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Fine structure of the receptors at the myotendinous junction of human extraocular muscles

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Summary. The myotendinous junction of the human extraocular muscles was studied by electron microscopy. Some peculiar receptorial structures have been found in the majority of the samples examined. These structures are very small and consist of 1) the terminal portion of one muscle fibre, 2) the tendon into which it inserts and 3), within the tendon, a rich nerve arborization, whose branches are always very close to the muscle component. Only one discontinuous layer, made up of flat cells, which lack a basal lamina and often show pinocytotic vesicles, encapsules every musculo-tendinous complex. The tendinous component consists of amorphous ground substance of different electron density, of collagen and elastic fibres and is divided in compartments by ramified cells, which make an inner capsular-like covering to the nerve fibres. Three types of afferent nerve endings can be identified. One type is usually more frequent than the others, possesses a large number of neurotubules and neurofilaments and few mitochondria and is always surrounded by a Schwann cell which forms finger-like processes penetrating into the axoplasm. The second type is only partially enveloped by the Schwann cell. The axoplasm is devoid of neurotubules and contains few neurofilaments, several mitochondria and groups of small clear vesicles placed in the areas uncovered by the glial sheath. The third one is completely surrounded by the Schwann cell, but is devoid of neurotubules and neurofilaments and full of mitochondria. These morphological features correspond well with the probable role of these receptorial structures, which is to ensure very exact and precise ocular movements.

Key words: Receptors, Extraocular muscles, Myotendinous junction, Man

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Introduction

The proprioceptors known as tendon organs were first identified by Golgi in 1880 in skeletal muscles. They were first described at electron microscope level by Merrillees in 1962 and later by other authors (Schoultz and Swett, 1972, 1974; Barker, 1974; Zelenà and Soukup, 1977; Soukup and Zelenà, 1985; Ovalle and Dow, 1983). In the extraocular muscles (EOM) the presence of tendon organs was first excluded by Golgi himself, but further investigations (Dogiel, 1906; Loffredo-Sampaolo, 1952; Bonavolontà, 1956, 1958) led to their identification and description at light microscopy level in several animal species. More recently Ruskell (1979) described the ultrastructural features of the EOM tendon organs in the monkey. These receptors showed some analogies and a few differences when compared with the tendon organs of skeletal muscles. The main differences were found in the size of the receptors and in their relationships with the muscle fibres. In fact, in monkey EOM these receptors are significantly smaller and connected only with one or two muscle fibres, and not with ten or more as in the skeletal muscles. Moreover, in the monkey EOM, Ruskell (1978) also identified other sensitive nerve endings, that he called «myotendinous cylinders».

Without doubt, these types of receptors play an important role in the oculomotor control. However, in humans there are no detailed investigations about this subject. In fact, using light microscopy, only peculiar structures, considered as receptors, the so called «palisade nerve endings», have been described at the humans myotendinous junction of the extraocular muscles, first by Dogiel (1906) and later confirmed by Cooper and Daniel (1949), Richmond et al. (1984) and Steinbach (1986). However these structures have never been investigated using electron microscopy; whereas, using electron microscopy only, Mukuno (1983) reports the observation of a structure «similar to tendon organs», but does not describe it.

The aim of the present work was to confirm, using electron microscopy, the presence of sensorial structures at the human EOM myotendinous junction, and to decide if they could be related to Golgi tendon organs, to Dogiel's «palisade» structures, to monkey «myotendinous cylinders», or even others.

Materials and methods

We considered the EOM of six patients who underwent enucleation for different ocular pathologies, without any disturbance of the ocular motor system. Three of the enucleated eyes suffered from choroidal melanomas, two from penetrating injury and one from absolute glaucoma. Age ranged from 36 to 62 years with a mean of 52.5 years.

During surgery the muscle was completely excised about two centimeters from its scleral insertion. Immediately after the operation, the specimen was separated from the sclera and divided into longitudinal strips. All samples were immersed in a fixative solution of 2% glutaraldehyde in 0.1 M cacodylate buffer, pH 7.4, and remained in this solution for two to six hours. The specimens were then washed in the same buffer, diluted half and half in a sucrose solution 0.44 M, for twelve hours or longer. The strips were then postfixed in 1% osmium tetroxide in phosphate buffer 0.1 M, pH 7.4. The samples were dehydrated in acetone at increasing concentrations and embedded in epoxy resin, using flat capsules in order to allow their orientation. We placed the muscle strips in such a way to obtain both cross and longitudinal sections. Semithin and ultrathin sections were obtained using the Porter-Blum MT I and LKB-Nova ultramicrotomes. The semithin sections, 0.5 μm thick, were stained with a water solution of toluidine blue and sodium borate for light microscopy. Some of the ultrathin sections were stained with uranyl acetate and lead citrate and the others with uranyl acetate and concentrated bismuth and finally examined and photographed under the Siemens Elmiskop 1 A and 102 electron microscopes.

Results

Some musculo-tendinous complexes were identified in the muscle component of the myotendinous junction of all the medial recti and four lateral recti.

With light microscopy, these complexes look like cylindrical structures made up of the ending of one muscle fibre and the beginning of the corresponding tendinous collagen bundle (Figs. 1, 2). The whole structure seems to be surrounded by one layer of thin capsular cells (Figs. 1-3, 4A,B and C). In cross-section, the tendinous component appears to be divided into polygonal compartments by cells with deeply stained cytoplasm and well developed ramifications (Figs. 3, 4A,B,C and 5A). For these reasons these musculo-tendinous complexes can easily be identified; in fact, the surrounding muscle fibres end in a common tendinous component, without any capsular or tendinous compartment formations.

