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REVIEW ARTICLE

Secondary endings of muscle spindles: Structure, reflex action, role in motor control and proprioception

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Abstract

Kinaesthesia and the control of bodily movement rely heavily on the sensory input from muscle spindles. Hundreds of these sensory structures are embedded in mammalian muscles. Each spindle has one or more sensory endings and its own complement of small muscle fibres that are activated by the CNS via fusimotor neurons, providing efferent control of sensory responses. Exactly how the CNS wields this influence remains the subject of much fascination and debate. There are two types of sensory endings, primary and secondary, with differing development, morphology, distribution and responsiveness. Spindle primary endings have received more attention than secondaries, although the latter usually outnumber them. This review focuses on the secondary endings. Their location within the spindle, their response properties, the projection of their afferents within the CNS and their reflex actions all suggest that secondaries have certain separate roles from the primaries in proprioception and motor control. Specifically, spindle secondaries seem more adapted than primaries to signalling slow and maintained changes in the relative position of bodily segments, thereby contributing to position sense, postural control and static limb positioning. By highlighting, in this way, the roles of secondary endings, a final aim of the review is to broaden understanding of muscle spindles more generally and of the important contributions they make to both sensory and motor mechanisms.

KEYWORDS
group II afferent, kinaesthesia, motor control, muscle spindle, position sense, spindle secondary ending

1 | INTRODUCTION

The mammalian muscle spindle was recognized as a sensory organ towards the end of the 19th century. Despite numerous reviews on its structure and function and on its roles in posture, locomotion and kinaesthesia (i.e., sense of position and movement), our knowledge remains at best fragmentary. One component of the muscle spindle that consistently receives little attention is the secondary ending. The dominant presence of the primary ending in response to muscle stretch, in eliciting the monosynaptic stretch reflex and in vibration illusions are some reasons that have led to the focus on primaries. By directing attention to secondary endings in this review, we aim to redress the balance, draw attention to what is not known and stimulate future research. The structure, function, distribution and abundance of the secondaries, their central connections, reflex actions and roles in posture, locomotion and kinaesthesia are reviewed. In writing the review, we were motivated and inspired by Peter Matthews who, while attending a symposium in Durham, UK (Bewick et al., 2015), remarked, 'Don't forget the secondaries'. He reiterated his conviction of their importance during an oral history for the Physiological Society shortly before his death in 2020 (available at https://static.physoc.org/app/uploads/2021/08/26163028/Peter-BC-Matthews.pdf).

2 | RECOGNITION OF THE SECONDARY ENDING

By the second half of the 19th century, the presence of large, myelinated nerve fibres ending within the expanded capsule was recognized as characteristic of all muscle spindles of tetrapod vertebrates, but although each capsule in non-mammals received one such nerve fibre (Cipollone, 1897; Regaud & Favre, 1904), those of humans (Kerschner, 1888) and other mammals (Cipollone, 1897; Huber & DeWitt, 1898) were reported to receive anything from one to four. Sherrington (1894) had shown that these were the peripheral axons and endings of dorsal-root ganglion cells and therefore sensory. Secondary endings were first named by Ruffini (1898), as distinct from the primary ending and supplied by separate nerve fibres. According to Ruffini, the primary was invariably present and almost always single, whereas secondaries might be absent or there might be one or two in an individual capsule. He also noted that 'The nerve-fibres of the secondary ending are never so large as those of the primary', an observation confirmed many times since, at least for individual spindles. Huber and DeWitt (1898) accepted the existence of primary and secondary endings, although they rejected Ruffini's alternative names of 'annulo-spiral ribbon ending' and 'flower-wreath ending', stating that these forms of terminals could be found contributing to any of the sensory endings. Nevertheless, Ruffini's influence prevailed, and even now the name 'flower-spray' is used frequently and uncritically as an alternative to 'secondary', without further consideration of the properties or functions of secondaries. Tello (1922) reported that primary endings were formed by the first axons to arrive at the developing spindle, whereas those that would form the secondaries, when present, followed later, thus further emphasizing their separateness.

It was half a century after Ruffini before Barker (1948) confirmed Huber and DeWitt's opinion on the various forms of the sensory terminals in a study of the complete innervation of a rabbit quadriceps spindle. Barker emphasized the relationship between the sensory endings and the structure of the underlying intrafusal muscle fibres, especially their nuclei. As early as 1897, Cipollone had illustrated these nuclei, located in Sherrington's (1894) equatorial region under the sensory terminals (for the key features of the mammalian muscle spindle, see Figure 1). Barker recognized not only the great cluster of roughly spherical nuclei he called the nuclear bag, but also that this cluster tapered on either side into a row of more elongate nuclei, which, owing to their resemblance to nuclei in developing muscle, he named myotubes. According to Barker's analysis, the primary and secondary endings were associated with the nuclear bag and myotubes, respectively, and therefore closely adjacent. In the rabbit, both had the annulo-spiral form, although secondaries were supplied by smaller nerve fibres (6–9 μm) than primaries (8–12 μm), when measured close to the spindles (Barker, 1948).

