Morphological and Morphometric Studies with the Electron Microscope on the Merkel Cells and Associated Nerve Terminals of Normal and Denervated Skin*

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Summary. Merkel cells and associated nerve endings of dog snout skin as well as foot and toe pads of rats were studied with the transmission electron microscope. Normal Merkel cells are characterized by the following morphological features: 1) localization restricted to the basal layer of the epidermis, 2) adjoining afferent nerve endings containing many mitochondria, 3) specific small round granules usually accumulated in the cytoplasm on one side of the nucleus facing the junction of the nerve ending, 4) highly lobulated irregular shape of the nucleus, 5) well developed Golgi apparatus with a few immature granules situated on the side of the nucleus opposite the junction at the ending, 6) spine-like processes extending from the cell surface where no nerve endings abut, 7) desmosomes and desmosome-like membrane thickening on the cell surface both abutting the surrounding keratinocytes and the nerve endings.

The Merkel cells with nerve endings were observed and measured at various days after denervation. The experiments were carried out on rats whose sciatic nerves were transected. The samples of skin of foot and toe pads of the denervated legs were taken almost every day from 1 to 30 days. Almost no changes were noticed after 24 hrs, but within the next day the nerves retracted and were no longer observed in the epidermis. The Merkel cell granules increased in number in 1-3 days but decreased again to about a half of the value of the control at 30 days. The polarity of granule distribution showing a strong accumulation in the cytoplasm near the nerve ending became less marked after denervation. Some cells sustained severe degeneration in the later stage of experiment.

It was remarkable that the activity of Merkel cells might depend on the associated nerves, but they never completely disappeared even after a long period of denervation.

* The authors wish to dedicate this paper to the late Professor W. Bargmann, who repeatedly gave kind encouragement and helpful criticism for about twenty years on many occasions through the first author's career in microanatomical studies.

The substance of this paper was presented at the workshop of the 15th International Congress of Dermatology in Mexico City 1977, at the 83rd Annual Meeting of the Japanese Association for Anatomists at Ube 1978, and at the 9th International Congress on Electron Microscopy in Toronto 1978. Furthermore, the first author gave a seminar at the Department of Anatomy, University of Kiel in Germany on December 7, 1977 on the methods and results of morphometry on the electron microscopic level including this study and some other results in research on hypothalamic neurosecretion. It was the last chance for the author to have discussions with Professor W. Bargmann about mutual results of ultrastructural studies on nervous tissues.

In spite of these great numbers of ultrastructural studies, the Merkel cell still retains several points of unsolved problems. For example, the direct evidence of the receptor function of Merkel cells has not been demonstrated, although the close contact of the cell to the nerve ending strongly suggests this. The chemical nature of the substance filling the specific granules of this cell has not been clarified. The origin of this specific cell type among various cells of the epidermis has been debated for a long time and is not yet fully settled. For instance, Munger (1965), Kurosumi et al. (1969), Smith (1970) and English (1977b) said that the Merkel cells might be modified epidermal cells (keratinocytes), while others argued that the Merkel cells have migrated from the dermis or neural crest into the epidermis at a certain stage of development (Breathnach, 1971, 1977; Hashimoto, 1972; Winkelmann and Breathnach, 1973; Winkelmann, 1977).

Dependence of Merkel cells on the peripheral nerves which make close contact with the cells may be clearly shown by observation of the cell after transection of nerves that innervate the cells (Palmer, 1965; Smith, 1967; English, 1977a). Details of changes in Merkel cells after denervation, however, are to be studied more, because no pursuit of minute changes within frequent intervals after denervation has been performed. In the present study, further observations on the ultrastructure of normal and denervated Merkel cells are reported as well as the results of quantitative studies, of specific granules of the cells after the nerve transection. Detailed discussions on the origin of Merkel cells and the probable function of the cells are also given in this paper.