Using electron microscopy, it is possible to identify only one discontinous layer of flat cells very poor in organelles, devoid of pinocytotic vesicles and basal lamina (Figs. 4D, 6) around these complexes. These cells can be considered as constituting something similar to an outer capsule. The tendinous compartments are delimited by the ramified cells (Figs. 4A, 7-10), which overlap and interdigitate each other with their branches (Figs. 7-10), forming one to three layers, sometimes concentric and continuous (Figs. 7, 8), sometimes not (Figs. 7, 10, 11), and determining for every compartment an inner capsule-like structure. These cells have a dark nucleus (Fig. 4D) and in the cytoplasm there are some mitochondria, a small Golgi apparatus, a poorly developed rough (RER) and smooth (SER) endoplasmic reticulum and several filaments (Fig. 9). Sometimes pinocytotic vesicles are also present (Figs. 6, 8, 10, 13, 15). Some long, thin cell processes often envelop a small bundle of collagen or elastic fibres (Figs. 4D, 9, 15). Also the inner capsular-like cells always lack a basal lamina (Figs. 4D, 6-15).

The terminal part of the muscle fibre is comprehensive of its tip (recognizable for its irregular border, Figs. 1, 2, 5B) and of a tract of variable extension ensheathed by a thin collar of connective tissue in continuity with the tendon. Also this collar can be divided in small compartments by the ramified cells of the inner capsule and incompletely delimited by the cells of the outer capsule. In the compartments nearest to the terminal part of the muscle fibre, the nerve fibres and the nerve endings are located. One-three nerve endings can be contained in every compartment. Close to the muscle fibre insertion into the tendon it is always possible to find one blood vessel (Figs. 1, 5B).

The connective tissue component located between the nerve endings and the inner capsular-like cells may have a peculiar aspect. The amorphous ground substance is electron transparent mainly in the subcapsular space (Figs. 7, 8, 14), whereas it is electron dense close to the nerve endings (Figs. 7, 8, 10, 12, 14). The collagen fibres are grouped in bundles which are often few and located near the nerve endings (Figs. 8, 10, 15). These bundles are orientated parallel to the long axis of the musculo-tendinous complex or slightly obliquely. Finally, the presence of elastic fibres should be noted, composed both of microfibrils and amorphous substance (Figs. 6, 9, 15). These fibres usually run both on the outer and inner sides of the inner capsular-like cells.

One myelinated nerve fibre can be found near the extremity of the muscle fibre inserting into the tendon (Figs. 5A, B); its perineurium is made up of one layer of cells rich in pinocytotic vesicles and surrounded by a basal lamina (Fig. 5B).

Entering the tendinous compartments, the nerve fibre loses the myelin covering and its arborizations maintain the Schwann cell sheath through to their endings. At this level the perineurium cannot be identified yet, and it is partially substituted by other cells, the inner capsular-like cells. Each Schwann cell sheath usually envelops one nerve fibre (Figs. 7, 8, 10-13) and exceptionally two

(Figs. 4D, 6, 8, 14, 15). A poorly developed RER, rather large mitochondria, several lysosomes and some microtubules are observed in the cytoplasm of the sheath cells. The nucleus is spherical or oval, often with a nucleolus. The chromatin is distributed in coarse clumps, mainly in the peripheral area (Figs. 4D, 7, 8, 10, 15).

Inside the preterminal nerve fibres the mitochondria are few, small and oval-shaped; scant neurotubules and neurofilaments are also present (Fig. 6).

At the level of the majority of the nerve endings we could identify (Figs. 7, 8, 10-13), the Schwann cell sheath shows a tortuous profile due to deep invaginations and thin evaginations, which partially delineate more electron dense connective tissue (Figs. 8, 10, 12, 14). From one to three short, thin, finger-like cytoplasmic processes of the Schwann cells penetrating into the nerve endings were also noted (Figs. 11, 13).

The Schwann cell completely surrounds these nerve endings and a basal lamina is always present. These nerve endings have a circular profile, and are very rich in neurofilaments and neurotubules. The latter are mostly near the axolemma, especially in the area in correspondence with the Schwann cell protrusions (Figs. 12, 13). The gap between the nerve endings and the muscle fibre is sometimes reduced to 750 nm (Figs. 8, 12) and always contains thin processes of the inner capsular-like cells. Very rarely these nerve endings are found in the compartments

Fig. 1. Longitudinal section of a musculo-tendinous complex. The insertion of the muscle fibre into the tendon is clearly recognizable. At this level the border of the muscle fibre has long, thin evaginations (arrows). In the tendinous component, near to the tip of the muscle fibre, numerous, but not identifiable, cells are located. BV=one blood vessel. The whole complex seems to be delimited by a thin capsule. Semi-thin section, toluidine blue. × 800

Fig. 2. Oblique section of a musculo-tendinous complex. The irregular extremity of the muscle fibre is clearly recognizable. Several cells, dividing the tendinous component in compartments, are located near the muscle fibre insertion and form a structure like a cup. The arrow indicates one probable outer capsular cell. Semi-thin section, toluidine blue. × 800

Fig. 3. Oblique section of a musculo-tendinous complex at its purely connective level. The asterisk indicates the tendinous component divided in compartments by deeply stained and extremely ramified cells surrounded by a thin capsule (arrow). This tendinous component continues (upper side) in a thinning tendinous structure, devoid of capsule and not divided in compartments. Semithin section, toluidine blue. × 800

Fig. 4 A,B,C. and D. Serial cross sections of a musculo-tendinous complex. One muscle fibre (upper side) and its tendon (right side). The tendon is divided in large compartments by deeply stained and ramified cells. With light microscopy (Figs. 4 A-C), this complex is apparently surrounded by a continuous capsule. By electron microscopy (Fig. 4 D), only one incomplete layer of thin processes (arrows) of capsular-like cells can be seen. In the compartments nearest to the striated muscle fibre (asterisk) the nerve fibres (NF) and nerve endings (NE) are contained. A-C: semithin sections; toluidine blue, × 800. D: × 6,250

Fig. 5 A and B. Slightly oblique sections of two different musculo-tendinous complexes at the level where the myelinated nerve fibre (NF) enters the receptor body. BV=one blood vessel. The terminal border of the muscle fibre is tortuous on its insertion in the tendon (tendon). A: semithin section, toluidine blue. × 800 B: × 7,500

