Myotatic, Kinesthetic and Vestibular Mechanisms

Ciba Foundation Symposium
Edited by A.V. S. de Reuck
and Julie Knight

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The Ciba Foundation

The Ciba Foundation was opened in 1949 to promote international co-operation in medical and chemical research among scientists from all parts of the world. Its house at 41 Portland Place, London, has become a meeting place well known to workers in many fields of science. Every year the Foundation organizes from six to ten three-day symposia and three or four one-day study groups, all of which are published in book form. Many other informal meetings also take place in the house, organized either by the Foundation or by other scientific groups needing a place to meet. In addition, bedrooms are available for visiting scientists, whether or not they are attending a meeting in the building.

The Ciba Foundation owes its existence to the generosity of CIBA Ltd, Basle, who, realizing the disruption of scientific communication caused by the war and by problems of distance, decided to set up a philanthropic institution whose aim would be to overcome such barriers. London was chosen as its site for reasons dictated by the special advantages of English charitable trust law, as well as those of language and geography.

The Foundation's many activities are controlled by a small group of distinguished trustees. Within the general framework of biological science, interpreted in its broadest sense, these activities are well summed up by the Ciba Foundation's motto, *Consocient gentes*—let the nations come together.

Preface

This is the third in a series of symposia designed to cover the various areas of sensory function, the previous volumes having been "Colour Vision" and "Touch, Heat and Pain". The entire series has been planned by the Deputy Director of the Ciba Foundation in conjunction with Professor Otto Lowenstein, whose involvement in the present symposium was, however, more than usually close, for his own work has been primarily in the area of vestibular function. The Foundation is particularly grateful to Professor Lowenstein for his valuable work in the planning of the symposium and for his lively chairmanship of the meeting itself.

Illness unfortunately prevented the participation of Sir Terence Cawthorne, of The National Hospital, London, but we were glad to welcome Dr. Margaret Dix in his place.

We were sad to learn, during the preparation of these proceedings for publication, of the death of a member of the symposium—Professor F. C. Ormerod, former Director of Research at the Institute of Laryngology and Otology and previously professor in these subjects in the University of London.

CHAIRMAN'S INTRODUCTION

PROFESSOR O. LOWENSTEIN

THE objective of this symposium, the third in the Ciba Foundation's series of meetings on sensory function, is to bring together those people who are interested in the sensory control of posture and movement. So very often these people meet separately. The "vestibular club" is a closely knit society, and those working on muscle are also nowadays beginning to form a very intimate family, but it is not often that the two can meet. This field of the sensory control of posture and movement is of course an extremely wide one, and it has obviously not been possible to invite everyone in it to this meeting—in fact, it is the strict but wise policy of the Foundation to limit the size of its meetings to roughly twenty-five people, in order that they shall be able to discuss informally together. The task of selecting the members has been a hard one, for besides those engaged in the academic pursuit of this range of interests, there are also the clinicians. The continuing discussion between clinicians and laboratory workers is a very frequently interrupted one and it is a further purpose of this meeting to bring together the two groups.

Although there is a limit set to the number of direct participants, it is our hope that by including in the published volume a record of the discussions at the meeting, we shall make accessible to all those interested in our field the thinking aloud of those actually present.

I spoke of roughly twenty-five of us at this meeting. In actual fact I feel that we shall number one more, because there will be among us during this symposium an uninvited but immensely welcome participant; the spirit of Charles Sherrington. It is strange that although it may well be that Sherrington will not often be mentioned in the formal papers, everyone of us is, I think, aware of what he owes to his pioneer work. Let us, then, make the concept of integration the guiding principle of the symposium.

SECTION I
MYOTATIC AND KINESTHETIC MECHANISMS

THE INNERVATION OF MAMMALIAN SKELETAL MUSCLE

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The classic work on muscle innervation by Ruffini, Cajal, and Dogiel, among many others, consists of observations made on nerve endings prepared by the gold chloride, silver nitrate, or methylene blue techniques. Until recently, silver impregnation, the most precise and complete of the traditional trio, was limited to sectioning methods, but by a modification of one of these (Barker and Ip, 1963) it is now possible to obtain whole, teased preparations. These are greatly superior to their gold chloride and methylene blue counterparts, and the information derived from them provides an essential guide for studies made with histochemical techniques and the electron microscope. Over the past few years these histological innovations have revealed much about muscle nerve endings that was previously inaccessible. I shall discuss some of these findings and make a general survey of the distribution and termination of muscle nerves.

MOTOR INNERVATION

The motor supply comprises skeletomotor (α) fibres that terminate in extrafusal motor end-plates; fusimotor (γ) fibres that innervate muscle spindles; and mixed (β) fibres (Bessou, Emonet-Dénand and Laporte, 1963; Adal and Barker, 1965*a*) that innervate both extra- and intrafusal muscle fibres. Intensive research on fusimotor innervation over the past decade at last seems within sight of reaching a full understanding of the complexities involved. The present position is as follows (unless otherwise stated, the information relates to work on the cat).