MATERIALS AND METHODS

Adult and young dogs as well as albino rats of Wistar strain were used for simple observation. Pieces of snout skin were taken from normal dogs and puppies. For denervation experiments, albino rats were used. They were anesthetized with intraperitoneal injection of Nembutal and the trunk of the sciatic nerve in the right hind leg was transected at the place immediate outside of the greater sciatic foramen. In order to prevent reinnervation during the period of experiment, about 0.5 cm of the nerve trunk was removed at the place of transection. After the surgery above mentioned, animals were sacrificed at 1, 2, 3, 5, 7, 10, 14, 20 and 30 days after denervation. The samples were removed from the foot and toe pads of the leg from which the sciatic nerve had been cut. Control samples were taken from the same places on the foot on the other side.

The specimens were doubly fixed with aldehyde mixture and osmium tetroxide.
The first fixative was either 2.5% glutaraldehyde buffered to pH 7.2 with 0.2 M cacodylate buffer or a mixture of 0.02% 2, 4, 6-trinitroresorcinol, 1.8% paraformaldehyde and 2.3% glutaraldehyde buffered with cacodylate, that is a slight modification of the method recommended by Ito and Karnovsky (1968). After 2 hr fixation with one of these primary fixatives, the samples were refixed with 1% osmium tetroxide buffered to pH 7.2 with cacodylate or phosphate buffer for about 1 hr. The embedding was performed into a mixture of Epon and Araldite. Polymerized samples were sectioned with a Porter-Blum MT-2B ultramicrotome with glass knives. Thin sections were stained with uranyl acetate and lead citrate. They were examined with a Hitachi HU-11D electron microscope with an accelerating potential of 75 or 100 kV.

Morphometry was performed on the micrographs at the final magnification of 15,000 times. The Kontron MOP/AM 01 system was used for planimetry and counting the number of granules. To determine the distribution pattern of granules in the cell, concentric circles or parallel lines with a distance of 5 mm each (corresponding to 3 μm when it was applied on the magnification of 15,000 times) were superimposed on the micrograph, setting a line or circle just upon the boundary between the Merkel cell and the associated nerve ending as a standard line. Zones with the constant width were thus made in the area of the Merkel cell, where the zones were parallel to each other and also to the boundary against the nerve terminal. These zones were named Zone 1, 2, 3 etc. starting from the zone at the boundary between the Merkel cell and nerve ending. The numbers of granules contained in each zone were counted and converted to the percent of the total number of granules in the cell. After denervation nerve terminals often disappear, but the setting of the standard line was done on the boundary of the cell that was thought to be the place on which the nerve ending had been attached before the operation, that usually corresponded to the basal surface of the Merkel cell.

RESULTS

1. Fine structure of Merkel cells and associated axons in normal skin

The morphological characteristics of the Merkel cell are as follows: 1) localization of the cell in the epidermal basal layer, 2) a close contact to the afferent nerve endings, 3) small round dense granules about 50 nm in diameter especially accumulated in the cytoplasmic area adjacent to the contiguous nerve ending, 4) irregularity of nuclear outline, 5) localization of the Golgi apparatus in the cytoplasm opposite to the nerve ending, 6) spine-like cytoplasmic processes extending to the intercellular space, often invading into the keratinocytes, and 6) desmosomes on the cell surface abutting the neighbouring keratinocytes.

The irregular outline of nucleus forming strong processes and deep indentations is one of the most striking characteristics of the cell (Fig. 1, 3). The nucleolus is not so large in size and often adheres itself on the inner surface of the nuclear membrane. Such an irregular shape of the nucleus is similar to that of the Langerhans cells, but it is not suggestive that the two cell types are related to each other, because other characteristics in the morphology of cytoplasmic structures including unique granules for each cell type are quite different between the Merkel cell and
Fig. 1. A Merkel cell (ME) of the snout skin of a puppy. The nucleus is highly lobulated. The cytoplasm basal to the nucleus is filled with abundant granules intermingled with mitochondria (M). Lipid droplets (F) are also seen. In the other side of cytoplasm, Golgi apparatus (G) and immature granules (arrow) are situated. The nerve ending (NE) is cup-shaped and contains many mitochondria (M) and lysosomes (L). Desmosomes (arrow heads) are observed along the cell surface. NL nucleolus, DE dermis. Ito and Karnovsky’s fixation. ×20,000
Fig. 2. A Merkel cell (ME) and associated axon (AX) of the snout skin of an adult dog. Schwann cell cytoplasm (SW) can be traced to the inside of epidermis (arrows). Mitochondria (M) and lysosomes (L) are seen in the cup-shaped ending. Granules are few in number, but the Golgi apparatus (G) is well developed. Many vesicles and tubules with or without dark internal substance are associated to the Golgi lamellae. Arrow heads indicate desmosomes. BM basement membrane, DE dermis. Glutaraldehyde and osmium fixation. ×16,000
After fixation with trinitroresorcinol-containing fixative followed by osmium postfixation resulted in dark staining of Merkel cell granules (Fig. 1, 3, 5-7), while the conventional method of double fixation with glutaraldehyde and osmium tetroxide may have caused the features of so-called cored vesicles for most of the specific granules of this cell (Fig. 2). In the normal state the granules are distributed preferentially in the cytoplasmic area facing the adjacent nerve ending.