Fig. 6. On the lower left side: one thin process of an outer capsular-like cell surrounding a musculo-tendinous complex. One amyelinated nerve fibre is present, embedded in a connective tissue rich in collagen and elastic fibres. This nerve fibre is to be considered as a preterminal one, since the neurotubules and neurofilaments are not numerous, the mitochondria are small and few and the Schwann cell has a regular outline (compare with figures 8, 9-13). × 20,000

Fig. 7. A musculo-tendinous complex sectioned at the level where two receptorial compartments are clearly distinguishable. The muscle fibre (not visible in the micrograph) is not far from them. One of these compartments (upper side, asterisk) is completely encapsulated, the other is partially encapsulated. Both contain two nerve fibres of a very different size. × 7,500

Fig. 8. Three nerve endings, each one completely surrounded by the Schwann cell, placed near the muscle fibre (upper left side) inside a compartment delineated by three layers of flat (inner) capsular-like cells. × 20,000

Fig. 9. Detail of one contact area between two capsular-like cells delimiting a receptorial compartment (upper side). Elastic fibres (E) are present near one of these cells, on the side facing the inner part of the receptor compartment. The arrow indicates one collagen bundle enveloped by one capsular-like cell process. × 25,000

Fig. 10 Detail of the Figure 7. Two nerve endings (asterisks), partially encapsulated, placed in the same compartment, but with very different size. The Schwann cell surrounding the largest one has an irregular profile (arrows) in correspondence of the nerve ending. × 20,000

Fig. 11. One partially encapsulated nerve ending placed in the purely tendinous area, but not far from the muscle component. The arrow indicates a finger-like process of the Schwann cell penetrating into the nerve ending. × 13,000

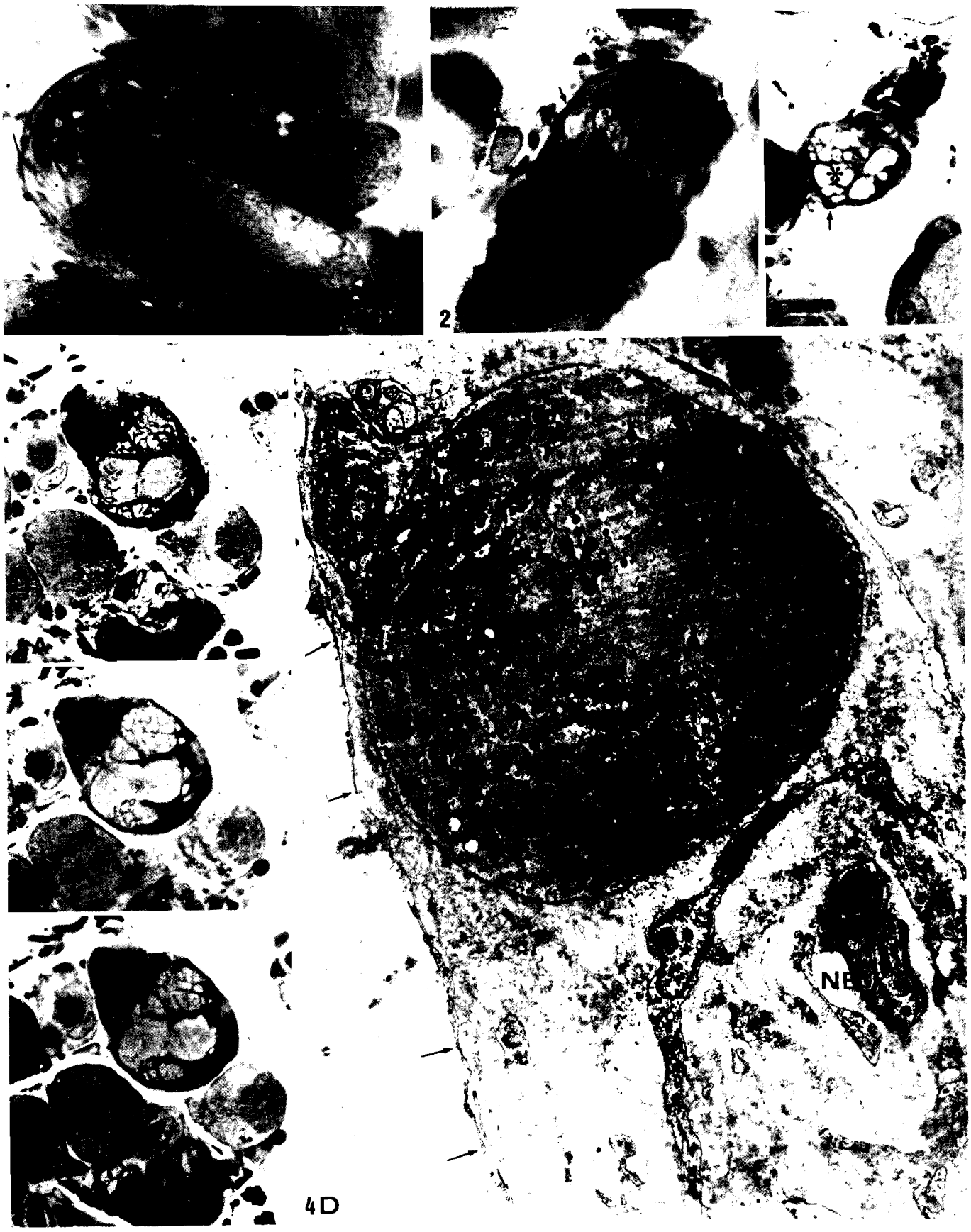
Fig. 12. One nerve ending placed very near to the muscle fibre. One thin process of a capsular-like cell separates them. The Schwann cell shows two invaginations (arrows) delineating two more electron dense connective tissue areas. Squares: groups of neurotubules located close to the axolemma facing the Schwann cell invaginations. × 25,000

Fig. 13. One nerve ending of the more frequently found type, rich in mitochondria, smooth endoplasmic reticulum cisternae (SER), neurofilaments and neurotubules (squares). In this section, the Schwann cell shows three finger-like processes (arrows) entering the nerve ending. × 20,000

Fig. 14. Two nerve endings (very rarely found), both completely enclosed in the same Schwann cell. These nerve endings are devoid of neurotubules and neurofilaments and full of mitochondria. On the lower right side the muscle fibre. × 20,000

