cortex. ○ and □, Spine.

DISCUSSION

Previous studies of afferent connections to visual and somatic sensory cortical areas have shown a close similarity between the different areas in several species (e.g. Colonnier 1964; Colonnier & Rossignol 1969; Lund & Lund 1970; Jones & Powell 1970*e*; Garey & Powell 1971; Fisken, Garey & Powell 1975; Peters & Feldman 1976). The motor cortex has however been considered on the basis of light microscopy to be a different type of neocortex from the primary sensory areas and so it is of interest to compare its afferent connections with those of of the sensory areas. The e.m. study of the normal structure of the motor cortex, done in

conjunction with this experimental work (Sloper, Hiorns & Powell 1979; Sloper & Powell 1979*a*) has indicated that the motor cortex is in fact remarkably similar to area 3*b* of the somatic sensory cortex in many respects. The findings of this study and that of Strick & Sterling (1974) of the thalamo-cortical projection in the cat show that the afferent projections to the motor cortex are also very similar to those of the sensory areas in the types and proportions of post-synaptic site contacted. The main differences between the projections to the motor and sensory cortices are in their relationship to the different cortical laminae but these would appear to be reflections of differences in the degree of development of the various laminae; such differences in lamination are present between different sensory areas of cortex as well as between motor and sensory areas.

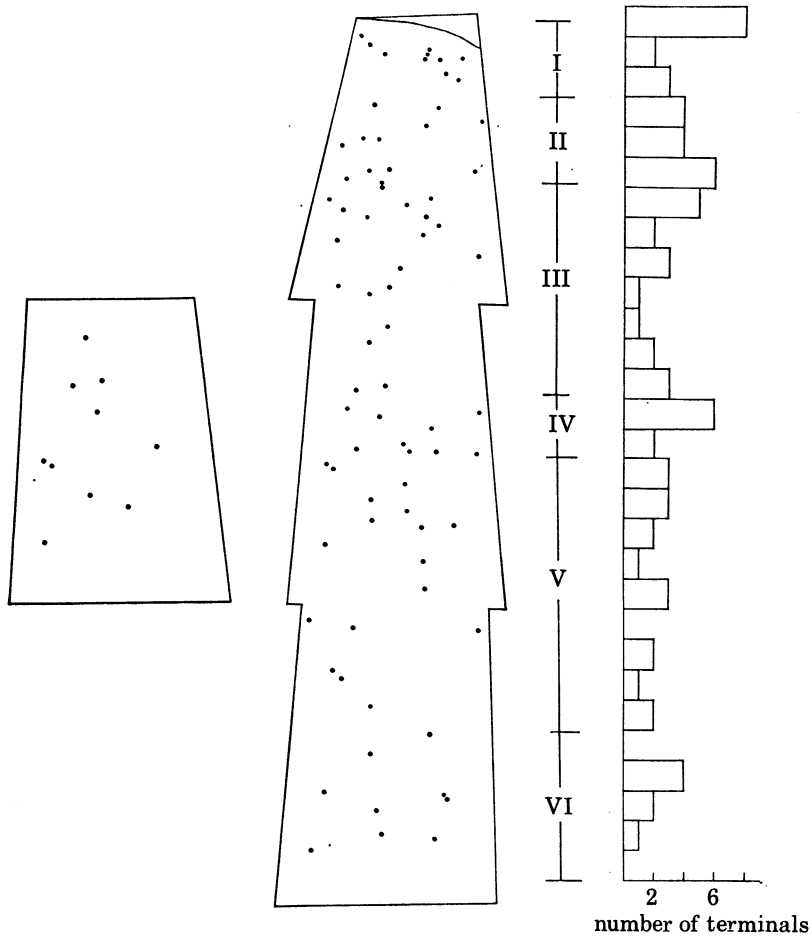


FIGURE 63. A map and histogram showing the depth distribution of degenerating association axon terminals in the motor cortex following a lesion of the somatic sensory cortex. The map to the left is of a single section of the middle third of the cortex to show the density of degeneration; the composite map consists of two superimposed maps at each of the three levels. Degeneration occurs in all cortical layers but appears to be a little more dense in the superficial half of the cortex.

Thalamo-cortical connections

Because most of the spines in the neocortex are seen in Golgi preparations to arise from pyramidal cells, Jones & Powell (1970*e*) considered that the spines receiving synapses from degenerating thalamo-cortical axon terminals were those of pyramidal cells. The failure of

impregnation of spines on pyramidal cell dendrites in the visual cortex following eye removal was also interpreted as showing this site of termination (Globus & Scheibel 1967*b*; Valverde 1968). However, the existence of stellate cells with spiny dendrites in the visual cortex has been emphasized by Garey (1971), Garey & Powell (1971) and Lund (1973); they have suggested that although these stellate spines form only a small proportion of the total number of spines in the cortical neuropil, it is possible that thalamo-cortical terminals end specifically on them.

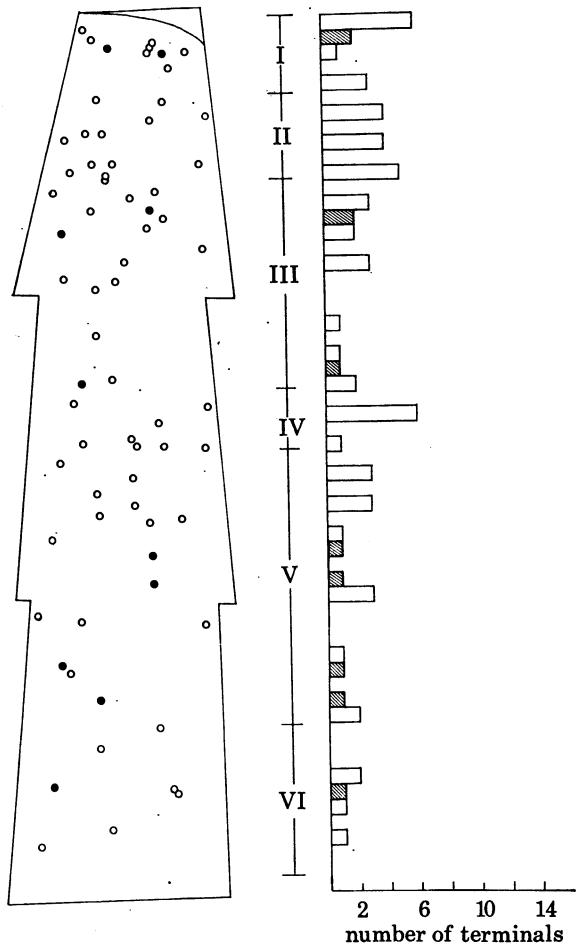


FIGURE 64. Map and histogram of the same sections of the motor cortex as figure 63 showing the depth distribution of the different types of postsynaptic profiles which receive synapses from SI association axon terminals. Dendrites (• and ▨) postsynaptic to these terminals occur throughout the depth of the cortex. o and □, Spines.

However, spiny stellate cells are much less frequent in the somatic sensory cortex (Jones 1975*b*). In an attempt to resolve this question a considerable number of parent dendrites of spines receiving synapses from degenerating thalamo-cortical terminals were studied and, with rare exceptions, these dendrites received few other synapses, contained few organelles and were not varicose in outline. They were therefore not the dendrites of large or small stellate cells, although the former do have occasional spines (Sloper, Hiorns & Powell 1979), but their characteristics are those of the small and medium sized dendrites of pyramidal cells (Jones & Powell 1970*a–c*); the few large parent dendrites found were almost certainly main apical or

basal dendritic branches of pyramidal cells. There would therefore seem to be little doubt that many of the spines receiving synapses from thalamo-cortical axon terminals arise from pyramidal cells and, since most thalamo-cortical terminals contact spines, it would seem that a considerable proportion of these afferent fibres make synapses directly on to pyramidal cells. This conclusion is in agreement with physiological studies of the thalamic projection to the motor cortex as stimulation of the thalamus produces monosynaptic EPSPs in pyramidal tract cells (Amassian & Weiner 1966). However the ultrastructural features of the dendrites of the spiny stellate cells described by Le Vay (1973) in the visual cortex are very like those of the dendrites of pyramidal cells, and so it is possible that a proportion of the thalamic afferents contact spines of the few spiny stellate cells in the sensori-motor cortex.

Peters & Feldman (1977) reconstructed fifteen dendrites from serial sections of rat visual cortex which had spines contacted by geniculocortical afferents. The dendrites described here with spines receiving thalamo-cortical afferents appear very similar to their group. However, they conclude from the variability within their dendrites that the spines receiving geniculocortical afferents probably arise from the dendrites of more than one type of neuron.

The remainder of the thalamo-cortical terminals made synapses on to dendrites and cell somata which were of the large stellate type and a gap junction was found on one of these dendrites, which also received synapses from two degenerating thalamo-cortical terminals. Three thalamo-cortical terminals made synapses on to dendritic shafts which were not of the large stellate type; two of them had spines and all three were probably of pyramidal origin.

All the cell somata receiving synapses from degenerating thalmo-cortical axon terminals were those of large stellate cells and if the histograms of the mean cell diameters and numbers of synapses received by these cells are compared to the corresponding histograms for large stellate cells in normal material the populations correspond (Sloper, Hiorns & Powell 1979). The thalamo-cortical projection therefore appears to consist of two main components: pyramidal cells receive synapses from the majority of the terminals by way of their spines and large stellate cells are contacted by a small proportion of the terminals on their dendrites and somata.

There is general agreement from e.m. studies that the great majority of degenerating thalamo-cortical terminals are found in a band in the region of layer IV in the adult animal (e.g. Jones & Powell 1970*e*; Garey & Powell 1971; Strick & Sterling 1974). In the monkey this band of degeneration extends well up into layer III in both the motor cortex (Sloper 1973) and area 3*b* of the somatic sensory cortex and these e.m. findings were confirmed by light microscopy and are in agreement with Jones (1975*a*). Using similar techniques Hubel & Wiesel (1969, 1972) and Garey & Powell (1971) have described a separate band of degeneration superficial to the stria of Gennari in area 17 of the monkey visual cortex following thalamic lesions. In area 3*b* of the monkey, where the outer band of Baillarger is not prominent, there is only one band of dense degeneration which extends well up into layer III; in the motor cortex there is a separate band of degeneration in layer V that may have been separated from the main band in a similar way to that in the visual cortex but by the deep fibre plexus. The basic laminar pattern of the thalamo-cortical projection in the monkey may be that seen in the somatic sensory cortex, of a single dense band extending from the middle of layer III to about two thirds of the way through layer IV with some scattered degeneration below this level, and with this having been modified in the other two cortical areas by the prominence of the inner or outer bands of Baillarger. In the cat the laminar termination of thalamo-cortical afferents

has been studied in areas 17, 18 and 19 of the visual cortex (Colonnier & Rossignol 1969; Garey & Powell 1971) and in the somatic sensory cortex (Jones & Powell 1970*e*). In both functional areas the degeneration appears to extend less into layer III than in the monkey and no separate band is apparent in area 17, which may be a reflection of the less marked development of the stria of Gennari in the cat.

There is a difference in the laminar distribution of thalamo-cortical terminals contacting spines compared to those contacting dendrites and somata. The dendrites receiving synapses from degenerating thalamo-cortical terminals are mostly of the type arising from large stellate cells and their laminar distribution corresponds to that of large stellate cell somata in normal material (Sloper, Hiorns & Powell 1979). Those cell somata receiving synapses from degenerating thalamo-cortical terminals are found within the band of dendrites receiving them and within the normal distribution of large stellate somata. With their different laminar distribution, it seems unlikely that the spines receiving synapses from degenerating thalamo-cortical terminals arise from the same cell type. The reasons for believing that these spines are those of pyramidal cells are discussed above and it is not surprising that the two components of the thalamo-cortical projection should have different laminar distributions if they contact two cell types which themselves have different distributions.

As an association has been found between degenerating thalamo-cortical axon terminals and apical dendrites, it is relevant that the bundles of apical dendrites are most prominent at the level of the dense band of thalamo-cortical degeneration. The most obvious interpretation would be that a proportion of the spines receiving synapses from the degenerating terminals in fact arise from the apical dendrites, but if all the spines receiving synapses from degenerating thalamo-cortical terminals were on apical dendrites all the degenerating terminals would be closely associated with them. In fact the degree of association overall is that which would be found if about one third of the degenerating terminals were specifically and closely related to apical dendrites and the remainder were unrelated and distributed evenly throughout the section both inside and outside the apical dendrite bundles. This is of course a hypothetical figure and the evidence from the examples where a spine receiving a synapse from a degenerating thalamo-cortical terminal has been traced to its parent dendrite indicates that most of the parent dendrites are of small to medium diameter and of pyramidal type, although in a few instances both in this study and those of Garey & Powell (1971) and Strick & Sterling (1974) they do appear to be apical dendrites. The most likely interpretation is that a small number of thalamo-cortical terminals end on spines on the main shafts of apical dendrites and that a much larger number end on side branches of apical dendrites. The small number of terminals making synapses on to spines on apical dendritic shafts may however contact a *large proportion* of the relatively few spines at this site and so produce the considerable reduction in spine density seen in Golgi material following enucleation or lateral geniculate nucleus lesions whereas the greater number ending on the side branches of apical dendrites may only contact a *small proportion* of the high density of spines present and produce a small percentage reduction.

Commissural connections

The finding that all but a few commissural terminals in both the motor and somatic sensory cortices of the monkey make synapses on to spines agrees with findings in the visual cortex of the rat (Lund & Lund 1970), cat and monkey (Fisken, Garey & Powell 1975) and the somatic sensory cortex of the cat (Jones & Powell 1970*e*). In all studies a few commissural terminals

have been found to make synapses on to dendritic shafts and Lund & Lund (1970) reported cell somata receiving synapses from commissural terminals. When spines receiving synapses from degenerating commissural terminals were traced to their parent dendrites they rarely received synapses, contained few organelles and were not varicose in shape. Therefore most were clearly not large or small stellate dendrites but had the characteristics of pyramidal dendrites (Jones & Powell 1970*a–c*). All were of small or medium size which suggests that commissural terminals may not make synapses on to spines on the main dendrites of pyramidal cells. The number of pyramidal spines impregnated in Golgi sections following callosal section is reduced on side branches of apical dendrites (Globus & Scheibel 1967*a*) and the dendrites which have been traced here could be side branches of apical dendrites on the basis of their size.

Of the dendritic shafts receiving synapses from commissural terminals about half could be identified as those of large stellate cells and a few were probably from small stellate cells. The one cell soma contacted by a commissural terminal was a large stellate cell and so this type receives contacts from commissural terminals on both its dendrites and somata. The termination of the commissural pathway is therefore probably upon spines of pyramidal cells, the dendrites and somata of large stellate cells and the dendrites of small stellate cells.

Light microscope studies of Wiitanen stained sections indicate that the laminar pattern shown by the e.m. maps is fairly typical, and it is interesting that the commissural afferents have a less dense band in the middle of layer V, like the thalamo-cortical afferents; this would appear to correspond to the inner band of Baillarger. However, in layers III and IV where both projections are more dense, the commissural and thalamo-cortical afferents appear to have a reciprocal relation; the commissural afferents are dense in the upper half of layer III but the lower border of this dense region corresponds to the upper border of the very dense band of thalamo-cortical afferents.

The dense patch of degeneration which was found in layers II and III of the somatic commissural map probably corresponds to the lateral variations in the density of commissural degeneration that have been described in the somatic sensory cortex using light microscopy (Jones, Burton & Porter 1975; Shanks, Rockel & Powell 1975). It also seems significant that the lower border of the dense degeneration in layer III of area 3*b* corresponds to the upper border of the dense band of the thalamo-cortical afferents and this confirms the apparent reciprocal relation between the commissural and thalamo-cortical afferents at this level.

Association connections

Although the degeneration following lesions of area 6 was sparse, it was similar to that found after damage of the somatic sensory cortex. The majority of the terminals of both projections made synapses on to spines and when the parent dendrites of these spines were identifiable they were of the type arising from pyramidal cells as with the thalamo-cortical and commissural connections. A greater proportion of the terminals of both these association connections made synapses on to dendritic shafts than of the thalamo-cortical or commissural connections (table 1). The proportions of each type of postsynaptic profile contacted correspond to the findings in relation to the association connections from SII to SI in the cat (Jones & Powell 1970*e*) and to those between areas 18 and 17 of the visual cortex of the cat (Fisken, Garey & Powell 1975). The majority of the dendritic shafts receiving synapses from terminals from SI or area 6 were of large stellate type, and the association connections therefore end mainly on

pyramidal spines, with some contacting large stellate dendrites and a few probably contacting dendrites of small stellate cells. In spite of the large size of the lesions and the wide range of survival period the degeneration after lesions of SI was less dense than the commissural degeneration.

Synthesis

All the afferent connections to the sensori-motor cortex studied here share a basically similar pattern of termination which is summarized in figure 65. All have asymmetric membrane specializations and the majority of the terminals of each projection contact dendritic spines which probably arise from pyramidal cells, with a small proportion contacting the dendrites and somata of large stellate cells. Physiologically both thalamic and commissural afferents to the motor cortex excite pyramidal tract (p.t.) cells monosynaptically (Amassian & Weiner 1966; Asanuma & Okada 1962) and p.t. neurons have been shown by dye injection to be pyramidal cells (Naito, Nakamura, Kurosaki & Tamura 1969). Thus there is good agreement between the anatomical and physiological findings with respect to the major site of termination of afferents to the motor cortex and in addition the correlation between the asymmetric membrane specializations and the excitatory action of the afferents confirms the correlation between structure and function made in the cerebellum (Uchizono 1965) and elsewhere (Gray 1969).

The major difference between the afferent connections would appear to be in their relation to the cortical laminae but they differ also in the exact proportions of each which contact spines, dendritic shafts and cell somata (table 1). For both the thalamo-cortical and commissural

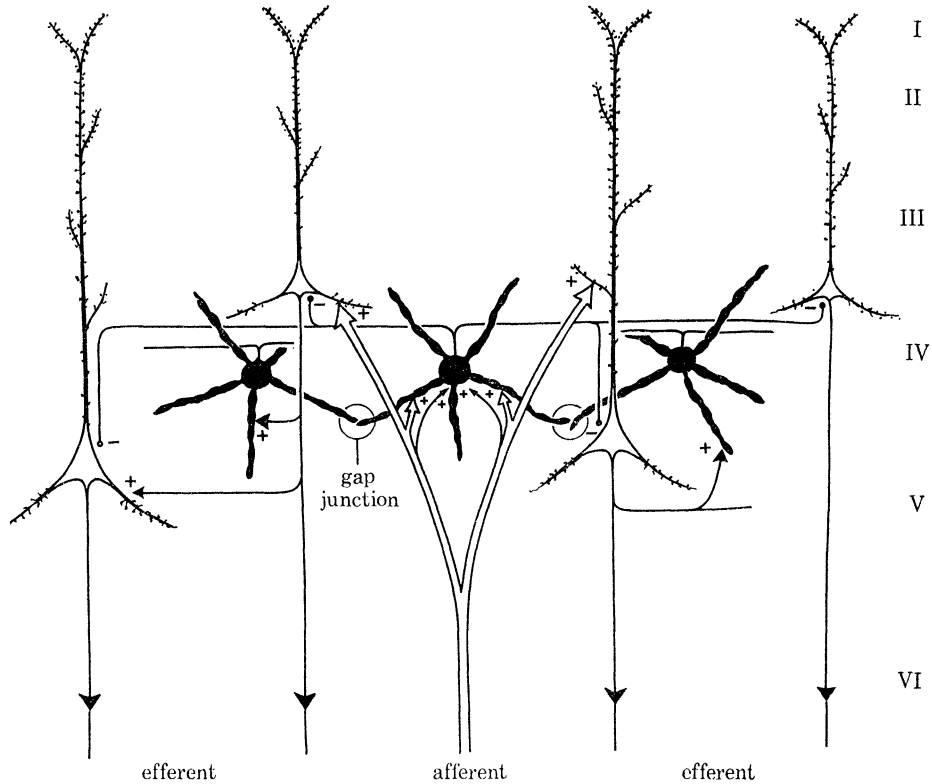


FIGURE 65. Schematic diagram showing afferent and intrinsic cortical connections based on a correlation of anatomical and physiological evidence (see text). The connections shown are for the thalamo-cortical projection to the motor cortex but those of the other afferents studied are essentially similar.

connections the proportions of terminals contacting each postsynaptic site are very similar in the motor and somatic sensory cortices and, considering the relatively small sample of terminals from area 6, the two association connections to the motor cortex are comparable. This suggests that the proportion of each type of postsynaptic profile is a feature of the *type of connection* rather than whether it goes to the motor or somatic sensory cortex. The greater proportion of thalamo-cortical afferents contacting stellate cell somata and the larger size of some of the stellate dendritic shafts contacted by thalamo-cortical afferents compared to commissural afferents suggest that the thalamo-cortical terminals extend more on to the proximal parts of large stellate cells than do the commissural terminals and the same is probably true for pyramidal cells.

Pyramidal cells project to a number of sites, both cortical and subcortical and their action has been shown to be excitatory. Pyramidal cell axons also have extensive collaterals within the cortex. Antidromic stimulation of the pyramidal tract activates these collaterals and excites monosynaptically other pyramidal tract neurons and 'pyramidal tract interneurons' which in turn are thought to mediate the delayed inhibition of pyramidal tract cells. The evidence that these 'pyramidal tract interneurons' correspond to the large stellate cells of electron microscopy and to the basket cells shown by the Golgi method has been considered elsewhere (Gatter, Sloper & Powell 1978) and of particular importance are the findings that a pyramidal cell axon makes a synapse upon a stellate cell dendrite (Sloper & Powell 1979*b*) and that after small lesions within the cortex degenerating fibres with the features of basket cell axons make symmetrical synapses upon pyramidal cells (Gatter *et al.* 1978). Thus, the large stellate/basket cell is excited by both afferent fibres and pyramidal cell collaterals, and in turn it inhibits adjoining pyramidal cells. In addition, as large stellate cell dendrites and somata are linked with other large stellate cells by gap junctions they are probably electrically coupled (Sloper & Powell 1978*a*) and this may coordinate their activity.