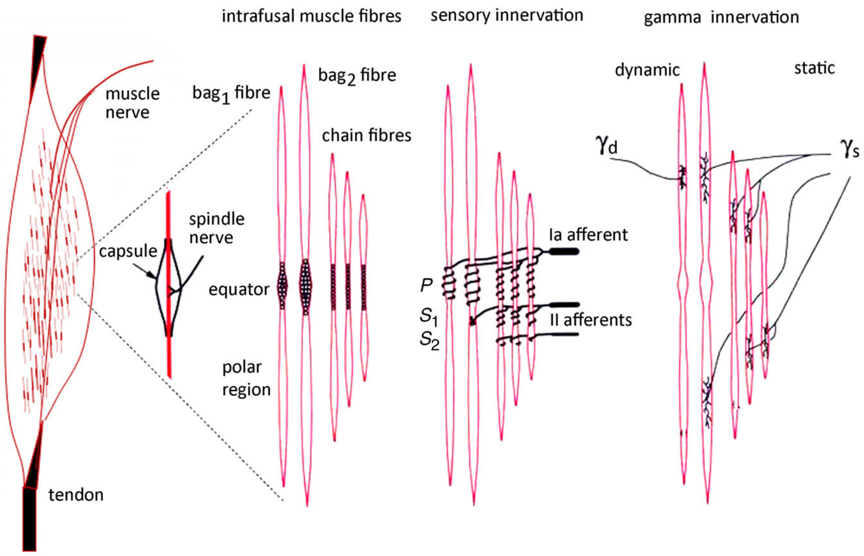
Barker's (1948) study was a preliminary to his interest in the recovery of the knee-jerk reflex following denervation and reinnervation of the quadriceps muscle. His close attention to the secondary was attributable to its previous identification as the sensory ending responsible for the tendon-jerk reflex by B. H. C. Matthews (1933), who had made the first recordings of single afferents from mammalian muscle, mainly peroneus longus and soleus of the cat. He identified four groups, calling them: A1 and A2, both from spindles; B, from tendon organs; and C, from rapidly adapting sensory endings in fascia that responded to muscle contraction. The distinction between A1 and A2 was that only A2 afferents were excited by slightly supramaximal nerve stimulation (relative to muscle force). Matthews argued that the A1 group represented 'flower-spray' (i.e., secondary) endings and were excitatory for the stretch reflex, whereas the A2 group represented 'annulo-spiral' (i.e., primary) endings and were of unknown reflex function. The A1 and A2 classification lasted a couple of decades before it became clear that both groups probably contained primaries and secondaries (Hunt, 1954). And although the subsequent identification of the tendon-jerk reflex as monosynaptic is not directly relevant to the present review, Lloyd's (1943) demonstration that the afferent limb of the reflex conducted at 116 m/s in the cat hindlimb meant that only the largest axons, innervating primaries, could be responsible.

By functionally isolating single afferents in dorsal-root filaments, Hunt (1954) could accurately measure conduction velocities, converting them into total fibre diameters (i.e., axon plus myelin sheath) for comparison with Lloyd and Chang's (1948) classification into groups I–IV. Hunt identified group II fibres in cat soleus and medial gastrocnemius with afferents almost exclusively from muscle-spindle secondaries. Although there was some overlap between groups I and II, Hunt found that a convenient division could be set at 72 m/s

New Findings

- **What is the topic of this review?**
  We describe the structure and function of secondary sensory endings of muscle spindles, their reflex action and role in motor control and proprioception.
- **What advances does it highlight?**
  In most mammalian skeletal muscles, secondary endings of spindles are more or much more numerous than primary endings but are much less well studied. By focusing on secondary endings in this review, we aim to redress the balance, draw attention to what is not known and stimulate future research.

FIGURE 1 Diagrammatic representation of the mammalian muscle spindle. From left to right: parent muscle, typically containing many spindles; capsule, enclosing a bundle (red) of intrafusal muscle fibres and the spindle nerve supply; the different types of intrafusal fibres composing the bundle (bag_1, bag_2 and chain), with nucleated equatorial regions; sensory innervation, showing a single primary afferent (group Ia axon) innervating (*P*) all intrafusal fibres (bag_1, bag_2 and chain) and two secondary afferents (group II axons) innervating (S_1) both bag_2 and chain fibres or (S_2) solely chain fibres; fusimotor innervation, showing a dynamic gamma axon (γ_d) restricted to the bag_1 fibre and static gamma axons (γ_s) innervating chain and bag_2 fibres. Modified from Chin et al. (1962) and Ellaway et al. (2015)



(which fitted the soleus data rather better than the medial gastrocnemius). This value has had a somewhat similar fate to the use of ‘flower-spray’, in that it has found its way into elementary accounts of human physiology, where it is applied indiscriminately and is almost certainly wrong. But as far as those distal hindlimb muscles of the cat are concerned, Hunt found that group II conduction velocities ranged from ∼18 to ∼72 m/s, approximately equivalent to total fibre diameters of 3–12 μm, and therefore covering a wide size range of all myelinated afferents. Hunt (1954) reported that the responses of the presumed primaries and secondaries to phasic stretch, muscle contraction and small motor fibre (γ) stimulation were qualitatively similar. Also, both were slowly adapting, but secondaries had a higher average threshold for passive stretch (19 g or ∼186 mN) than primaries (3.3 g or ∼32 mN). A qualitative difference relating to what is now generally known as the dynamic response was soon reported by Cooper (1961), however. She found that the greater response of a muscle-spindle sensory while being stretched, compared with its adapted response to maintained stretch, was more prominent in primaries than secondaries of cat soleus. Cooper related this difference to the locations of the endings, citing the recent observations of Barker and Ip (1960) that most secondary endings in cat hindlimb were associated with intrafusal-fibre myotubes (including nuclear chains) and were of annulo-spiral form, as in the rabbit; only the more polar endings, where cross-striations of the muscle fibres were evident, adopted a spray-like form.