Spindles receive three kinds of motor ending, a diffuse, multi-terminal, trail ending (Barker and Ip, 1965), and two kinds of end-plates designated as Types I and II (Barker, 1966*b*), abbreviated as p_1 and p_2. The trail ending (see Figs. 19, 20 and 21) was first detected by the cholinesterase technique which revealed diffuse enzymic activity near the equatorial region, in contrast to that shown by discrete subneural apparatuses of plates located further along the poles (Coërs and Durand, 1956 [rat, cat, man]; Kupfer, 1960 [man]; Hess, 1961*a* [mouse, rabbit]; Coërs, 1962 [rat, cat, man]). Boyd (1962) provided the first information about the form of such a diffuse termination, which he described in gold chloride preparations as "a network of fine axons and small elongated nerve endings". Though figures and photographs of the trail ending have since appeared (Barker and Ip, 1965; Barker, 1966*a*), a full description has yet to be published. Two of its main characteristics are the considerable distance that usually occurs between the terminal node and the final ramification making synaptic contact, and the presence of many ramifications given off from preterminal nodes. Trail endings bear a remarkable resemblance to the extrafusal *en grappe* ending of Tschiriew (1879) that occurs in the skeletal muscles of various vertebrates (Hess, 1960, 1961*b*, 1963), and in mammalian extraocular muscles (Hess, 1961*c*, 1962; Hess and Pilar, 1963), as illustrated in Fig. 22. Work on the fine structure of the trail ending shows that this resemblance includes the nature of the myoneural junction, where post-junctional sarcolemmal folds are absent (Adal and Barker, unpublished), as in the *en grappe* terminals of the cat superior oblique muscle (Pilar and Hess, 1966). Moreover, preliminary observations on spindles in sheep extraocular muscles show that the intrafusal trail innervation and the extrafusal *en grappe* innervation frequently originate from the same motor axon (Barker and A. B. Purdy, unpublished observations). Trail endings typically occupy an area just under one millimetre long on either side of the equatorial region, extending through the S_1, S_2, and part of the S_3 regions. Jones (1966) has described diffuse spray endings in methylene blue preparations of opossum spindles; these appear to correspond to trail endings.

FIGS. 1–10. Photographs of teased preparations of cat muscle receptors. The preparations illustrated in Figs. 1 and 9 are gold chloride, the rest silver (modified de Castro technique). *P*, primary ending; p_2, end-plate of the p_2 type; pf.c., paciniform corpuscle; S_1, S_2, S_3, secondary endings located in positions increasingly distant from the primary ending; t.o., tendon organ; Ia, primary ending nerve fibre; Ib, tendon organ nerve fibre; II, secondary ending nerve fibre.

FIG. 1. Muscle spindle with primary and three secondary endings from normal flexor digitorum longus.

FIG. 2. Muscle spindle with primary and three secondary endings from normal tenuissimus. Note clarity of motor innervation in this silver preparation as compared with that in the preceding gold chloride preparation.

FIG. 3. Enlargement of the sensory innervation of the spindle shown in Fig. 2. The secondary endings are located mainly on the nuclear-chain muscle fibres (coursing through on the left-hand side of the spindle) and only to a small extent on the nuclear-bag muscle fibres.

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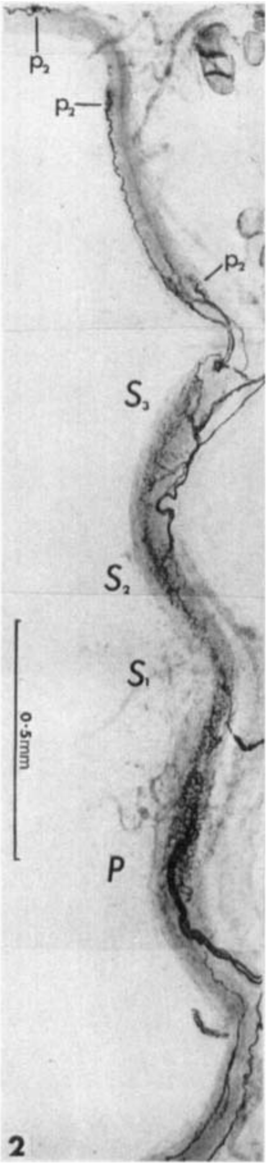

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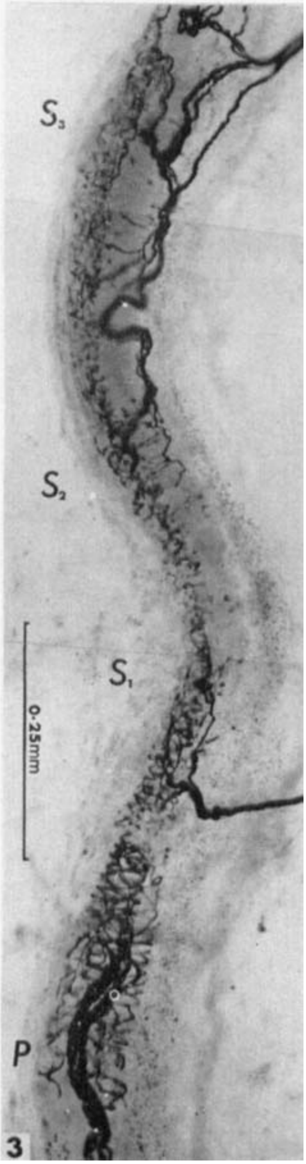