Fig. 15. Detail of the Figure 4D. One nerve ending (rarely found) looking similar to those of typical Golgi tendon organs. In fact, this nerve ending has a tortuous profile and is partially devoid of glial sheath (arrows). Several mitochondria are present. Neurofilaments are not numerous. A peculiar feature of this nerve ending is the presence of groups of clear vesicles (about 50 nm in diameter) in the axoplasm beneath the areas devoid of glial sheath. E=elastic fibres enveloped by thin processes of the capsular-like cells. × 20,000

Fig. 16. One nerve ending full of mitochondria and round clear vesicles (50-80 nm in diameter) near one striated muscle fibre at the level where this fibre inserts in a capsulated tendinous component, forming with this a musculo-tendinous complex (the same complex where the nerve ending of the Figure 13 is located). The muscle fibre, in correspondence to this nerve ending, forms tubular invaginations covered by one basal lamina identical to those of a typical subneural apparatus. The nerve ending, in correspondence to this subneural apparatus, is devoid of a glial sheath and is apposed to this apparatus, like nerve endings of motor end plates do. This type of nerve ending, therefore, has been considered as an efferent one. × 25,000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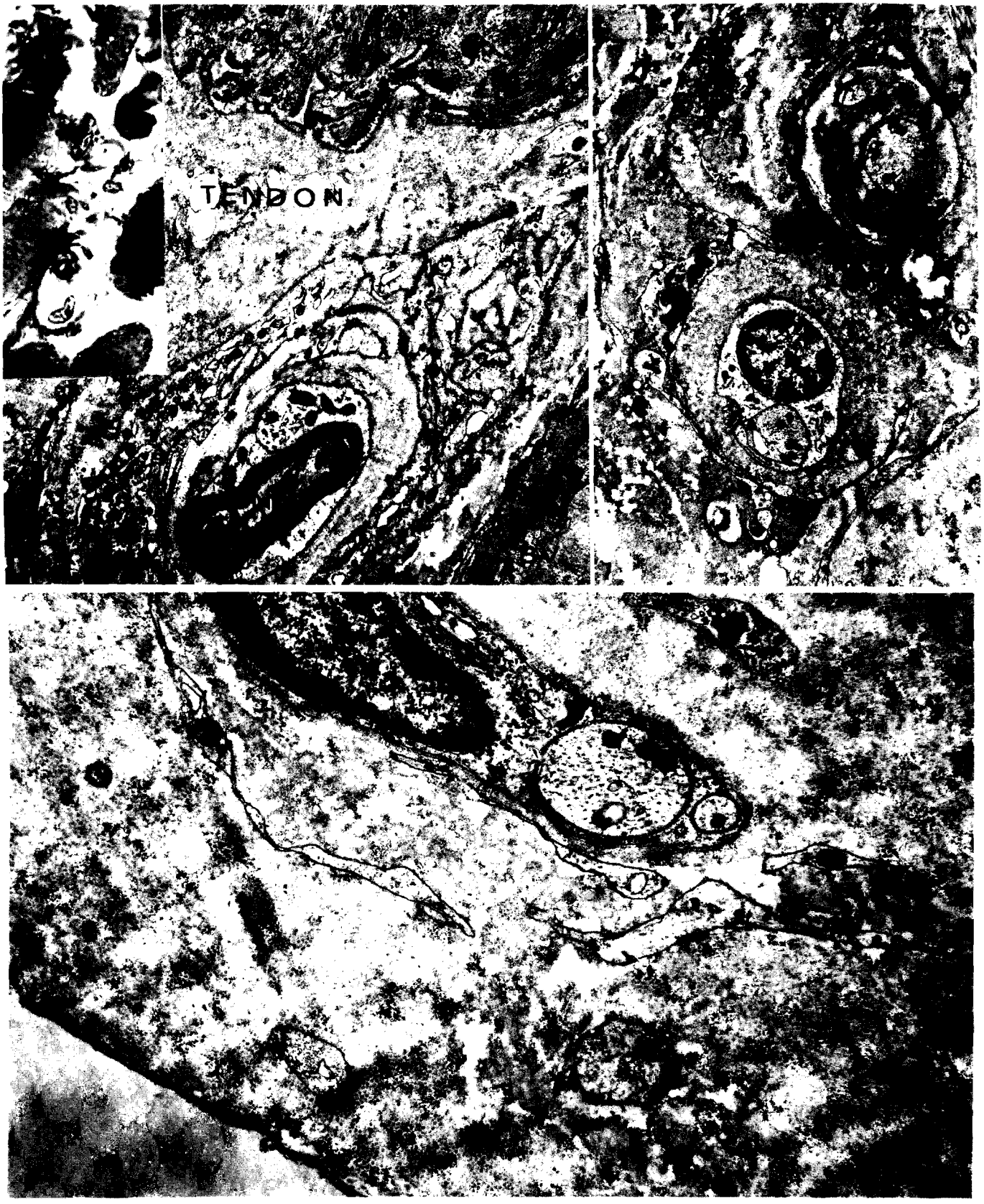
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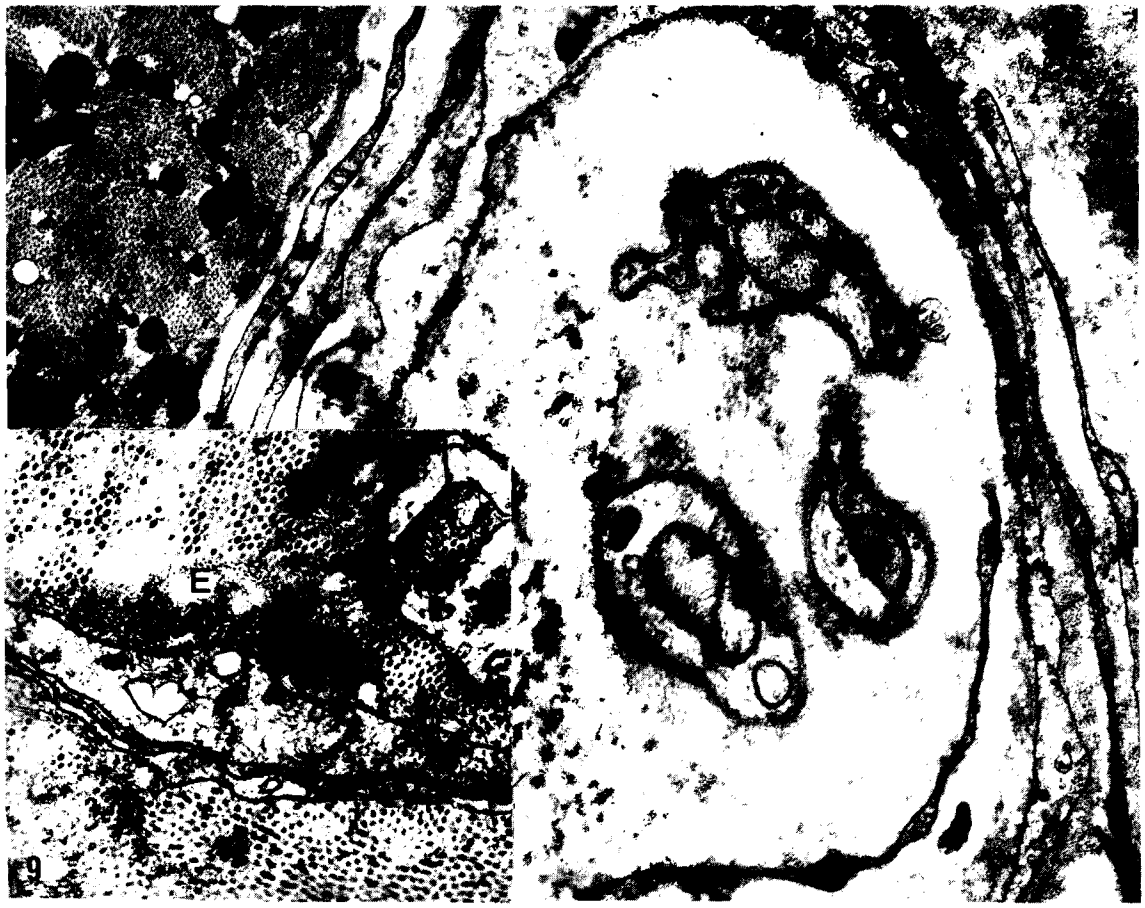
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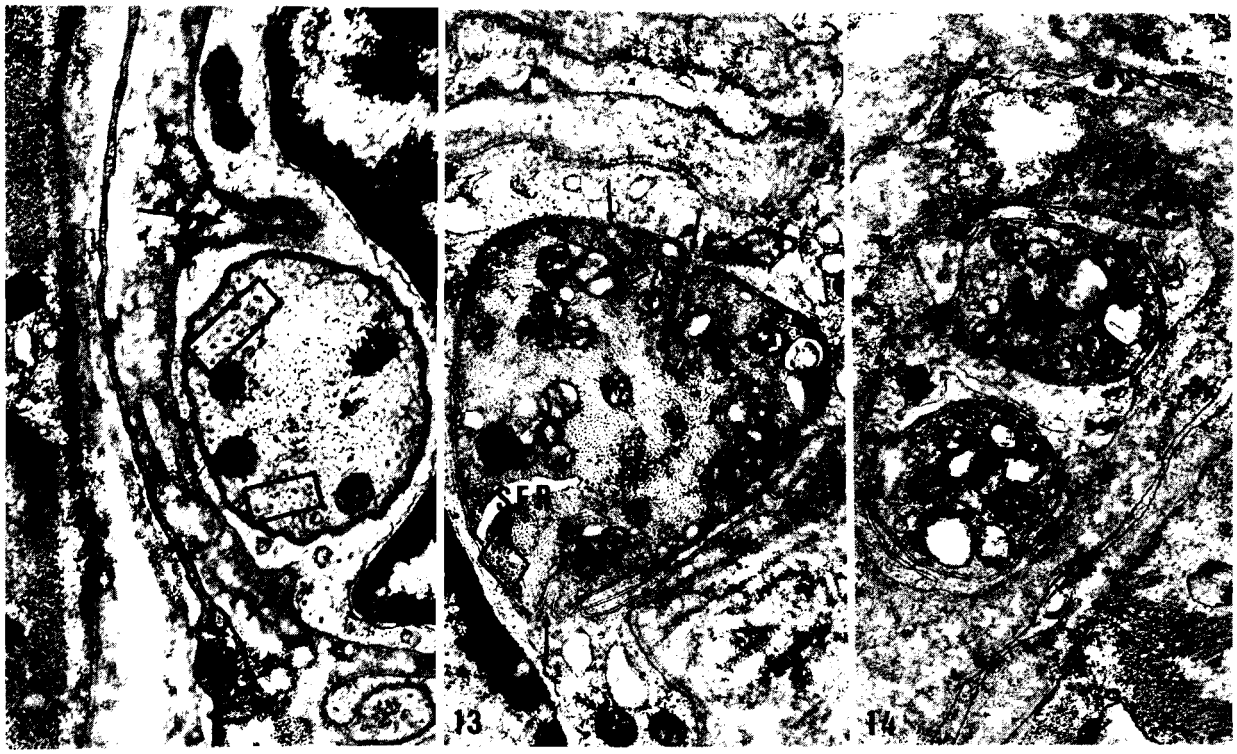

