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The fine structure of human extraocular muscle spindles and their potential proprioceptive capacity

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INTRODUCTION

For many years the presence of receptors in human extraocular muscles was doubted, for despite a clear description of muscle spindles in sheep (Cilimbaris, 1910) nothing comparable was found in human material. The occasional observation of muscle fibre encapsulation hinted at the possibility of the presence of spindles but not until Cooper & Daniel (1949) and Merrillees, Sunderland & Hayhow (1950) published their detailed accounts were the doubts dispelled. Yet although they described spindles bearing features that were sufficient to warrant their classification both groups of workers found them to have an unusual appearance. For example, intrafusal muscle fibre diameter varied and often compared with that of extrafusal muscle fibres, in contrast to the substantially reduced diameters characteristic of other spindles. From the small maximum spindle diameter noted in these and subsequent reports (Cooper, Daniel & Whitteridge, 1955; Winckler, 1956; Maier, DeSantis & Eldred, 1975) one may infer that the periaxial space is limited, for which the published micrographs bear adequate witness. These factors had presumably hindered spindle identification by earlier workers.

Other than a brief description of the ultrastructure of sensory endings (Mukuno & Nomura, 1969) human extraocular muscle spindles have attracted little further attention and their peculiar structural features remain unexplored forty years after they were described. The purpose of this study is to present a detailed analysis of the structure of spindles and to consider whether or not they are likely to function in a similar manner to their counterparts in other muscles, notwithstanding their dissimilarities.

In contrast to man, sheep extraocular muscle spindles are in most respects of standard form, and a description of them is included to provide a comparison.

MATERIALS AND METHODS

Six human extraocular muscles consisting of two medial, one lateral, one inferior and one superior rectus and one inferior oblique muscle were obtained from three patients aged 58, 70 and 74 years undergoing ocular enucleation for choroidal melanoma. The patients had no record of impairment of eye movements or of neurological or muscular disease. Long lengths of each of the muscles were removed and immersed after a delay of less than 5 minutes in 5% cacodylate-buffered glutaraldehyde at pH 7·4. Muscles were cut longitudinally into four or five strips and cut transversely into lengths of about 1 cm and transferred, after washing, to a 1%

unbuffered solution of osmium tetroxide for 1 hour and then dehydrated in graded ethanols, cleared in xylene and embedded in Araldite. Sheep material was obtained from a local abattoir. After decapitation the right orbit of three animals was dissected swiftly to free the area around the superior rectus muscle to permit injection of glutaraldehyde. The muscle was then removed, immersed in the fixative and prepared in the same manner as the human material.

Sections 0·75 μm thick were cut transversely and retained at 50 μm intervals from pieces taken well away from, and mainly distal to, the motor end-plate band. A few pieces were cut longitudinally. When spindles were identified sections were retained at 10 μm or 3 μm intervals or mounted serially. Sections were stained in a solution of equal parts of 1% toluidine blue and 2·5% sodium carbonate. Thin sections for electron microscopy were cut at appropriate intervals, mounted on copper grids and immersed in a saturated solution of uranyl acetate in 30% or 70% ethanol for about 20 minutes and then, after washing, in 0·4% lead acetate in 0·2 N sodium hydroxide for 10 minutes.

RESULTS

Human extraocular muscle spindles

Spindles were often identified without difficulty and 27 of them were analysed in detail, either from end to end or from one pole to beyond the equator, so that the full sensory region was included. Spindles contained from one to 16 muscle fibres with a mean of 8 and varied in length from 130 to 1360 μm with a mean of 542 μm. Maximum widths at the equator varied from 49 to 182 μm (mean 97 μm) and the mean spindle fibre diameter (15·3 μm) measured near a pole was smaller than that of neighbouring extrafusal fibres (21·9 μm). The fibre diameter spectra were unimodal in both groups with considerable overlap between the two (Fig. 1).

Nuclear chain fibres

Of a total of 215 intrafusal muscle fibres only 90 (42%) were nuclear chain fibres. They were rather more common in the younger (48%) than in the two older groups of muscles (25% each). Their structure was essentially similar with a prominent Z-line, an M-line and a narrow I-band. In the myotube region the mainly oval nuclei occupied a central position, well separated at first, with undifferentiated sarcoplasm filling the interspaces at the core of the fibres. The interspaces reduced or stopped at the equator so that nuclei were almost touching, retaining their oval shape, or were in contact and flattened against each other (Fig. 2). Long rows of central nuclei were common but occasionally they were short, consisting of as few as three central nuclei. Myofibrillar material was reduced in the myotube region and at the equator it was represented by thin strands undulating peripherally in phase with the bulging nuclei and often a mere one or two myofibrils thick. Transverse sections showed that some myofibrillar material was always present. Fibre diameters were reduced at the equator often to little more than, and sometimes less than, half that measured towards the poles of the spindles and striations became less discrete. Some of the fibres were surprisingly large and their non-equatorial diameters and those of extrafusal fibres were similar (Figs. 1*a*, 3). Even the finest of them had a greater girth than many of the chain fibres in sheep spindles; intrafusal fibres with polar diameters less than 10 μm were rare in man whereas they were common in sheep (Fig. 1).

Sensory endings were located opposite and often slightly beyond the myotube region (Figs. 3, 4). By inspection of serial sections terminals could be seen to coil

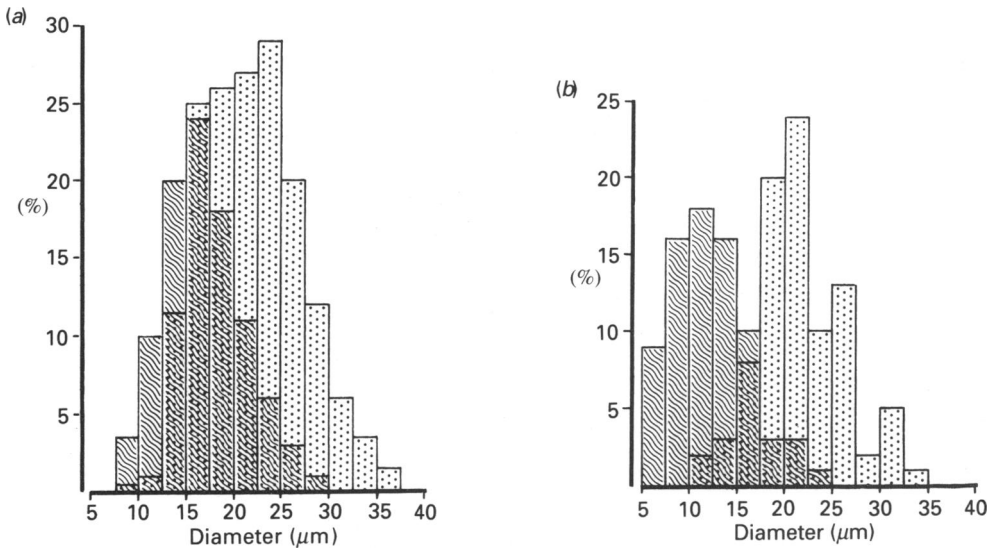


Fig. 1 (*a–b*). Diameter distributions for intrafusal (i) and extrafusal (e) fibres of human (*a*) and sheep (*b*) extraocular muscles. Intrafusal fibres were measured close to a spindle pole (n = 172 human, 78 sheep) where they are largest and extrafusal measurements were made from fibres immediately adjacent to spindles (n = 297 human, 95 sheep). ▨, (i); ⁘, (e).