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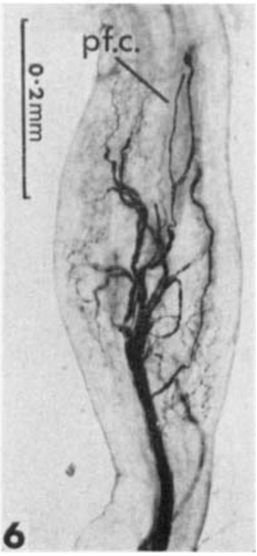
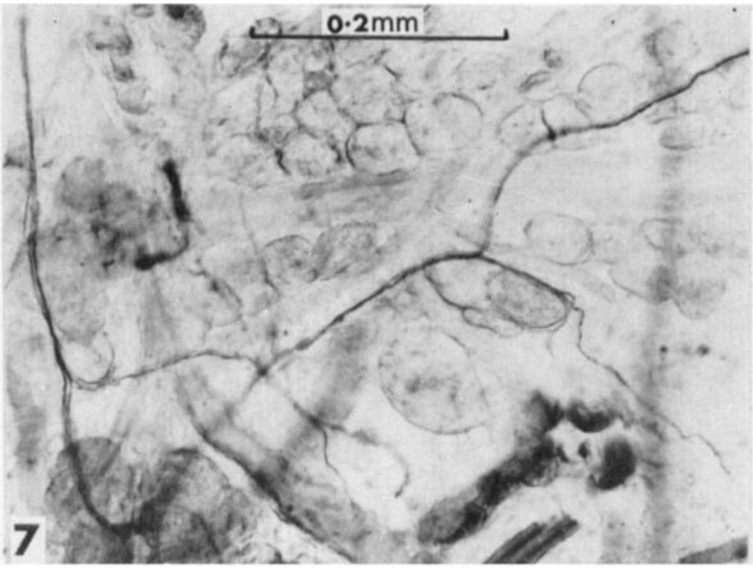
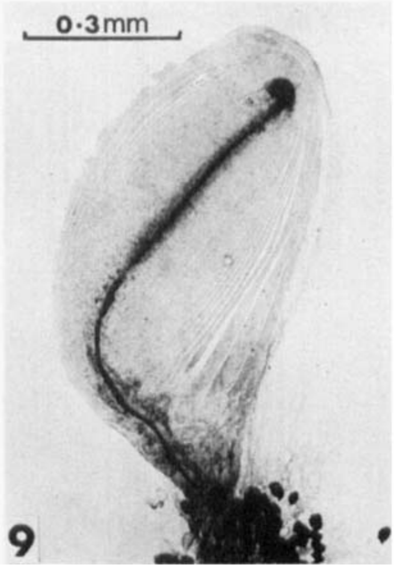


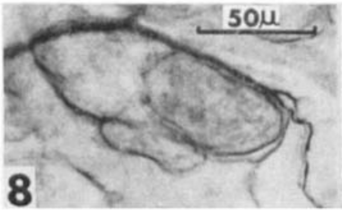
FIG. 4. De-efferentated and sympathectomized preparation from peroneal muscle showing a muscle spindle, a tendon organ and two paciniform corpuscles, one of which is associated with the tendon organ.

FIG. 5. Secondary ending of the flower-spray type in de-efferentated peroneal spindle.

FIG. 6. Tendon organ from de-efferentated extensor digitorum longus innervated by one 10 μm. Ib fibre. Six paciniform corpuscles are present underneath the receptor capsule (two only visible in photograph) innervated by a 7·5 μm. Group II fibre.