Coërs and Durand (1956), in describing the location of cholinesterase activity on intrafusal muscle fibres, found that it was absent only from the region occupied by the primary ending. In addition to localized concentrations in polar regions indicative of motor end-plates, they found a diffuse activity throughout the juxta-equatorial region, where secondaries were known to occur. They concluded initially that all secondaries were therefore motor. Following Boyd's (1959) confirmation of the sensory nature of secondaries, Coërs (1962) continued to suggest that ‘the “flower-spray” includes both motor and sensory endings’, a conclusion that failed to attract any further support, especially after Boyd's full account of his denervation studies (Boyd, 1962).

3 | NUMBER AND DISTRIBUTION

The sensory innervation of spindles in non-mammalian tetrapods has not been studied as intensively as that of eutherian mammals, but it appears likely that secondaries are altogether absent (Barker, 1974). The characteristic monofibral spindles of squamate reptiles occur as two types, however, with each spindle having a single sensory ending (Proske, 1969), and they are structurally distinguishable by the dimensions of the sensory ending and its enclosing capsule. The endings of ‘short capsule’ spindles respond phasically to stretch, as do mammalian primaries, whereas those of ‘long capsule’ spindles respond tonically to similar stretches, thus resembling mammalian secondaries (Proske & Ridge, 1974). There are reports of more than one myelinated axon entering the sensory region in some bird spindles, including terminals identified as secondary (reviewed by Maier, 1992), but these await confirmation. Within mammals, the structure and innervation of metatherian spindles are similar to those of eutherians; in a variety of fore- and hindlimb muscles of the Australian opossum (*Trichosurus*), E. G. Jones (1966) found that ‘about 50%’ of spindles contained one or two secondaries. Nothing is known about the sensory innervation of monotreme spindles, although they do contain several intrafusal muscle fibres, like other mammals and archosaurs (turtles, crocodilians and birds) (Voss, 1963).

Boyd (1962) and Barker (1962) both presented quantitative data on muscle receptors in several, mostly hindlimb, cat muscles. Boyd studied tenuissimus, soleus and interosseus, presenting his results as the numbers of various primary (*P*) and secondary (*S*) complements (*P*, PS_1, PS_1S_2, etc.). In each muscle, there were more secondaries than primaries, with an overall ratio of 1.50 secondaries per primary (or, for direct comparison with what follows, *P*:*S* = 0.67:1). Barker (1962) presented a much larger total number of spindles obtained by teasing one to nine complete exemplars of rectus femoris, soleus, semitendinosus, flexor digitorum longus, interosseus V and intercostal IV. He gave total numbers of primaries and secondaries for each muscle, but also the range (0.7:1–2.3:1) of *P:S* ratios. Note, therefore, that Barker found fewer secondaries per primary than Boyd, but his total sample was dominated by large, proximal limb muscles (rectus femoris and semitendinosus) not studied by Boyd. The range of ratios and their averages for each muscle indicated that there could be consistent differences between muscles, which would, presumably, reflect their roles in posture, locomotion and rhythmic activity. In addition to these results from the cat, Fox et al. (1975) reported that in distal hindlimb muscles from the baboon (peroneals, tibialis posterior and gastrocnemius) 60% of spindle sensory endings were secondaries; and in a mixed sample of mainly upper-limb muscles from human fetuses of gestational ages ranging from 26 to 41 weeks (Dissin, 1973) ~51% of the sensory endings were identified as secondaries.

In his histological study of cat hindlimb spindles, Boyd (1962) differentiated nuclear-bag and nuclear-chain fibres and reported that, although primaries were distributed to both types, any secondaries ended predominantly on nuclear-chain fibres. Following recognition of two types of nuclear-bag fibres in addition to nuclear-chain fibres (Banks et al., 1977), Banks et al. (1982) re-examined the innervation of cat spindles using reconstructions from serial sections in addition to silver-stained and teased muscles. The reconstructions included a primary and S_1 secondary from the same tenuissimus spindle, allowing quantitative comparisons between the two (see Section 5). The silver-stained material was mainly sampled from tenuissimus, but also from distal hindlimb and foot muscles. The great majority (270 of 310) were spindle units or capsules that contained the full complement of intrafusal-muscle fibre types ('b_1b_2c'). Most of these (258) had a single primary and from zero to six secondaries, with one of each (PS_1) being the commonest arrangement (34%), followed by a primary and two secondaries (either S_1PS_1 or PS_1S_2, total 29%) and a single primary (16%). The remaining b_1b_2c capsules each contained two primaries and one to five secondaries. Additionally, there were 40 capsules that lacked a nuclear-bag fibre (b_2c capsules) and were usually in tandem with a larger b_1b_2c capsule. Most (36) had a single ending, conventionally identified as a primary; the remainder had one other ending, conventionally identified as an S_1 secondary. Banks et al. (1982) went on to show that the distribution of the various sensory complements in all b_1b_2c capsules could be described accurately by binomial statistics. They suggested that this is consistent with a model in which, as presumptive group II afferents course through the developing nerve, they associate randomly with pioneer Ia afferents responsible for initiating intrafusal-fibre differentiation.

