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ELECTRON MICROSCOPY OF MERKEL'S "TASTZELLE", A POTENTIAL MONOAMINE STORING CELL OF HUMAN EPIDERMIS*

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In 1875 Merkel (10, 11) described specialized epidermal cells near the tip of the rete ridges. In osmium tetroxide-fixed preparations they could be distinguished from the surrounding epidermal cells by their less opaque cytoplasm and more irregular nuclei and by their intimate contact with a neurite. He believed that the function of these cells was that of touch receptors and called them "Tastzellen". Merkel's prophesy has been recently substantiated by combined histological and electrophysiological studies of Iggo (4). Small mechanical forces applied to the localized skin areas wherein the Merkel cell-neurite complexes were found, evoked a persistent discharge of high-frequency impulses in the afferent nerve fibre. A slowly adapting response is compatible with a secretory mechanism of transduction. The chemical nature of the transduction remains to be determined. It is possible that it might be based on noradrenaline release similarly to the process at post-ganglionic sympathetic nerve terminals.

This study concerns the observation in a Merkel cell of human epidermis of a multitude of membrane-coated dense-cored granules, about 1000 Å in diameter. Similar granules characterize monoamine-containing cells of various neural tissues and have been found also in presso- and chemoreceptors.

Material and Methods

The material consisted of 20 small punch biopsies, taken without anesthesia from healthy almost glabrous skin of the midvolar forearm of ten young adult males. After bisection, the specimens were fixed for 2 to 6 hours in 2 per cent, phosphate-buffered glutaraldehyde (pH 7.3), post-fixed in 1 per cent osmium tetroxide (18), dehydrated in the graded ethanol series and embedded in Epon 812 (8). Thin sections were stained with lead citrate (17), examined with an electronmicroscope[1] and photographed at original magnifications (×2500 to ×15,000).

Results

Merkel's "Tastzelle", the fourth of the specialized cell types of the interfollicular epidermis, appears to be infrequent in the midvolar forearm epidermis of young adult males. It was encountered only once in one single specimen. The thin section with the Merkel cell originated from a healthy 20 year-old finnish man.

The Merkel cell was characteristically

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[1] Siemens Elmiscope I.

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located within the basal cell layer at the tip of a rete ridge and was embraced by a neurite. The electron microscopic field around the cell contained neither myelinated axons nor structures belonging to hair follicles or eccrine sweat ducts.

The Merkel cell appears to be a stationary cell having not only a close union with the adjoining intraepidermal neurite but also desmosomes providing strong contacts with the flanking keratinocytes. The relatively short desmosomes showed some evidence of the typical striated internal structure between the dense attachment plates of cytoplasmic filaments converging from both the keratinocyte and the Merkel cell (Fig. 2). While representing the strongest cell-to-cell contacts, the desmosomes are apt to transmit even the slightest mechanical displacements of the epidermis to this mechanoreceptor cell.

The Merkel cell has a highly lobulated nucleus (Figs. 1–3), not unlike that of the Langerhans cell, and a sparce feltwork of fine cytoplasmic filaments (Figs. 2–4) similar to those of the melanocyte. However, the mere presence of desmosomes in the Merkel cell and their absence in both the Langerhans cell and the melanocyte speaks against a common ontogenic lineage between the Merkel cell and these two other secretory cells of the epidermis.

In the cytoplasm of the Merkel cell the most characteristic finding was the presence of numerous membrane-enveloped dense-cored osmiophilic granules (Figs. 1–4). They were most abundant in the basal portion of the cell, but occasionally were scattered anywhere in the cytoplasm. The granules measured 600 to 1500 Å and had a relatively uniform appearance. In some of the granules, the finely granular internal core was somewhat less electron-opaque suggesting a linearly striated internal structure. The limiting membrane of about 50 Å in thickness was separated from the central dense core by an almost translucent halo of about 80 Å in width. Apart from the specific granules the cytoplasm possessed three dense much larger bodies enveloped by a hardly resolvable membrane (Figs. 2 and 3). In addition, there were two multivesicular bodies as well as numerous lead-stained, roughly isometric, 200Å-particles, which may be glycogen or some other polysaccharide (Figs. 2–4). Neither elements of the Golgi complex nor agranular endoplasmic reticulum could be detected in this section of the Merkel cell, and only few minute profiles of rough-surfaced membranes were visible in one pole of the cell.