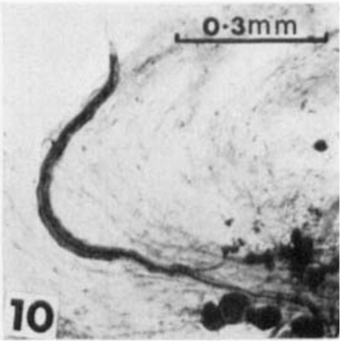
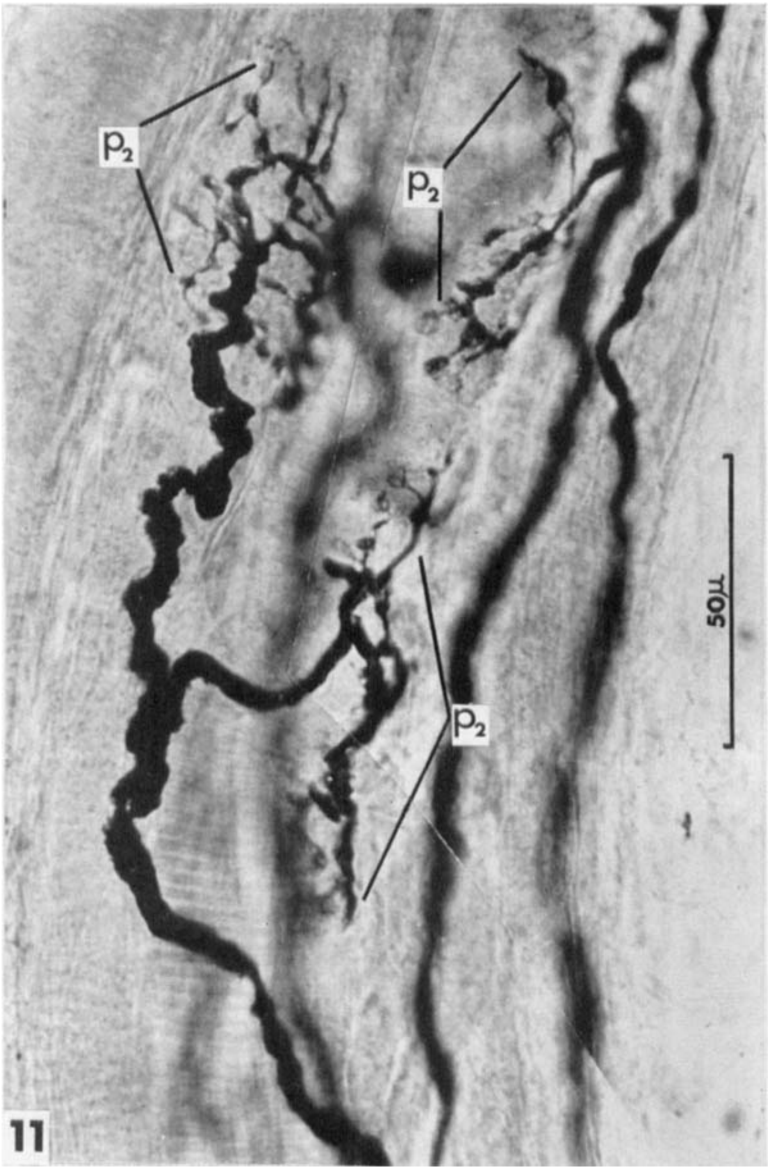


FIG. 7. De-efferentated and sympathectomized preparation of fat, connective tissue and blood vessels in tibialis posterior muscle, demonstrating innervation by two Group III fibres with stem diameters of 2·0 and 2·5 µm.

FIG. 8. Enlargement of the area just to the right of centre in Fig. 7, showing innervation of fat.

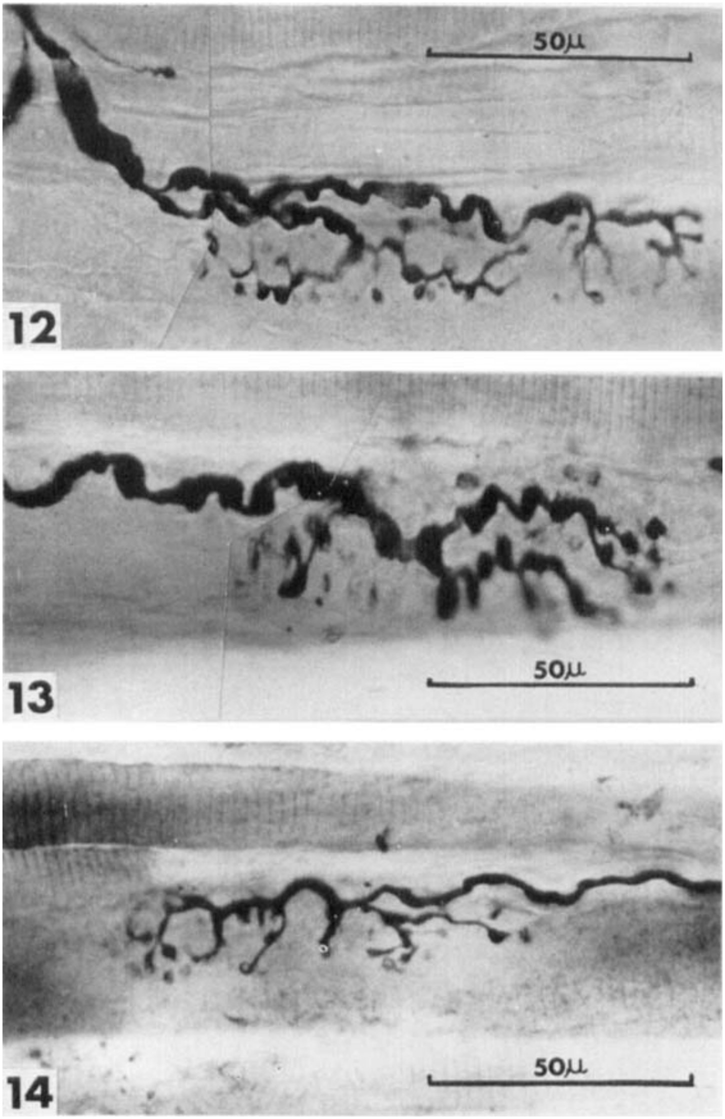
FIG. 9. Pacinian corpuscle from fascial covering of interosseous muscle.