The Golgi apparatus is always localized in the cytoplasm of the other side of the nucleus opposite to the nerve ending. They comprise several stacks of lamellated sacs. Among the stacks, ribosome-rich cytoplasmic matrix is inserted and holds the entire Golgi field. It contains mitochondria, lysosomes and a few immature granules, which look like cored vesicles even after fixation with trinitroresorcinol-containing fixative (Fig. 1, 3). Small vesicles are often accumulated near the Golgi stacks, and sometimes a dark substance fills some of the vesicles and tubules, which may be formed by coalescence of vesicles (Fig. 2). They are probably primary lysosomes. Multivesicular bodies are also observed (Fig. 1). Cytoplasmic filaments are almost evenly distributed in the Golgi area.

The rough endoplasmic reticulum is very poorly developed in this cell type, namely a few tubules or vesicles studded with ribosomes are randomly distributed in the cytoplasm. They have no preferential distribution like the Golgi apparatus and specific granules in the cell. Mitochondria are mostly elongate and contain a relatively dark matrix and a few cristae which are often arranged in oblique position. A few lipid droplets are observed (Fig. 1).

Cytoplasmic filaments are variable in amount. They are clearly shown in Merkel cells of a dog fixed with glutaraldehyde and osmium (Fig. 2). They are seen not only in the Golgi region but also found in the cytoplasm near the attachment to the nerve ending. They form loose bundles, but they are very scarce as compared to the tonofilbrils (tonofilament bundles) in the keratinocytes.

Merkel cells often extend spine-like processes. These spines arise from the surface of the other side of the cell than that associated with a nerve terminal. They often penetrate the neighbouring keratinocytes (Fig. 3-5). Because the cytoplasm of a Merkel cell is lighter than that of the keratinocytes, it is easy to find profiles of Merkel cell processes embedded in the dark cytoplasm of keratinocytes. Microfilaments of the cytoplasm are continuous to those in the spines, but their amount is not ample (Fig. 4). They are usually oriented parallel to the long axis of the spine. The spines never contain any other organelles or inclusions except for filaments. On the surface of spines no desmosomes develop, but they appear at the bottom of the interspinous pits. These spines look straight and strong. As they extend usually towards the skin surface on which mechanical pressure may be applied, external force may bend the spines and stimulate the cell. Therefore, the spines may play a role in sensory reception of mechanical stimuli.

Between the Merkel cell and the keratinocytes surrounding it many desmosomes are observed (Fig. 1-5), though the size and complexity in structure are a little lower than the typical desmosomes occurring between two adjacent keratinocytes.

When the nerve fiber penetrates the epidermis, the Schwann cell sheath disappears just after entry into the epidermis (Fig. 2). The basement membrane covering the Schwann cells is continuous to the membrane of the same nature along the
Fig. 3. A Merkel cell (ME) in the foot pad skin of a normal rat. A darkly stained nucleus is quite irregular in shape. Granules are arranged along the boundary between the Merkel cell and nerve ending (NE), which is watery clear and contains mitochondria (M) and vesicles of various sizes. Desmosomes (arrow heads) are seen on the cell surface. Many spines (S) extend to the surrounding epidermal cells. G Golgi apparatus with immature granule (arrow), DE dermis with collagen bundles. ITO and KARNOVSKY's fixation. ×15,000
basal surface of the utmost basal cells of the epidermis. Immediate after penetration in the epidermis, the axon becomes swollen and flattened to form a cup-like shape attaching the lower surface of the Merkel cell, as if the nerve terminal supports the cell (Fig. 1, 2).