The Merkel cell was embraced by a neurite covered on the dermal side by a Schwann cell process. The latter showed a faintly resolvable discontinuous basement membrane, tubular fibrils and large mitochondria (Figs. 1, 3 and 4). The tightly interposed unmyelinated basal axon abounded with about 500 Å-vesicles, a few of them showing small inner cores (Fig. 3). In addition, the basal axon possessed synaptic-like cell membrane condensations with the Merkel cell (Fig. 4). The richness of small mitochondria in the axon apposed upon the Merkel cell (Figs. 1 and 6) provided further evidence of intense functional activity at the site of junction of the neurite and the Merkel cell.

Discussion

The content of monoamines in various tissues appears to be correlated with the number of membrane-limited dense-cored granules indistinguishable from those of the Merkel cell studied (5). However, secretory products of a very different nature may reside in dense granules that cannot be morphologically differentiated. Moreover, the ultrastructure alone does not identify the nature of the content of the monoamine-storing granules. Both unsubstituted catecholamines and indole amines, such as 5-hydroxytryptamine (20), form with the electron microscopic fixative glutaraldehyde an insoluble polymer which gains electron density on subsequent exposure to one of several metal-containing oxidizing agents, such as dichromate, iodate, ammoniacal silver or osmium tetroxide (2, 19).

The contribution of electron microscopy to the solution of the continuing contro-