FIG. 10. One of two paciniform corpuscles innervated by a 2·5 µm. Group III fibre.

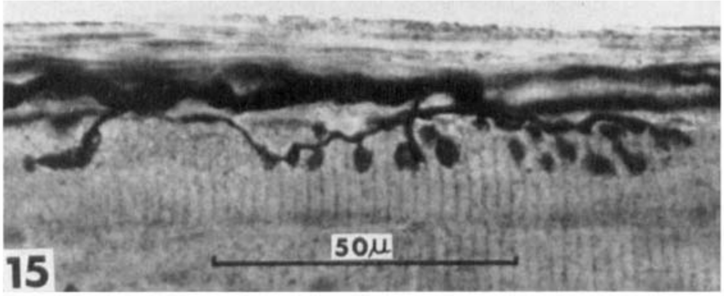


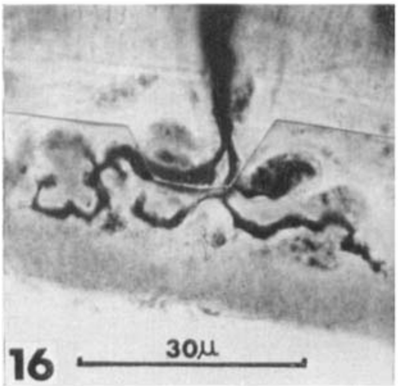
Figs. 11-22. Photographs of teased, silver preparations (modified de Castro technique) illustrating (except Fig. 22) the motor innervation of cat muscle spindles. c., spindle capsule; j., myoneural junction formed by ramification of trail ending; *P*, primary ending; p_2, end-plate of the p_2 type; r., trail-ending ramification; tr.e., trail ending.

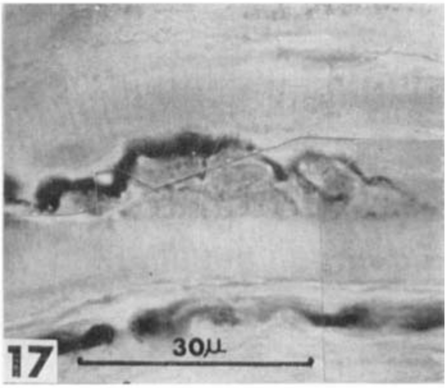
Fig. 11. p_2 plates in de-afferentated interosseous spindle.



Three examples of p_2 plates innervating de-afferentated spindles in peroneus brevis (Figs. 12 and 13) and 2nd deep lumbrical muscle (Fig. 14).







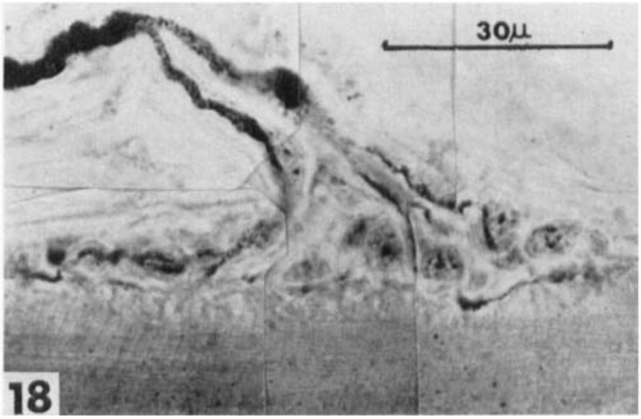
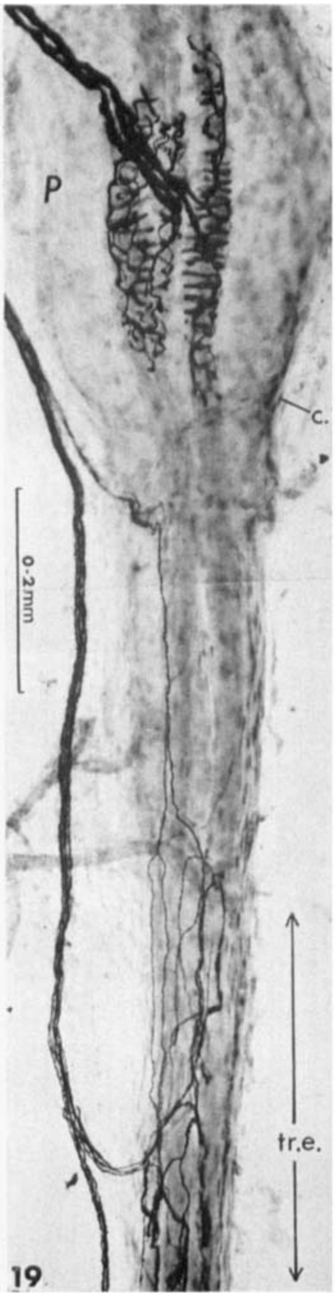