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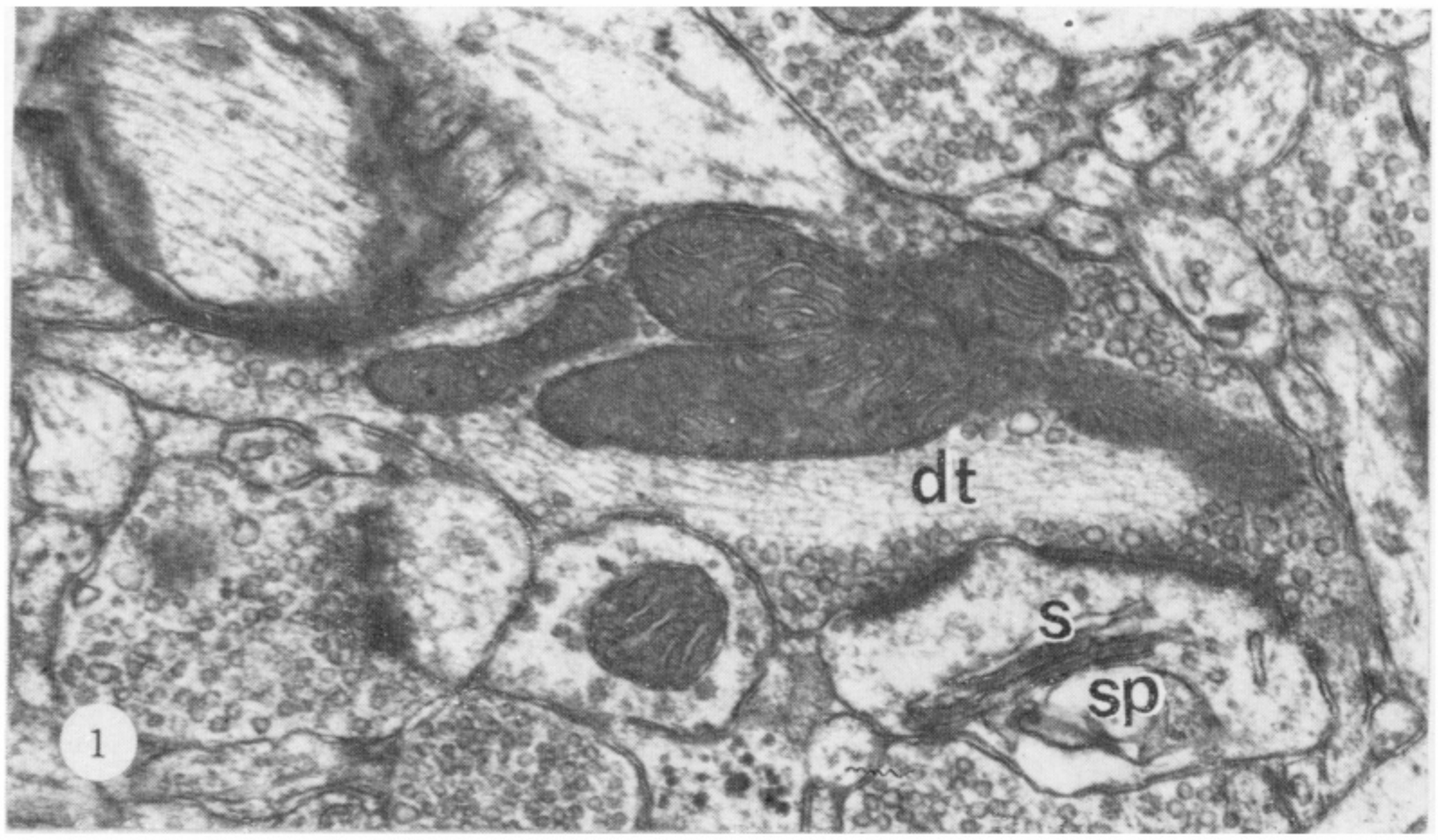
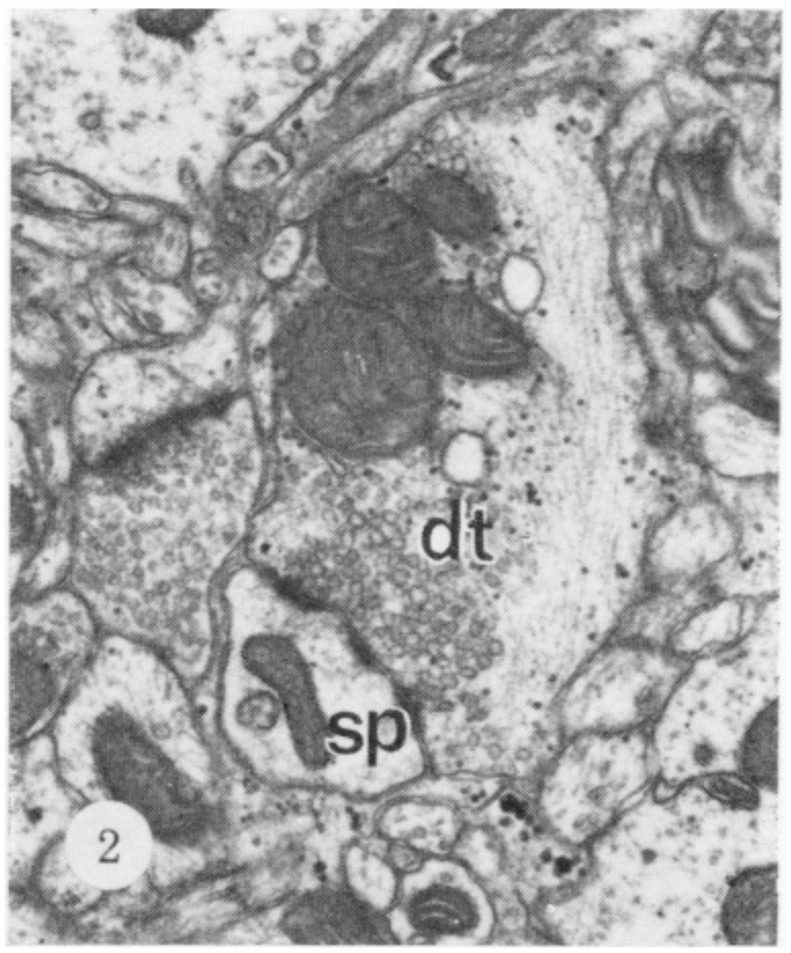
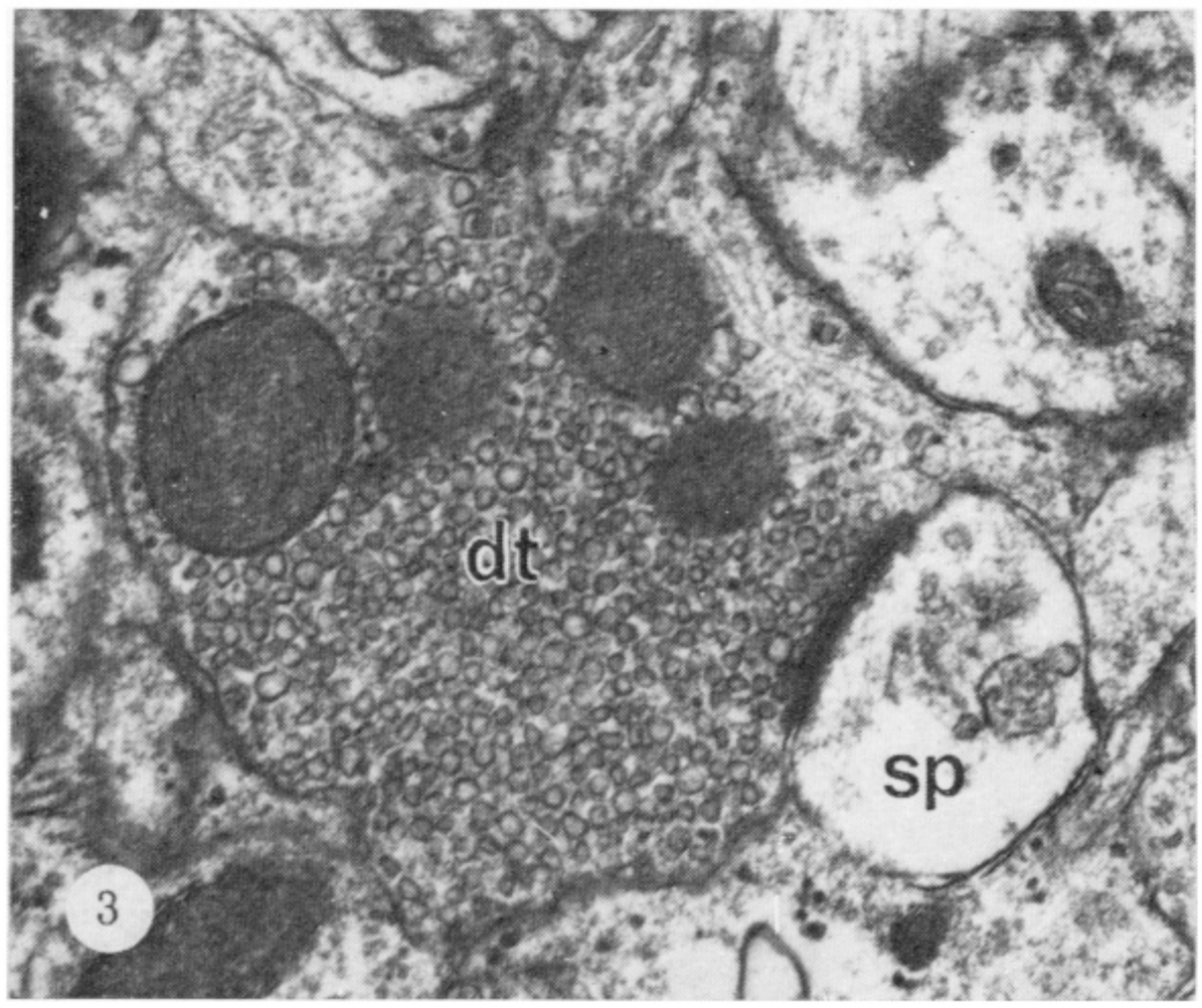
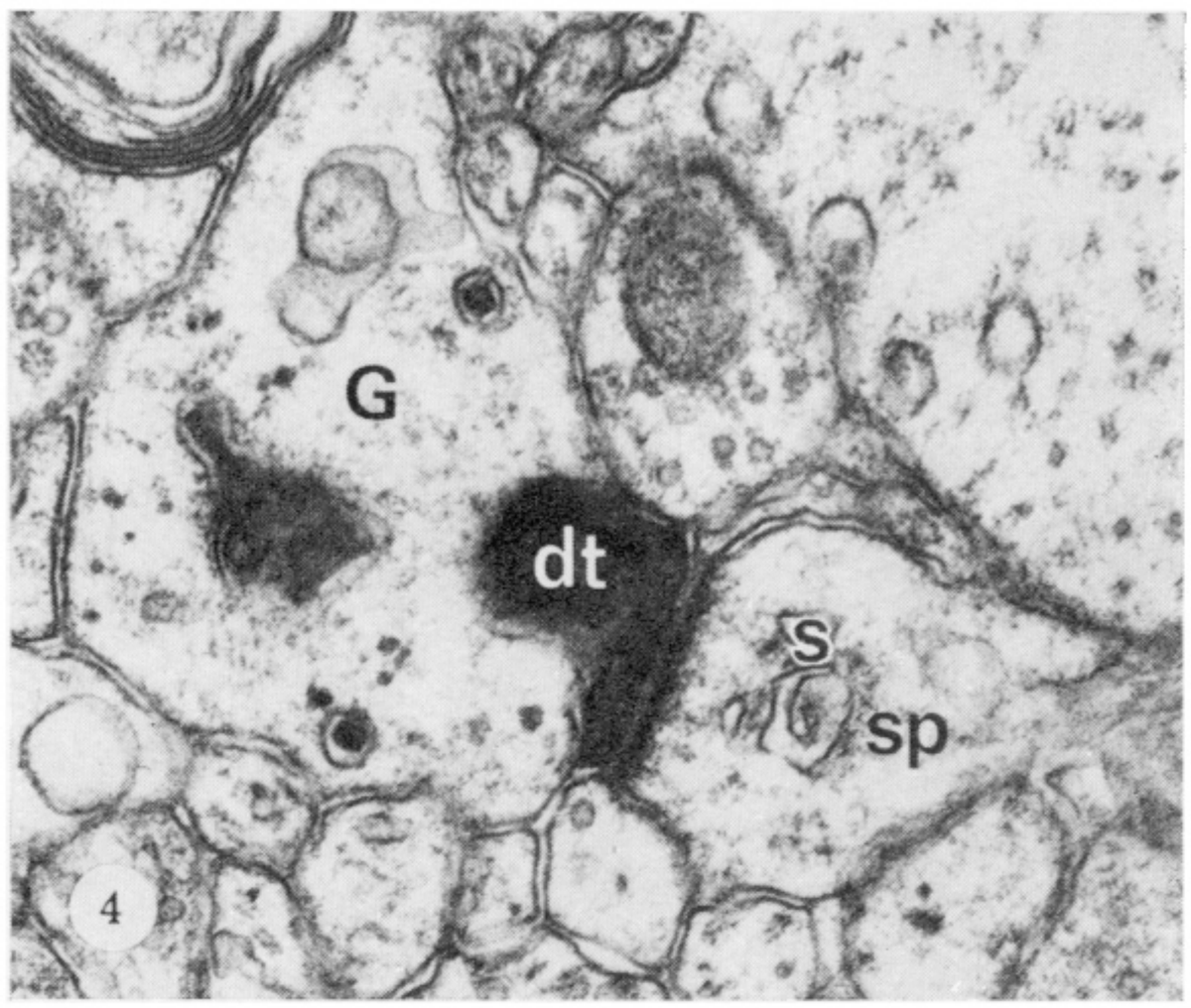
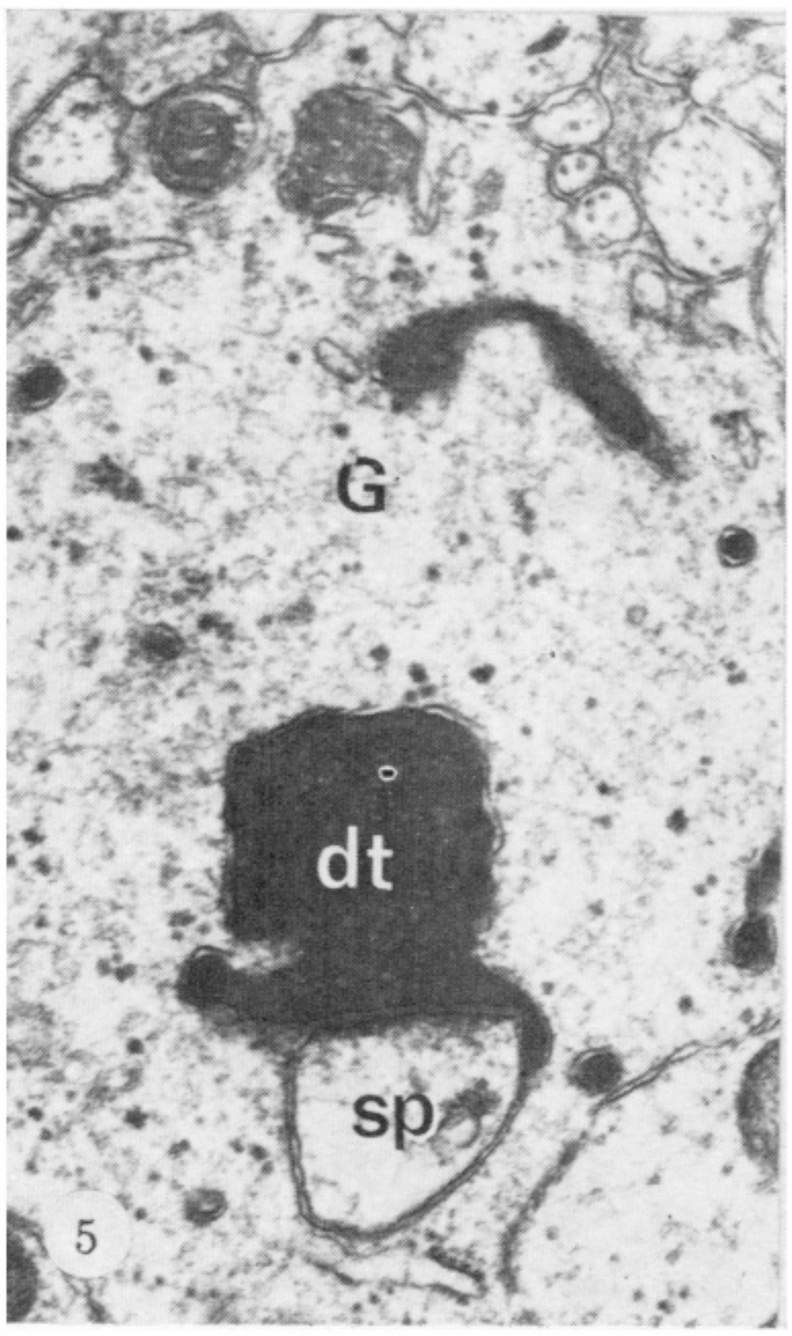
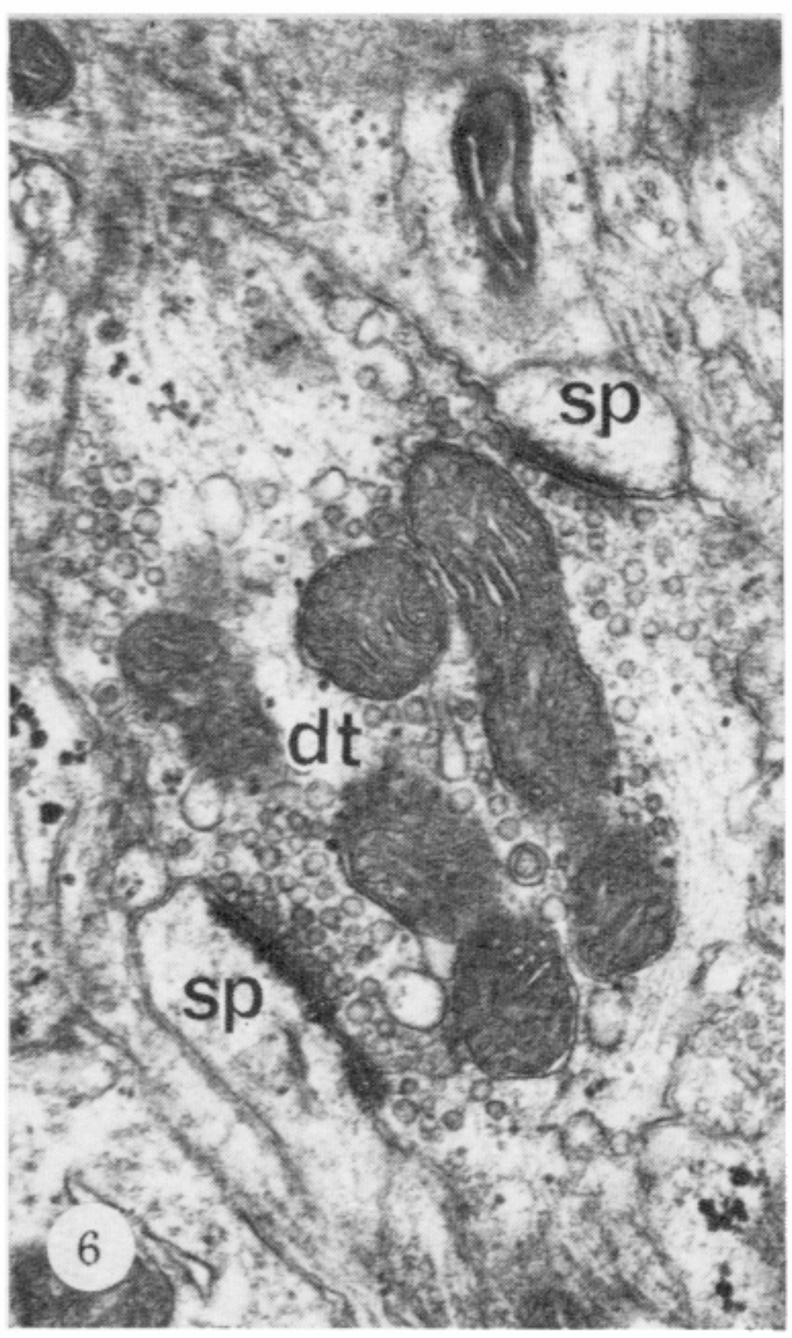