The cytoplasm in the axons and endings is watery clear, but contains microfilaments and microtubules (Fig. 1–3, 5–7). In the expanded portion at the final ending, many mitochondria are accumulated. Most of them are elongate, worm-like and closely packed together. A few empty vesicles of various sizes are observed, but they are mostly larger than the so-called synaptic vesicles found in the efferent nerve terminals. There are some spots of membrane thickening at the boundary between the nerve ending and the Merkel cell (Fig. 1), but no accumulation of vesicles in these spots could be observed. The morphological characteristics of Merkel cell-associated nerve terminals, that is, ample mitochondria and absence of synaptic vesicles, may suggest the nature of this ending to be afferent. The endings often contain moderate-sized dense bodies which may be identified as lysosomes. Lysosomes are often found in a heap of mitochondria.

In some cases, a variety of unusually shaped nerve endings could be found both in the normal control and 1 day after operation (Fig. 5–7). It is not likely that these unusual forms of nerve endings are the results of denervation, because they also

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Fig. 4. The upper half of a Merkel cell (ME) of a normal rat. A few granules (arrows) and mitochondria (M) are seen in the apical cytoplasm. Many spines (S) extend and pierce the neighbouring keratinocytes (KE). Desmosomes (arrow heads) are seen at the bottom of interspinous pits. ITO and KARNOVSKY's fixation. ×16,000
appear in the normal control state of the rat. In rare cases two endings are formed for one Merkel cell (Fig. 5, 7). In such a case, the Merkel cell stands up perpendicularly to the basement membrane, and the endings are seen on both sides of the cell (Fig. 5). In the case of Fig. 5, however, the main ending is on the left-hand side and that on the right-hand side may be accessory, because specific granules are accumulated on the left ending but no granule accumulation is found on the right-hand side. Furthermore, the Golgi apparatus is situated on the right-hand side of the cell.

Fig. 5. A Merkel cell (ME) with two nerve endings (NE) from the skin of foot pad of a normal rat. Granules are accumulated near the ending on the left-hand side, while Golgi apparatus (G) with immature granules (arrows) is situated in the cytoplasm on the right-hand side. Typical desmosomes (arrow heads) are developed at the junction between the Merkel cell and the adjacent keratinocytes (KE). M mitochondria, L lysosomes, S spines, DE dermis. 1	no and KARNOVSKY's fixation. ×13,000
Fig. 6. Unusual form of nerve ending (NE), surrounded by the cytoplasm of a Merkel cell (ME), from the rat foot pad 1 day after denervation. The ending is strongly expanded and contains many mitochondria (M) and lysosomes (L). Microfilaments and vesicles are also found. Merkel cell granules are scattered around the perimeter of the nerve ending. KE keratinocytes, BM basement membrane, DE dermis. ITO and KARNOVSKY's fixation. ×12,000
An axon may penetrate a Merkel cell and expand within the cell. In such a case, cytoplasm of the Merkel cell almost completely surrounds the irregularly expanded nerve ending (Fig. 6). Accumulation of granules may be found in some places around the ending. The nerve fiber makes several swellings along its course and probably makes contact with two or three Merkel cells (Fig. 7). That is a case of the so-called synapse en passant (De Robertis, 1964) of afferent nerve fibers.

2. Changes in fine structure of Merkel cells and associated axons after denervation

One day (about 24 hrs) after transection of the sciatic nerve, the Merkel cells and associated nerves in the foot and toe pads are not remarkably altered. Only one noticeable change in the Merkel cell structure at 1 day denervation is considerable increase in the number of specific granules (Fig. 6, 7), but it decreased again several days after surgery (Fig. 8, 9). Even after several days, the Golgi apparatus of the Merkel cell is still considerably well developed and immature granules are observed in the Golgi region (Fig. 8). This suggests that the Merkel cell continues granule production after denervation, though to a lesser extent.