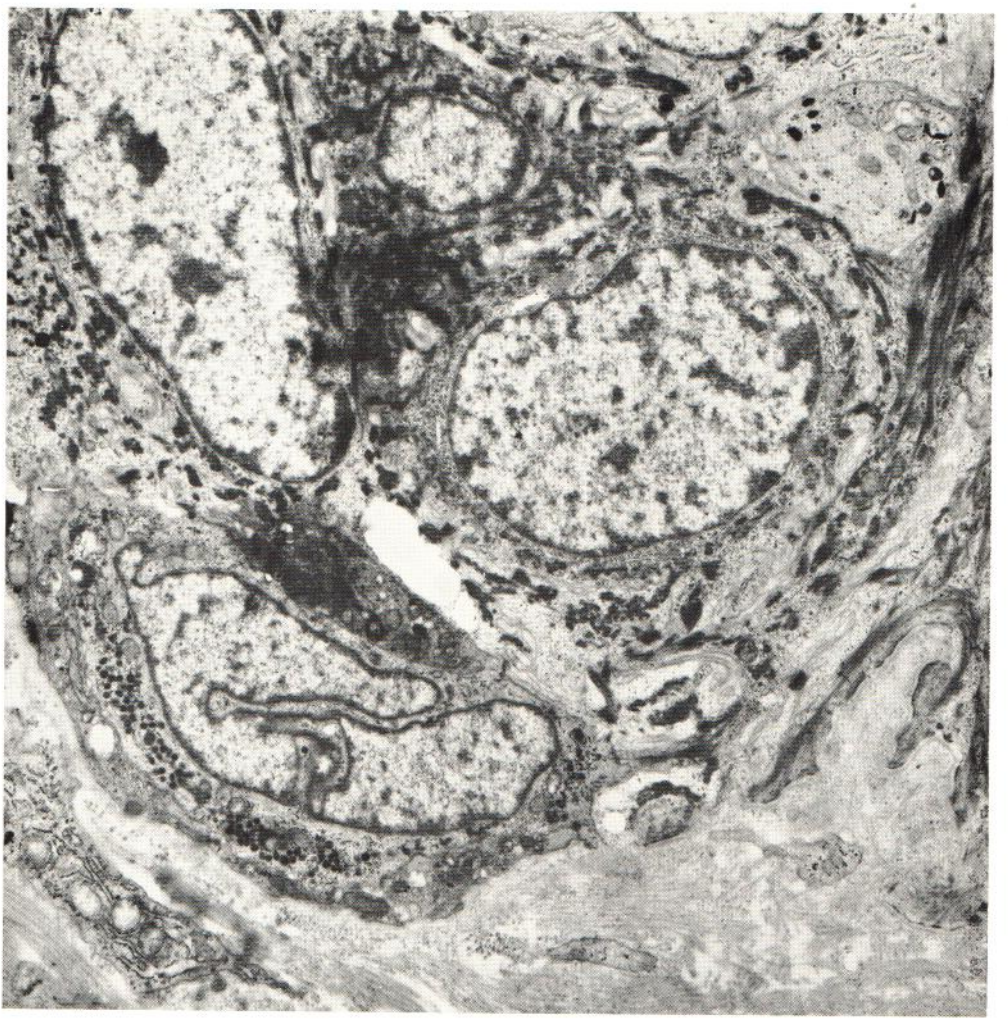

Fig. 1. Topographical relations of a Merkel cell-neurite complex within the basal cell layer at the tip of a rete ridge of human forearm epidermis. Note the highly convoluted nuclear profile and the spherical dense granules at the basal cytoplasm. ×7000.