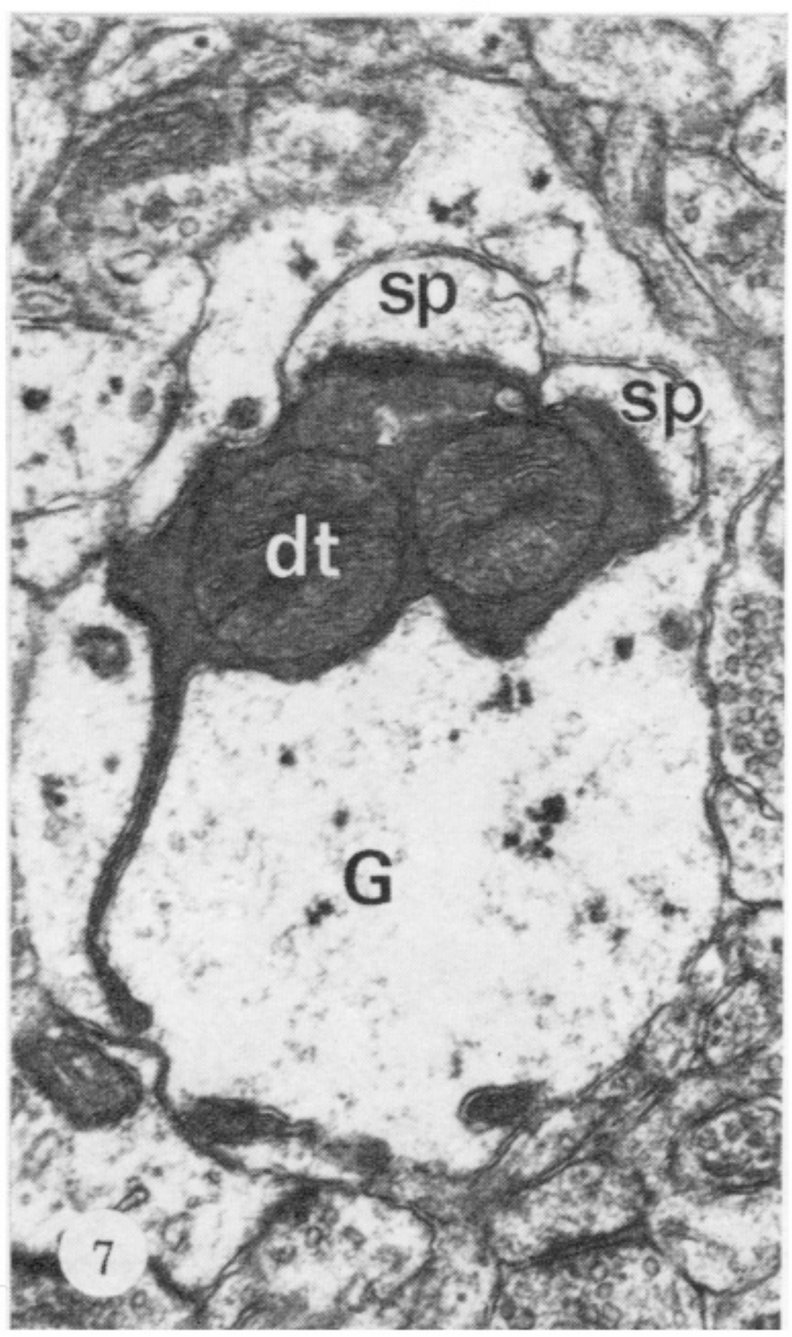




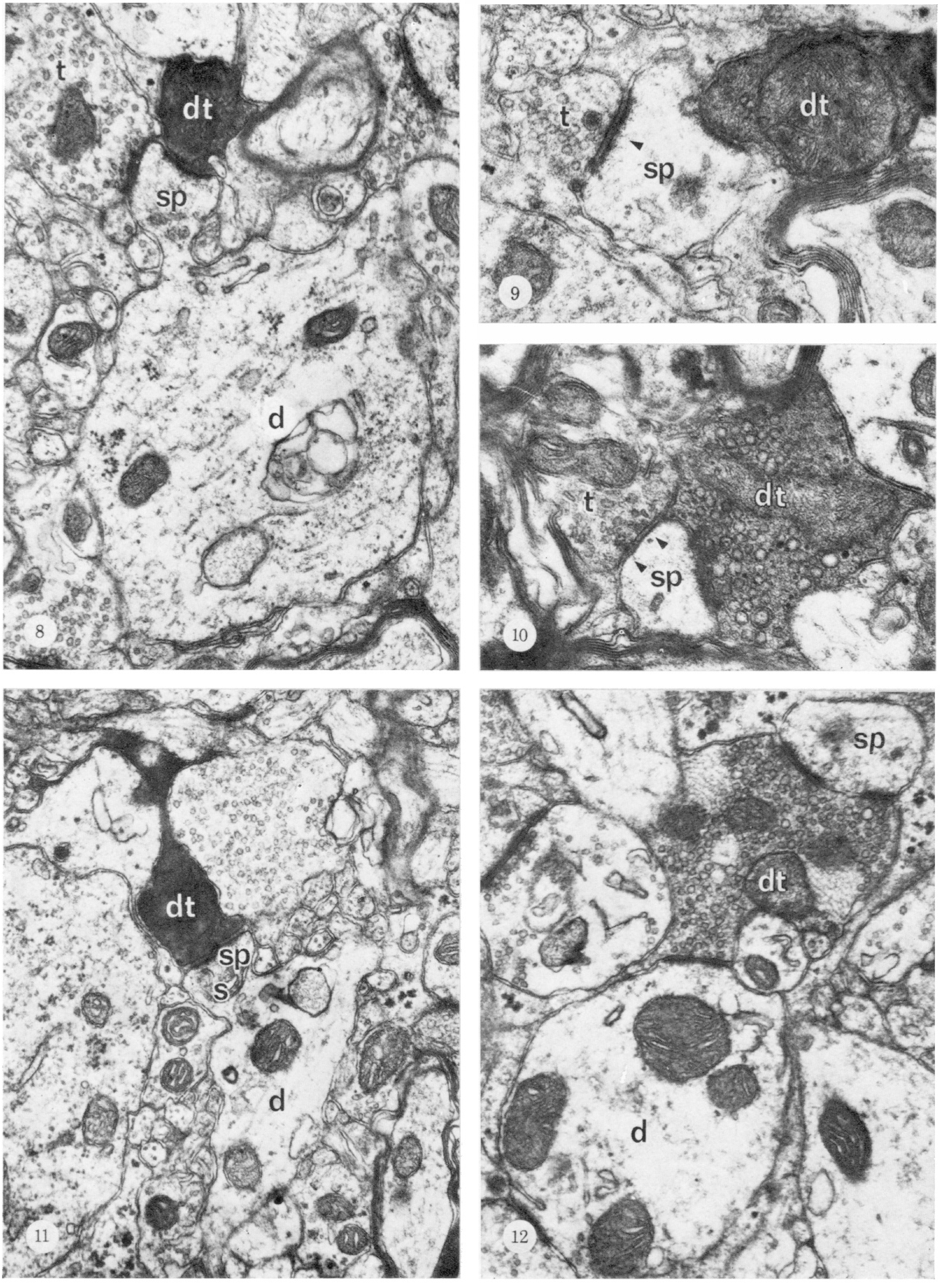




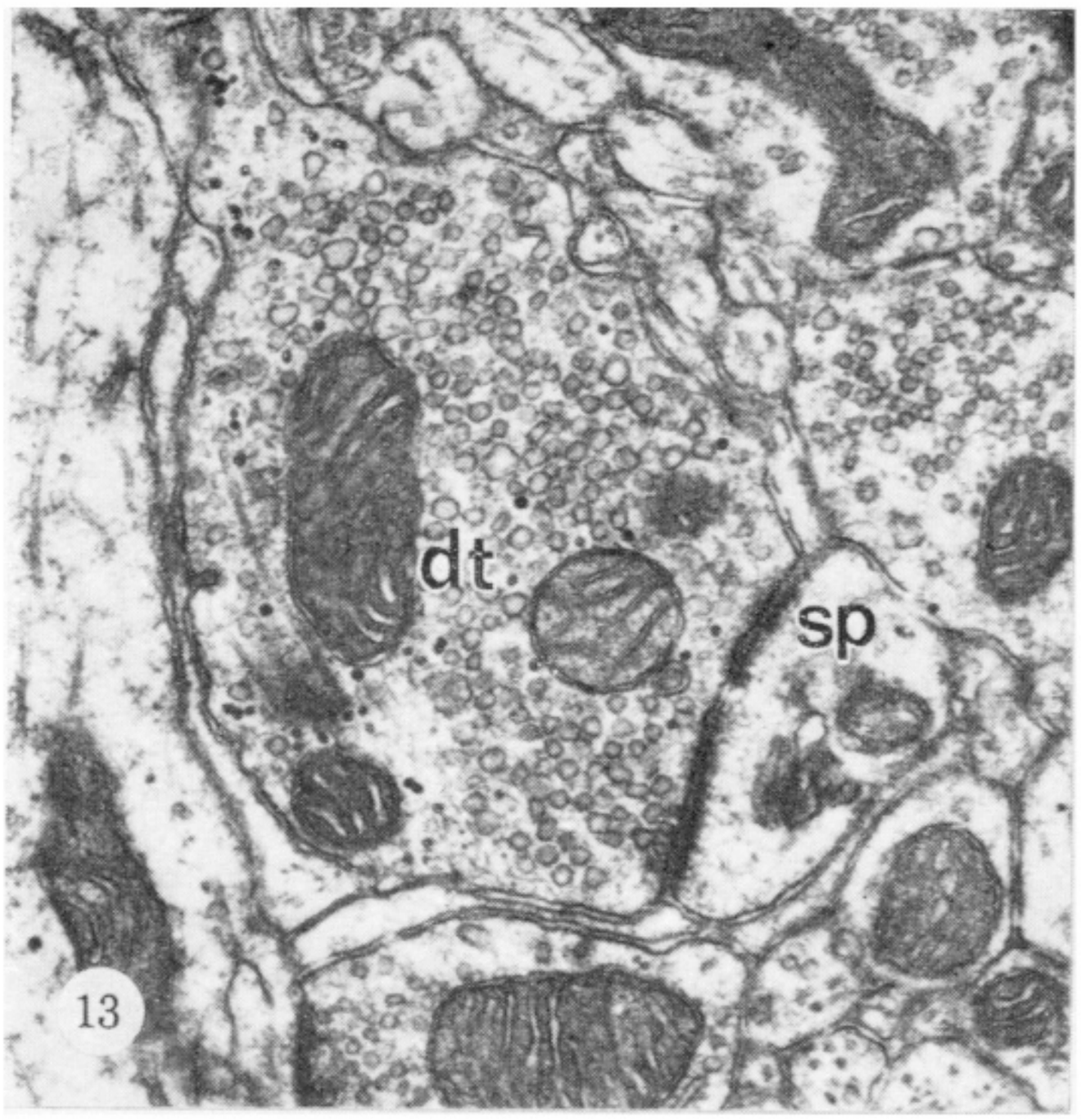


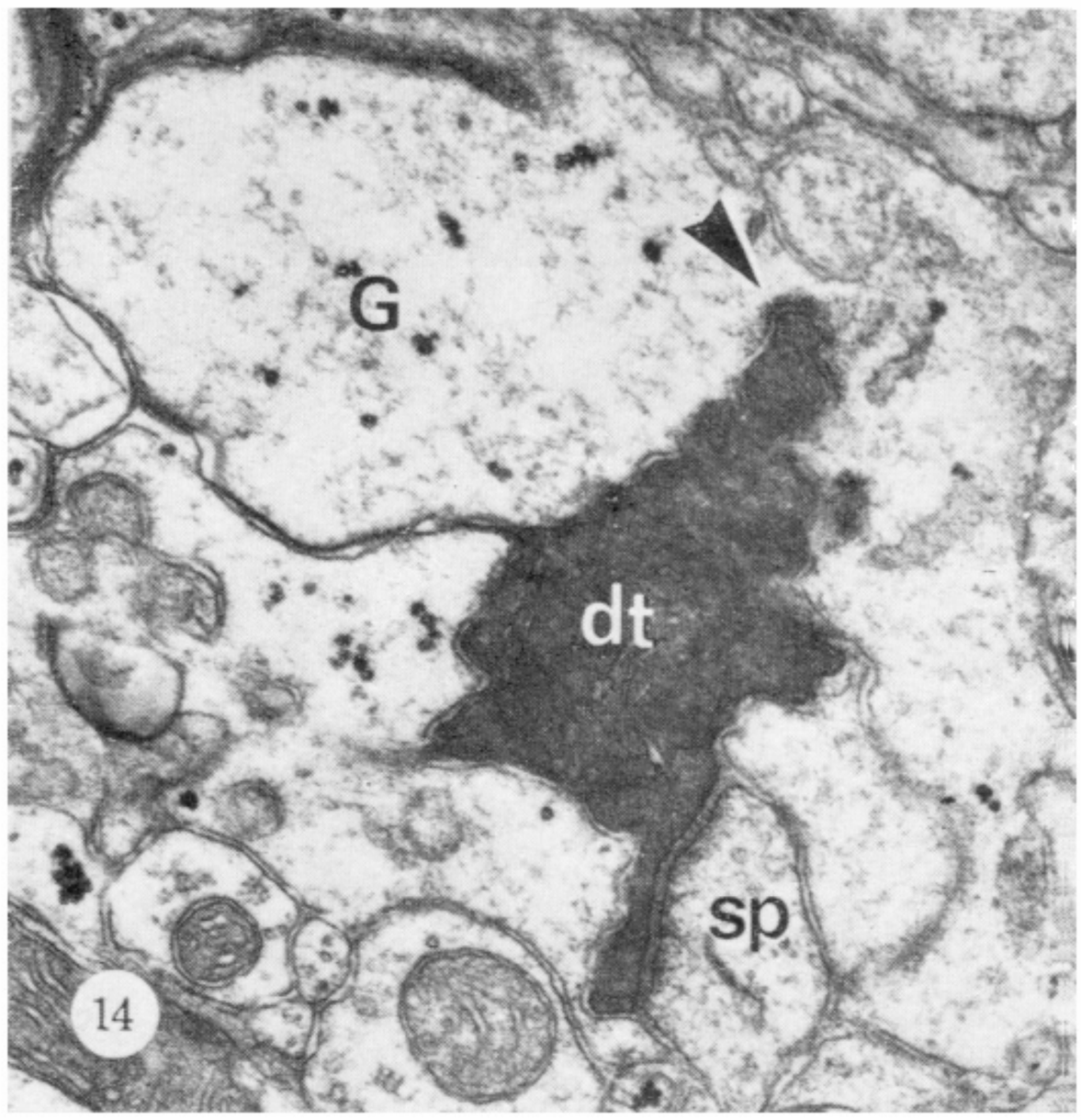


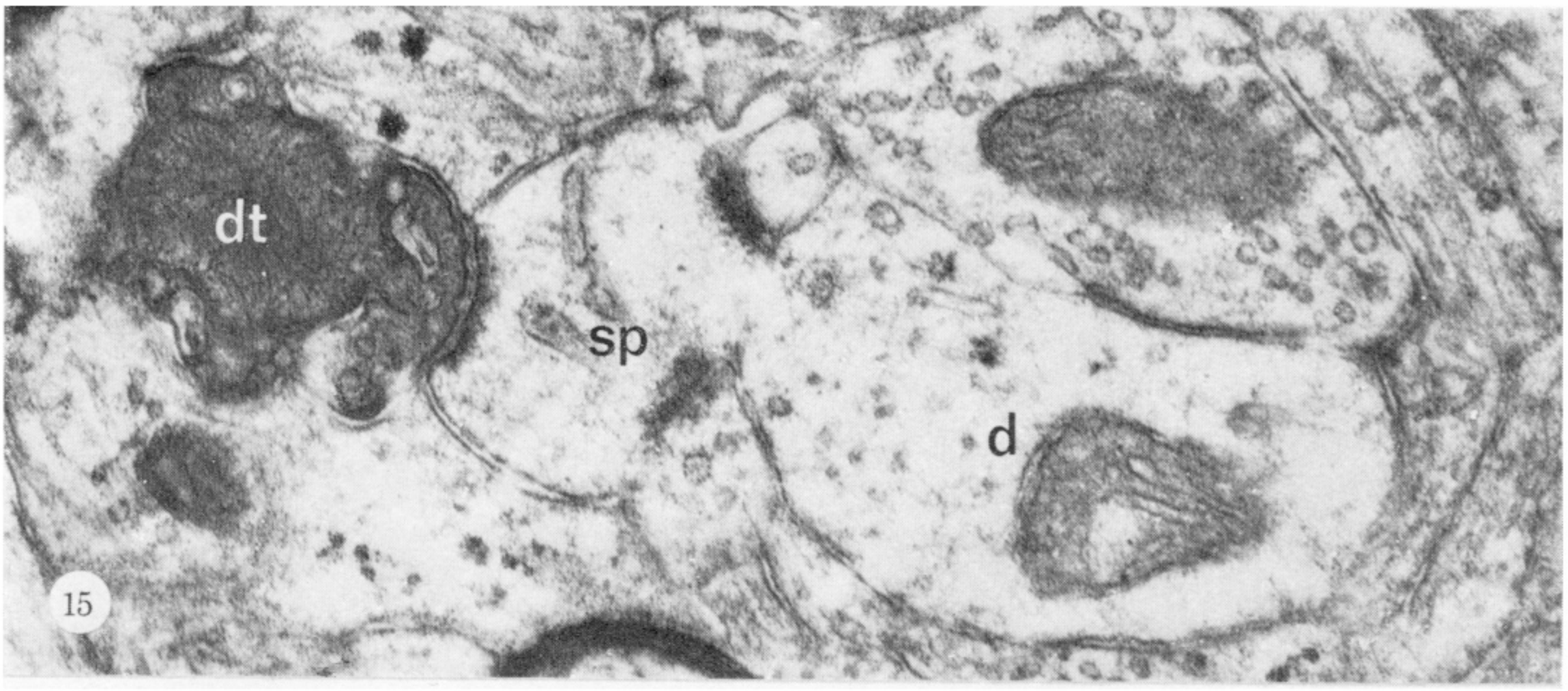
FIGURES 1–7. For description see opposite.

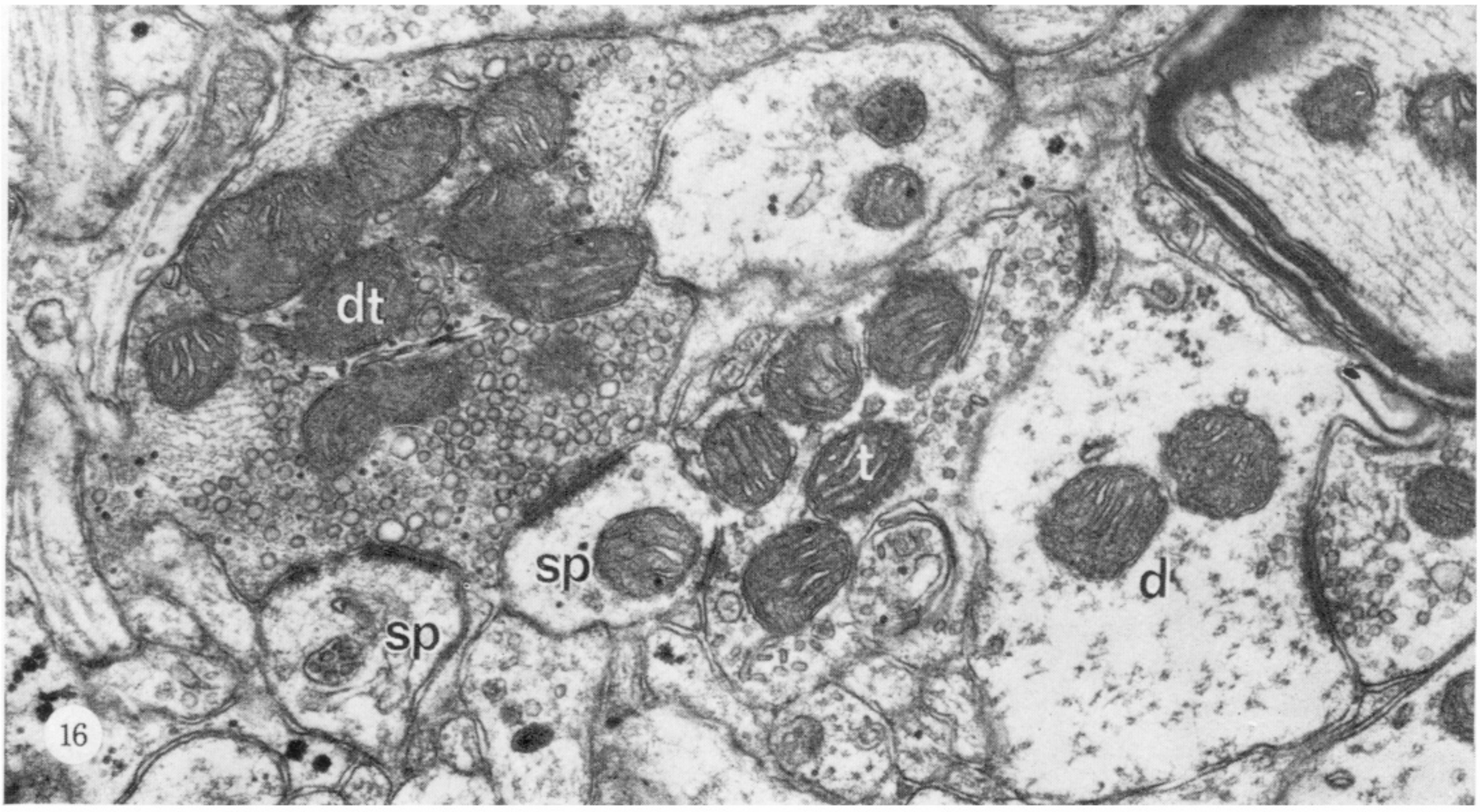


FIGURES 8–12. For description see page 202.