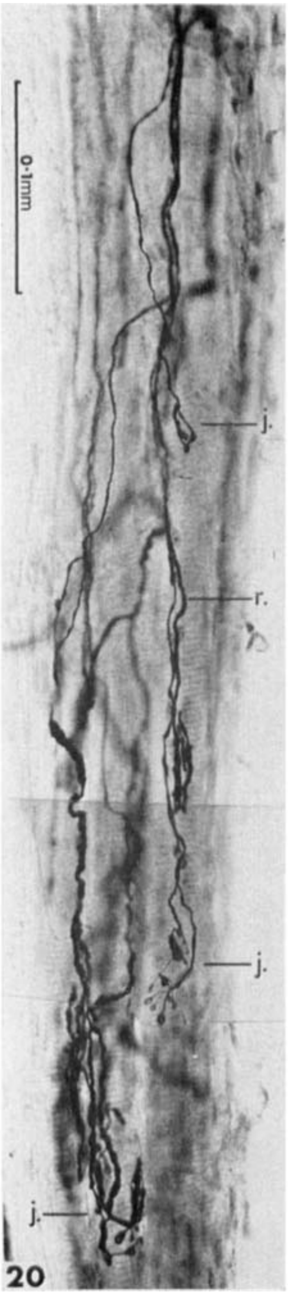
FIG. 15. p_2 plate in de-afferentated soleus spindle.

FIG. 16. Surface view of p_1 plate in de-afferentated interosseous spindle.

FIG. 17. Side view of p_1 plate in de-afferentated interosseous spindle. Note nucleated sole plate, Doyère eminence.

FIG. 18. Side view of p_1 plate in de-afferentated spindle from peroneus brevis.





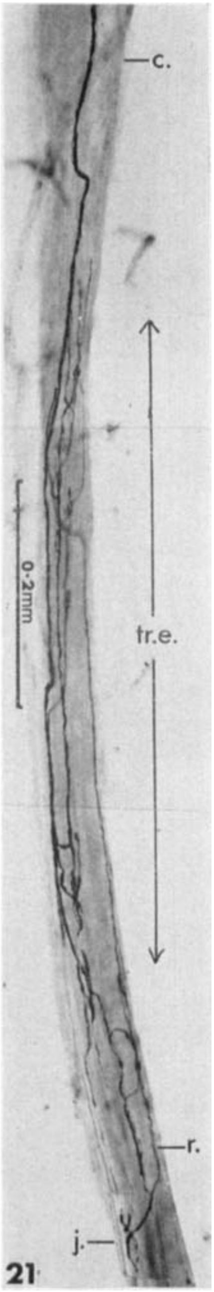


FIG. 19. Normal spindle from peroneus brevis showing primary and trail endings.

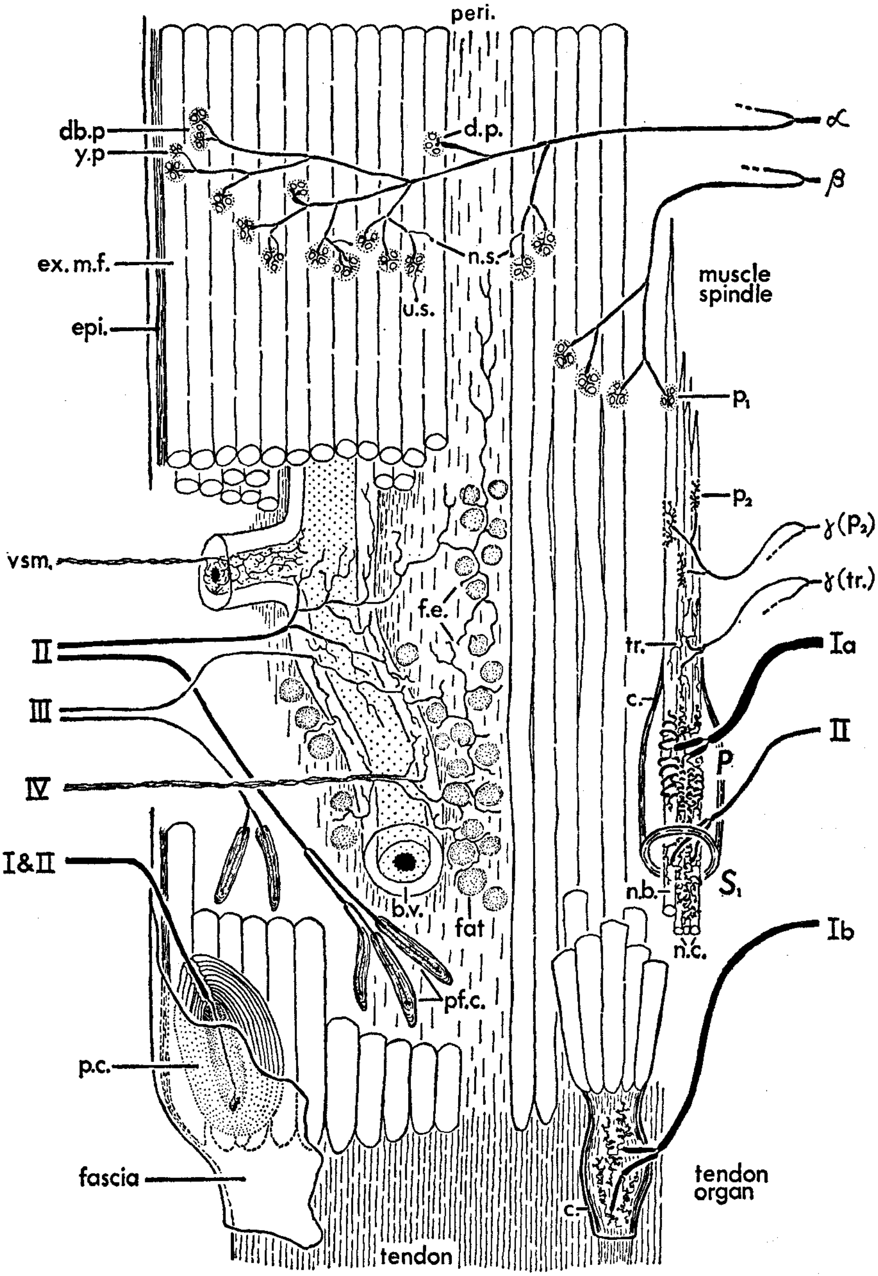
FIG. 20. Enlargement of part of the trail-ending area shown in Fig. 19. At this focus three myoneural junctions (j.) formed by trail-ending ramifications (r.) are shown.