Fig. 2. Montage of electron micrographs through a myotube of a nuclear chain fibre. The central nuclei are almost in contact, myofibrils are confined to a narrow peripheral zone, most of the fibre surface is covered by nerve terminals (*t*) and it is enclosed by a delicate inner capsule (*c*). The varicose nature of terminals is indicated in two positions (*v*) and one terminal is buried deep within the fibre adjacent to a nucleus (*b*). Marker, 5 μm.

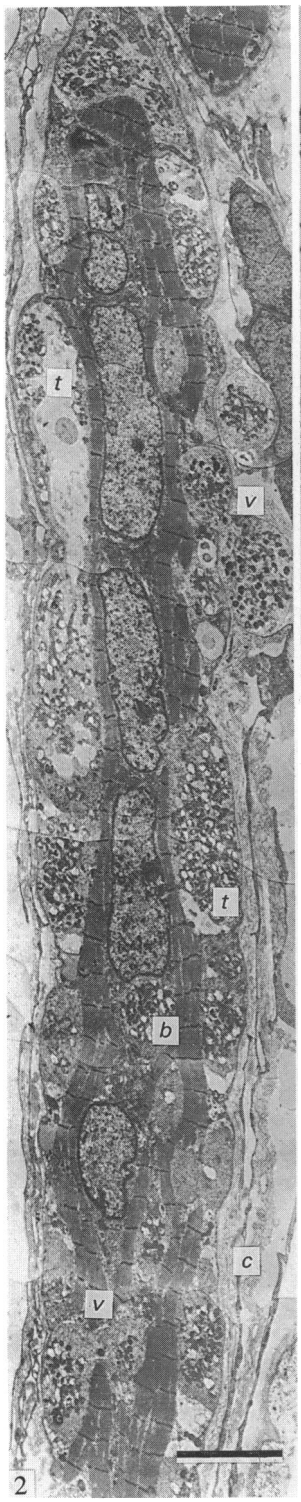
Fig. 3. Transverse section through a spindle close to the entry of a nerve (*n*). Two of the fibres identified in serial sections as chain fibres are separately enclosed by inner capsules (*i*), one of them fused with the outer capsule at *c*. Both chain fibres are at pre-myotube level with nuclei still peripheral (one is shown at *u*) but both have sensory terminals (*t*) and both compare in size with extrafusal fibres (*e*) and the three other intrafusal fibres that were unmodified (see text). Marker, 10 μm.

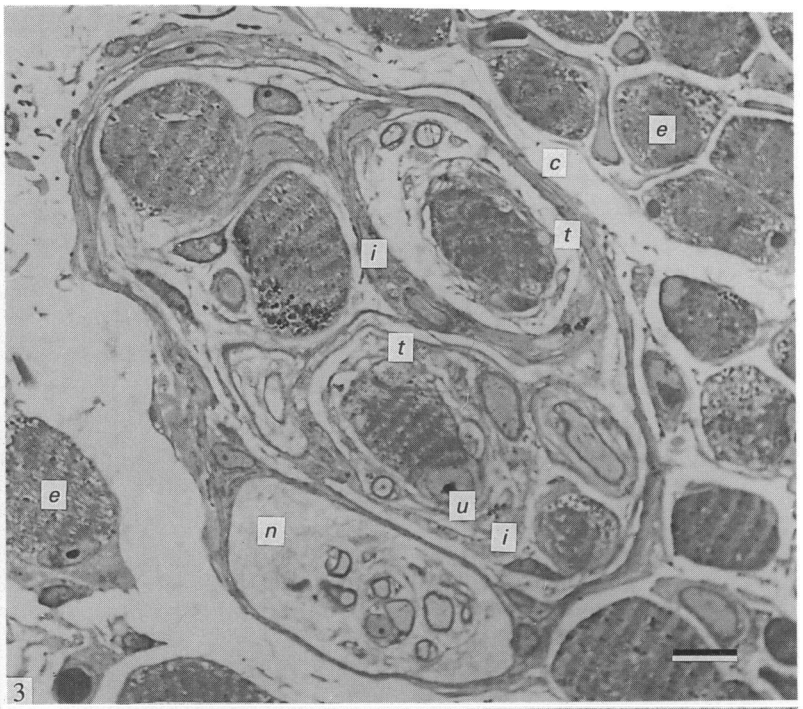
Fig. 4. Electron micrograph of part of a sensory terminal (*t*) at the myotube level of a nuclear chain fibre sectioned longitudinally. Most of the area shown is occupied by mitochondria and a few clear vesicles are present. The narrow synaptic cleft is empty apart from material forming part of the dense plaques (*p*). The ill-defined banding of the muscle fibre is typical of the equatorial region of a spindle and the two M-lines shown are very faint. Marker, 0·5 μm.

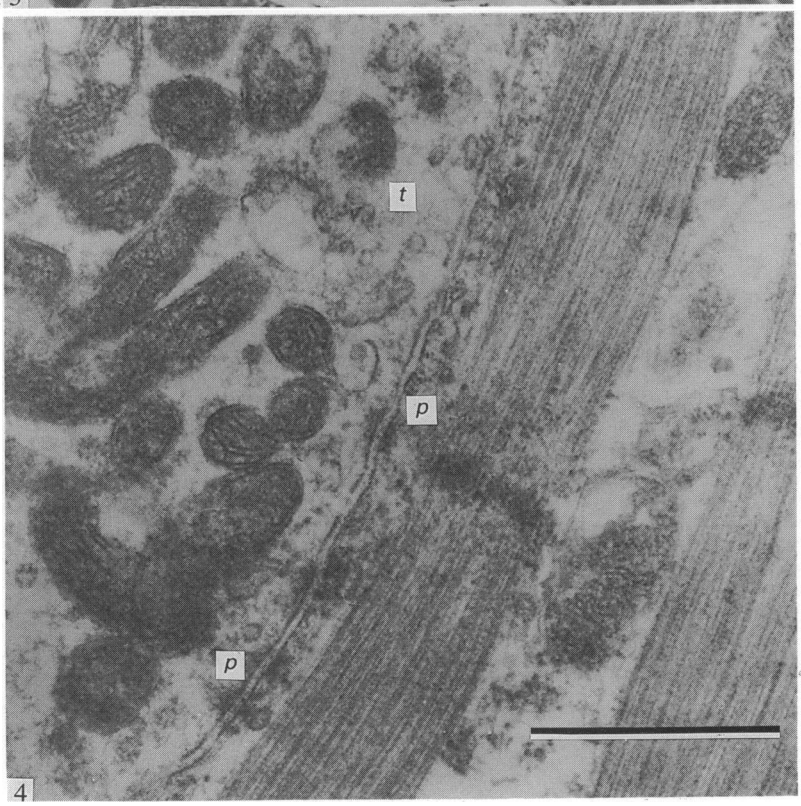
Fig. 5 (*a–c*). Three sections through the same area of a spindle separated by a few microns. A chain fibre (*c*) increases slightly in diameter from 5(*a*) to 5(*c*) through a myotube and a larger nuclear bag fibre (*b*) is seen at myotube level at 5(*a*) and at bag level at 5(*b*) where the nuclei are double stacked. Dark myofibrillar material is present in each section and is least in area in the chain fibre at 5(*a*) and in the bag fibre at 5(*b*). The two fibres display terminals in each section and they share an inner capsule (*i*). An extension of the capsule surrounds two of the other three fibres in 5(*a*), all of which proved to be unmodified. *p*, outer capsule. Marker, 10 μm.