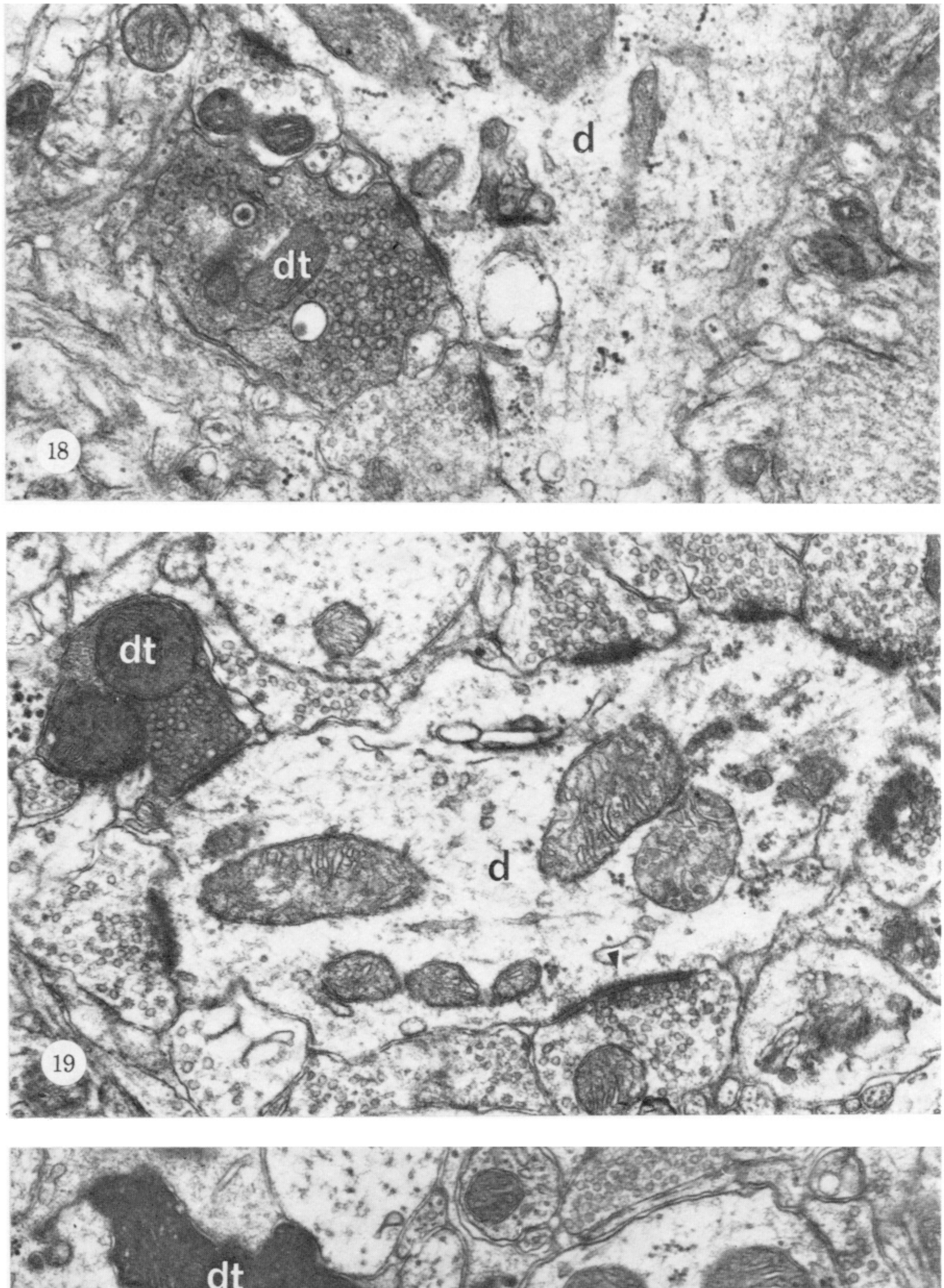




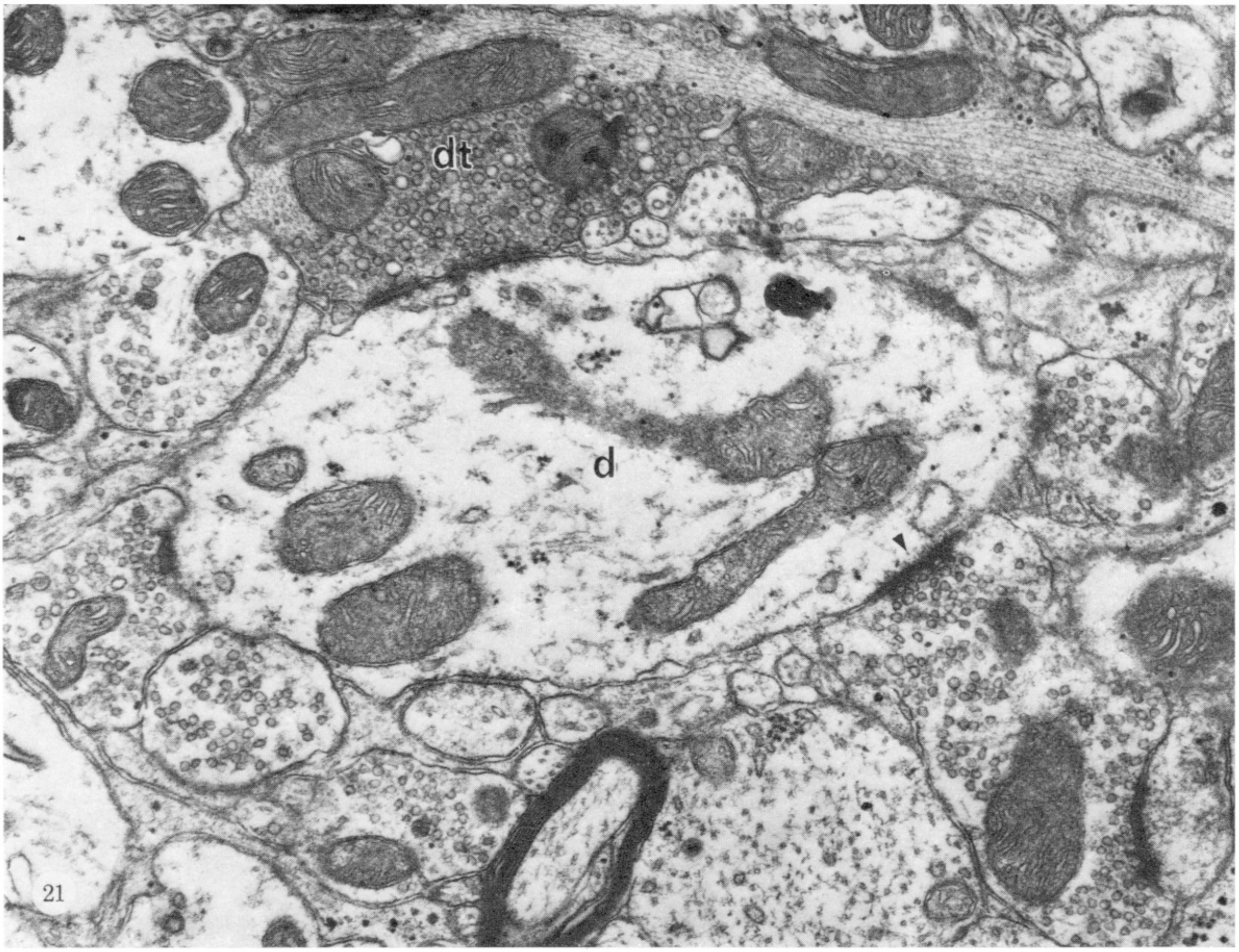


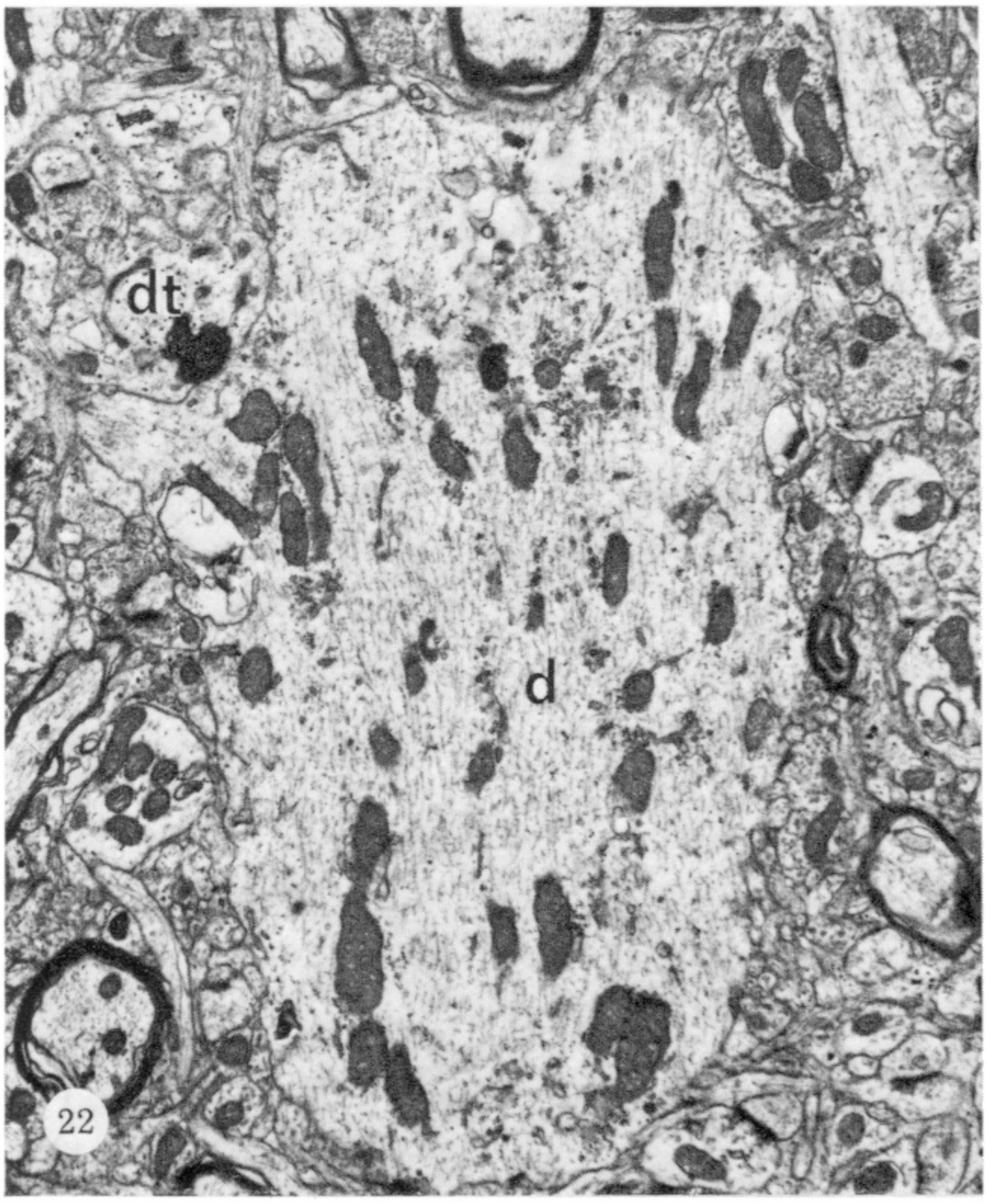


FIGURES 13–16. For description see page 203.



FIGURES 17–20. For description see opposite.





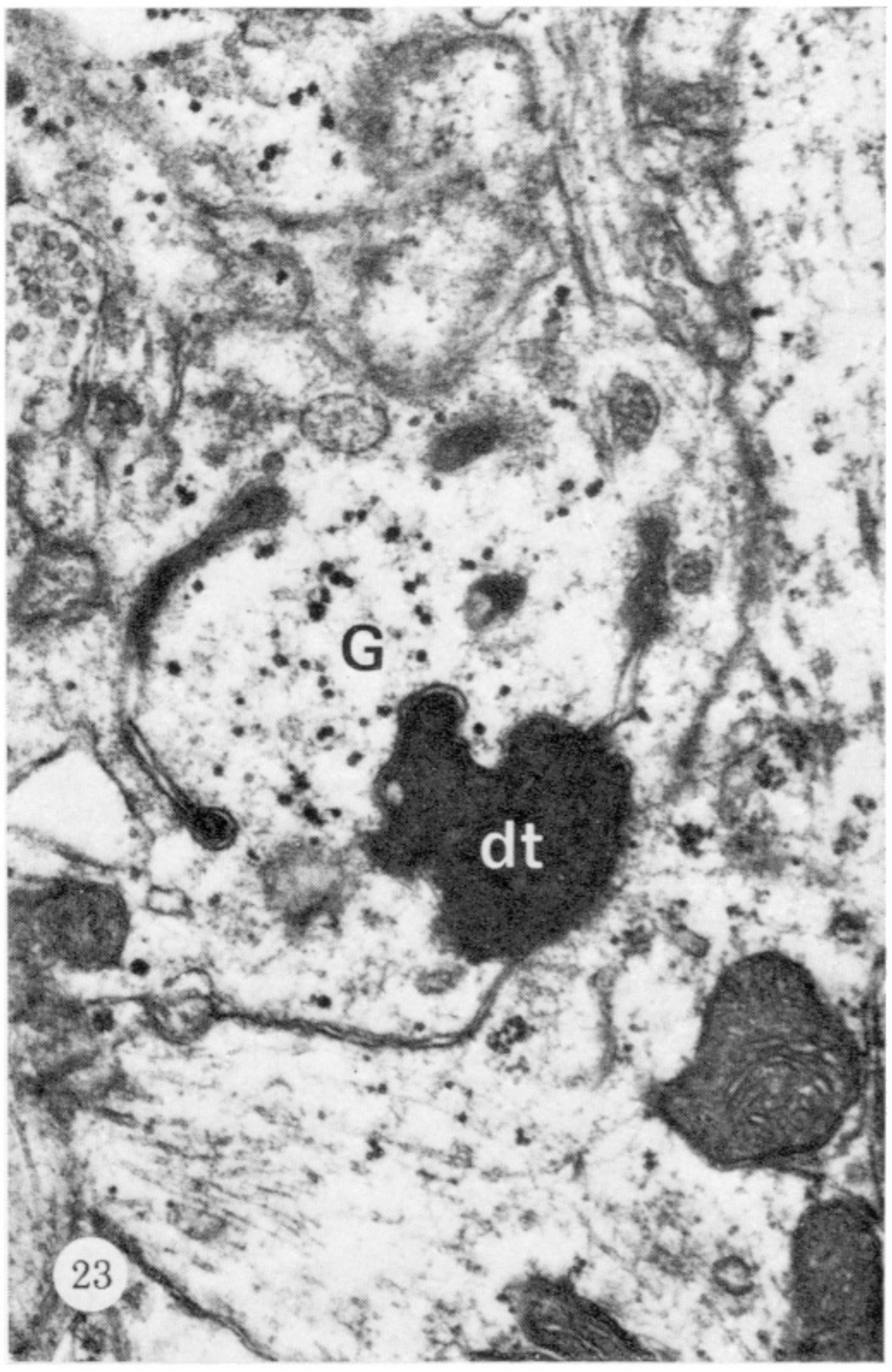
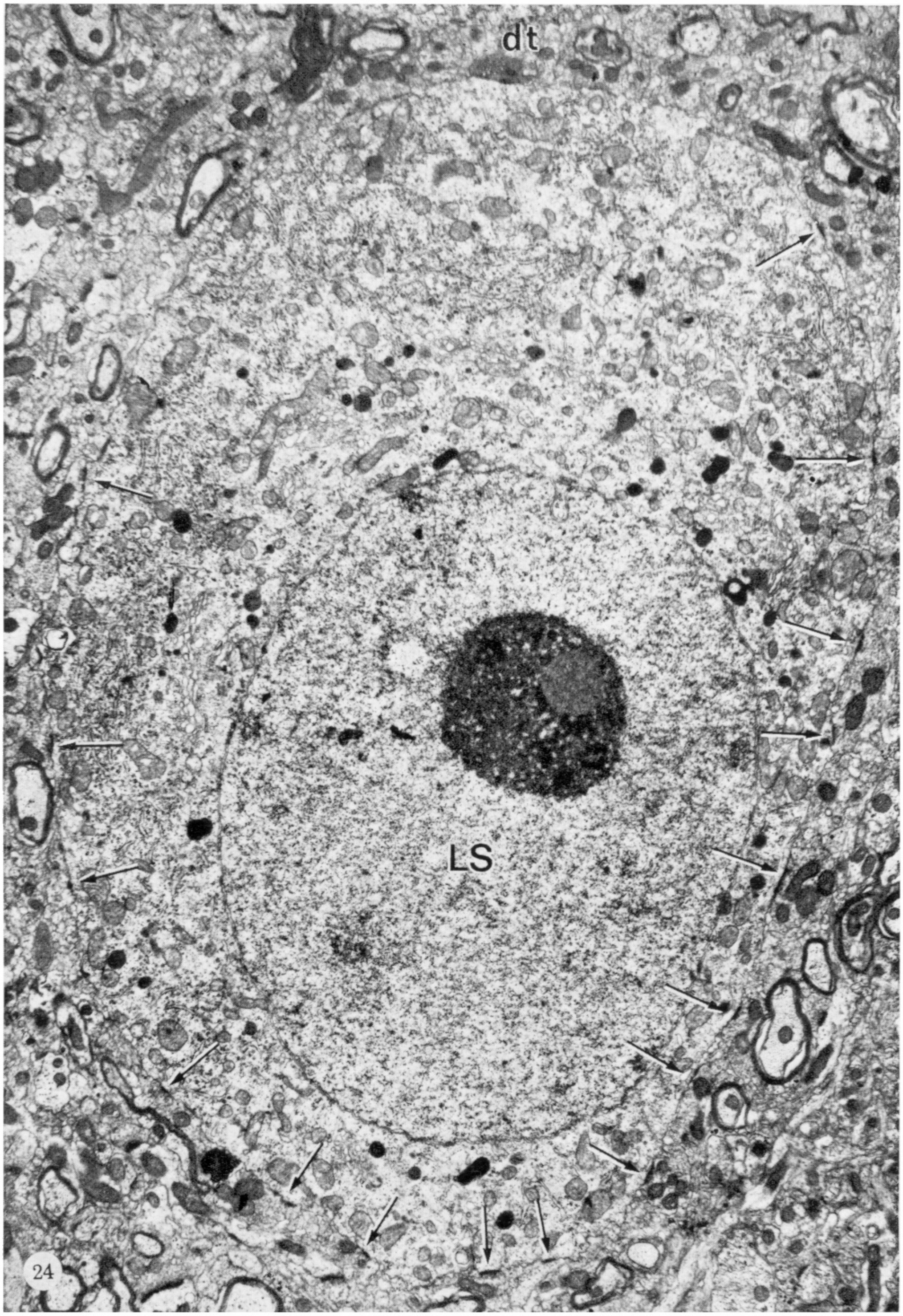
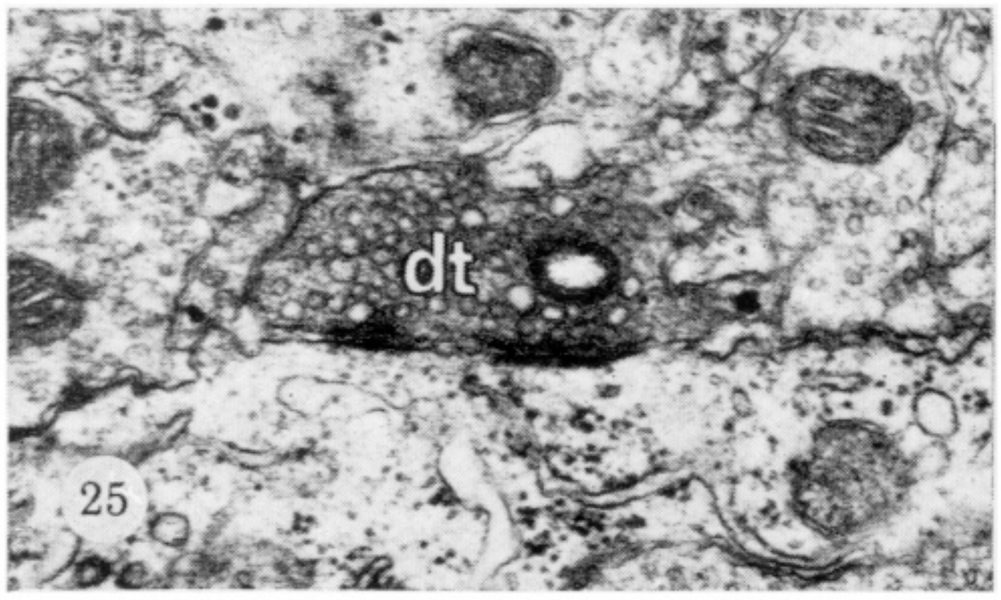


FIGURE 21. A degenerating thalamo-cortical axon terminal (dt) which makes an *en passage* synapse on to a dendrite (d) in the somatic sensory cortex. Note the large size of the dendrite and the other synapses it receives, one of which is clearly of the asymmetric type (arrowhead). (Magn. × 29 000.)

FIGURE 22. A degenerating thalamo-cortical terminal which makes a synapse on to a very large vertically running dendrite at the base of a side branch in layer IV of the somatic sensory cortex. This dendrite is probably the apical dendrite of a pyramidal cell in layer V. (Magn. × 8400.)

FIGURE 23. Higher magnification of the degenerating thalamo-cortical terminal of figure 22. Note the glial engulfment (G). (Magn × 29 000.)





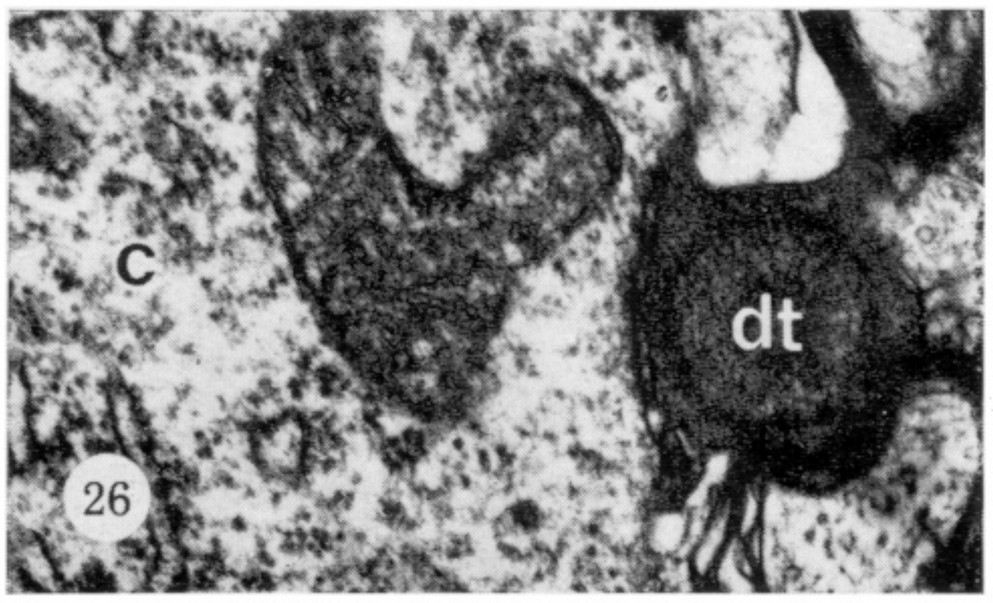


FIGURE 24. A degenerating thalamo-cortical axon terminal (dt) which makes an axo-somatic synapse on to a large stellate cell (LS) in layer IV of the motor cortex. Note the large number of other synapses received by the cell soma (arrows) and its abundant cytoplasm full of organelles. (Magn. × 8400.)

FIGURE 25. Higher magnification of the degenerating thalamo-cortical terminal of figure 24. (Magn. × 29000.)

FIGURE 26. A degenerating thalamo-cortical axon terminal making an axo-somatic synapse on to part of a large stellate cell soma (c). This large stellate cell received 8 normal axo-somatic synapses in the same section. (Magn. × 29000.)