Banks and Stacey (1988) extended the binomial analysis by examining, as far as possible, complete spindle populations of several muscles of the cat. This indicated that the random distribution of secondaries to particular spindles depends on at least two factors that could represent: (1) the probability of a presumptive group II fibre associating with a Ia afferent in a developing muscle; and (2) the maximal number of such associations (alternatively, the duration over which such associations are possible). Banks et al. (2009) extended the sample of muscles, including some comparative data from rats, rabbits and guinea pigs. They confirmed rigorously that overall sensory complements vary characteristically in different muscles, as had often been suggested previously without proof. Moreover, the several components of the sensory complement, which include the number and distribution of secondaries, vary independently of each other in different muscles (Figure 2). The average number of secondaries per spindle for the complete sample of cat muscles ranged from 0.42 for calcaneometatarsalis to 3.7 for rectus capitis posterior, equivalent to the proportion of secondaries amounting to ~31% and 79%, respectively.

The cat data of Banks et al. (2009) indicate that there is no overall fixed relationship between primary and secondary numbers, but their relative numbers and distributions are characteristic of each muscle, presumably reflecting its functional role(s), in turn depending on the size and mode of life of the animal. The rat data of Banks et al. (2009) add emphasis to this point; despite being a much more restricted sample of only four different muscles, sensory complements were very different from those of the cat, being dominated by primaries. In peroneus longus and soleus, some 30% of afferents ended as secondaries, roughly half the proportion seen in hindlimb muscles of the cat and baboon. In addition, several afferents branched to supply both primary-like (equatorial) and secondary-like (juxta-equatorial) terminals. As in the cat, however, spindles in an axial muscle (intertransverse caudal) contained a much higher proportion of secondaries (66%) than limb muscles (Gladden, 1969). Axial muscles are postural, controlling the relative positions of the head, torso, hip and legs. High positional resolution of sensory input is presumably required here, whereas limb muscles tend to be more physically active, generating dynamic movements where velocity information might be more important. Although we can be sure, therefore, that there is a vital relationship between mode of life and sensory provision for motor control, it remains one of the major areas of our ignorance.

4 | PHYSIOLOGICAL PROPERTIES

Hunt's (1954) demonstration that group II afferents supply cat hindlimb spindles provided the impetus to compare the responses of primaries and secondaries in detail. Lloyd and Chang's (1948) soleus fibre-diameter spectrum showed a minimum at 12 μm, corresponding to the minimum conduction velocity of 72 m/s, as seen by Hunt (1954). Thus, at least in cat soleus, afferents from primaries and secondaries are well separable by conduction velocity alone. Such a clear distinction could not be relied on in other species or even in other muscles of the cat. Could other physiological criteria, equally good or better, be found to distinguish primaries from secondaries? How, and to what extent, do the responses of secondaries and primaries differ?

Bessou and Laporte (1962) made a direct comparison by recording the responses to muscle stretch and fusimotor stimulation of a primary and secondary in the same spindle of cat tenuissimus. They