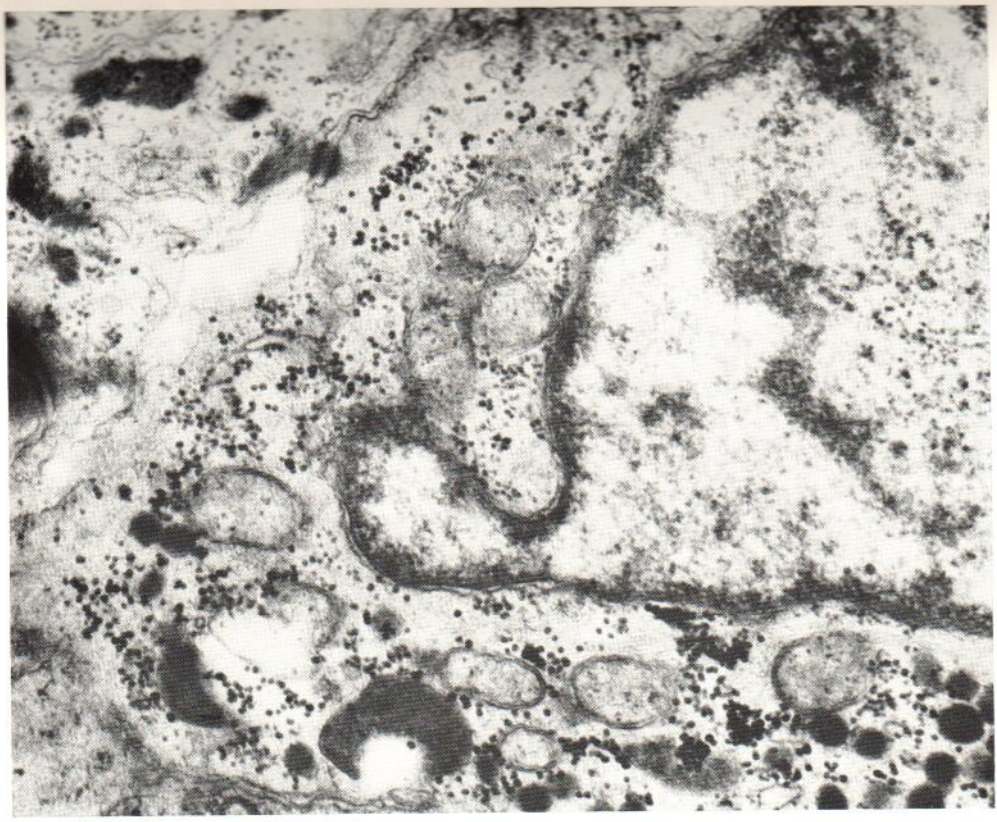

Fig. 2

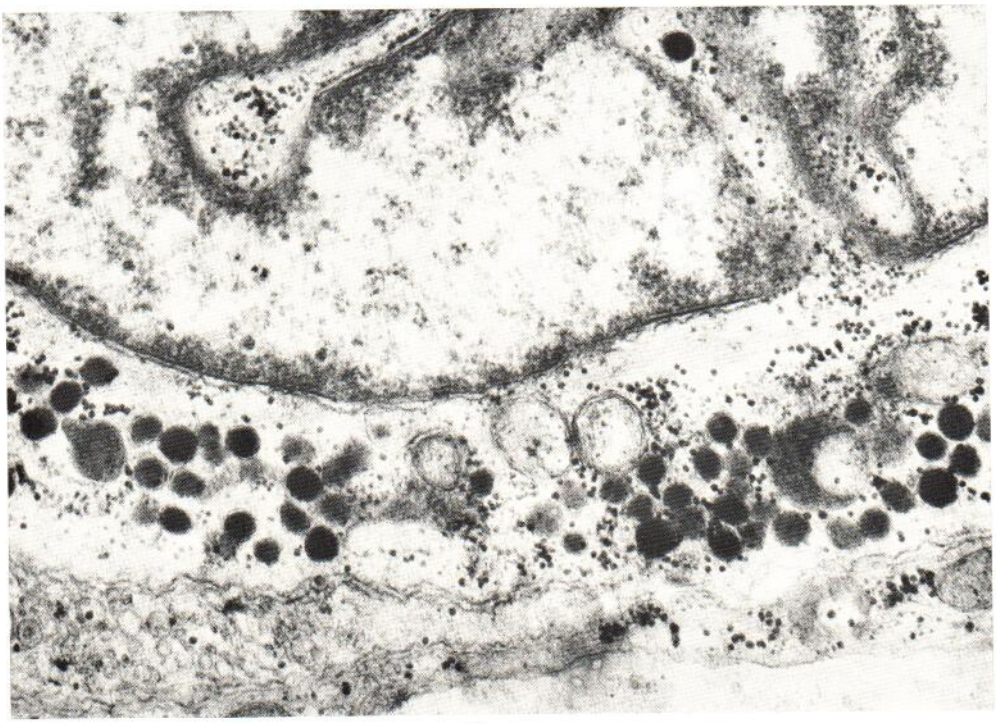

Fig. 3

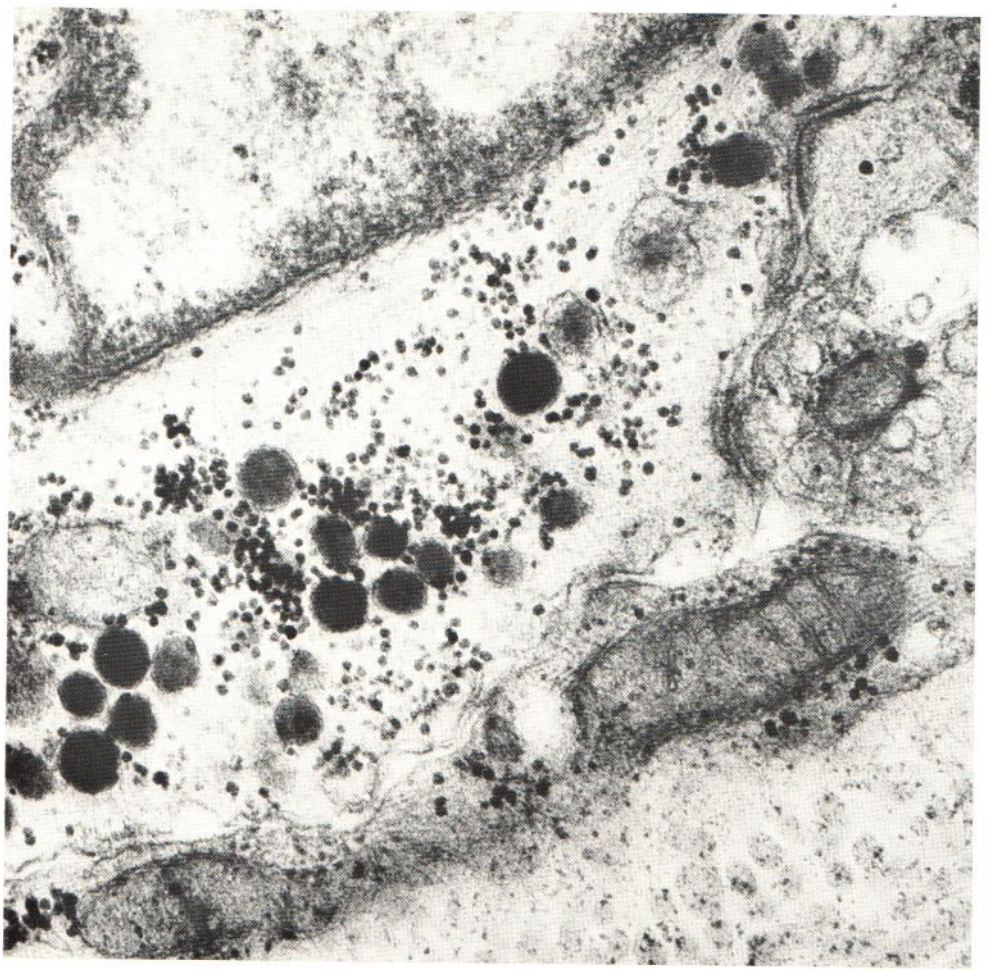

Fig. 4. At the upper right corner two curved synaptic-like membrane condensations between the Merkel cell and an axon are seen. Unlike the desmosomes (cf. Fig. 2) they lack converging filaments but show poorly defined vesicular structure in the surrounding cytoplasm. Apart from characteristic dense-cored granules, the nearby cytoplasm contains two multivesicular bodies. ×56,000.

Fig. 2. A higher magnification of the left pole of the Merkel cell reveals a desmosome attaching the cell to an adjacent keratinocyte. Fine cytoplasmic filaments converge from both cells onto the attachment plates of the desmosome. The cytoplasm of the Merkel cell contains several membrane-lined dense-cored granules, numerous lead-stained 200 Å-particles, lightly stained mitochondria and two large crescentic lysosome-like dense bodies. ×36,000.

Fig. 3. The basal aspect of the Merkel cell cytoplasm abounds with characteristic membrane-limited granules, measuring 600 to 1500 Å in diameter. A feltwork of fine cytoplasmic filaments is visible in the juxta-nuclear area. Lowermost in contact with the dermis a Schwann cell-process wraps the Merkel cell and an axon at the lower left. The interposed axon demonstrates myriad vesicles of about 500 Å in width. ×35,000.