The nerve endings at 1 day after denervation showed almost no changes. Slight increase of lysosomes in size and number was noticed. After 2 days, however, the nerve endings completely disappeared from the epidermis. This change was very prompt and abrupt, it probably occurred at a moment between 24 and 48 hrs after the operation. Nerve fibers and endings with or without relation to Merkel cells were

Fig. 7. Two Merkel cells (ME) connected with a common nerve ending (NE) from the foot pad skin of 1 day denervated rat. The Merkel cell on the left-hand side has two nerve endings which might be continuous in another level of section. Many spinous processes (S) penetrate the surrounding keratinocytes (KE). DE dermis. ITO and Karnovsky's fixation. ×12,000
no longer observed from this point of postoperative time. Such an abrupt and complete disappearance of nerve fibers indicated that the change might be neither degeneration nor necrosis of nerve fibers, but it had probably been retracted away to some extent into the dermis or adjacent underlying tissue. It may be conjectured that the axons might be severely damaged after retraction. Degenerated nerve fibers with damaged myelin sheaths were found in a deeper portion of subcutaneous tissue, but neither degenerated nor normally structured nerve fibers could be found in the dermis closely subjacent to the epidermis containing the Merkel cells. It is in striking contrast that the nerve endings completely disappeared so early in the course of the denervation experiment, while the Merkel cells themselves were almost intact even to 20 or 30 days as well as immediately after denervation (Fig. 10).

A few Merkel cells in some later stages of denervation experiment sustained severe degeneration. For example, a Merkel cell show in Figure 11 appeared to be
damaged, i.e., its nucleus was pycnotic, the cytoplasm was also dark, but mitochondria were vacuolated (very clear). A large vacuole containing glycogen-like particles was observed.

3. Changes in numerical density and distribution pattern of Mekel cell granules after denervation

The number of granules of each Merkel cell was counted, and the area of cytoplasm was measured using Kontron morphometric apparatus. The numerical density of granules was calculated by dividing granule numbers by the area of the cytoplasm. Changes in numerical density of Merkel cell granules are demonstrated in both Table 1 and Figure 12. It was evident that the numerical density of granules significantly increased at 1–3 days, while it showed gradual diminution especially at 7 days.

Fig. 10. A Merkel cell (ME) of the rat foot pad skin 20 days after denervation. No nerve fibers are found. Even in this stage considerable numbers of granules are contained. Mitochondria (M) are also numerous. KE keratinocytes, BM basement membrane. Ito and KARNOVSKY's fixation. ×9,000

Fig. 11. A Merkel cell (ME) of the rat 30 days after denervation. No nerve endings can be observed. The cell sustained a marked degeneration characterized by pycnosis of the nucleus, dark cytoplasm and vacuolated mitochondria (M). A large vacuole (V) filled with less dense particles is observed. KE keratinocytes, BM basement membrane, DE dermis. Ito and KARNOVSKY's fixation. ×11,000
as well as 30 days. The numerical density of granules at 30 days was about a half of that of the control, and about one third of the increased number of granules at 1 day after denervation.

The Merkel cell cytoplasm was divided into zones by a series of straight or curved imaginary lines parallel to each other and also to the boundary between the cell and nerve ending. Zone 1 is the nearest part to the nerve ending and Zone 2 is the next. In normal state the granules are markedly gathered to Zones 1 and 2, but sharply decrease as the zone transits far away from the ending (Fig. 13). A small elevation at Zone 7–8 indicates the site of the Golgi apparatus, where granules of rather immature stage are accumulated. Such a remarkable polarity of granule

<table>
<thead>
<tr>
<th>Condition (Days after denervation)</th>
<th>Numerical densities of granules (Number/μm²)</th>
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<tbody>
<tr>
<td></td>
<td>Mean ± S.E.</td>
</tr>
<tr>
<td>Control</td>
<td>3.47 ± 0.43</td>
</tr>
<tr>
<td>1 day</td>
<td>5.24 ± 0.65*</td>
</tr>
<tr>
<td>2 days</td>
<td>3.64 ± 0.86</td>
</tr>
<tr>
<td>3 days</td>
<td>4.03 ± 0.92</td>
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<tr>
<td>5 days</td>
<td>3.29 ± 0.52</td>
</tr>
<tr>
<td>7 days</td>
<td>1.45 ± 0.29**</td>
</tr>
<tr>
<td>10 days</td>
<td>2.83 ± 0.54</td>
</tr>
<tr>
<td>14 days</td>
<td>3.47 ± 0.54</td>
</tr>
<tr>
<td>20 days</td>
<td>2.47 ± 0.58</td>
</tr>
<tr>
<td>30 days</td>
<td>1.79 ± 0.29***</td>
</tr>
</tbody>
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* p < 0.05, ** p < 0.001, *** p < 0.005 vs control