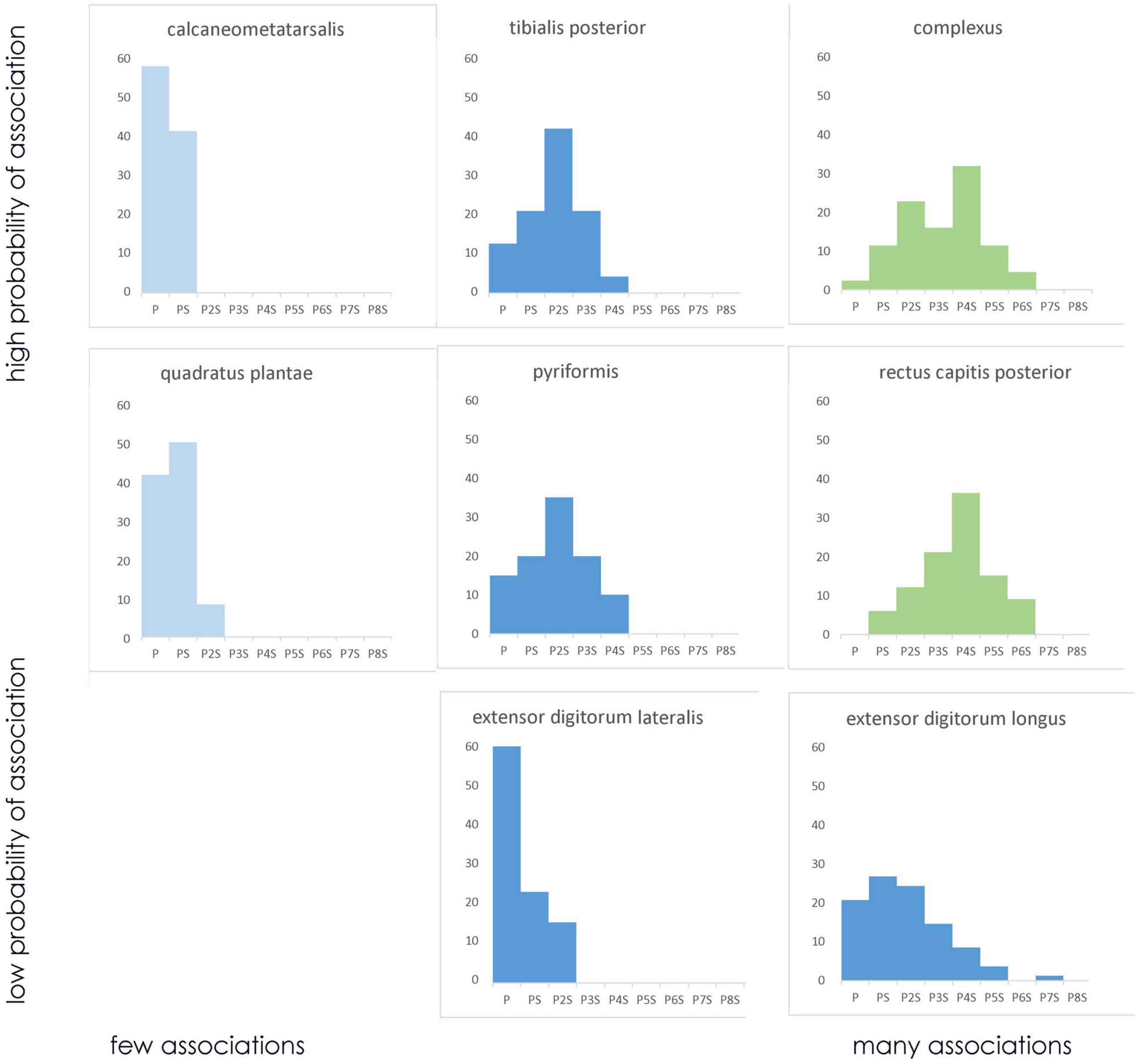


FIGURE 2 Muscle-specific sensory complements of cat spindles. The range of frequency distributions of sensory complements of spindles in the cat, displayed on the basis of a developmental model, whereby Ia afferents initiate spindle differentiation, and later-arriving group II afferents associate randomly with the nascent spindles. The distributions can be modelled by binomial statistics, suggesting that two independent factors are important: probability of association; and maximal number of associations. P, spindles with a single primary ending; PS, P2S, …, spindles with a primary ending and one, two, …, secondary endings. Further details are given in the Appendix (Figure A1)

confirmed that in passive spindles the primaries were usually more sensitive to changing muscle length than the secondaries (the dynamic response), and the secondary of a pair usually had a higher threshold to maintained (static) stretch than the primary, but the sensitivity of the secondary to such static stretch was, on average, twice that of the primary (3.2 and 1.6 impulses/s/mm, respectively). Parallel excitation of a primary and secondary pair usually occurred on stimulation of a single fusimotor axon, but in one instance the secondary discharge decreased while the primary increased markedly. This is best explained by contraction in a nuclear-bag fibre unloading a secondary ending located on nuclear-chain fibres lying in parallel.

A further difference reported by P. B. C. Matthews and Stein (1969) was greater variability of the discharge of primaries than secondaries; coefficients of variation for passive spindles in cat soleus were 5.8% and 2.0%, respectively, at mean frequencies of ~30 impulses/s. There was no overlap between the two ranges, but afferents were identified as from primaries or secondaries by conduction velocity; those with velocities between 60 and 80 m/s were omitted. Botterman and Eldred (1982) studied the length sensitivity of passive spindle afferents responding to maintained (static) stretches of cat gastrocnemius, confirming and extending Bessou and Laporte's (1962) conclusion described above; on average, length sensitivity was 50% greater for

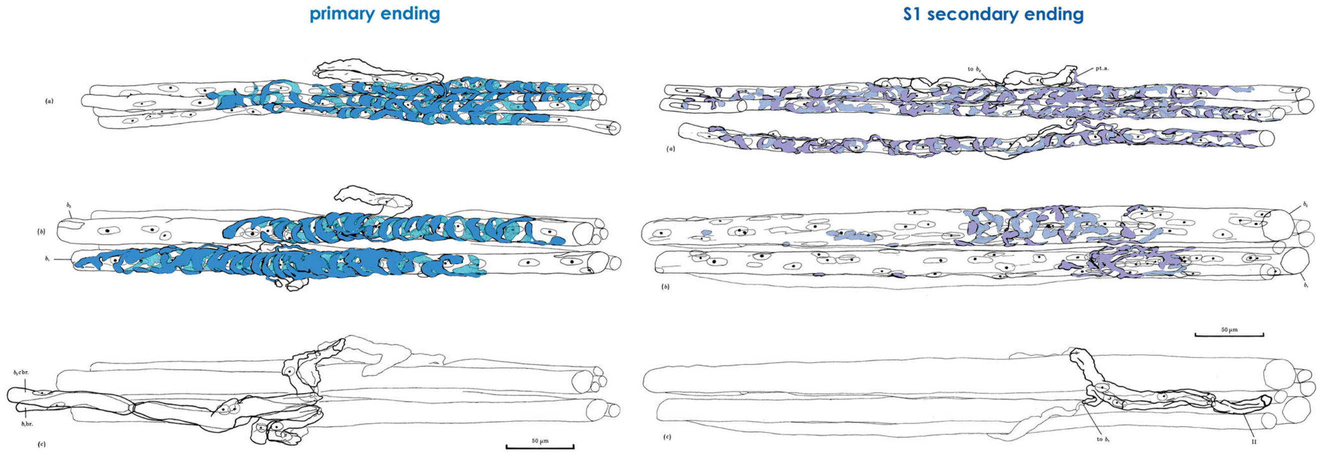


FIGURE 3 An example of the sensory innervation of a cat tenuissimus spindle that contained a primary and one secondary ending. Graphical reconstructions from serial, 1-μm-thick, transverse sections through a primary (left) and an adjacent S_1 secondary (right) from cat tenuissimus. Sensory terminals are shown coloured; other features (intrafusal fibres, myonuclei, preterminal axon branches and Schwann cell nuclei) are shown in outline. Top, the group of four chain fibres; middle, the bag$_2$ (upper) and bag$_1$ (lower) fibres; and bottom, overall outline with remaining preterminal axonal branches. The predominantly chain-fibre distribution of the S_1 ending is apparent; with a contact area on the chain fibres of almost 9,500 μm^2, the terminals on the chain fibres represent ~75% of the total contact area of the secondary. Modified from Banks et al. (1982)