Fig. 6. A muscle spindle turning so that its fibres are cut transversely on the left and obliquely on the right. One of the oblique fibres is a nuclear bag fibre with several nuclei (*n*) in a cluster with sparse adjacent myofibrils and abundant terminals (*t*). *c*, capsule. Marker, 20 μm.

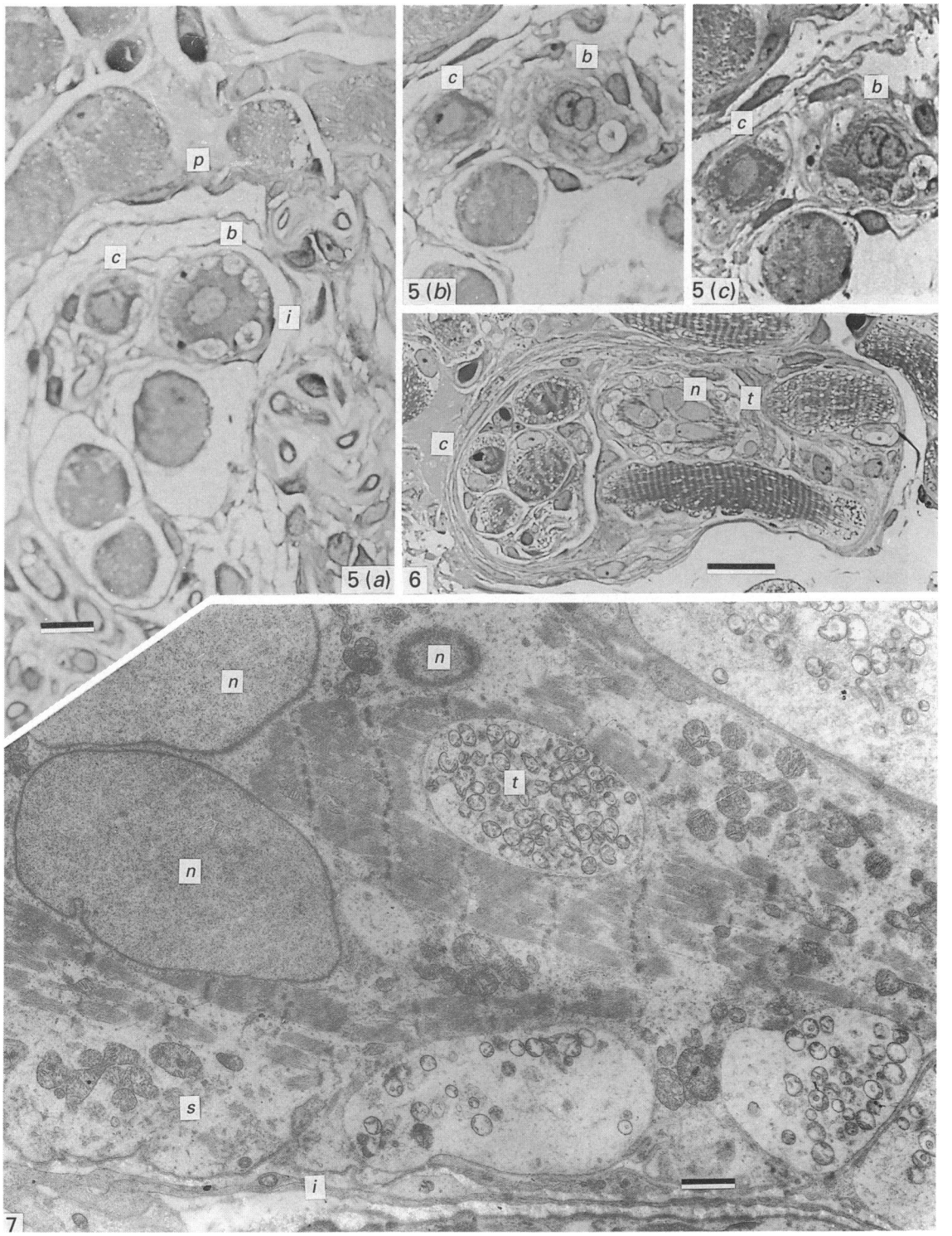
Fig. 7. Electron micrograph of part of the nuclear bag fibre of Figure 6 in a subsequent section. One of the terminals (*t*) is buried deep in the fibre. The nuclei (*n*) straddling the fibre identify the nuclear bag region and myofibrils were found throughout. The ill-defined myofibrillar banding is exaggerated by the obliquity. Note the large areas of undifferentiated sarcoplasm (*s*) next to the cell membrane; it regularly filled the interspaces between the deeply indenting terminals. *i*, inner capsule. Marker, 1·0 μm.







Figs. 2–4. For legends see p. 201.



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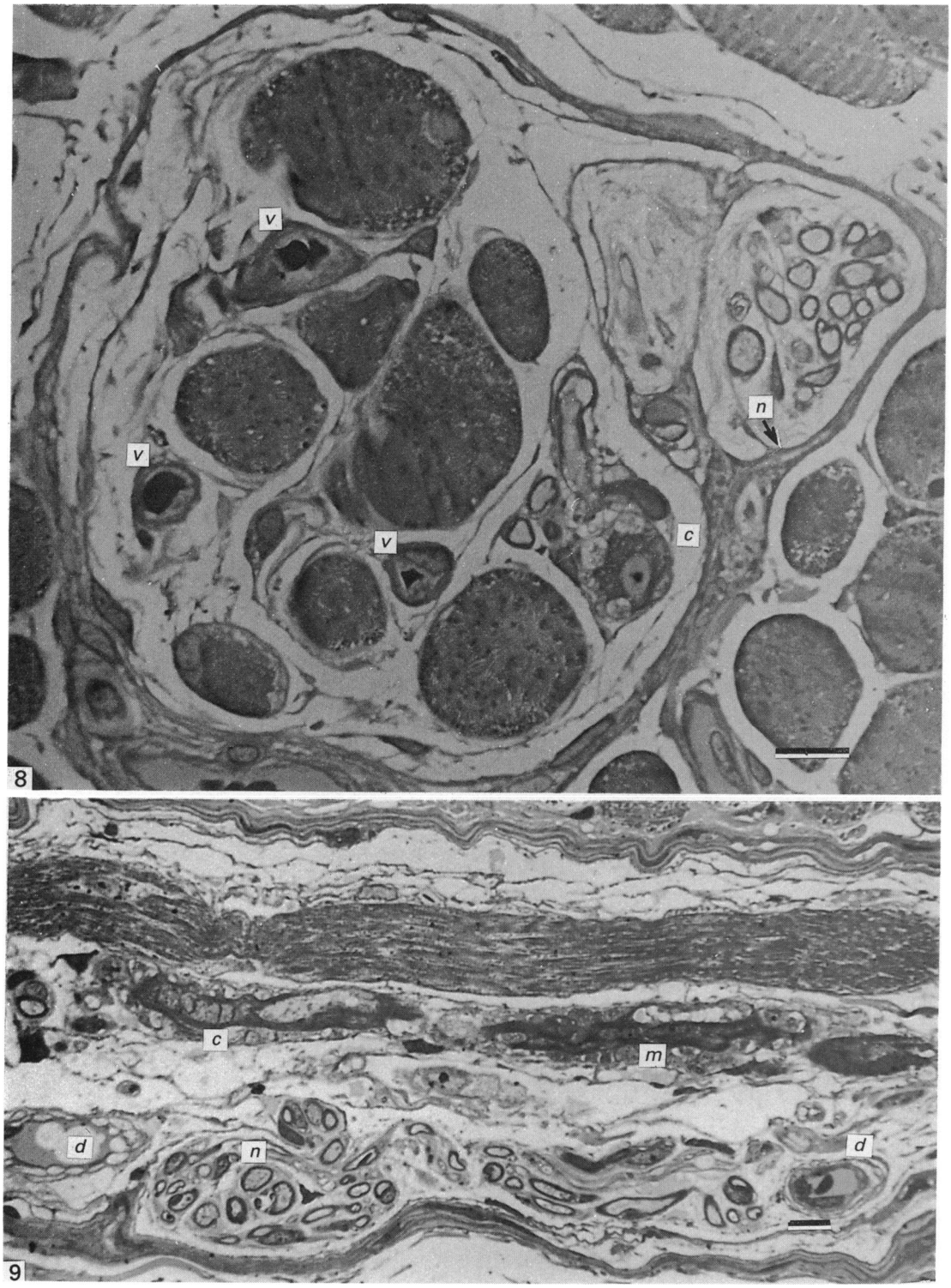