Fig. 12. Fluctuation of numerical densities of rat Merkel cell granules after denervation. Mean values with standard errors on each step of the experiment are shown, and also the numerical density of granules of each cell examined are plotted in order to show the width of variation.
distribution was still observed shortly after denervation, but became less marked as the postoperative time lasted. A small elevation at the position of Golgi apparatus almost disappeared after denervation (Fig. 13). These results may indicate that the preferential distribution of granules of Merkel cell depends on the presence of a contiguous nerve ending.

**DISCUSSION**

Since the first description by Merkel (1875) this specific cell in the epidermis has been known to be closely related to the nerve fiber and assumed to be one of the mechanoreceptors of skin. The presence of specific dense granules is the most salient feature of this cell as observed by electron microscopy first reported by Cauna (1962). It was suggested that these granules might be secreted from the cell and initiate the nerve impulse in the adjacent afferent nerve ending (Munger, 1965). Mustakallio and Kustala (1967) suggested that the Merkel cell might produce monoamines from the morphological resemblance to the adrenal medullary cells. However, Munger (1965) failed to demonstrate positive results for detection of chromaffin reaction and of catecholamines. Kurosumi (1976) tried the autoradiography in electron microscopic level after administration of tritiated DOPA to mice, but the Merkel cells did
not incorporate $^3$H-DOPA, though the melanocytes, mast cells and adrenomedullary
cells did uptake DOPA. These results suggested the substance of specific granules
was not monoamines and the assumption that the Merkel cell might be one of the
paraneurons (or of APUD system) would not be tenable.

The developmental origin of the Merkel cell, however, was repeatedly assumed
to be the neural crest by some authors (Breathnach, 1971, 1977; Hashimoto, 1972;
Winkelmann and Breathnach, 1973) and the idea that the cell might belong to the
APUD system (Winkelmann, 1977) has been a strong argument. An alternate theory
concerning the origin of the Merkel cell is a concept that the cell may derived from
a modified epidermal cell (keratinocyte). The authors (Kurosumi et al., 1969) as well
as Munger (1965) suggested that the Merkel cell might be differentiated from the
epidermal (epithelial) cells. The presence of typical desmosomes at the junction
between the Merkel cells and keratinocytes was the major evidence for our hypo-
thesis. We thought that a few synaptic vesicles in the nerve ending abutting on
the Merkel cell might be related to the induction of differentiation of sensory cells
from the epithelial cells (Kurosumi et al., 1969). In later studies on the morphogenesis
of Merkel cells, English (1977b) demonstrated conspicuous features of Merkel cell-
adjoining nerve terminals containing clear-cored, synaptic-sized vesicles in a Haar-
scheibe of a newborn rat. In adult animals these vesicles markedly diminished in
number or disappeared. These vesicles may have a significance in trophic action of
nerves, and probably related the differentiation of tactile sensory cells in the young
less differentiated epidermis.

Iggo and Muir (1969), Smith (1970) and Nafstad (1971b) as well as English (1974,
1977b) demonstrated so-called "transitional cells" which had the characteristics of
both Merkel cells and keratinocytes. They contain thick bundles of tonofilaments
like those of keratinocytes on one hand, while the cells contain specific granules
similar to those of the Merkel cells, although the transitional cells generally lack the
associated nerve endings. English (1974) said, "Merkel cells may be formed without
direct neuronal contact, but innervation is necessary for maintenance or differentia-
tion of these cells."