secondaries than primaries. Both primaries and, usually, secondaries show history-dependent responses, however; thus, for a given muscle length, instantaneous firing rate is less at constant length than during lengthening and less again when the same length is reached during shortening (Harvey & Matthews, 1961). Aspects of this hysteretic behaviour, such as the proportional reduction in firing rate at the transition from ramp to maintained stretch then to ramp release, are typically more marked in primary than secondary responses. The differences themselves depend on the rate of stretch or release and, typically, increase more rapidly in primaries than secondaries (Lennerstrand, 1968; P. B. C. Matthews, 1963), albeit sub-linearly in both cases (Houk et al., 1981). Baboon triceps surae gave similar results, although conduction velocities differed from those of the cat, with a minimum between groups Ia and II at 60–65 m/s (Cheney & Preston, 1976; Koeze, 1973). In rat soleus, also, De-Doncker et al. (2003) were able to recognize groups of primary-like and secondary-like afferents based on their responses to a range of ramp–hold–release and sinusoidal stretches. Conduction velocities of primary-like afferents ranged from ~36 to 56 m/s and of secondary-like afferents from ~24 to 40 m/s.

The greater dynamic response of primaries than secondaries is also manifest during repetitive and constantly changing length stimulation, such as sinusoidal stretch (Bessou & Laporte, 1962). With increasing frequency into the acoustic range (> 20 Hz) the hysteresis seen with ramp–hold–release or triangular stretches may eventually result in firing of a single action potential during each stretch cycle (1:1 driving). Bianconi and Van Der Meulen (1963) examined vibration sensitivity in cat triceps surae using an electromagnetic vibrator with a 1.5 mm probe, driven between 40 and 500 Hz at amplitudes down to < 200 μm. With the probe positioned on the muscle surface so as to excite a single afferent maximally, they found that 1:1 driving with maximal frequencies between ~150 and 350 Hz could be elicited in virtually all afferents with conduction velocities > 70 m/s, whereas half of the afferents with conduction velocities < 70 m/s could not be driven in this way. Moreover, when the tendon was vibrated, driving could usually still be elicited in the faster group but never in the slower group. Although the different responses of faster- and slower-conducting afferents to phasic stimuli of various types are usually attributed to the different mechanical properties of the equatorial locations of the primary endings and the adjacent, juxta-equatorial locations of the secondary endings, this particular difference between local- and tendon-evoked responses has yet to be explained.

5 | STRUCTURAL PROPERTIES AND THEIR RELATIONSHIP TO FUNCTION

Serial-section reconstructions of a primary and adjacent secondary (Banks et al., 1982; Figure 3) confirmed the relationship between sensory terminals and the underlying structure of intrafusal muscle fibres. Beneath the primary terminals, all three types of intrafusal fibres were reduced in diameter to a local minimum, whereas only the chain fibres retained similar small diameters beneath the secondary terminals. Indeed, in this example, both bag$_1$ and bag$_2$ fibres attained local maximal diameters where each received some secondary terminals. A clear spatial correlation existed between intrafusal myonuclei and sensory terminals, whether primary or secondary. Nuclear bags, myotubes and nuclear chains were associated with primary terminals, whereas looser chains or myotube-like rows of nuclei were found under secondary terminals, including those on the bag fibres. Sensory terminals were densely packed in the primary, especially on the bag$_1$ fibre, where about half the fibre surface was covered; less so in the secondary, which was, nevertheless, more extensive. At a little over 12,600 μm^2, the contact area of the secondary with the