FIG. 21. One pole of a de-afferentated peroneal spindle innervated by a single trail motor fibre.

FIG. 22. *En grappe* innervation in cat inferior oblique extraocular muscle. Its diffuse multiterminal nature is similar to that of the fusimotor trail innervation, and contrasts with the discrete *en plaque* end-plate, an example of which (e.p.) is seen in the top right-hand corner of the photograph.

The p_1 plate (see Figs. 16, 17, and 18) is similar in every respect to the extrafusal motor end-plate and may on occasion be quite clearly seen to derive its axon as a collateral of a β fibre. After nerve section, p_1 plates and extrafusal end-plates degenerate simultaneously, while p_2 plates and trail endings persist for a further 24 to 36 hours (Barker and C. L. Negus, unpublished observations). This differential in motor degeneration may partly be a feature of the different kinds of myoneural junctions involved, and may also be related to axon size, since the extremities of large axons appear to degenerate more quickly than those of small ones. Taken in conjunction with other evidence, the existence of such a differential suggests that the relatively large and predominantly skeletomotor β fibres provide the p_1 innervation, while the smaller γ fibres supply the p_2 and trail endings. The location of p_1 plates is typically towards the extreme ends of the polar regions, but they may occur anywhere along the poles and may lie as close to the equator as the S_2 region. The p_1 plate occurs with less frequency than the other two fusimotor endings, and unlike them is usually supplied to only one or two muscle fibres in the spindle. The p_2 plate (see Figs. 11–15) is on average about twice as long as the p_1, and there is no nucleated sole plate or Doyère eminence. Synaptic contact is made by irregular knobs or rings applied closely to the surface of the muscle fibre somewhat like *boutons terminaux*. These plates are characteristically mid-polar and several are usually supplied to each intrafusal muscle fibre. The fine structure of p_1 and p_2 plates has not yet been described. In favourable silver preparations of p_1 plates there are indications of a subneural apparatus with postjunctional sarcolemmal folds. These do not appear to be present in p_2 plates whose synaptic knobs seem to lie on simple cushions of sarcoplasm.

The distribution of three kinds of motor ending to cat muscle spindles results in the occurrence of seven different patterns of polar innervation, and there is an eighth variant in which one of the two poles sometimes receives no motor innervation at all. Jones (1966) has also encountered such barren poles in opossum lumbrical spindles. Of 64 possible combinations of polar innervation in complete spindles, I have so far found 19 in analysing a sample of 59 spindles teased out from various hindlimb muscles. The most common pattern of innervation in this sample was for trail endings and p_2 plates to be distributed to both poles: 91 per cent of the spindles received trail endings, usually at both poles; 78 per cent received p_2 plates; and 58 per cent received p_1 plates. None of the endings is exclusively distributed to one type of intrafusal muscle fibre, though trail endings are more frequently located on chain than on bag fibres, and p_1 plates more


peri.
db.p
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α
y.p
β
ex.m.f.
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muscle spindle
epi.
u.s.
p_1
p_2
γ(p_2)
vsm.
γ(tr.)
f.e.
II
tr.
Ia
c.
III
II
P
IV
I&II
S_1
n.b.
b.v.
fat
n.c.
Ib
pf.c.
p.c.
tendon organ
fascia
c.
tendon

frequently on bag than on chain fibres. The p_2 plates, however, are more or less equally distributed to both bag and chain fibres. Boyd (1966) still adheres to his original view (1962) that one type of fusimotor ending specifically innervates one type of intrafusal muscle fibre, while Jones (1966) finds, on the contrary, that in over a third of his sample of opossum spindles motor endings were supplied to both bag and chain fibres by the same motor axon. Rabbit spindles, in which all muscle fibres are of the bag type (Barker and Hunt, 1964), receive both trail endings (Barker and Ip, 1965) and p_1 plates; the presence of a p_2 innervation awaits future analysis.