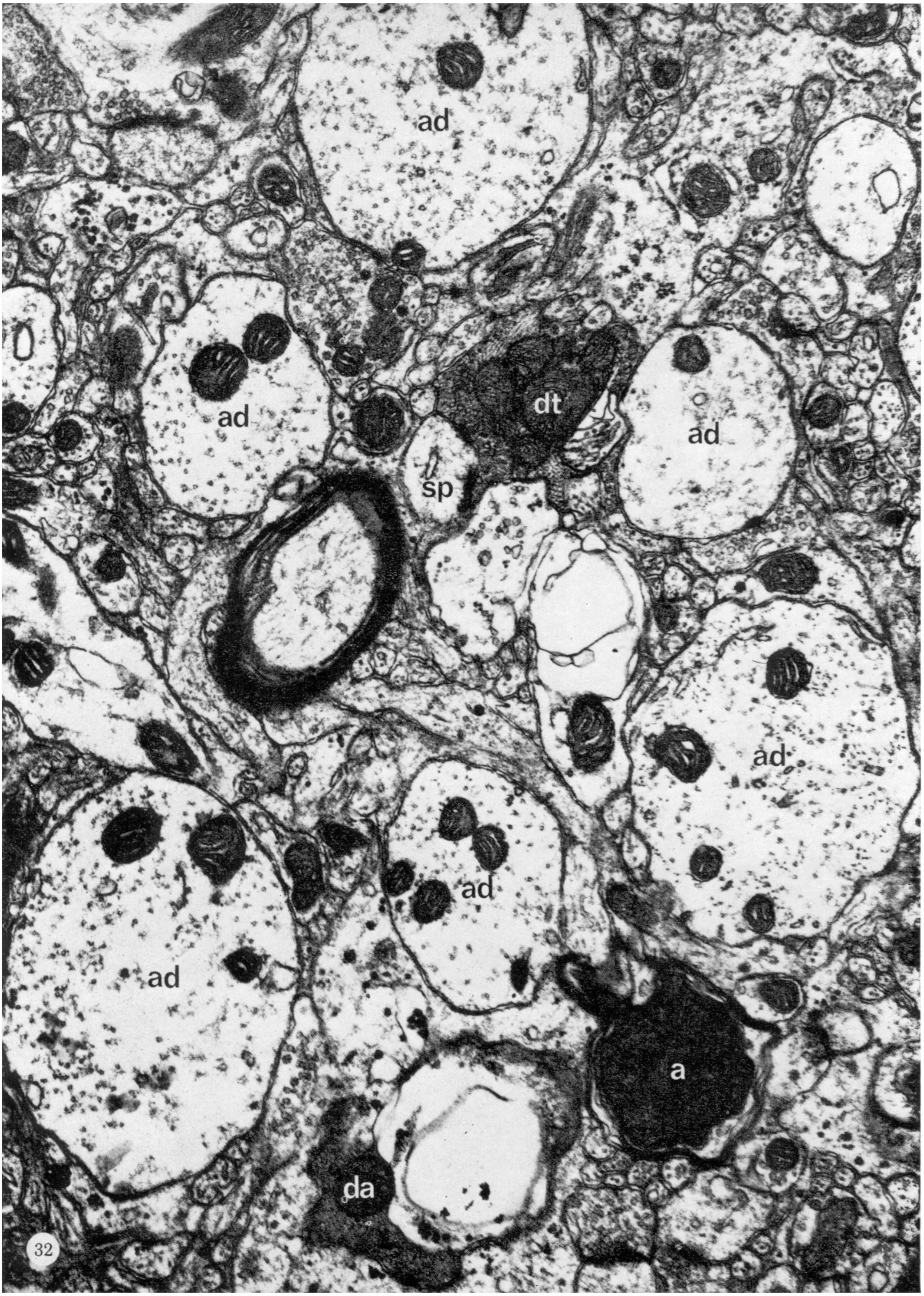
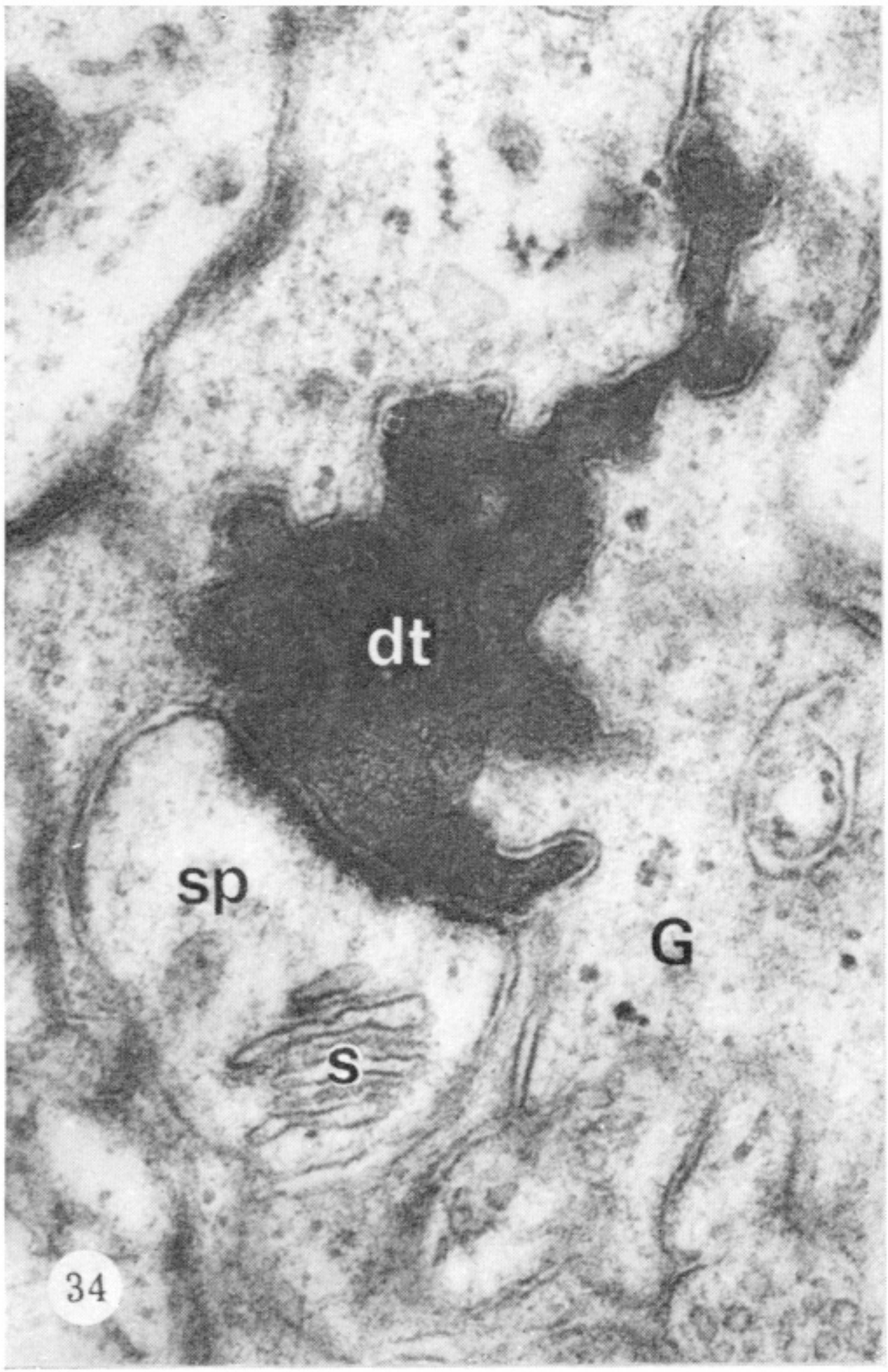
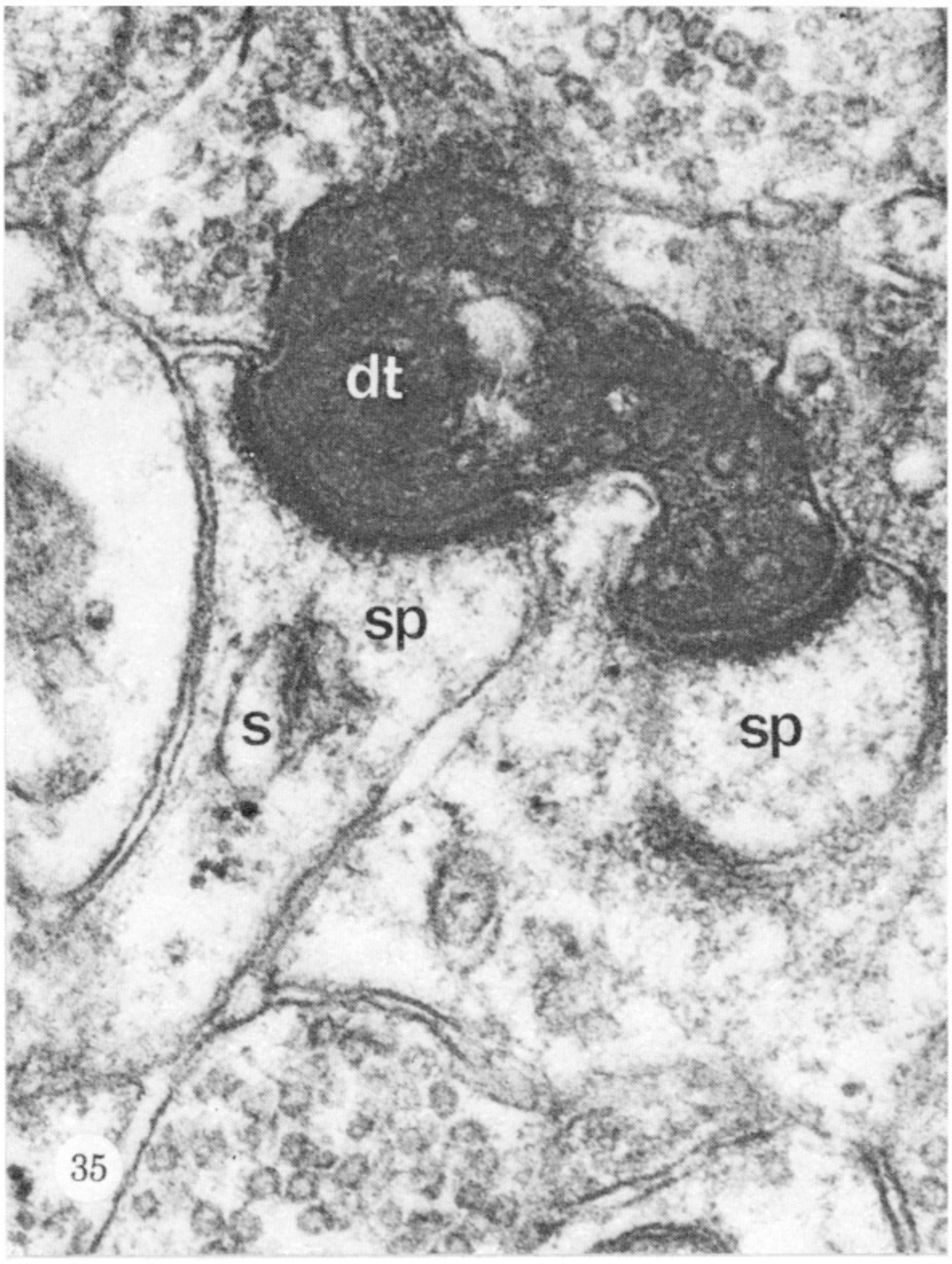
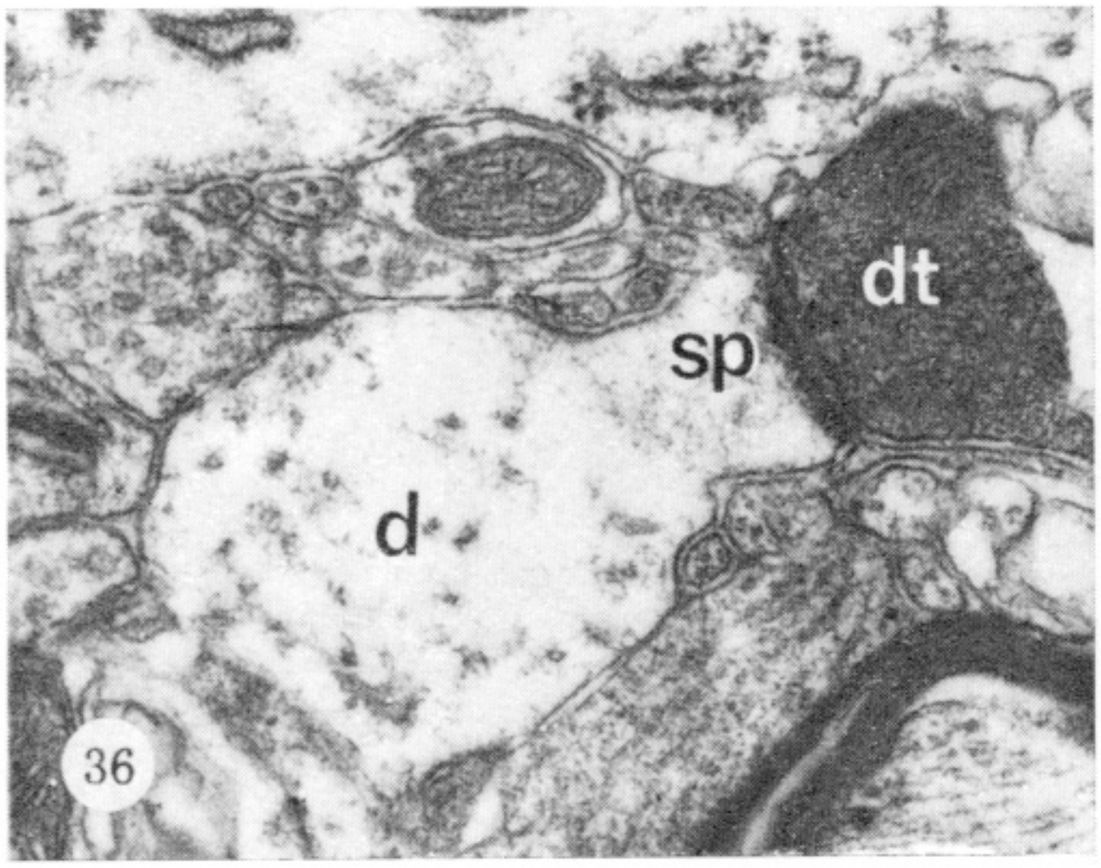
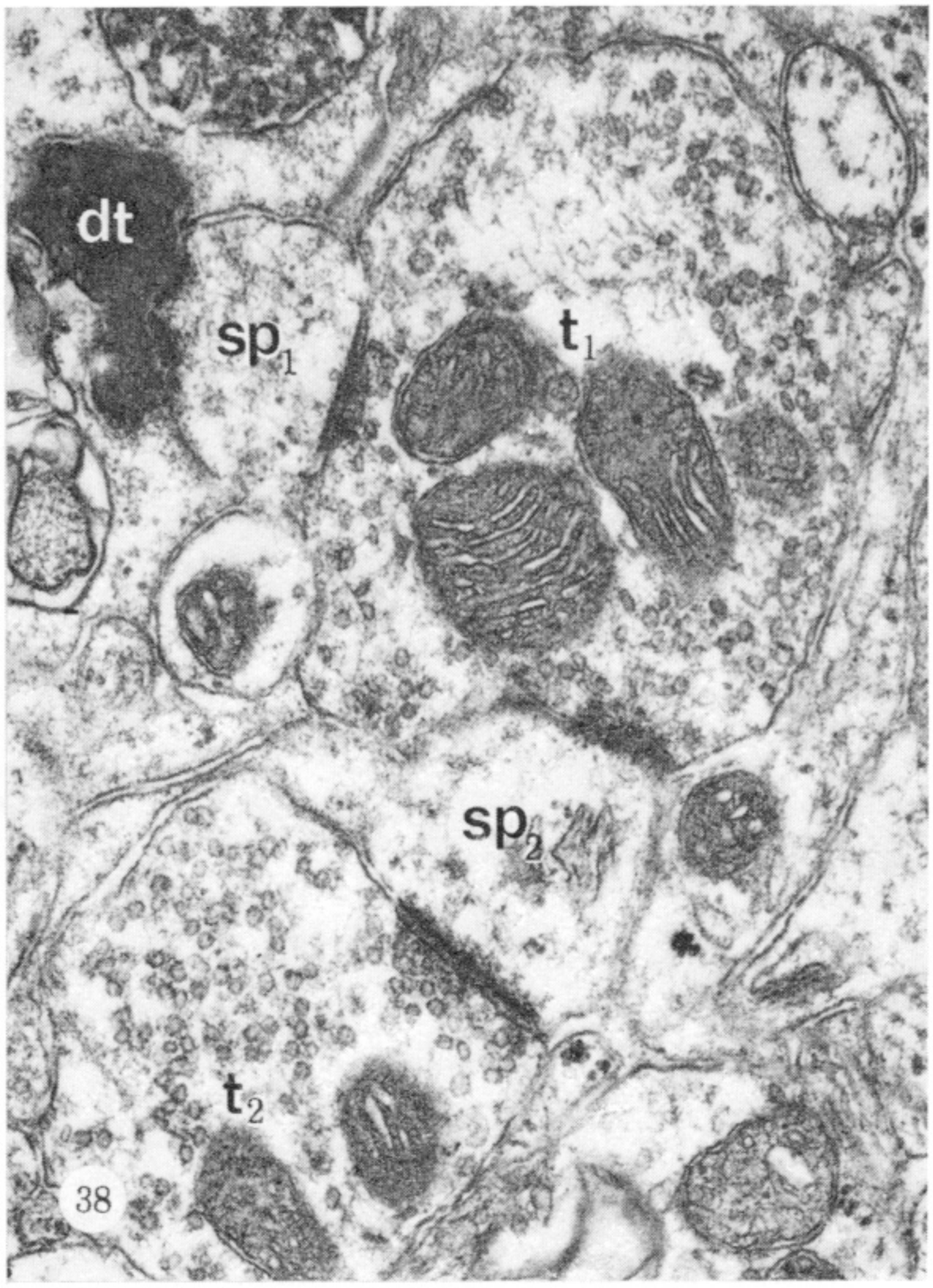


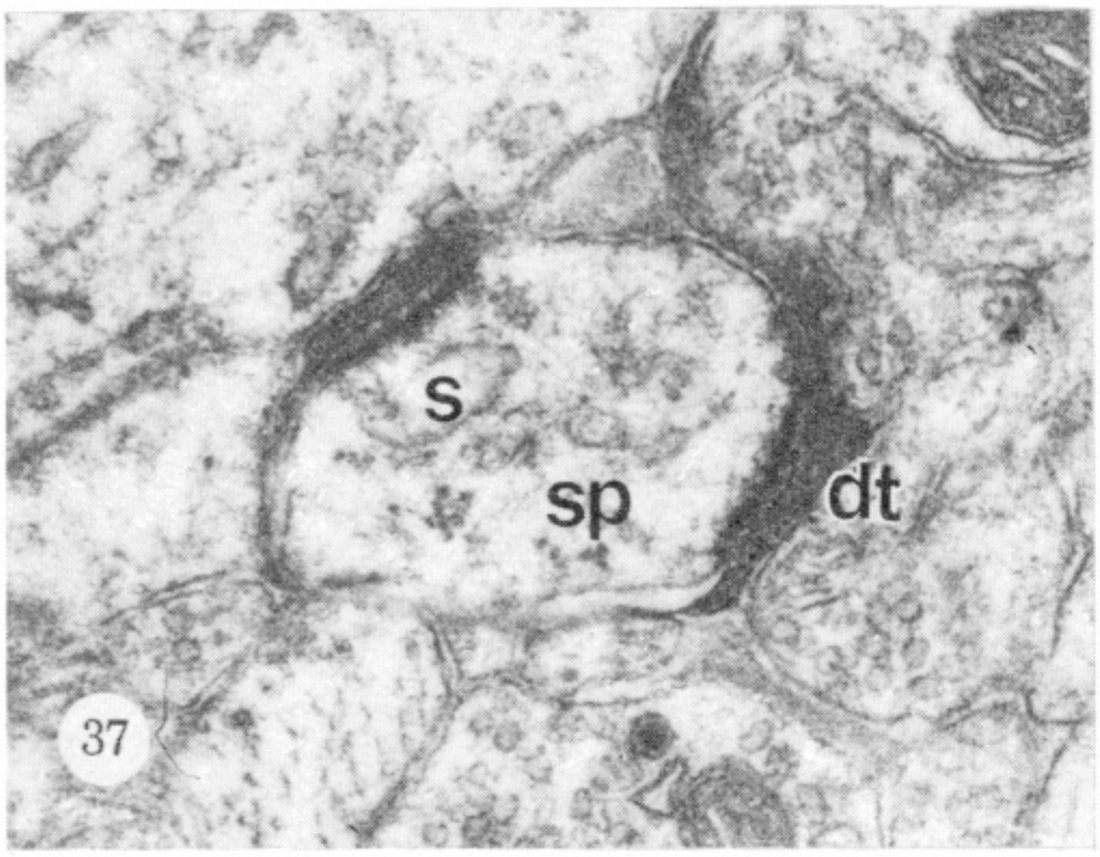
FIGURE 32. A section of layer IV of the motor cortex taken parallel to the pial surface showing a bundle of apical dendrites (ad) cut in transverse section, together with a degenerating thalamo-cortical axon terminal (dt) which makes a synapse on to a spine (sp), a degenerating myelinated axon (a) running vertically with the bundle of apical dendrites and a degenerating preterminal axon (da). (Magn. × 29000.)