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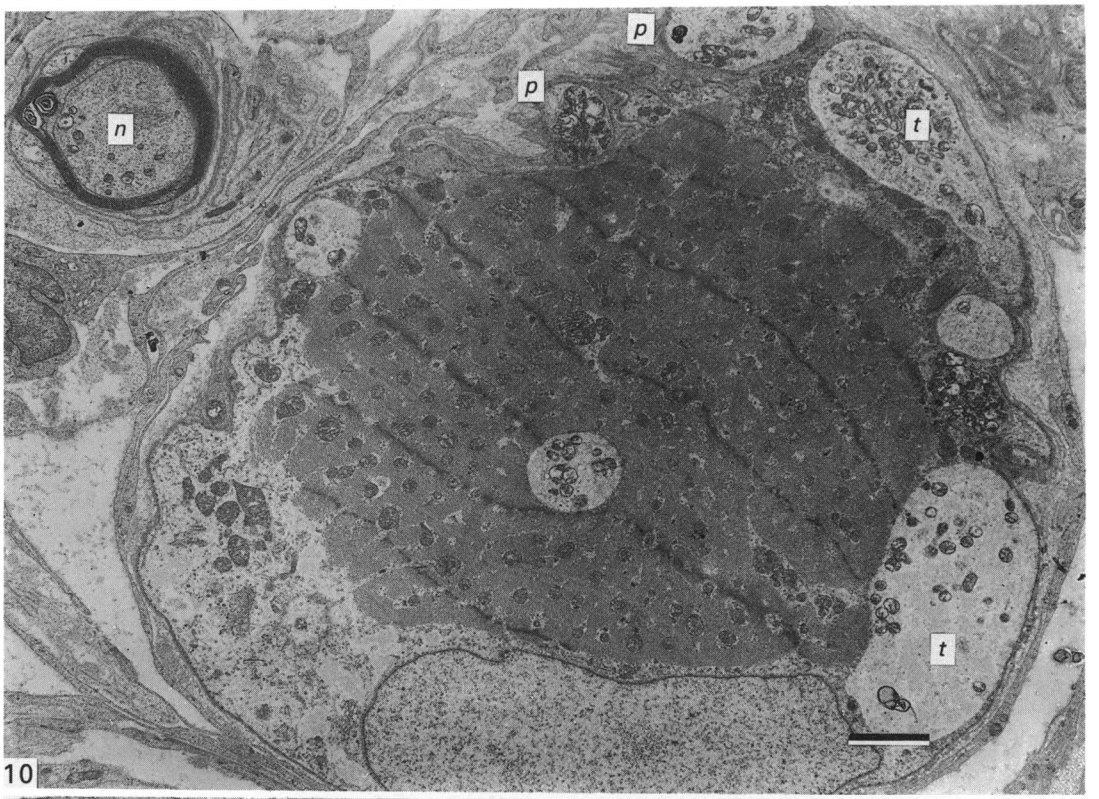
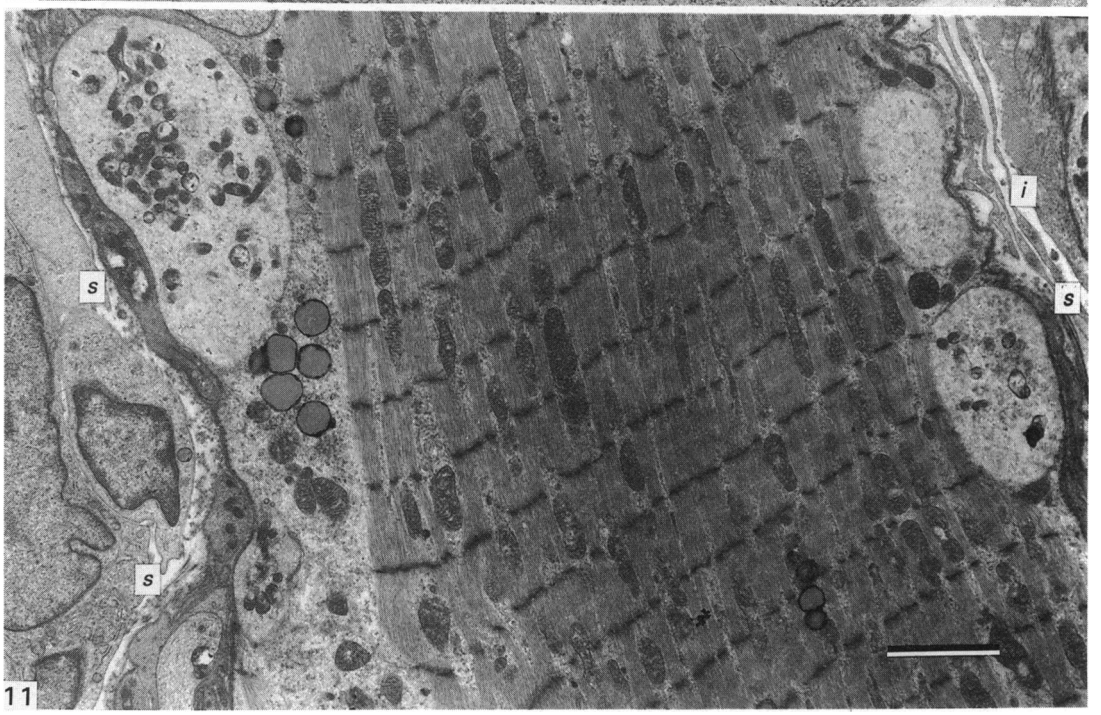




Figs. 10–11. For legends see p. 206.

tightly around individual fibres in a helical fashion with frequent dilations and short spurs. Occasional double stacking of terminals suggested the presence of double helices or overlapping by spurs. The terminals indented the surface of muscle fibres and it was quite common to find deeply penetrating spurs where they ended as expansions (Fig. 2).

Terminals were separated from muscle fibres by a cleft of about 20 nm and were covered externally by a common basement membrane. The cleft was empty apart from maculae of dense material bridging the cleft and linking dense plaques on the apposed cell membranes; several plaques were seen in single sections of most terminals (Fig. 4). Otherwise the cell membranes were unmodified. Aggregations of mitochondria frequently occupied much of the area of the terminal but the packing density was variable and they were few and scattered in the narrow necks connecting expansions. The mitochondria were set in a fine regularly disposed granular matrix interrupted occasionally by circular or oval clear patches which were possibly the result of inadequate fixation. Vesicles were present in small groups or scattered but they were seldom numerous; a large majority were about 50 nm in diameter and agranular (Fig. 4). A few larger vesicles were often present including some with dense cores. The vesicles were unrelated to the plaques.