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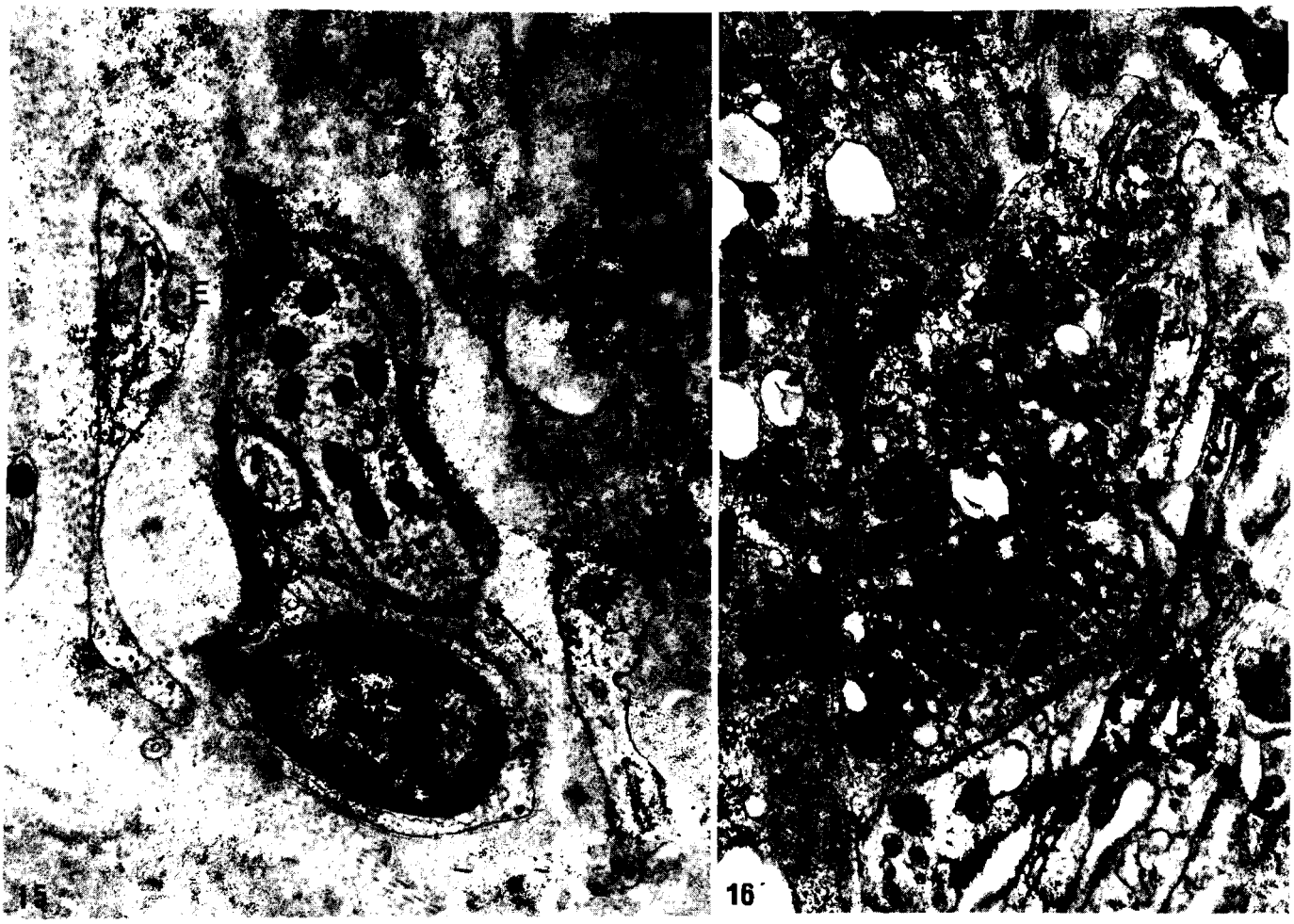