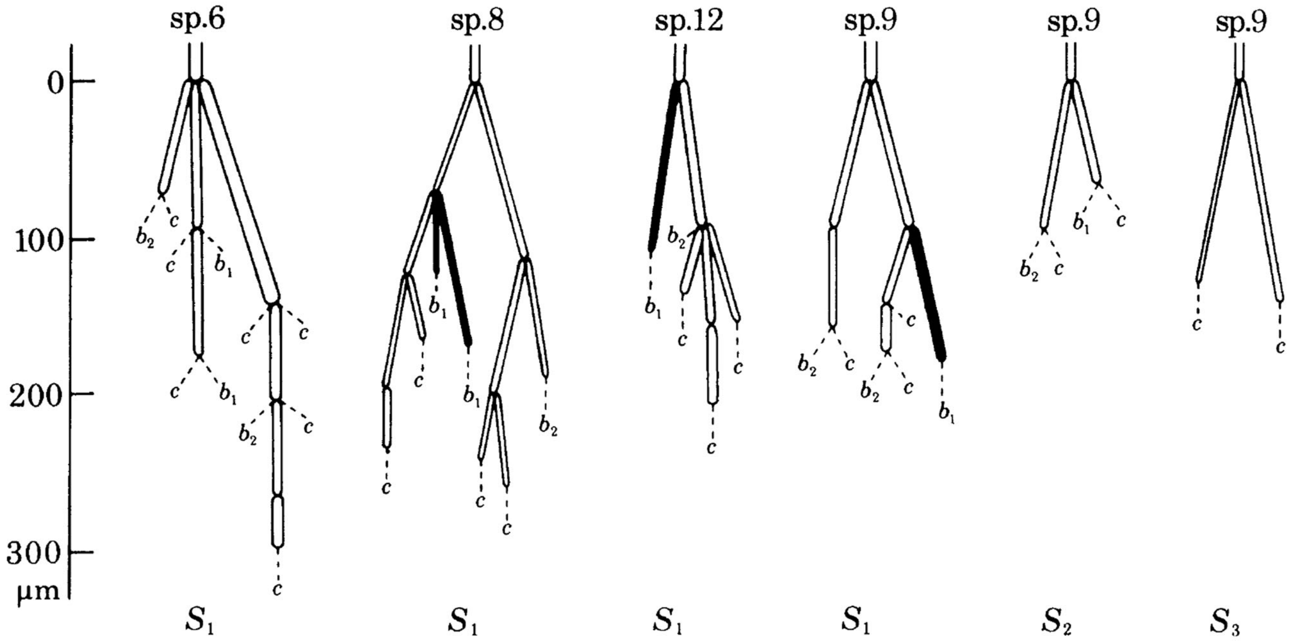


FIGURE 4 Examples of preterminal axonal branching to secondary endings. Semi-schematic reconstructions of group II preterminal axonal branches that supplied four S_1, one S_2 and one S_3 secondary ending from four spindles (sp.) of cat tenuissimus. Myelinated internodes are shown as closed outlines; branches to the bag$_1$ fibre alone are shown filled. Note the occurrence of unmyelinated branches (dashed lines) arising from nodes of Ranvier and all the hemi-nodes. Spindle 6 S_1 is the ending reconstructed in Figure 3. From Banks et al. (1982)

intrafusal fibres was only about two-thirds that of the primary. Chain-fibre terminals predominated, however, with a contact area of almost 9,500 μm^2, some 30% greater than that of the primary terminals on the same fibres.

The predominance of the chain-fibre component of secondary endings is reflected in the preterminal branches of the afferents. In the sample shown in Figure 4, all 13 first-order branches are myelinated and all but one supply chain-fibre terminals, unlike primaries, where one of the branches usually supplies the bag$_1$ fibre exclusively (Banks et al., 1982). In group II preterminal branches, too, unmyelinated branches connecting with sensory terminals commonly arise from upstream nodes of Ranvier in addition to final hemi-nodes, again in contrast to primaries, where unmyelinated branches arise almost exclusively from final hemi-nodes. The whole preterminal branching system in secondaries may therefore be expected to be more electrotonically compact than in primaries and only rarely to possess encoding sites accessible to separate dynamic and static motor inputs (see Banks et al., 1997).

Sensory nerve endings clearly exert a powerful morphogenetic influence on intrafusal fibres, causing the accumulation of myonuclei and, usually, a correlated reduction in myofibrillar content and fibre diameter (Zelená, 1994). This must have profound effects on local mechanical properties, as studied in isolated spindles by Poppele et al. (1979) and Poppele and Quick (1985). In the example of Figure 5a,b, a primary was located at the equatorial region S, with an S_1 secondary in juxta-equatorial region IM$_2$. The opposite juxta-equatorial region IM$_1$ lacked any sensory ending. Both primary and secondary sensitivities, measured in conditions of low velocity, were proportional to local strains. Local strains of S and IM$_2$ increased with passive spindle extension, whereas that of all other regions and the external capsule decreased. Thus, the regions occupied by sensory endings exhibited spring-like behaviour, in contrast to the other components, whose stiffness tended to increase with increasing length. More surprisingly, perhaps, is the observation that sensory regions were initially, and for most of the applied extension, stiffer than the polar sarcomeric regions. The structural basis for this is not clear, but one element could be prominent branching and converging bundles of elastic fibres around the intrafusal fibres (Figure 5c) (Cooper & Gladden, 1974), some arising in one polar region before crossing the equatorial region to insert on bag fibres in the opposite juxta-equatorial region (Banks, 1984). The outer capsule also plays an important mechanical role, because its removal reduced local strains in IM$_1$, IM$_2$ and S, compensated by increased strain of the contractile polar regions (PM). In a spindle with an intact capsule, sarcomeres in the juxta-equatorial regions are shorter than those in the adjacent polar regions (Boyd, 1976; Poppele & Quick, 1985; Figure 5d); hence, removal of the capsule results in extension of equatorial and juxta-equatorial sarcomeres, with a corresponding shortening of polar sarcomeres.

6 | EFFECTS OF FUSIMOTOR STIMULATION

The discovery of separate functional categories of static and dynamic fusimotor fibres (P. B. C. Matthews, 1962) initiated a period of experimentation and debate about their intrafusal distribution and the nature of intrafusal-fibre contractions elicited by their actions. Secondary-ending responses influenced the debate, because they could be assumed to be attributable to the predominantly