Nuclear bag fibres

Five spindles contained a single nuclear bag fibre. Four of them were identified in transverse sections and qualified as being nuclear bag in type because their nuclei lay two abreast over a short length of each fibre (Fig. 5). The fifth nuclear bag fibre was cut obliquely and was larger than the others with a greater concentration of nuclei stacked two to three across (Figs. 6, 7). Since none of the five was seen in longitudinal section the nature of the fibre banding was unclear and their diameters were similar to those of nuclear chain fibres apart from the wider equatorial zone. The limited difference between bag and chain fibres presented the hazard of confusing the two but as all sections or every third section were retained on approaching areas of increasing nuclear density the chance of error was minimised. The content of terminals and their relationship with the muscle fibres were indistinguishable from that found in nuclear chain fibres.

Fig. 8. Transverse section of a spindle containing nine muscle fibres and showing the continuation of the thin capsule with the perineurium of a spindle nerve (*n*). Three small vessels are present (*v*). The smallest muscle fibre (*c*) is sectioned in a myotube region showing a central nucleus with nucleolus and several terminals and proved to be a nuclear chain fibre in serial sections. All other fibres are anomalous, lacking equatorial nucleation. Most of the nerve fibres failed to disperse within the spindle. The spindle is represented in Figure 12 as spindle C. Marker, 10 μm.

Fig. 9. Longitudinal section through the equator of a spindle showing parts of two nuclear chain fibres sectioned slightly obliquely, one at myotube (*m*) and the other at chain (*c*) level showing flattened abutting nuclei. The larger, lighter fibre is without equatorial nucleation. *n*, nerve fibres; *d*, capillaries. Marker, 10 μm.

Fig. 10. Electron micrograph of an innervated unmodified muscle fibre in transverse section. Terminals (*t*) lie in surface depressions and lack a Schwann cell investment in common with most chain and bag fibre terminals; one terminal lies at the centre of the fibre. An inner capsule invests the fibre and a medullated nerve fibre (*n*) lies outside the inner capsule – myelin was regularly shed before penetration of the inner capsule in human muscle spindles. Two pre-terminals (*p*) have a thin investment. Terminals were frequently larger than the nerve fibres of origin and an example is seen here. Marker, 2 μm.

Fig. 11. Electron micrograph of an innervated unmodified muscle fibre sectioned longitudinally at a spindle equator. Terminal content is similar to other spindle sensory endings with an empty, narrow synaptic cleft, and plaque densities can be seen in one of them. A thin Schwann cell process (*s*) covers the outer aspect of three terminals but these were unusual. Muscle fibre banding is bold in contrast to the poorly defined banding of chain and bag fibres at the equator. *i*, inner capsule. Marker, 2 μm.

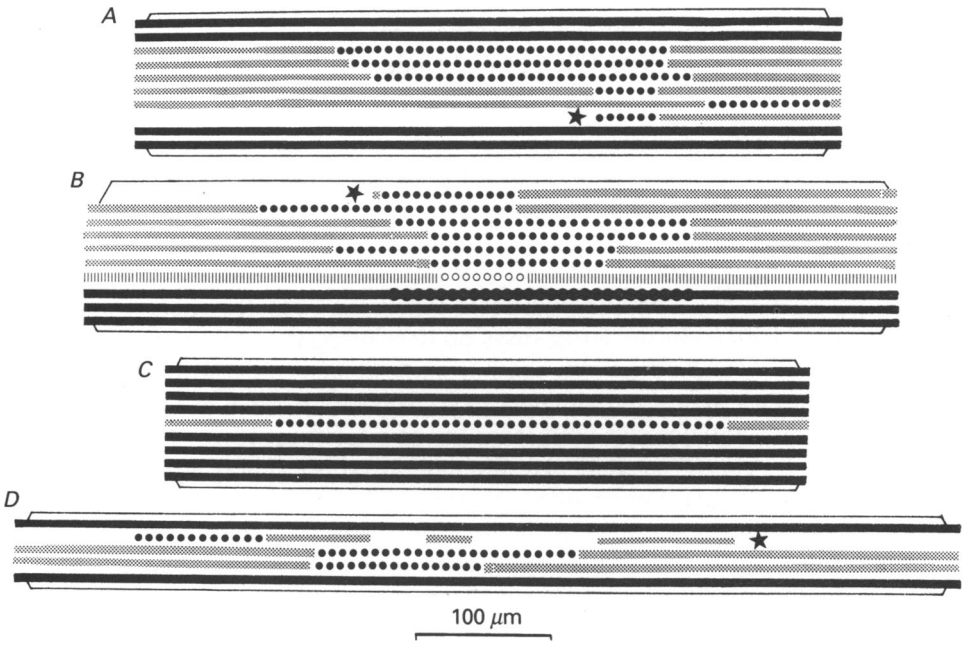


Fig. 12. Scheme of four representative muscle spindles illustrating the four fibre types encountered in this study. Solid thick lines represent anomalous fibres, stippled lines nuclear chain fibres and cross-hatched lines nuclear bag fibres. All circular profiles represent loci with sensory terminals Spindle *B* contained all four types including one nuclear bag and one innervated anomalous fibre. Note the poor registration of sensory loci and marked eccentricity in some cases. Most fibres extended beyond the capsules, indicated by the brackets; exceptions are shown in spindles *A* and *B* in which a chain fibre terminated at a myotube and in spindle D which contained a fragmented fibre. Chain and bag fibres amounted to 48% of all intrafusal fibres of muscle spindles of the 58 years old patient of which spindles *A*, *B* and *D* are examples; the comparable figures for each of the older muscle groups was 25%. Muscle fibre width is not to scale.

Anomalous fibres

Of the 215 intrafusal muscle fibres 120 were anomalous in that they lacked equatorial nucleation. Nuclei remained peripheral and myofilamentous material occupied the full width of each fibre throughout its length and the fibres continued beyond the spindle at each pole or pierced the capsule short of a pole (Figs. 8, 9). Only those fibres occupying a position within the main capsule of the spindle with chain or bag fibres qualified for inclusion in this group. Other fibres not included and regarded as extrafusal sometimes became enclosed within a division of the capsule leaving again without entering the main intrafusal chamber. All the larger fibres of spindles were anomalous but many others were of similar diameter to the larger chain fibres. With a single exception spindles contained at least one anomalous fibre and most spindles contained a majority of them. Their appearance and variety of form was shared by neighbouring extrafusal muscle fibres. Close to the orbital surface of muscles both intrafusal anomalous and extrafusal were similarly smaller than their equivalents lying nearer the muscle centre or ocular surface.

Eight of the anomalous fibres were generously supplied with sensory nerve terminals. The terminals had all the characteristics of sensory endings and were similar in organelle content to those serving nuclear chain and bag fibres but providing a rather less ubiquitous investment of the muscle fibres (Figs. 10, 11). However, the length of fibre in receipt of terminals was approximately the same.

The numerous motor terminals seen near the poles of spindles were identified by the circular, aggregated boutons and sole plate sarcoplasm.