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of the purely tendinous area, completely or incompletely enveloped by the inner capsular-like cells, but never far from the muscle fibre.

Very occasionally, it was possible to observe other types of nerve endings. One type (Figs. 4D, 15) is never located in the compartments nearest to the muscle fibre and is only partially enveloped by the Schwann cell sheath, but a basal lamina is always present. The axoplasm is devoid of neurotubules and contains only a few neurofilaments and a certain number of large, oval-shaped mitochondria. Groups of clear vesicles of about 50 nm in diameter are seen in the opposite areas uncovered by the Schwann cell sheath (Fig. 15). The shape of these nerve endings can be oval, or elongated or tortuous.

Another type of nerve ending (Fig. 14) has a circular profile and is completely surrounded by the Schwann cell sheath, as those more frequently found, but it is devoid of neurotubules and neurofilaments and full of large, round mitochondria. This type of nerve ending is found only near the muscle fibre, separated from this by an inner capsular-like cell. Rarely, it is possible to find another type of nerve ending (Fig. 16), located only in correspondence with the end of the muscle fibre. This nerve ending is very different from the previous ones. It is large, looks like a flat flask and is strictly apposed to the muscle fibre, with a gap of 50-100 nm only. At this contact area, the Schwann cell sheath is interrupted and the nerve ending is separated from the muscle fibre by only one basal lamina, which also penetrates in finger-like invaginations of the sarcolemma constituting a typical subneural apparatus. The axoplasmic portion of this nerve ending contains clusters of large, oval mitochondria, distal to the contact area, and a lot of clear vesicles of about 50-80 nm in diameter in the proximal one. We consider this nerve ending type as an efferent one because of its similarity to those of the end plates.

Discussion

In the myotendinous junctions of the human EOM we were able to identify numerous small musculo-tendinous complexes. These complexes possess an architecture and ultrastructural features never described before.

These musculo-tendinous complexes are incompletely capsulated and are made up of three components: 1) a muscular component, consisting in the terminal part of one striated muscle fibre ensheated by a capsulated tendinous collar; 2) a connective tissue component, the tendon in which the muscle fibre inserts, divided in compartments by ramified cells; 3) a nerve component, made up of a rich nerve supply, whose arborization is located inside the tendinous compartments.

The nerve supply needs to be discussed in order to identify the nature of these musculo-tendinous complexes, since the nerve fibres share peculiar ultrastructural features which are somewhat different to those already described in this area (Ruskell, 1978, 1979).

In the myotendinous junction of the extraocular muscles of mammals the motor innervation is usually considered absent, whereas various types of sensory nerve endings have been described: tendon organs, myotendinous cylinders, palisade nerve endings (Dogiel, 1906; Cooper and Daniel, 1949; Loffredo-Sampaolo, 1952; Bonavolontà, 1956, 1958; Ruskell, 1978, 1979; Mukuno, 1983; Richmond et al., 1984; Steinbach, 1986).