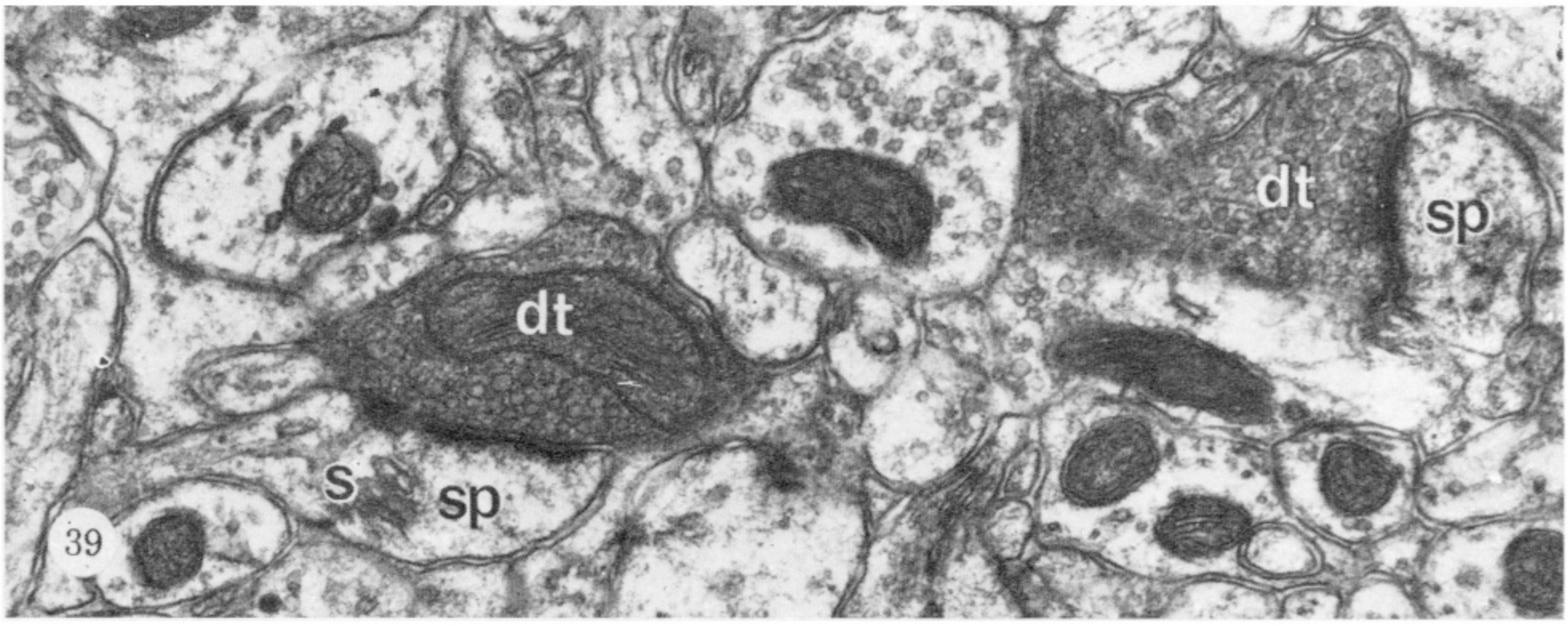


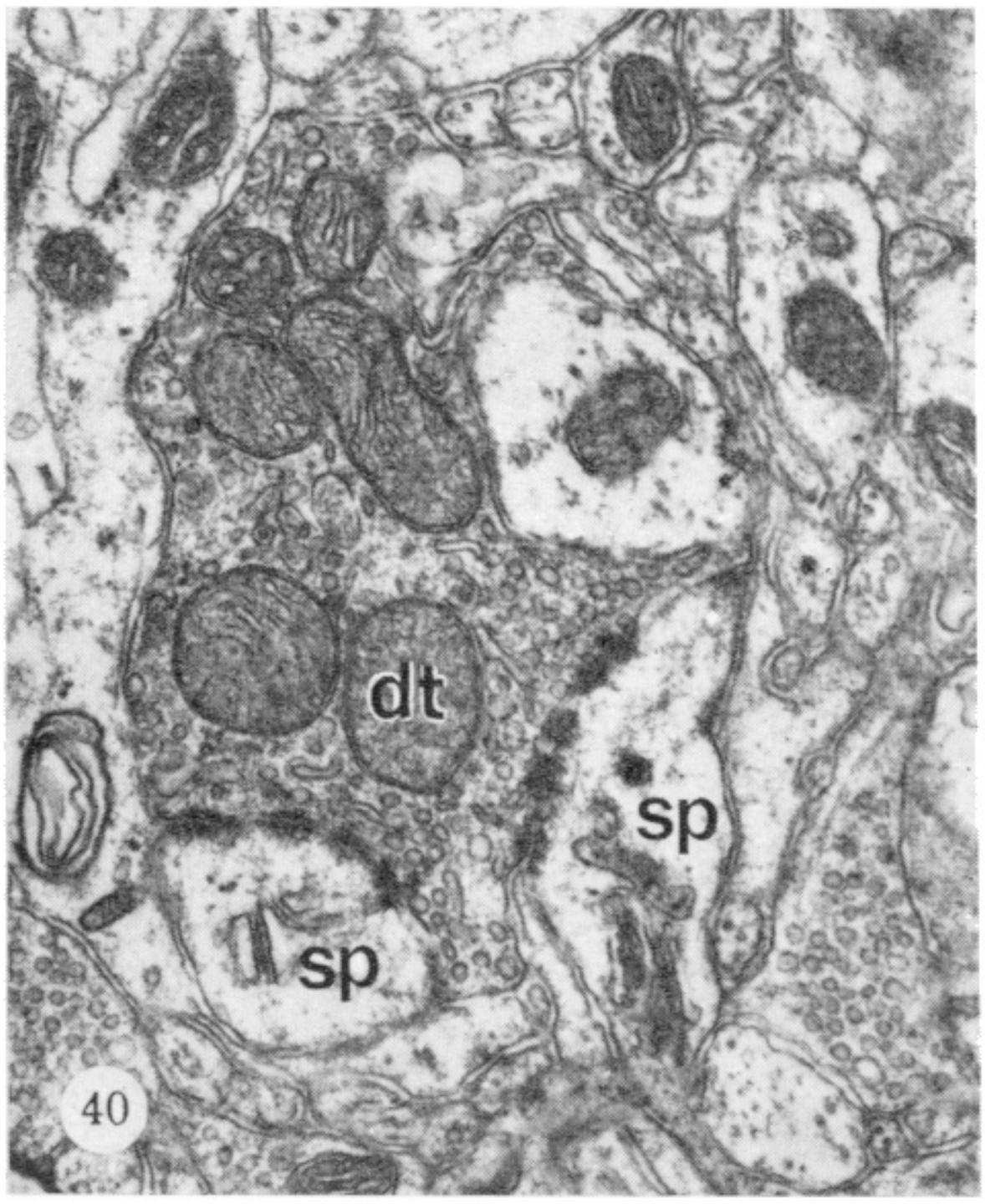


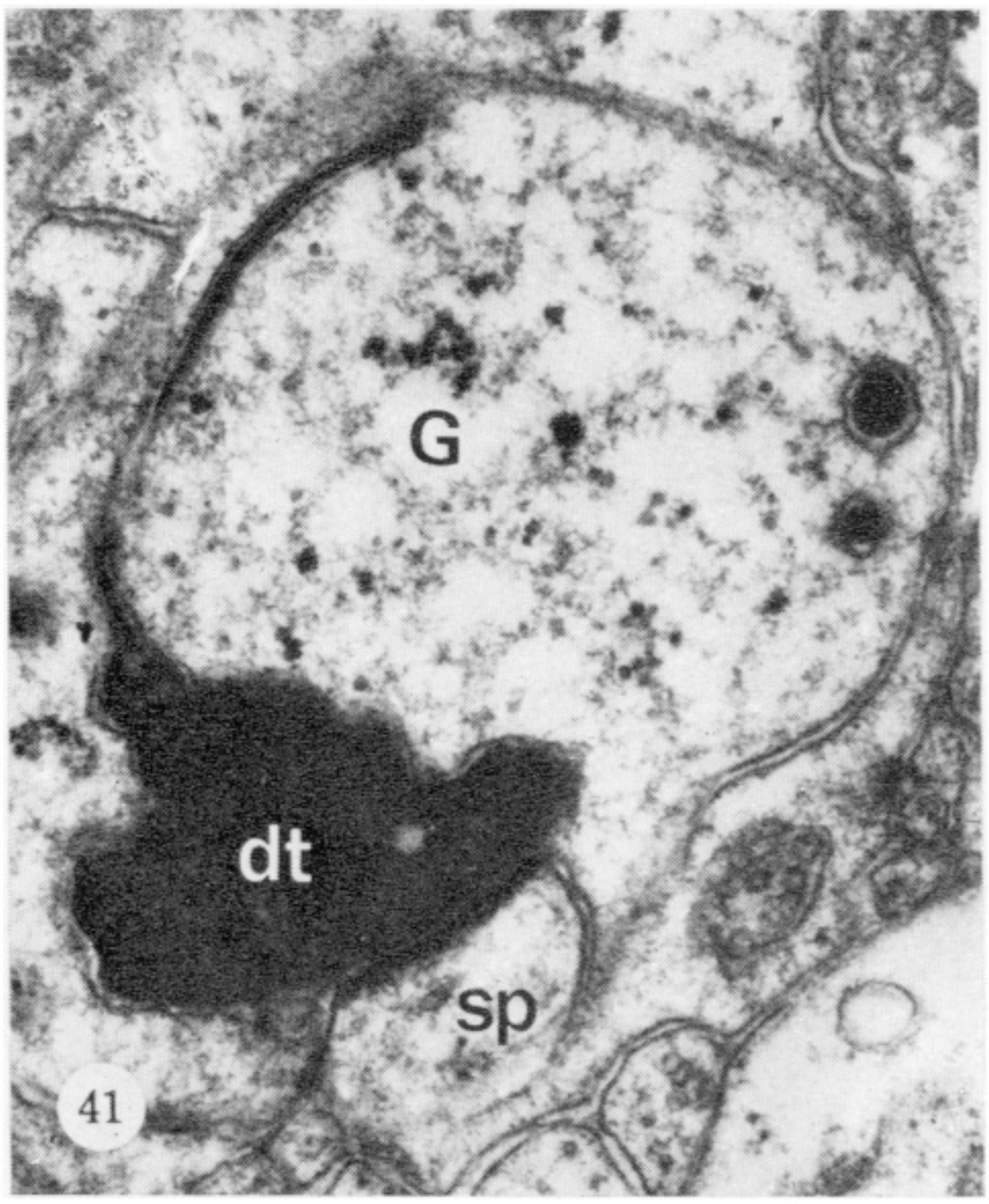


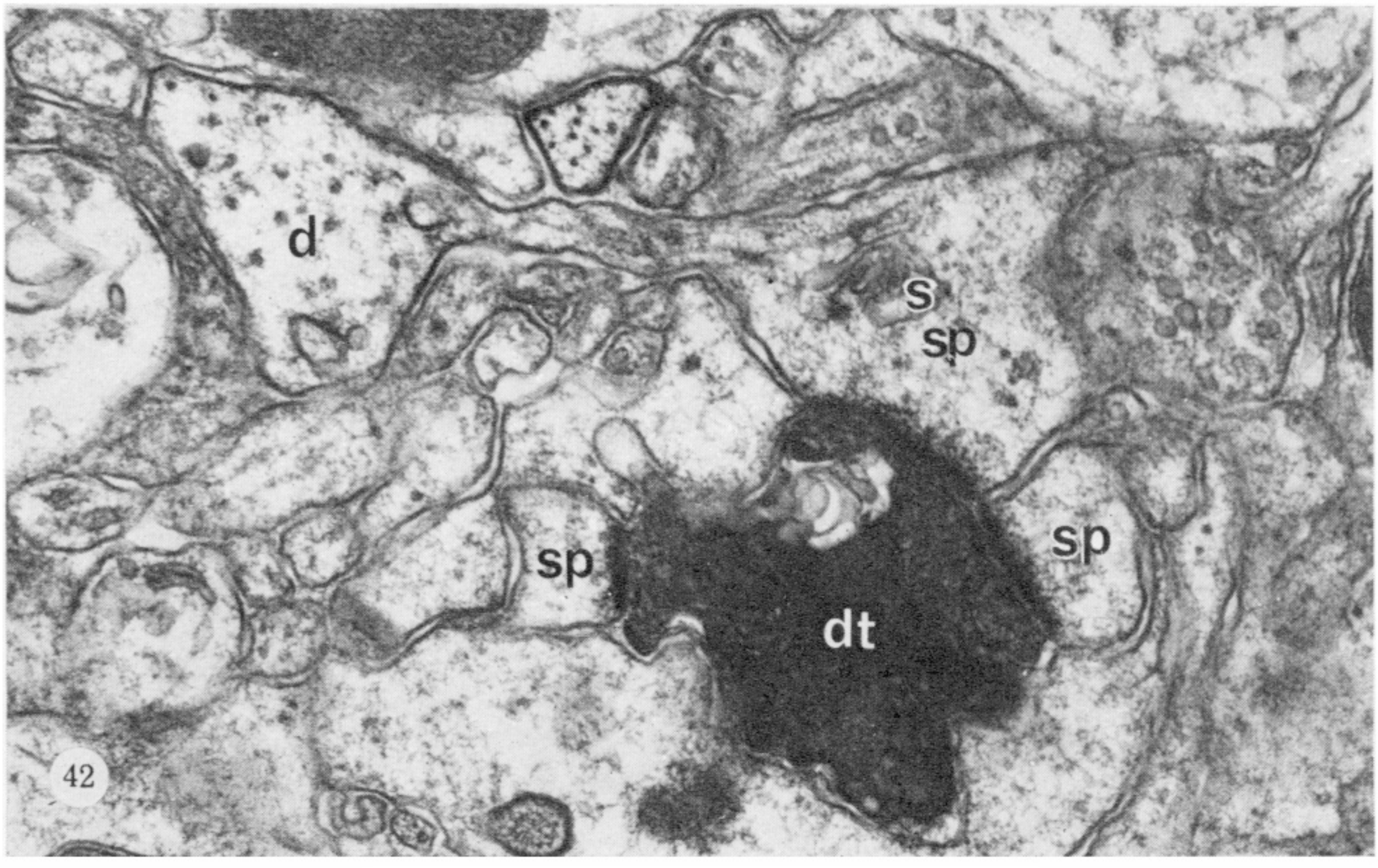


FIGURES 34–38. For description see opposite.

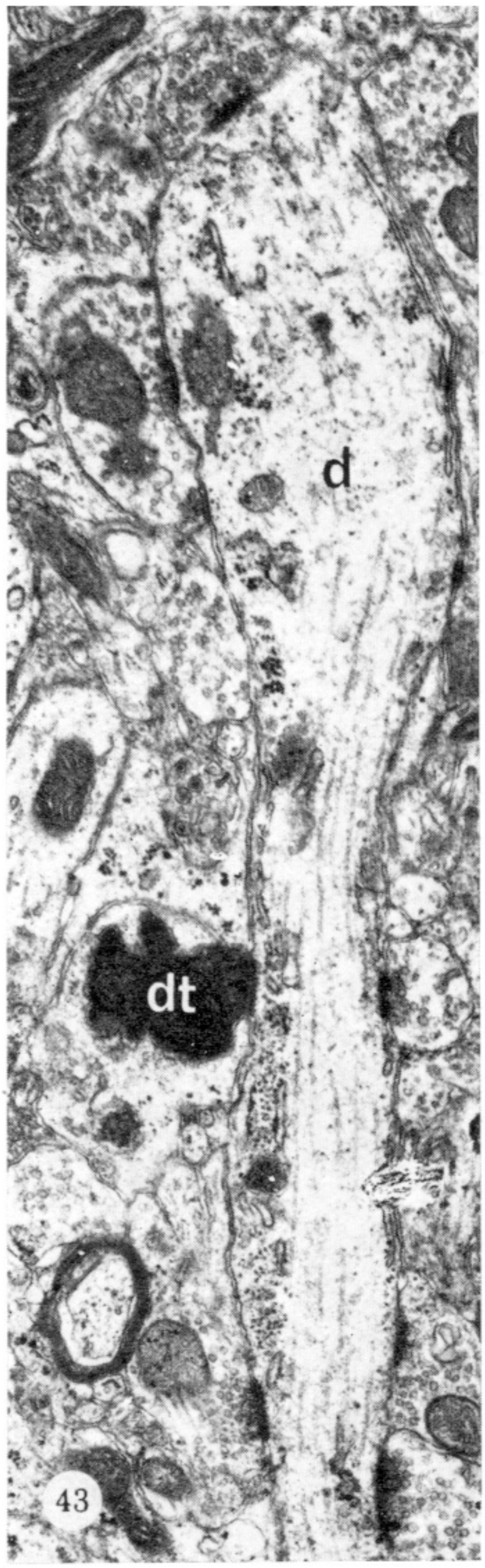




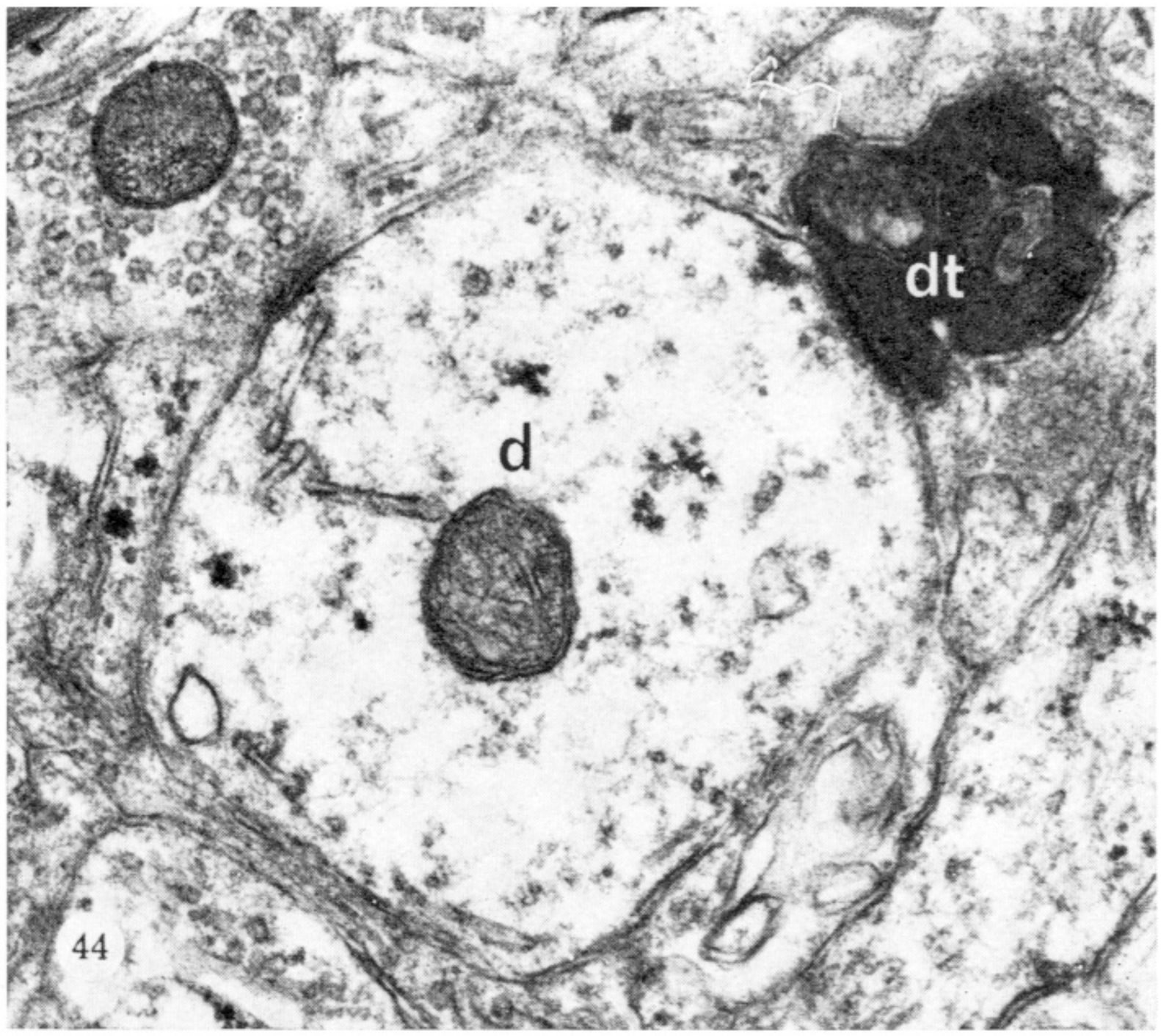




FIGURES 39–42 For description see opposite.