Examples of spindles illustrating each of the fibre classes are represented schematically in Figure 12.

Other spindle anomalies

A variety of other features, not general to muscle spindles, was observed. The equatorial zone was often ill-defined because the periaxial space was small or absent and the sensory regions of fibres were commonly out of register. The separation of intrafusal muscle fibres from the outer capsule by a substantial fluid space, typical of other spindles, was rarely seen although some expansion occurred equatorially in all but three of the spindles. In the latter cases no development of tissue-free space was detectable. Where several fibres with sensory endings were present in a spindle the majority of myotubes were approximately in register but as often as not one or two myotubes were substantially displaced from the equator (Fig. 12).

A discrete single inner capsule investing all intrafusal fibres was never seen. Connective tissue cells ensheathed single or pairs of intrafusal fibres and the sheaths were almost invariably in contact with the outer capsule (Fig. 3). In the smaller spindles a single sheath was sometimes present and in larger spindles there were usually two or three sheaths but numerous fibres, invariably of the anomalous type, lacked a cellular investment.

A number of the smaller fibres terminated within the spindle close to a pole attaching to the outer capsule wall or a connective tissue extension of it but in twelve spindles, representing material from each of the three patients, from one to three fibres stopped well short of the poles, frequently occupying a third or less of the spindle length. All of the short fibres were fine and most received sensory terminals and in all but one instance fibres terminated at or close to the innervated portion as shown in Figure 12. In two spindles fibres appeared to stop and in subsequent transverse sections they could be identified again; a double interval was noted in one of them (Fig. 12). They were regarded as single fibres because at all points along the spindle the same site was occupied by the two or three separated elements. The ends of short fibres were either tapered or they displayed granule-containing expansions interrupted by

Fig. 13. One of the two spindle fibres sectioned through a myotube shows a mass of densely stained material extending from a central nucleus to the surface. *c*, capsule; *e*, extrafusal fibres. Marker, 10 μm.

Fig. 14. False spindle showing the initial investment of four muscle fibres by the perineurium (*p*) of a nerve (*n*) which is incomplete below where a small vessel (*v*) enters. Marker, 10 μm.

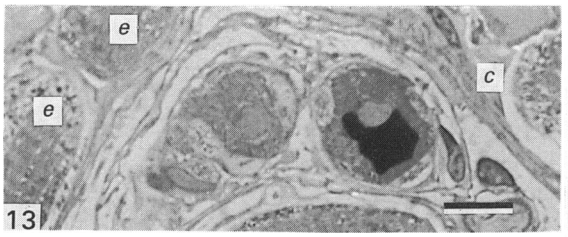
Fig. 15. The same false spindle about 100 μm further on, showing complete enclosure of the muscle fibres and the vessel (*v*). The nerve was axially orientated throughout the length of the false spindle and no nerve terminals or muscle fibre modifications were traced. Marker, 10 μm.

Fig. 16. Sheep muscle spindle sectioned transversely through the myotube region. Intrafusal fibre diameters are very small compared with the extrafusal fibres (*e*). The largest is a bag fibre and the others chain fibres of various diameters. One nerve fibre (arrow) lies within the inner capsule (*i*). Note the discrete inner and outer capsules. *n*, spindle nerve; *v*, spindle vessel. Marker, 10 μm.

Fig. 17. Sheep muscle spindle sectioned approximately 100 μm beyond Figure 16, through the equator, with three nuclei occupying most of the nuclear bag fibre and a single central nucleus in each of the chain fibres. Marker, 10 μm.

Fig. 18. Longitudinal section through the equator of a sheep muscle spindle showing a nuclear chain fibre and parts of two others. The nuclear chain region (*c*) of the uppermost fibre and the myotube (*m*) region of the lowermost fibre are shown. *i*, inner capsule; *t*, terminals. Marker, 10 μm.

Fig. 19. Longitudinal section through a nuclear bag fibre at the spindle equator of a sheep muscle. The large nuclei, stacked two abreast, occupy almost the full width with myofibrils reduced to fine strands next to the cell membrane. *m*, myotube region. Marker, 10 μm.



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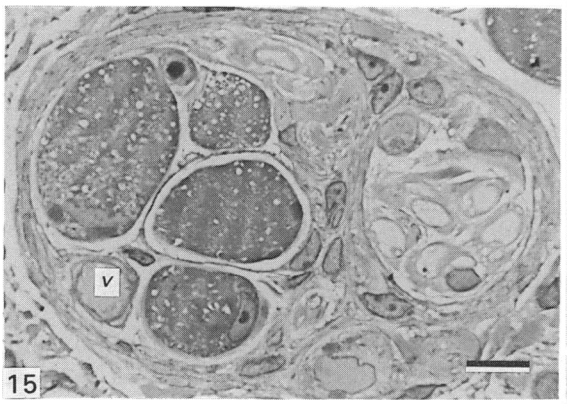

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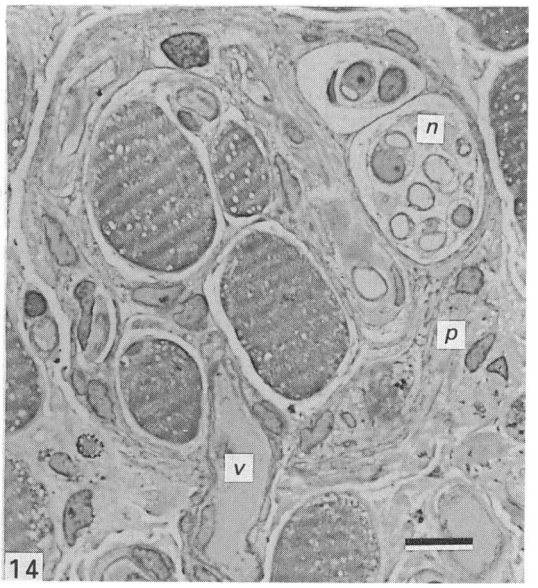

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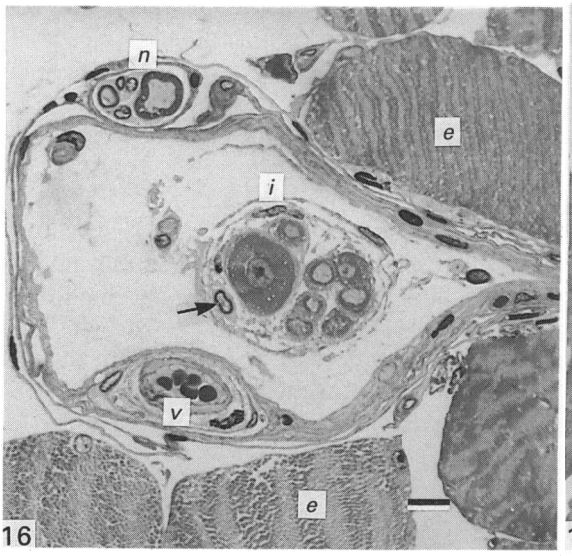