One type of the nerve endings we observed looks identical to those of the end plates. However, we found this type of nerve ending very rarely and, therefore, it cannot be considered as typical of this area. All other nerve endings we observed, on the contrary, are very numerous and are not similar to commonly described efferent nerve endings. Therefore, this seems to be a valid reason to exclude the possibility that we observed only motor terminals (except those afore-mentioned) and, on the other hand, also valid to consider the musculo-tendinous complexes as receptorial structures. However, as above mentioned, the nerve endings we described are different from those previously described in this area in monkey EOM (the only ultrastructural data we have for a comparison).

The unmyelinated nerve structures we found inside every musculo-tendinous complex are very numerous and share different features; these facts should indicate that some (few) of them might be preterminals and some (many) terminals. At least two types among these nerve structures have to be considered as nerve terminals (see Figs. 14 and 15) for their unequivocal features: one being partially devoid of the Schwann cell sheath and containing mainly vesicles and mitochondria (the possibility that this type is efferent is excluded, see later in the discussion); the other mostly containing numerous, large mitochondria and lacking neurotubules and neurofilaments (as commonly described for a large number of sensitive nerve endings). All other nerve structures, containing neurotubules and neurofilaments and completely surrounded by the Schwann cell sheath, have to be examined more carefully in order to distinguish between preterminals and terminals. Only few nerve structures (see Fig. 6), having normal features and looking identical to commonly considered amyelinated nerve fibres, can be identified as preterminals. The others which, on the contrary, are very numerous (as we can expect if these represent the terminal arborization of a receptorial nerve supply) share noticeable structural differences in respect to nerve fibres (preterminals included). In fact, the neurofilament and neurotubule content is enormous and the mitochondria are numerous, large, round and peripherally located. These features have been described also for other receptorial structures and considered characteristic of their terminal sensitive supply (Watanabe and Yamada, 1985). Moreover, the Schwann cell sheath at the level of the nerve structures we considered as nerve endings shows an irregular outline: on the outer side forms deep invaginations and thin evaginations branching electron dense connective tissue material; on the inner side penetrates into the axoplasm invaginating the axolemma

by means of finger-like protrusions. These features have not been described elsewhere (and will be discussed later) and are not characteristic for preterminal (neither motor, nor sensitive) nerve fibres.

For all the above mentioned considerations we are reasonably convinced of having found sensorial structures with peculiar ultrastructural features. It needs now to be seen if these musculo-tendinous complexes can be identified as tendon organs (until now not definitely confirmed in human EOM), as myotendinous cylinders (never mentioned in humans), as palisade nerve endings (the only ones certainly present in human EOM,) or as other receptorial structures unknown until now.

Their ultrastructural morphology is in some respect different from that observed in monkey EOM Golgi tendon organs and myotendinous cylinders and from Golgi tendon organs described in skeletal muscles. In fact, in comparison with the Golgi tendon organs of both skeletal muscles (Schoultz and Swett, 1972, 1974; Barker, 1974; Zelenà and Soukup, 1977; Ovalle and Dow, 1983; Soukup and Zelenà, 1985) and EOM (Ruskell, 1979) the structures we described are smaller (about 20μm in diameter), devoid of a typical outer capsule (we observed only one discontinous layer of flat cells), always found very near to the muscle component (even more than the tendon organs of the monkey EOM), with a gap from the sarcolemma to the capsular cell sometimes reduced to 750 nm. Moreover, only one type of nerve ending (see Fig. 15), very rarely found, looks similar to those commonly described in tendon organs. This type of nerve ending possesses some areas uncovered by the Schwann cell sheath, contacts with the connective tissue, has a tortuous profile and is poor in neurofilaments and neurotubules. At variance with the nerve endings of the tendon organs, but similarly to those of Ruffini and Pacini corpuscles (Halata et al., 1985), this type of nerve ending contains groups of clear vesicles clustered in the areas uncovered by the Schwann cell sheath. These nerve endings, because of some similarities with both those of tendon organs and Ruffini and Pacini corpuscles, and since they were never found close to the muscle fibre, have been considered as sensorial ones. The others, the most frequently observed, are very different form those of tendon organs, since the glial covering is always complete and, therefore, the nerve ending never directly contacts the connective tissue component. Moreover, most of these nerve endings are full of neurotubules and neurofilaments and show large mitochondria peripherally located. We must finally remember the peculiar behaviour of the Schwann cell which has an irregular outline (both on the outer and inner side of these nerve endings).

The structures we described also differ from the myotendinous cylinders (Ruskell, 1978) of the monkey EOM. In fact, the nerve endings we could observe closer to the muscle fibre and containing clear vesicles, at variance with those described in the myotendinous cylinders, are always in close contact with the muscle fibre, with a gap of 50-100 nm, and in presence of a typical subneural apparatus. Because of these morphological features we considered them as efferent. Moreover, this type of nerve ending was very rarely found and, therefore, does not characterize the musculo-tendinous complexes of humans.

Despite the afore-mentioned differences, the structures we found show, even if only a few, important similarities both with the tendon organs and the myotendinous cylinders. As in the tendon organs, we can observe a tendinous component divided into several compartments by cells which should correspond to those of the inner capsule. But really, in the structures we identified, it is not possible to distinguish between two different types of capsular cells, an outer and an inner one, because all the capsular cells we observed have intermediate features between those of the outer and those of the inner capsule of the tendon organs. In fact, all the capsular cells we identified lack a basal lamina (like the inner capsule cells) (Schoultz and Swett, 1972; Zelenà and Soukup, 1977; Ovalle and Dow, 1983), but very often show pinocytotic vesicles (like the outer capsule cells) (Ovalle and Dow, 1983). The characteristics of the connective tissue interposed between the nerve ending and the inner capsule are also similar to tendon organs (Schoultz and Swett, 1972; Soukup and Zelenà, 1985). The similarities with the myotendinous cylinders mostly consist in the small size, being both receptor types usually made up of only one muscle fibre and its tendon, and in the absence of a consistent outer capsule. In both these types of receptors the nerve endings are mostly located near the muscle fibre, but at variance with the myotendinous cylinders, we found them not only in correspondence of the tip of the muscle fibre, but also around its terminal part (the portion ensheathed in the capsulated tendinous collar).