The identification of the functionally separable dynamic and static fibres of Matthews (1962) with specific fusimotor fibres and endings remains to be satisfactorily elucidated. There have been two attempts to do so:

(*i*) *The dynamic/*γ_1*, static/*γ_2 *correlation.* This was suggested by Matthews (1962; Jansen and Matthews, 1962; Crowe and Matthews, 1964*a*, *b*; Brown, Crowe and Matthews, 1965) and is based on the concept developed by Boyd (1962; Boyd and Davey, 1962; Boyd and Eccles, 1963) of two γ motor systems in which large, fast γ-stem fibres reach the spindle as large branches ("γ_1 fibres") terminating as end-plates on bag muscle fibres, while small, slow γ-stem fibres arrive as thin branches ("γ_2 fibres") to supply a network of endings on the chain muscle fibres. One difficulty in the way of this interpretation is that the ranges of the conduction velocities of static and dynamic fibres overlap (Crowe and Matthews, 1964*b*) instead of giving the bimodal distribution that would be expected on the basis of a γ_1/γ_2 correlation. Moreover, by tracing the intramuscular course of γ fibres, Adal and Barker (1965*a*) showed that there is no correlation between the diameters of γ fibres in the muscle nerve and those of their branches at spindle entry, and found the distribution of γ fibres to be such that many cat spindles are innervated by large γ-stem fibres only. Further doubts were raised by work on rabbit spindles which, though composed of bag muscles only, nevertheless proved to be innervated by both large and small γ-stem fibres (Adal and Barker, 1965*b*), static and dynamic fusimotor fibres (Emonet-Dénand, Laporte

FIG. 23. Schema of the innervation of mammalian skeletal muscle based on a study of the cat. Those nerve fibres shown on the right of the diagram are exclusively concerned with muscle innervation; those on the left also take part in the innervation of other tissues. Roman numerals refer to the groups of myelinated (I, II, III) and unmyelinated (IV) sensory fibres; Greek letters refer to motor fibres. Features of terminal sprouting and degeneration are omitted from the spindle. b.v., blood vessel; c., capsule; db.p., double motor end-plate; d.p., degenerating end-plate; epi., epimysium; ex.m.f., extrafusal muscle fibre; n.b., nuclear-bag intrafusal muscle fibre; n.c., nuclear-chain intrafusal muscle fibre; n.s., nodal sprout; *P*, primary ending; p_1, p_2, two types of intrafusal end-plates; peri., perimysium; p.c., Pacinian corpuscle; pf.c., paciniform corpuscle; S_1, secondary ending; tr., trail ending; u.s., ultraterminal sprout; vsm., vasomotor fibres; y.p., young motor end-plate ("accessory ending").

and Pagès, 1964, 1966), and two kinds of motor ending (Hess, 1961*a*; Barker and Ip, 1965). Finally, Barker and Ip (1965) found no correlation in cat or rabbit spindles between the type of fusimotor ending and the axon diameter at the entry to the spindle of the fibre, or fibre branch, supplying it, and maintained that plate and trail endings are not segregated in their distribution to bag and chain muscle fibres respectively. At the Nobel Symposium held in Stockholm in 1965 (Granit, 1966), the γ_1/γ_2 concept and its dynamic/static correlation were therefore abandoned.

(*ii*) *The dynamic/trail-fibre, static/plate-fibre correlation.* This interpretation is put forward by Bessou and Laporte (1966) and is based mainly on their finding (1965) that stimulation of dynamic fusimotor fibres initiates a non-propagated potential near the equatorial region, whereas stimulation of some static fibres initiates a propagated action potential further away, more towards the middle and end of the polar region. Histological evidence (Barker, 1966*a*) suggested that the juxta-equatorial trail ending and its fibre should therefore be identified as dynamic, and that static fibres terminated in the spindle as end-plates. At the time of the Nobel Symposium, this correlation appeared to be the most probable one, even though it was at variance with the dynamic rather than static effect produced by stimulating the fusimotor collaterals of β fibres (Bessou, Emonet-Dénand and Laporte, 1963; Brown, Crowe and Matthews, 1965), an effect since shown to persist after curarization of the extrafusal myoneural junctions (Emonet-Dénand and Laporte, 1966).

Both these correlations were proposed before it was realized that there are two types of plates involved (p_1 and p_2) in addition to the trail ending. At this stage the only correlation that appears certain is to identify the p_1 plate and its β fibre as dynamic. In view of Bessou and Laporte's (1965) findings, and the close resemblance between trail and *en grappe* innervation (indeed their common identity in sheep extraocular muscles), it seems safe to conclude that trail endings produce slow, local contractions and initiate non-propagated potentials intrafusally, comparable with similar extrafusal responses produced by *en grappe* innervation in frog muscle (Kuffler and Vaughan Williams, 1953*a*, *b*) and cat extraocular muscles (Hess and Pilar, 1963). Such activity may also produce a dynamic effect, in which case the static fibres can be identified with the p_2 innervation. A possibility that has to be taken into account in future experiments is that this innervation may be capable of producing both contracture and propagated action potentials, like avian *en grappe* innervation (Ginsborg, 1960).

An essential preliminary to detailed studies of muscle innervation is to isolate the component under investigation by differential denervation. It