43



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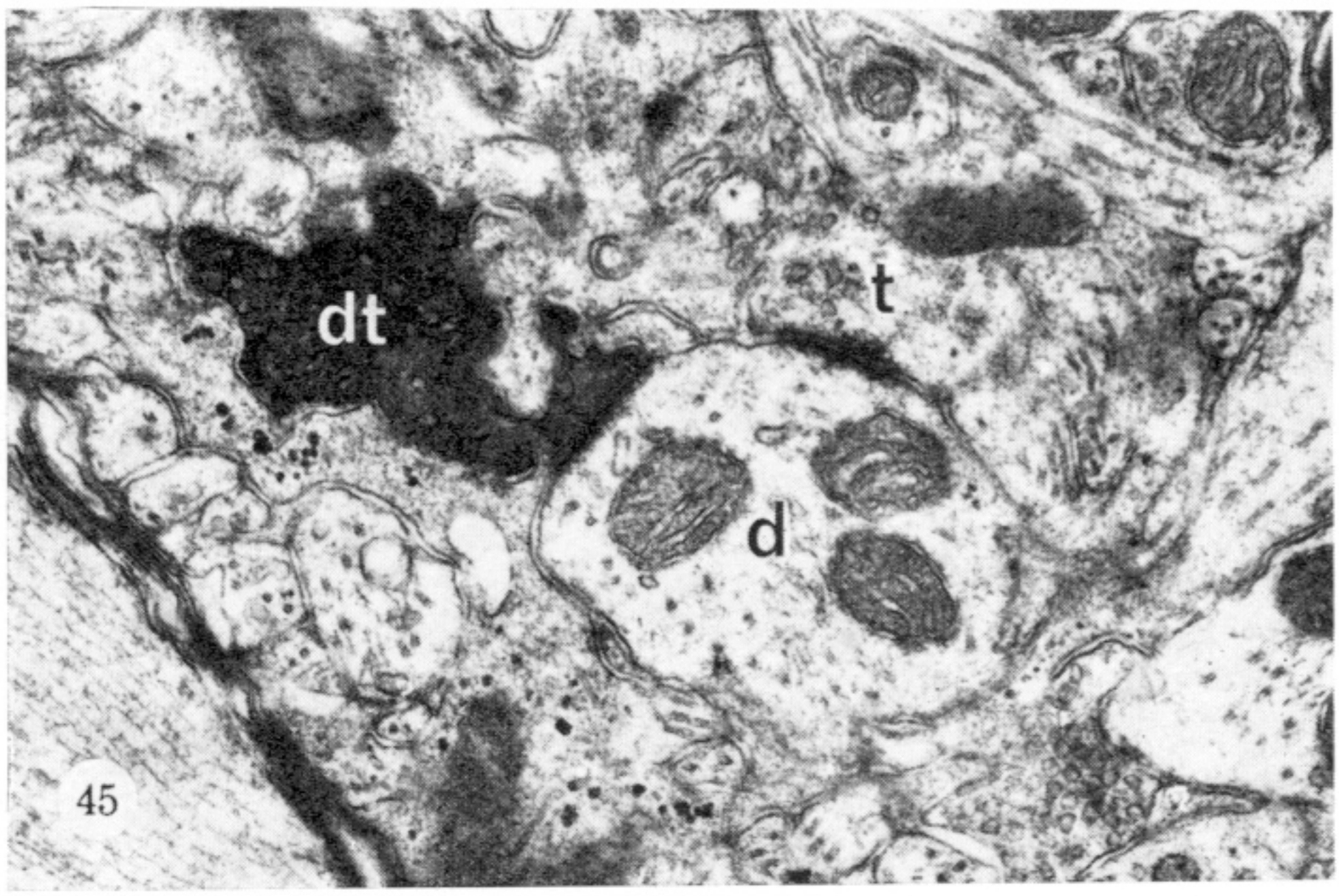

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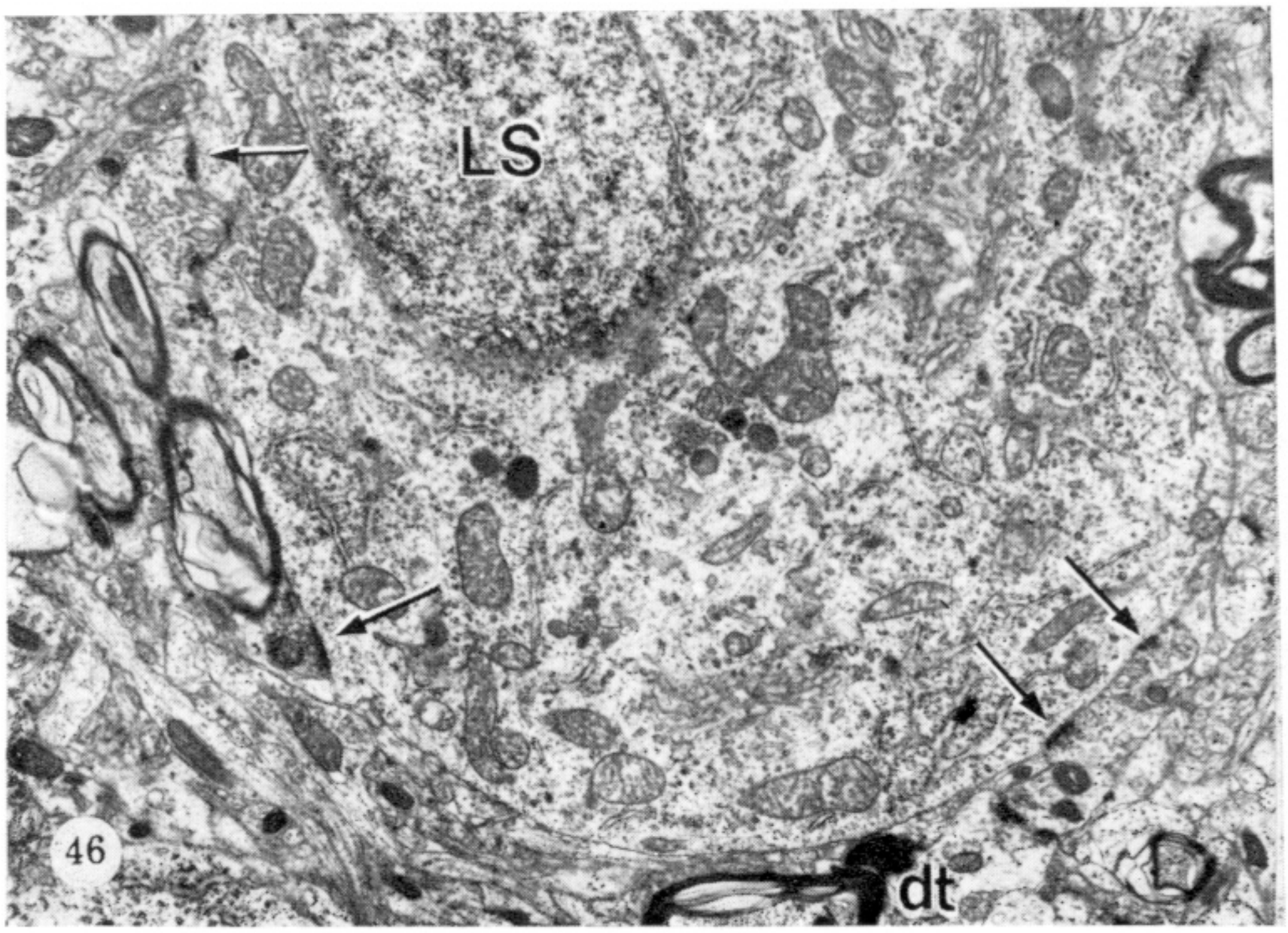

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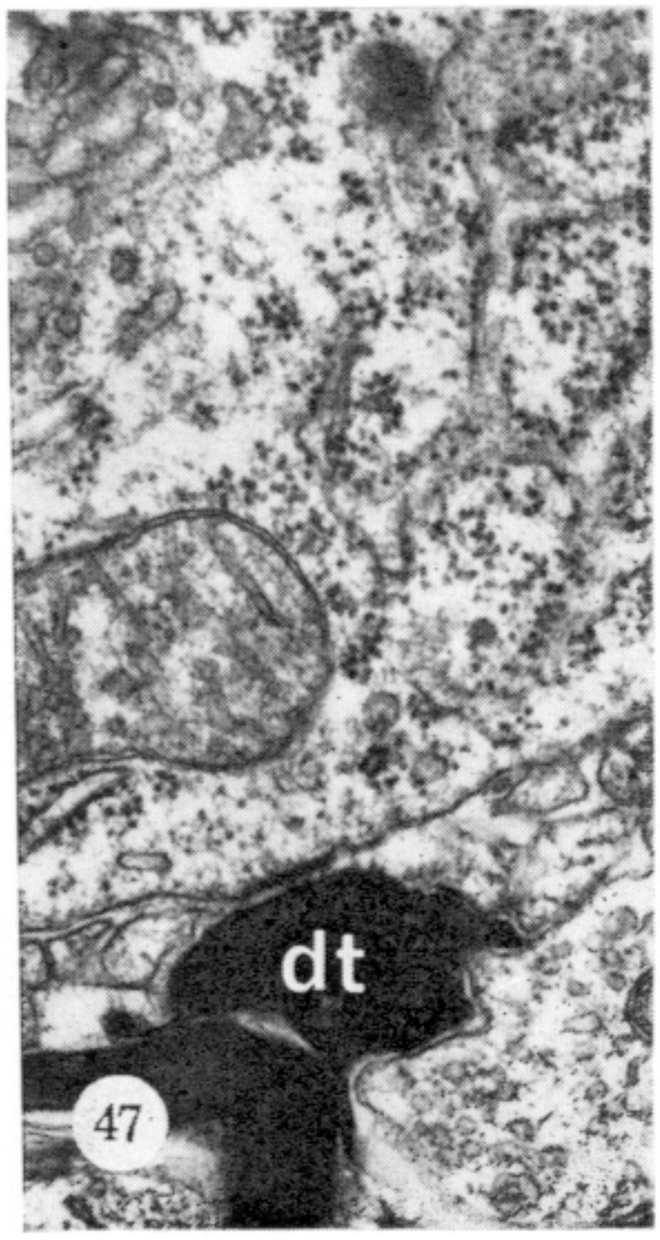

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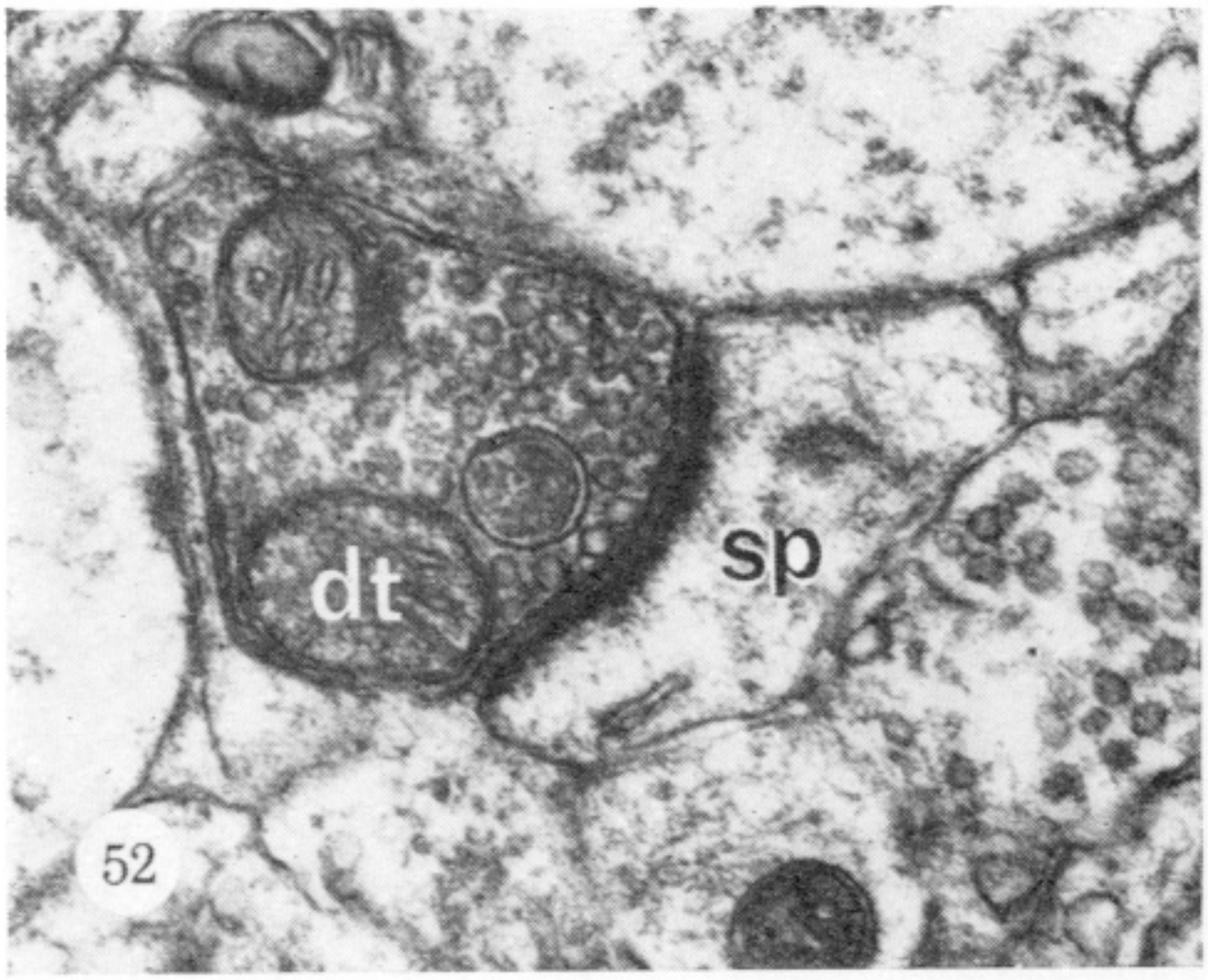
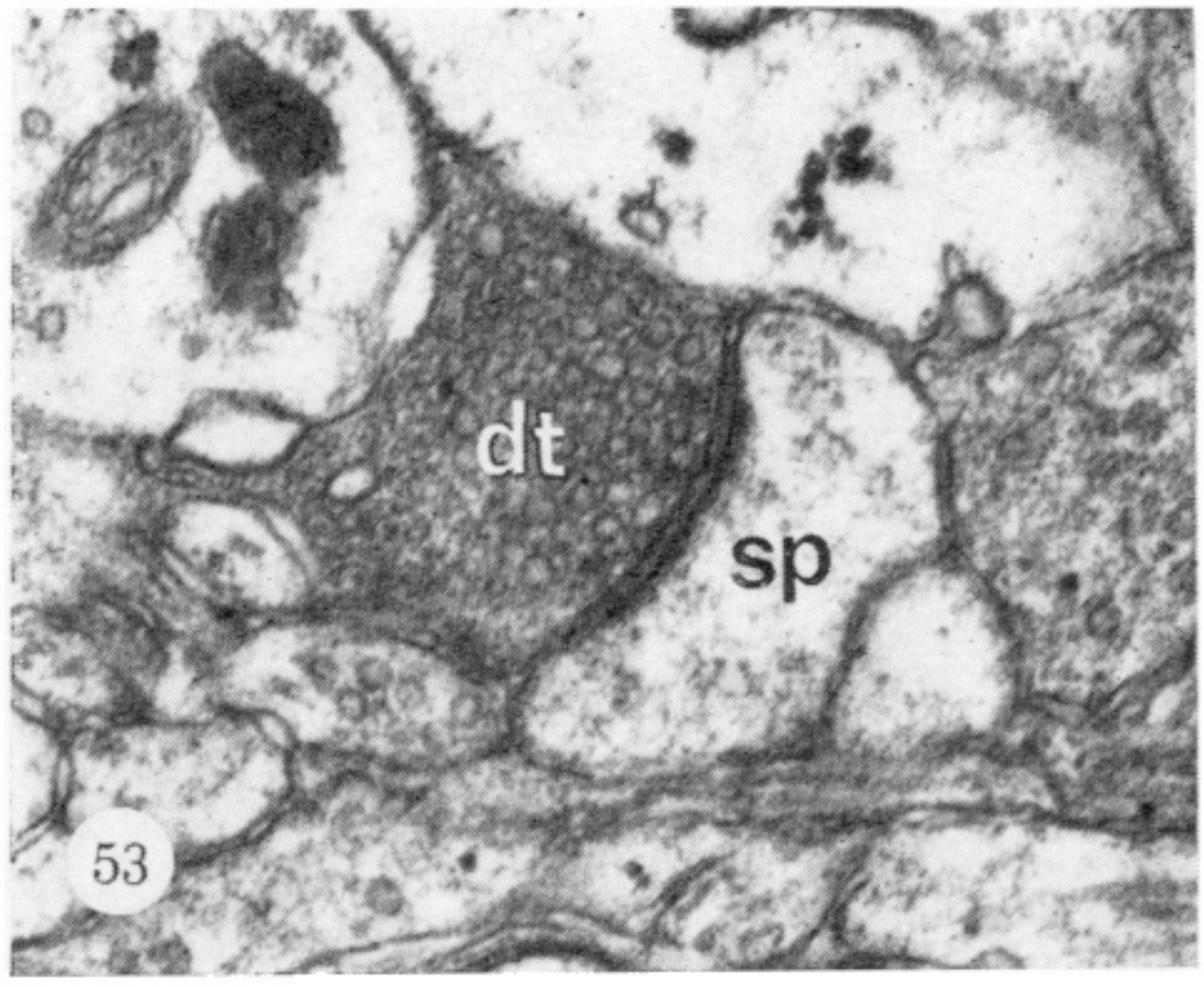
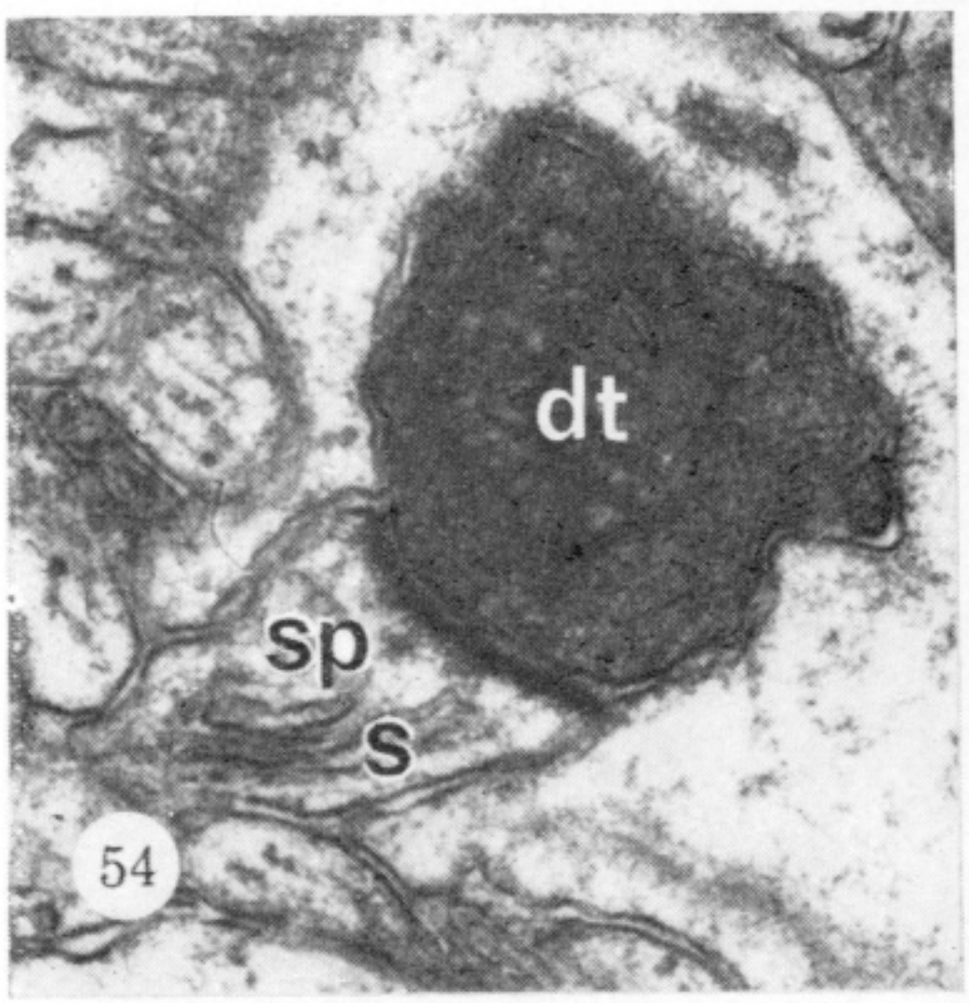
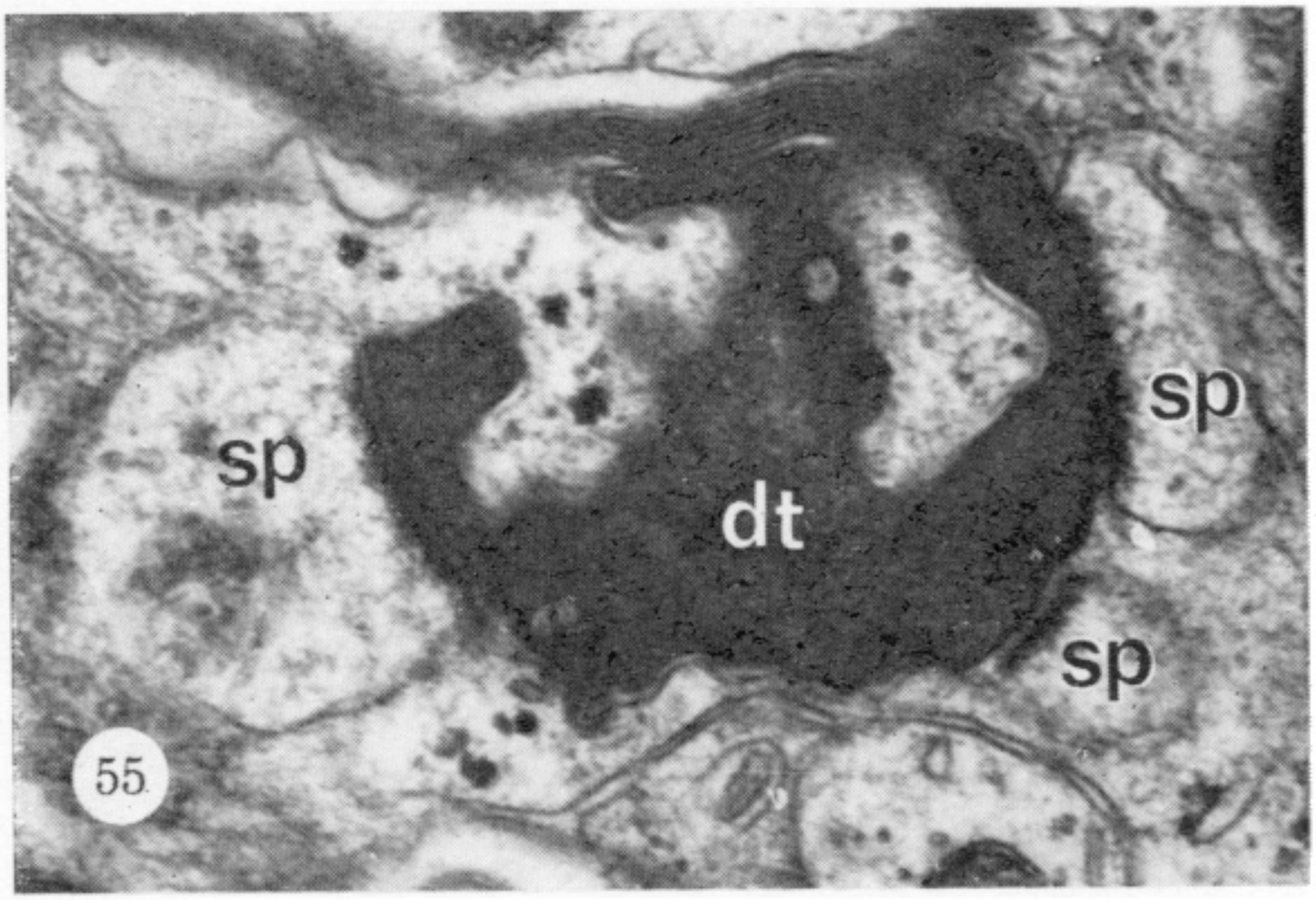
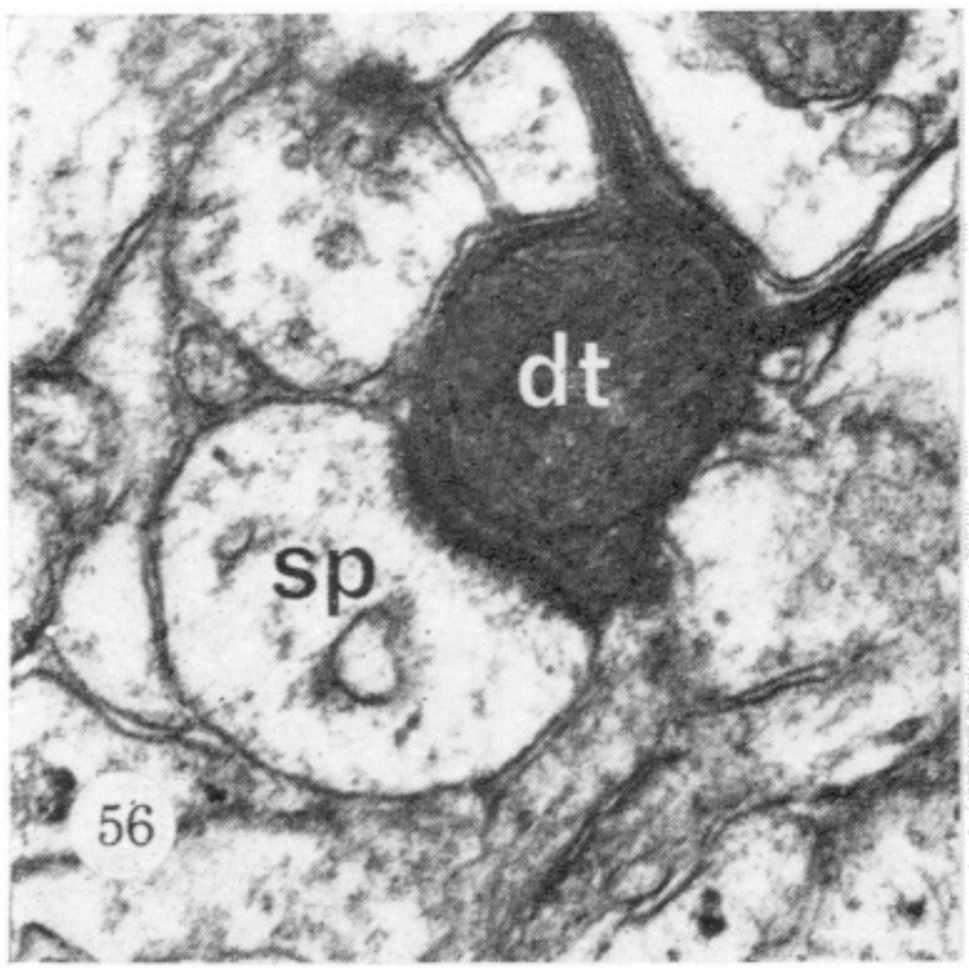
FIGURES 43–47. For description see page 212.