In conclusion, the human EOM, in the area of the myotendinous junction, show some structures that seem more similar to Golgi tendon organs than to myotendinous cylinders, but with important structural differences in comparison to both.

In humans, Dogiel (1906) described in this region peculiar sensorial structures, which he called «palisade endings» because of the typical nerve arborization. The presence of this type of receptor has been confirmed recently by others, using light microscopy (Cooper and Daniel, 1949; Richmond et al., 1984; Steinbach, 1986). Ruskell (1978, 1979) suggested that the «palisade» endings have an ultrastructural counterpart in the «myotendinous cylinders» he found in monkey EOM.

The nerve endings we described in human EOM show an ultrastructure different in many respects to that of myotendinous cylinders. We cannot, however, exclude the possibility that the nerve endings we described at electron microscopy correspond to Dogiel's «palisade» endings.

It is difficult to relate the light microscopy observations to our findings, obtained examining semi-thin sections (where nerve endings cannot be identified) and ultrathin sections (where it is difficult to understand exactly the three dimensional organization of the whole receptor). However, considering the similarities in the

location (myotendinous junction) and size (one muscle fibre and its tendon) of the receptor and the same relations the nerve supply seems to have with the striated muscle fibre (at the tip and along the terminal part of it), we think we can reasonably identify the Dogiel's «palisade» endings in those ultrastructurally found in human EOM, and here described. We want to point out, however, that, since the differences among animal species are not surprising, we must be prudent in stating that the «palisade» endings show a «unique» ultrastructure. Therefore, we think that both Ruskell and we have described a similar type of receptor, whose ultrastructural peculiarities are different among animal species.

Golgi tendon organs in human EOM have never been described using light microscopy. Only Mukuno (1983) reports the presence of receptorial structures «similar to tendon organs» in human EOM at the electron microscope, but he does not give any description of them. We couldn't find typical or atypical Golgi tendon organs, and we are, therefore, unable to confirm Mukuno's findings. However, because of some important morphological analogies between the structures we observed with electron microscopy and the tendon organs, and because several mammals have tendon organs in the EOM, we presume that a similar function is performed by the musculo-tendinous complexes, unique receptorial structure present in man in the EOM myotendinous area, and by the tendon organs.

The peculiar ultrastructural features we observed are difficult to understand and some problems persist, but some hypotheses may also be formulated. For example, the nature of the capsular cells we found is and remains a problem. In the literature, two types of capsular cells have been identified; the outer ones are considered as perineurium and the inner ones as connective tissue cells (see Ovalle and Dow, 1983 for review of literature). We found only one type of capsular cell, which has intermediate features between the two afore-mentioned. Even if we remain uncertain about their nature, we can reasonably conceive that they have functions attributed to both inner and outer ones, i.e. to envelope the receptorial area and to subdivide the tendon into smaller compartments in order to create inside them the microenvironment which is more favourable to receptorial function. Moreover, we think that the absence of an outer capsule involving a certain number of muscle fibres and nerve endings can allow the formation of small and numerous receptorial structures, each one transmitting signals from only one or a few muscle fibres.

It is not yet possible to understand the significance of the peculiar ultrastructural features of the nerve endings found. However, features similar to those more frequently found have been described in other sensorial endings such as those found in the rat cheek mucosa (Watanabe and Yamada, 1985) and are also considered to be mechano-receptorial. On the other hand, the coexistence in EOM of more than one type of nerve ending has previously been reported also in the monkey (Ruskell, 1978, 1979). This fact seems therefore to be related to the specific function of these receptors. Also the smaller size of these receptors, compared to those of the skeletal muscle, as shown in both human and monkey EOM, can be related to their specific role.

The behaviour of the plasma membrane of the terminal Schwann cells is interesting. Evaginations of the outer plasma membrane of these cells enveloping portions of the connective tissue have also been observed is skeletal muscle tendon organs (Schoultz and Swett, 1972), but in the latter and in those of the monkey EOM, the nerve terminals, with or without a Schwann cell sheath, do the same (Schoultz and Sweet, 1972; Ruskell, 1979; Zelenà and Soukup, 1985). This could easily be interpreted as the site where the nerve endings are closely anchored the tendinous portion, probably stretched directly by the contraction of the muscle fibre inserted on the receptor. On the contrary, the finger-like processes penetrating into the axolemma have never been described before. Merkel cells send similar processes into neighbouring keratinocytes (see Yeh and Byers, 1983, for review of the literature). Finger-like processes of the nerve terminal of the Pacini corpuscle protrude between the lamellae of the inner core (terminal Schwann cells) (Halata et al., 1985). It would be interesting to know their possible functional role, but until now no interpretation has been given for them. One hypothesis could be to see them, in particular the Schwann cell finger-like protrusions as in our case, as sensors that transmit or enhance all deformations (weak, medium, strong, etc.) received on the outer plasma membrane to that in contact with the specific area of the sensitive axolemma and/or axoplasm. The constancy and precise localization of the neurotubules in correspondence to these areas could have such an explanation.

Moreover, we consider important also the closer relationship found between nerve endings and muscle component, and also described by Ruskell for myotendinous cilinders (1978) and for some EOM tendon organs (1979) in monkey, because it is possible that this vicinity allows the generation of very detailed proprioceptive informations from EOM to the central nervous system.

The peculiar structural features we observed are, therefore, not surprising if we consider the kind of information these receptors have to transmit. In fact, the existence of an afferent system so precise and refined is essential in the oculomotor muscle apparatus which has to ensure very exact movements and a perfect coordination between the two eyes. This is fundamentally important for the development of a normal binocular vision. The presence of «efferent» nerve endings (like very small motor end plates) contacting the terminal portion of the receptorial muscle fibre, could perhaps be interpreted in this sense, assuring, as in the muscle spindle, a more accurate integration at the level of the central nervous system.

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