The dependence of Merkel cells upon innervation may have been more clearly
understood, when the experiments of transection or removal of nerves, which inner-
vate the Merkel cells in normal state, were carried out (Brown and Iggo, 1963;
Palmer, 1965; English, 1977a). English (1977a) performed denervation experiments
on cats and observed Merkel cells and also did morphometry. According to her, the
number of Merkel cell granules decrease remarkably from the control level that is
135/cell to 70/cell at 25 days after denervation. However, a few exceptional cells
containing more than 200 granules were left in this long term postoperatively. That
means the maximum values are not so different between the control and 25 day de-
nervated Merkel cells.

In our experiment, the maximum values in numerical density of granules were
not altered till 20 days (about 7-9/μm$^2$, mean: 7.73/μm$^2$), but in Merkel cells at 30
days the maximum value (3.84/μm$^2$) as well as the mean (1.79/μm$^2$) reduced to about
a half of the control (mean: 3.47/μm$^2$). The results of both ours and of English
(1977a) were in the same line, that the Merkel cell granules significantly decreased
due to denervation at later stages (25 or 30 days) of the experiments. But some de-
tailed aspects were not the same, for example, the difference in maximal value at
the last stage as mentioned above, and the transient increase in number of granules shortly after denervation (1-3 days) in our results could not be compared with that of English, because she did not count in such short periods after surgery. Such an increase of granule numbers at 1-3 days might be because the release of granules was blocked, as the target of stimulus transmission was altered or disappeared. However, in a later stage the formation of granules might become diminished as well, resulting in the decrease in number of granules left in the cell. In the present study, however, we observed new formation of granules in the Merkel cells even several days after denervation, indicating that some of the Merkel cells were still active after loss of their innervation.

English (1977a) also reported the striking decrease in number of Merkel cells in the denervated Haarscheiben by counting the cells by light microscopy. We did not perform light microscopic counting, nor electron microscopic morphometry in search of diminution of the number of the cells. However, we felt a little difficulty in finding the Merkel cells in specimens of denervated skin as compared with the control sample. It was due probably to the decrease in number of the Merkel cells after denervation.

It may be concluded from the results of our observation and counting of Merkel cells and their granules that the cells are very closely related in function to the nerve endings as shown by the alteration in structure and number of granules after denervation, but the maintenance of the cell does not absolutely depend on the presence of nerve fibers, for the Merkel cells with minor changes were still observed even 20 or 30 days after denervation, though the intact cells decreased in number.

正ならびに神経切断後のメルケル細胞と神経終末の電子顕微鏡による形態学的および形態計測的研究

黒住一昌, 黒住歌子, 井上金治

イスの鼻先・ラットの足底および指腹皮膚のメルケル細胞と、それに連結している神経終末を透過電子顕微鏡で観察した。正常なメルケル細胞は次のような形態学的特徴を有する。1）この細胞は表皮基底層に限局して位置する。2）多数の余粒体を含む求心性神経終末に密着する。3）小さな球形の特殊果粒が通常、神経終末と結合部に面する側の細胞質に集積する。4）核は高度に分裂した不規則形をなす。5）よく発達したゴルジ装置が少数の未熟な果粒を伴ない、神経終末との結合部とは逆の細胞側に位置する。6）細胞表面の神経終末と接触しない部位から、棘状の突起が多数突出している。7）デスモゾームおよびデスモゾーム様の橋粒厚が表皮（角化）細胞および神経終末に接する細胞表面に発達する。

ラットの坐骨神経を切断後、1〜30日の間ほとんど毎日、足底および指腹の皮膚を採取し、メルケル細胞とそれに連結する神経終末を観察し、計測した。神経切断後24時間では、ほとんど変化は見られないが、次の24時間内に神経は退縮して、その後は全く表皮内に神経線維を発見できない。メルケル細胞の果粒は神経切断後1〜3日に一過性に増加するが、その後は再び減少して、30日後には対照例の約半数に到達する。神経終末側に密集するこ
とによって示される。メルケル細胞内での果粒分布の極性は、神経切断後に不明瞭になる。実験の後期には重い変性に陥る細胞もある。

メルケル細胞の活性は、連結している神経に依存しているが、神経切断後、長期間を経ても、メルケル細胞が完全に消失してしまうことはない。

REFERENCES