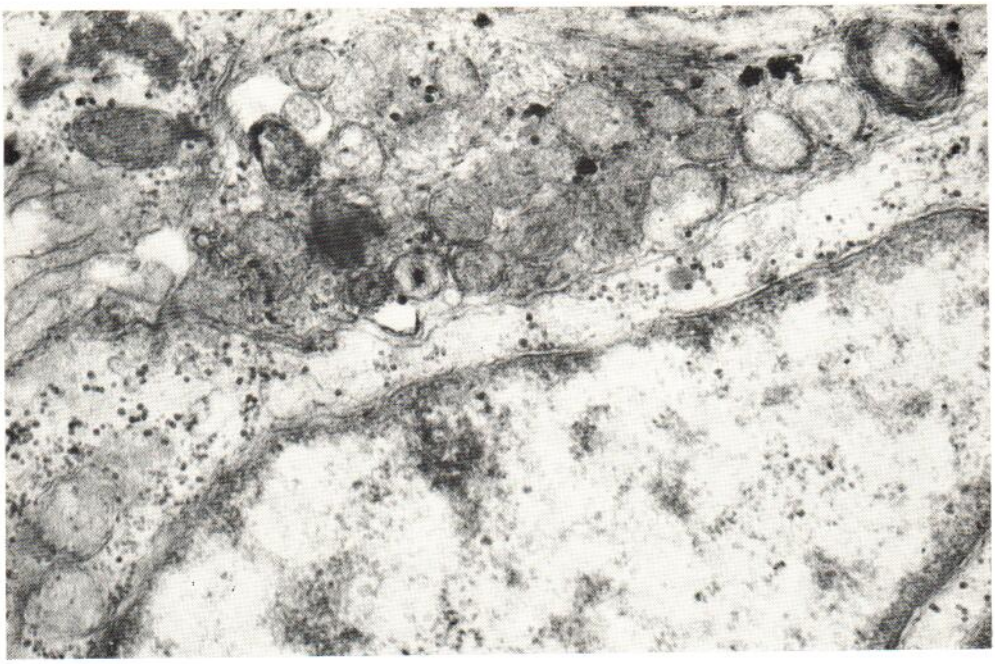

Fig. 5. The axon tightly upon the Merkel cell is crowded by small mitochondria. Note also the myelin figure in the upper right corner. ×35,000.

versy, whether or not monoamine-containing extraneuronal cells are present in the human skin (see 14 and 15), rested so far on one incidental observation. A single "chromaffin" cell, fulfilling the electron microscopic criteria of monoamine storage and showing appositional contact with unmyelinated axons was found by McGavran (9) in the dermis of the axillary skin of an 11 month-old boy with xanthogranuloma.

In the two low power electron micrographs of Cauna (1), depicting a Merkel cell from the finger-tip epidermis of a 43 year-old man, only "osmiophilic granules" but no limiting membranes could be seen. This may be due to the fact that Cauna's study was made before the glutaraldehyde-fixation was introduced for the preservation of monoamines.

On the other hand, in the highly specialized, exquisitely sensitive snout skin of the opossum, the numerous Merkel cells contain membrane-coated dense-cored granules of the monoamine storing type, as recently reported by Munger (12). His histochemical studies did not reveal catecholamines in these cells. However, for the chromate and periodate methods he used paraffin sections of formalin-fixed specimens instead of fresh tissue slices, i.e. a technique inappropriate for adequate preservation of chromaffin granules (16).

Obviously, further studies are necessary before the Merkel cell can be established as a monoamine storing or secreting cell, but it is tempting to speculate that the Merkel cell-granules, whatever their exact nature may be, could chemically alter the permeability of the afferent tactile nerve fiber, thus producing a burst of comparatviely slowly adapting impulses. The rather unspecific electron microscopic technique should be complemented by more specific histochemical methods, including the fluorescence method reported to be specific for catecholamines, indole amines and DOPA (3). Such studies may also result in revision of the concept that only melanocytes in the basal cell layer display specific fluorescence induced by formaldehyde vapor.

Finally, considering that the storage and release of monoamines appear to be associated with adenosine triphosphatase activity (7), the ATP-ase positive end-bulbs of the axons, shown by Mustakallio (13) to be in close contact with active cells in the basal cell layer of human epidermis, may in fact represent neurites of the Merkel cell-neurite complex rather than hypothetical neural connections of melanocytes or Langerhans cells (6).

Acknowledgements

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SUMMARY

A Merkel cell-neurite complex of human epidermis was observed in a single electron microscopic section. The sections examined were derived from 20 small punch biopsies taken without anesthesia from the midvolar forearm skin of 10 healthy young men.

The Merkel cell-neurite complex was located within the basal cell layer at the tip of a rete ridge. The Merkel cell, with a highly lobulated nucleus, exhibited desmosomal contacts with the surrounding keratinocytes and synaptic-like membrane condensations with the basal axon. The axon apposed upon the Merkel cell contained a multitude of mitochondria, also suggesting intense activity at the point of junction of the neurite and the Merkel cell. The most characteristic finding was the presence of numerous membrane-limited dense-cored granules of about 1000 Å in diameter in the basal cytoplasm of the Merkel cell. Morphologically they were indistinguishable from monoamine-storing granules.

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