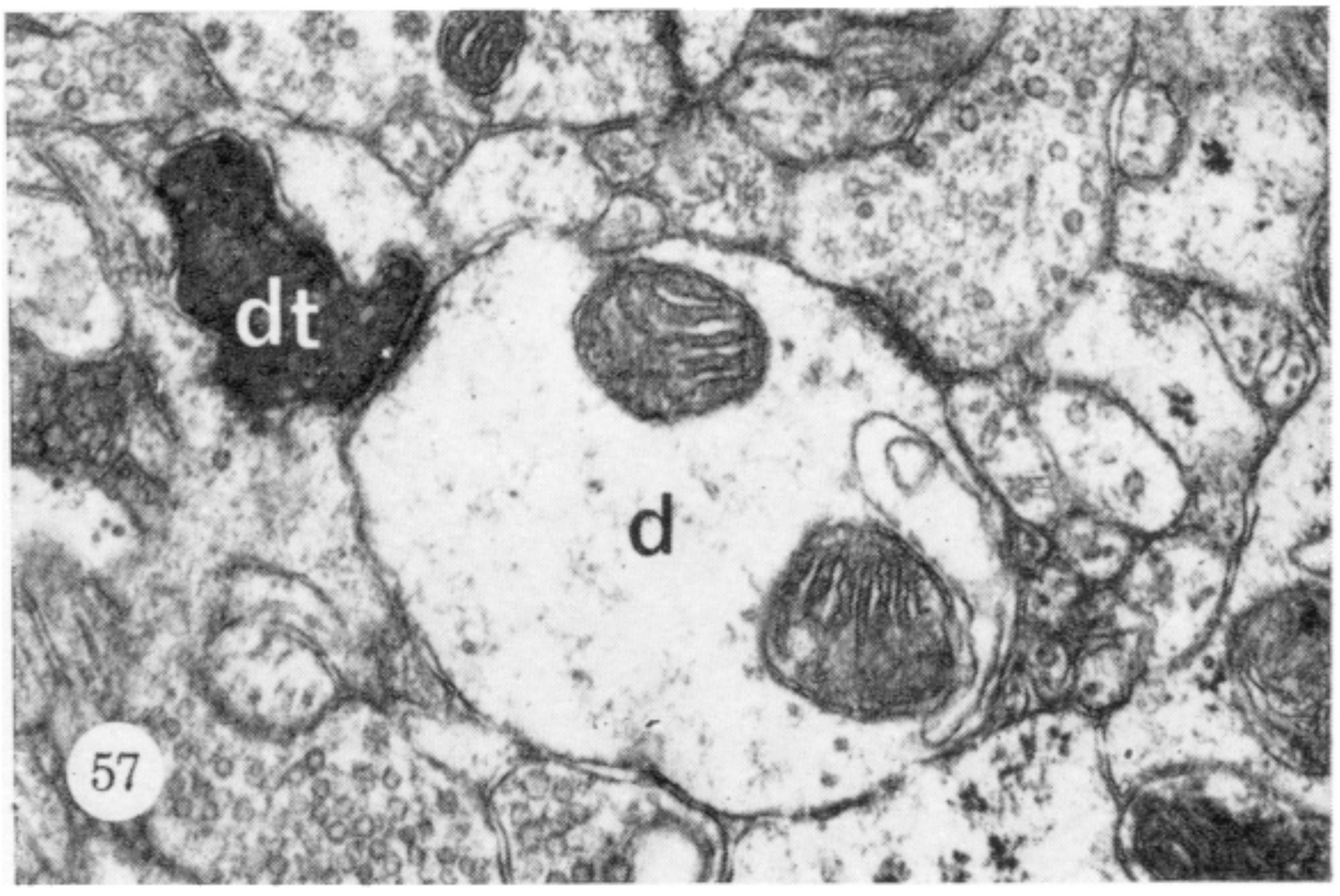




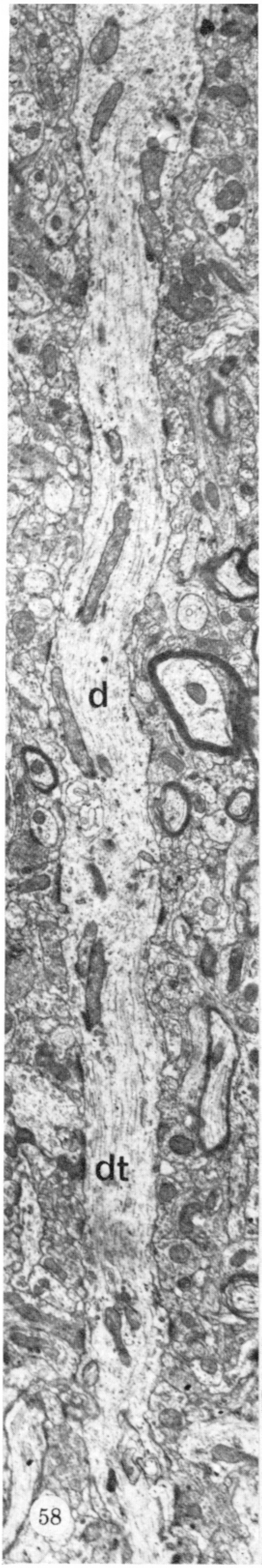


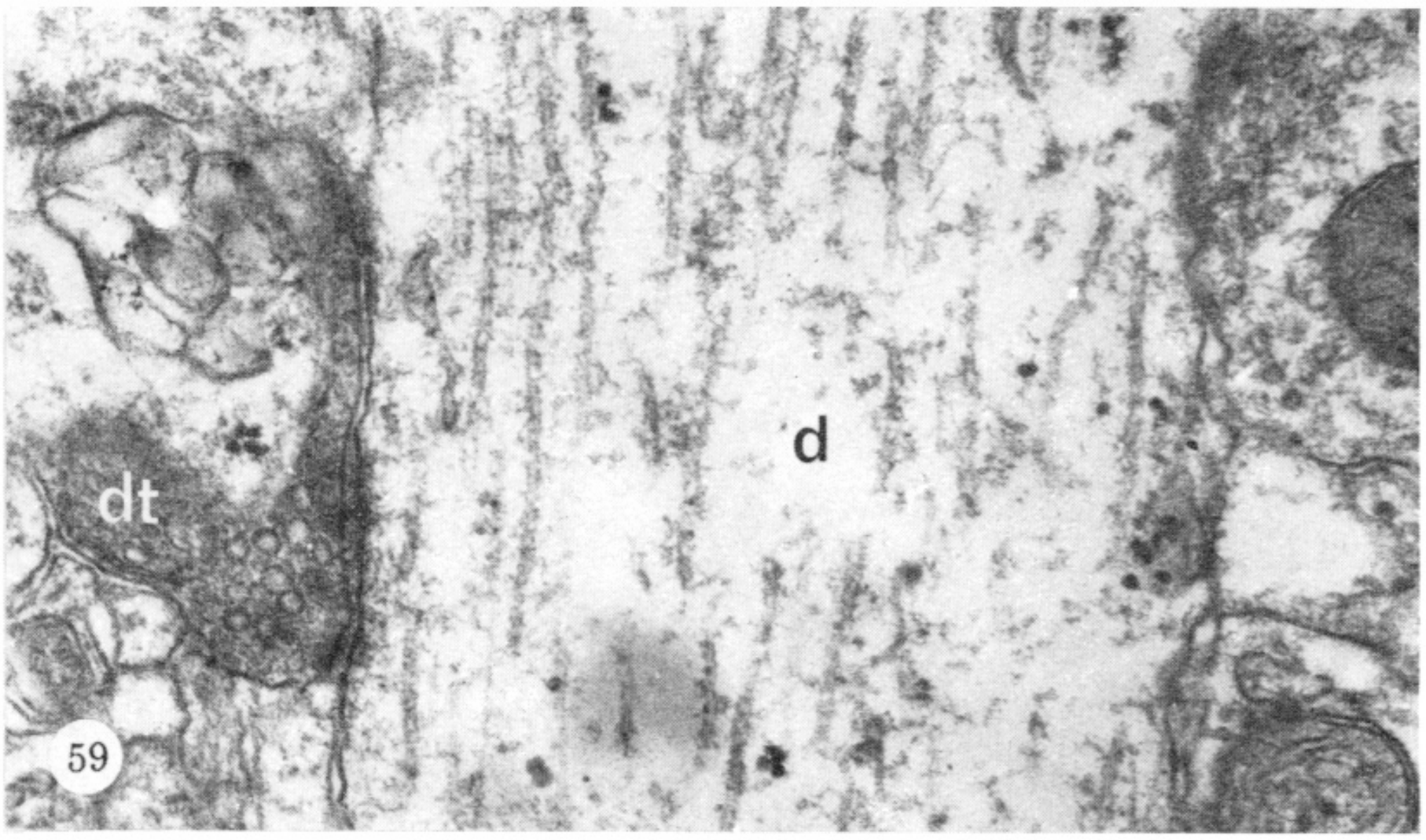


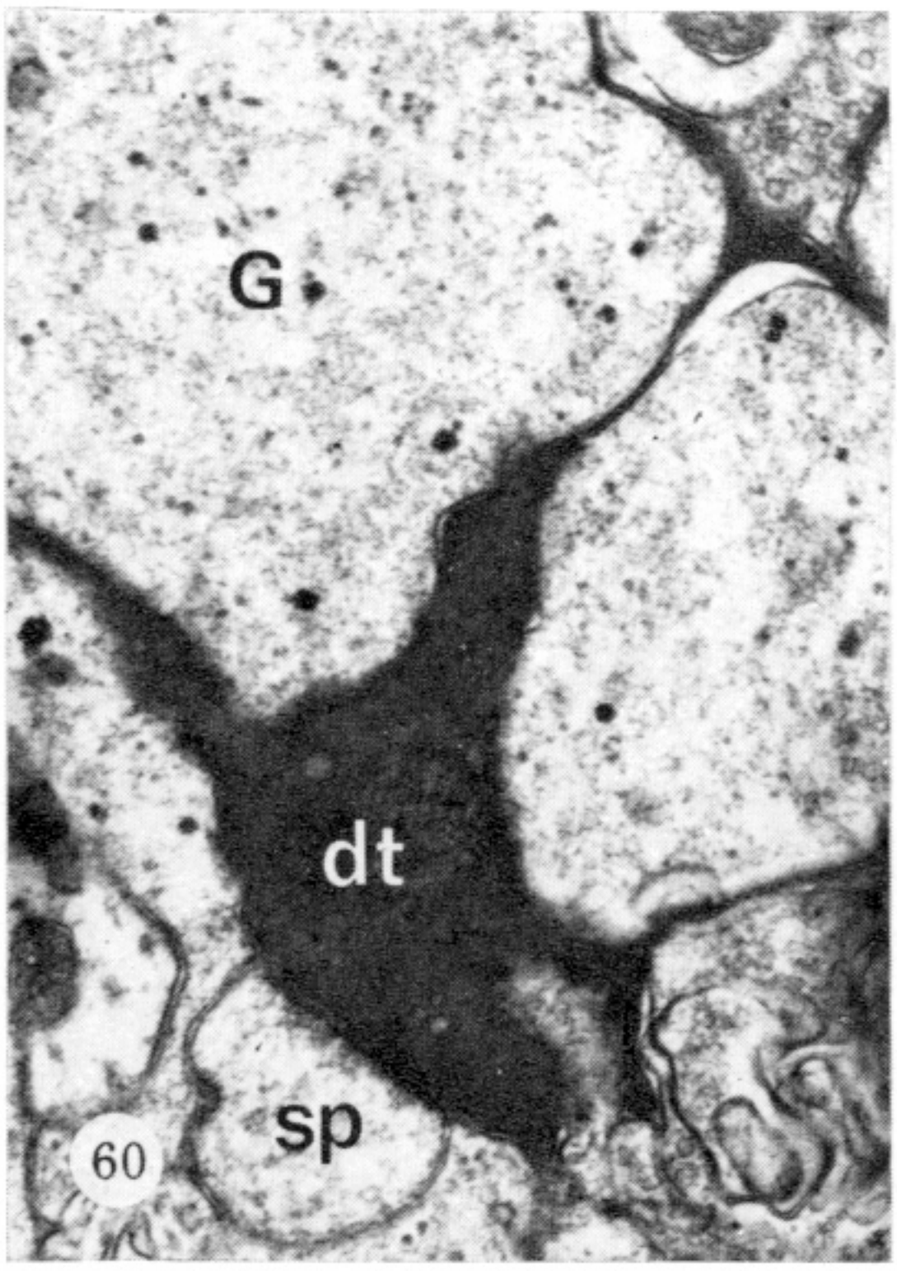


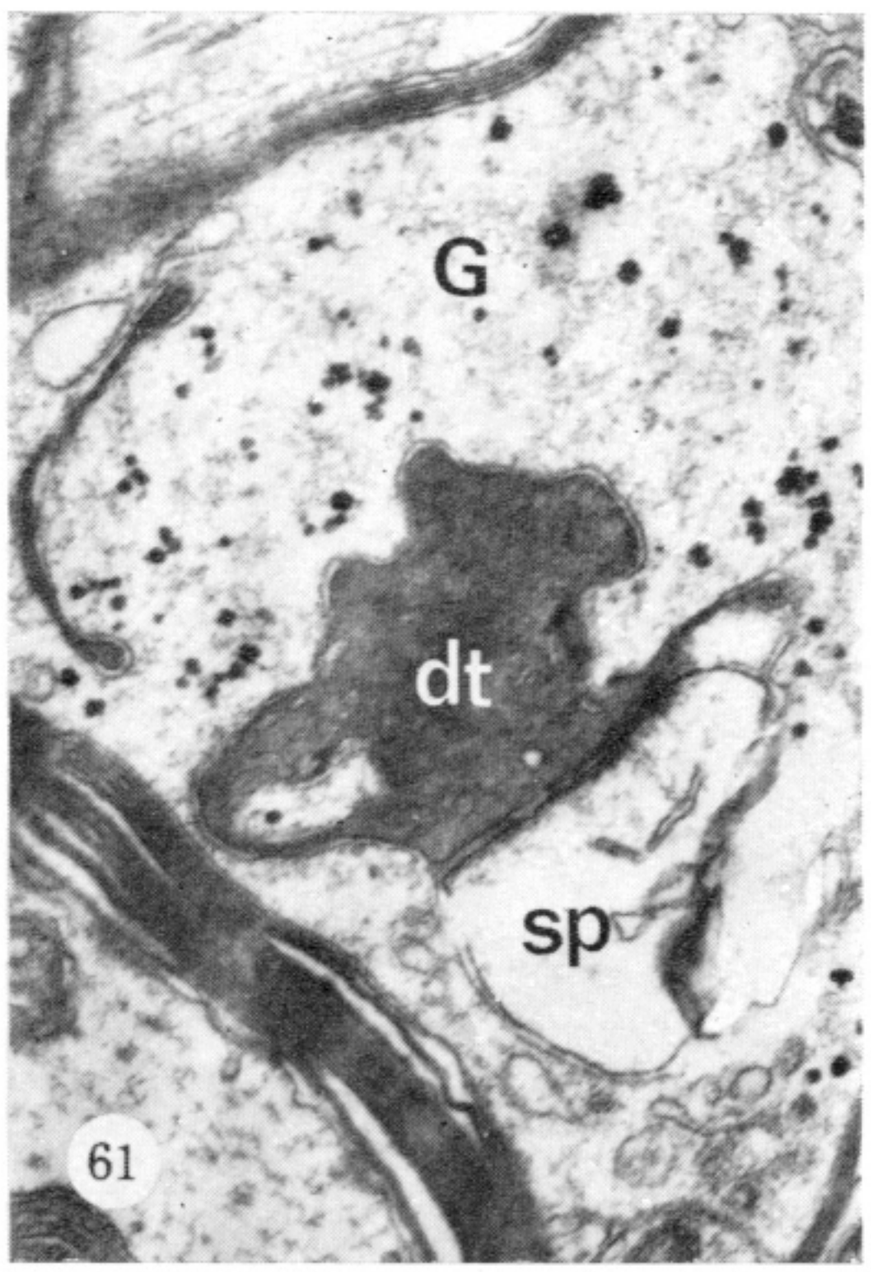


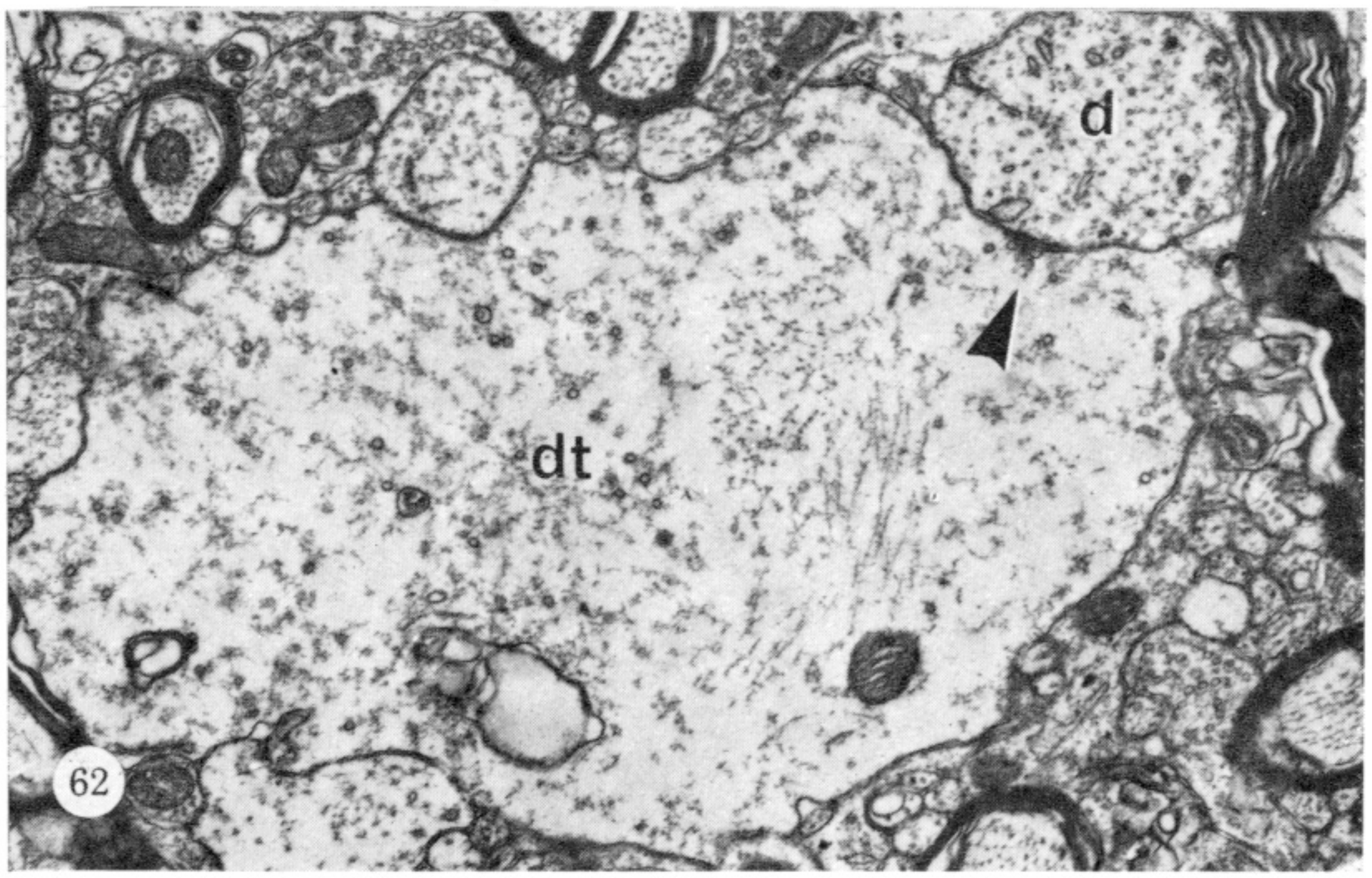
FIGURES 52–57. For description see page 213.











FIGURES 58–62. For description see opposite.