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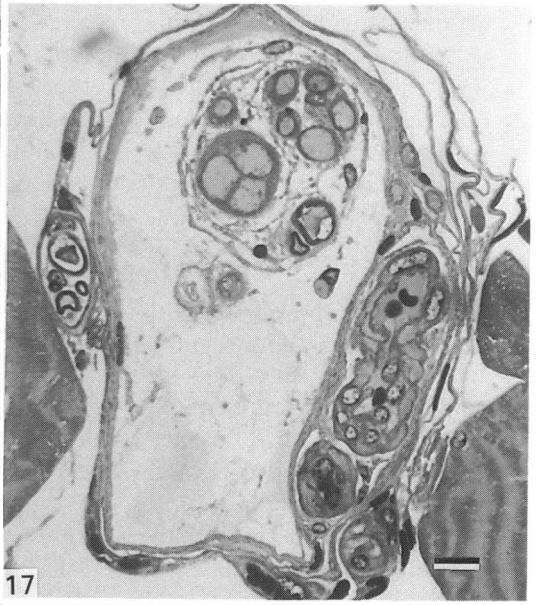
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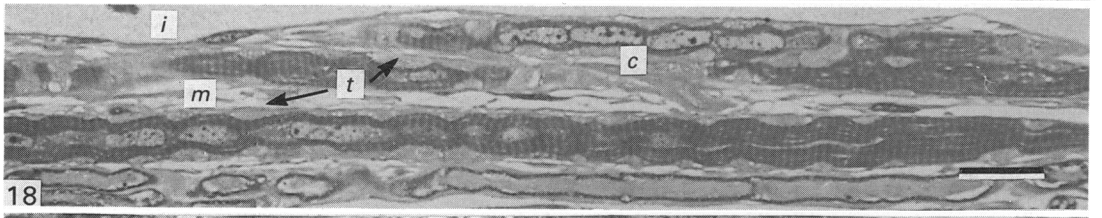

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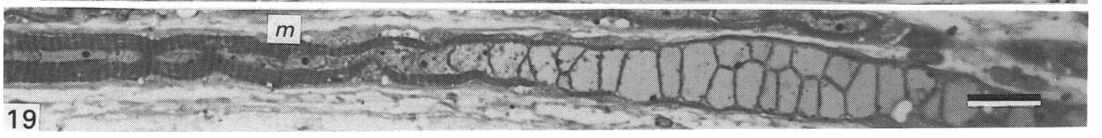

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numerous empty vacuoles varying in size and shape and enclosed by an irregular cell membrane.

A minority of intrafusal muscle fibres with sensory endings contained irregularly shaped masses of densely staining material, often speckled with mostly circular profiles of lower density. They were most commonly found in the undifferentiated sarcoplasm separating central nuclei in the myotube region of chain fibres. Several deposits of the material, assumed to be lipofuscin, were seen within a short length of some fibres and in a few instances it extended from the centre to the perimeter of a fibre crossing territory normally occupied by myofibrils (Fig. 13). Lipofuscin was also seen in extrafusal muscle fibres but with far less frequency.

These departures from expected muscle spindle structure were observed in material from each of the three individuals.

False spindles

Eight encapsulated structures were found containing fibres exclusively of the anomalous variety. The capsule was a division of the perineurium of an adjacent nerve producing a second attached chamber enclosing the group of muscle fibres with or without intrusion of some of the nerve fibres (Figs. 14, 15). Alternatively, the nerve and muscle fibres shared a single capsule and in one of the structures with this arrangement a muscle fibre received a motor end-plate. Sections retained for inspection of several of these structures were taken at rather infrequent intervals from the series and the possibility that other motor end-plates were present cannot be ruled out; sensory endings are unlikely to have been missed because they generally cover substantial lengths of muscle fibres and none was found. They are therefore false spindles. They contained between two and eight muscle fibres and the capsule varied in length from 90 to 650 μm.

Sheep extraocular muscle spindles

Obtaining appropriate data from sheep extraocular muscle spindles for comparison with the human equivalent was facilitated by their bold profiles, symmetry and high frequency. At least one spindle was present in any cross-section. However, its suitability as a representative of the typical muscle spindle was no more than an assumption based on earlier studies and twelve spindles were therefore analysed in detail in cross-section. Others muscle pieces were prepared in longitudinal section and the spindles were sampled.

Bag fibres were larger than chain fibres at all positions along spindles but chain fibre diameters varied two- or three-fold, producing an almost continuous range of diameters as expressed in the unimodal distribution (Fig. 1). However, in single spindles, bag and chain fibres could usually be distinguished in serial cross-sections well before the equator was reached (Fig. 16). Diameters peaked at 12 μm for intrafusal fibres and 21 μm for extrafusal fibres close to the spindle poles and the difference increased slightly towards the equator as intrafusal fibres became more slender. All spindles had a wide equatorial expansion (maximum diameter 95–175 μm, mean 120 μm) with a fluid-filled interval separating outer and inner capsules (Figs. 16, 17). The inner capsule enclosed all the muscle fibres which were aggregated and, unlike those in Figure 17, usually centrally placed.

Spindles contained from 3 to 16 muscle fibres with an average of 8. Nuclear bag fibres were often more easily recognised than in human material because the nuclear bag region was longer and broader with two or three central nuclei occupying the fibre width (Figs. 18, 19). One to three fibres in each spindle were nuclear bag in type and

the remainder were all chain fibres; in both groups the nuclei were invariably packed and flattened against each other.

Sensory terminal fine structure was indistinguishable in chain and bag fibres and was strikingly similar to that found in human spindles except that, in sheep, a terminal was frequently common to two adjacent fibres whereas this was rare in human spindles. All terminal-bearing regions of fibres were in register at the equator and no anomalous fibres without equatorial nucleation were seen.

DISCUSSION

Human extraocular muscle spindles differ from all other spindles so far subjected to detailed study. Not one of the several anomalous features recorded here has been noted in spindles of other human muscles or in extraocular muscle spindles of other species. These will be discussed in turn. The presence of intrafusal fibres as large as extrafusal fibres, confirming the findings of Cooper & Daniel (1949) and Merrillees *et al.* (1950) is partly explained by the anomalous fibre content. They have none of the characteristics of regular intrafusal fibres and are indistinguishable from extrafusal fibres apart from their position and so share their variety of diameters. Fewer than half (44 %) of the intrafusal fibres conformed to the usual pattern of spindles. consequently human intrafusal fibres fall into two distinct groups, one comprising mostly small diameter fibres with equatorial modifications and sensory innervation and the remainder, more than half the total, made up of mostly larger fibres having none of the customary features of spindle fibres.

There is no reason to doubt that terminals on the regular intrafusal fibres are functional. Equatorial terminals have an annulospiral form and contact muscle fibres in the usual fashion and the limited imperfections of axonal terminal structure can be attributed to delay and other difficulties in achieving fixation. Similarly, nerves entering spindle capsules were found to be in good condition and bore the expected complement of organelles. However, it is unlikely that they could function in a normal manner. Spindle fibres generally enjoy the privilege of functioning in a protected environment undisturbed by the local activities of extrafusal fibres. In human spindles this cannot be so – spindle afferents must be subject to the mechanical consequences of the contractions of unmodified fibres. The problem is exacerbated by their bulk and frequent preponderance.

A second major feature distinguishing human extraocular muscle spindles from other mammalian spindles is the limited or absent periaxial space. It is for this reason, more than any other, that spindles are sometimes difficult to find in sections. The large fluid-filled space surrounding a central assembly of intrafusal fibres typical of spindles in general, and present in sheep, is lacking even in the most generously proportioned human spindle and the segmented inner capsule, contrasting with the single common investment in sheep, adds to the cramped appearance. Accepting that the periaxial fluid-filled space acts as a buffer against external influences (Brzezinski, 1961), it follows that human extraocular muscle spindles do not enjoy such protection or, at best, it is diminished so that the risk of interference from extrafusal fibre contractions is added to that of unmodified intrafusal fibres.

Turning now to the regular intrafusal fibres in human spindles, although they are individually of usual construction, the ratios of chain and bag fibres are again singular. Since the discovery of bag fibres all reports appear to imply that they are regularly present in spindles and, among the larger surveys, at least one bag fibre is expressly stated to be present (Cazzato & Walton, 1968; Banker & Girvin, 1971). All the sheep

spindles examined contained at least one bag fibre, and most had two, whereas they appeared to be absent from most of the human spindles. Bag fibres in human spindles were not easily identified because, with one exception, they were maximally only two nuclei in width and the bag length was short; consequently others could have been identified incorrectly as chain fibres. The usual facility of identifying bag fibres in most positions within the spindle by their greater diameter, available in the sheep spindles, cannot be used in human material because of the wide spectrum of fibre diameters, but the possibility of error is insufficiently strong to question the conclusion that bag fibres are absent from most spindles.

The large calibre intrafusal fibres without cytoplasmic modifications equatorially, yet generously supplied with sensory endings, constitute another fibre class not previously described. They were more common than bag fibres and nearly a third of the spindles contained one. There is little reason to doubt that muscle fibre activity would excite the endings since all specialised muscle receptors are regarded as mechanoreceptors and since these fibres are presumably uniformly contractile throughout their length, the response characteristics would necessarily differ from those of chain and bag fibre endings.

Variations reported among mammalian spindles such as the different ratios of receptors, fibre diameters and incidence of secondary endings are minor compared to the aberrant features of human extraocular muscle spindles and consequently the literature provides no guide towards an explanation. In other circumstances the singular features of anomalous fibres indistinguishable from extrafusal fibres and the particular heterogeneity of spindle receptors might be considered the instruments of specialised function but their setting suggests that they are expressions of spindle reorganisation imposed by degeneration. The frequent deposits of densely stained amorphous material in spindle fibres, assumed to be lipofuscin, is an obvious indicator of degeneration. Although often confined to the undifferentiated sarcoplasm between central nuclei of nuclear chain fibres, territory normally occupied by myofibrils is also encroached upon. The deposits could represent a stage in degeneration leading to fragmentation and destruction of the fibre.

Evidence for loss of fibre lengths in these spindles was strong. Short pieces of muscle fibre occupying a small fraction of the length of the spindle are foreign to the normal complement of spindles. Small diameter chain fibres with normal configuration at one pole, with an equatorial zone served by sensory terminals stopping abruptly at or just beyond the equator, is evidence of effete receptors and no explanation other than fibre fragmentation and loss appears to fit (Fig. 12). Successive short lengths of muscle fibres found in two spindles, similar in diameter and occupying a similar position, are consistent with fibre break-up.

The anomalous fibres are arguably incursions of extrafusal fibres replacing degenerated intrafusal fibres. The absence of bag fibres from most spindles and the low numbers of chain fibres in some is consistent with this view. In this respect it is of interest that Swash & Fox (1972) found fewer intrafusal fibres in the spindles of older human skeletal muscles and attributed the difference to fibre degeneration. On the other hand, these authors found evidence of spindle nerve degeneration whereas none was identified in this study. Innervation of anomalous spindle fibres of extrafusal type could be the result of sensory terminals, made redundant by fibre degeneration, in search of a target. And finally the eight encapsulated muscle fibre groups without sensory endings, the so-called false spindles noted earlier in human extraocular muscles (Ruskell, 1984), may represent the culmination of spindle degeneration with all bag and chain fibres destroyed and replaced by erstwhile extrafusal fibres. Apart

from a single motor end-plate the fibres were not innervated and the numerous nerve fibres present in each case were presumably destined for other targets.

Given that the extraocular muscle spindles in the present study are in the course of degenerating, one needs to consider whether or not it is really a feature of ageing or an expression of phylogenetic redundancy. An answer to this question would have been facilitated had the material spanned a wider range of ages but the muscles used were taken from patients aged 58, 71 and 74 years; none was available from younger patients. Although the explanation of ageing is favoured by the fact that the youngest muscles contained twice the proportion of standard intrafusal fibres (48%) as the other two (25% each), this scarcely amounts to tangible evidence and no other helpful cues were recognised.

If spindle afference is ineffective in human extraocular muscles, are other sources of proprioceptive information available? Daniel (1946) described numerous muscle spirals consisting of nerve fibre terminals embracing single muscle fibres in a helical fashion and speculated that they might contribute to extraocular muscle sense. But this is unlikely as the terminals were shown to have the morphological characteristics of motor end-plates (Ruskell, 1985). The position regarding Golgi tendon organs is unclear. Initially Golgi tendon organs were considered to be absent from extraocular muscles (Golgi, 1880) but this was disputed by others who claimed to find tendon organs and other forms of terminal in man and animals (see Ruskell, 1979, for a review). Of these studies Dogiel's (1906) is the most expressive of the precise forms of endings present and shows that they do not conform to the elaborate encapsulated ending that we accept as a Golgi tendon organ today and one of the types he illustrated (the palisade ending) was recently described in human extraocular muscle (Richmond, Johnston, Baker & Steinbach, 1984). Free terminals, sometimes partially enclosed by capsular material, were described in the only published account of the ultrastructure of tendon nerve endings in human extraocular muscles and they were regarded as putative receptors (Sodi, Corsi, Faussone-Pellegrini & Salvi, 1988). The capsular material described, however, had the appearance of connective tissue cells rather than that of the perineurium normally associated with Golgi tendon organs. The contention that Golgi tendon organs are present in human extraocular muscles is therefore poorly supported and those terminals described are apparently unique, probably sensory and possibly fulfilling a special function. Alternatively, they could be regarded with the spindles as degraded as a consequence of ageing or phylogenetically redundant receptors. Further studies are needed for clarification.

SUMMARY

Twenty seven muscle spindles from six extraocular muscles removed following ocular enucleation from patients aged 58, 76 and 74 years were examined throughout all or most of their length by means of light and electron microscopy using serial transverse sections. Five others were prepared in longitudinal section. Twelve spindles of the superior rectus muscle from three sheep orbits were studied in a similar manner to provide a comparison.

The human spindles contained a total of 90 (42%) nuclear chain and 5 (2%) nuclear bag fibres with the usual complement of sensory endings, and 120 (56%) fibres were anomalous with continuous, unattenuated myofibrils throughout their length, a constant width and peripherally placed nuclei. Eight anomalous fibres received sensory terminals similar in form to those of chain and bag fibres. Most (26) spindles contained at least one chain and one anomalous fibre. The periaxial space was limited

or absent and the inner capsule was often segmented and in contact with the outer capsule. Abrupt termination of some chain fibres including several with one pole missing, together with evidence of fibre fragmentation and other structural anomalies, were indicative of degeneration. Eight further encapsulated fibre groups were identified as false spindles containing only anomalous fibres; associated nerves failed to terminate in the encapsulations.

Sheep spindle content was of regular form, all spindles containing several chain and at least one bag fibre enclosed by an inner capsule and surrounded by a substantial periaxial space equatorially.

The human extraocular muscle spindles have lost, either by ageing or phylogenetically, the privilege of contractile chambers isolated by a fluid periaxial space from extrafusal fibre activity and sensory terminals are subject to the direct mechanical influences of anomalous intrafusal fibres. These, and the other departures from normal structure described, must jeopardise monitoring of muscle activity in the manner normally attributed to spindles and their capacity to provide useful proprioceptive information is questionable.

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