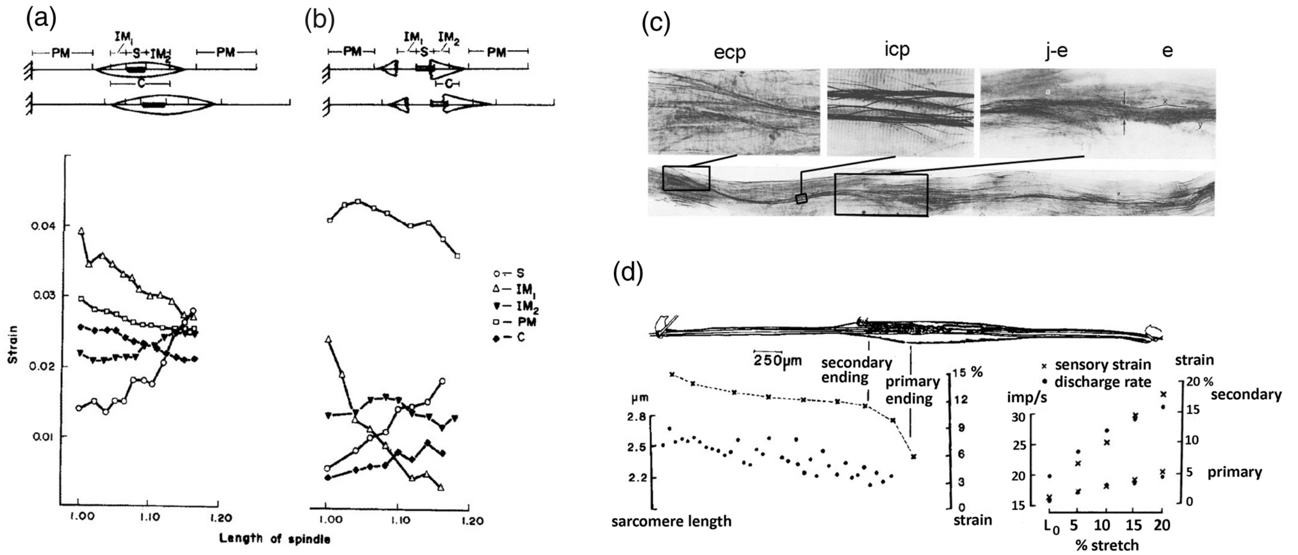


FIGURE 5 The mechanical environment of the secondary in passive spindles. (a,b) Differential strains (change in length/unit length) in various components of an isolated spindle from cat tenuissimus, measured at increasing overall length of the spindle: (a) with the capsule intact; and (b) with the capsule removed from the equatorial and a juxta-equatorial region. Key: C, capsule; IM_1, juxta-equatorial region devoid of sensory endings; IM_2, juxta-equatorial region occupied by an S_1 secondary; PM, average of both polar regions; S, sensory (equatorial) region occupied by the primary. With the capsule intact, strain increased with increasing length only in sensory regions, and the region occupied by the secondary is more extensible than that occupied by the primary for most of the increase in length. (c) Cat tenuissimus muscle spindle in situ, stained with Resorcin–Fuchsin for elastic fibres. Details of the extracapsular polar (ecp), intracapsular polar (icp), juxta-equatorial (j-e) and equatorial (e) regions are shown above as indicated. (d) Isolated muscle spindle from cat tenuissimus with an S_1P sensory complement, showing: (left) strain distributions and sarcomere lengths along a nuclear bag fibre, following an extension of 12.5% of resting length, and demonstrating equatorial-region stiffness; and (right) close correlation of sensory discharge rates with local strain, the secondary region being more extensible than the primary region, resulting in greater length sensitivity. (a,b) Modified from Poppele et al. (1979), copyright 1979 with permission from Elsevier. (c) Modified from Cooper and Gladden (1974), copyright 1974 the Physiological Society. (d) Modified from Poppele and Quick (1985), copyright 1985 Society for Neuroscience

chain-fibre location of the endings; Appelberg et al. (1966), for example, explicitly used their observation that static γ axons routinely activated both primary and secondary endings in the same tenuissimus spindle, whereas dynamic axons rarely did so, to attempt to infer their intrafusal distribution. Likewise, Bessou and Pagès (1969) used their frequencygram technique to conclude that single action potentials in static γ axons often resulted in rapid twitch contractions consistent with chain-fibre properties. Resolution of the problem of static and dynamic γ axonal distribution was possible only after bag_1 and bag_2 fibres were recognized as distinct types (reviewed by Banks, 1994). The usual paucity of secondary-ending terminals on bag_1 fibres readily explained the minimal effects of dynamic fusimotor actions on the endings; conversely, static fusimotor actions involve bag_2 in addition to chain fibres and need to be looked at more closely.

One may speak of dynamic and static fusimotor fibres because the action of each fibre on the primaries of all the spindles innervated by it is recognizably dynamic or static (Crowe & Matthews, 1964). The adapted response to a maintained stretch, also known as position sensitivity, of a primary or secondary might be increased, unaltered or, rarely, decreased by the action of a single static γ axon (Lennerstrand & Thoden, 1968), but the effect was inconsistent when pairs of primaries activated by the same static γ axon were studied (M. C. Brown et al., 1969). Jami and Petit (1978) examined this problem in a study of secondaries in cat peroneus tertius. They found that when a single secondary was acted on by three to six γ axons, only one or two produced an increase in position sensitivity, and about half of all such axons increased secondary-ending position sensitivity progressively as the stimulation rate increased from 30 to 100 stimuli/s, whereas in the remainder the effect peaked at stimulation rates of ~50 stimuli/s. When position sensitivity increased, stimulation at 50 stimuli/s led to an average doubling compared with that of passive endings. Furthermore, the response of a secondary to low-frequency sinusoidal stretch (0.5–1 Hz; $>$ 0.1 mm extent) was usually enhanced by static γ stimulation at 50 stimuli/s if the stimulation also increased position sensitivity during a slow ramp stretch (Jami & Petit, 1981). The glycogen-depletion technique (Jami et al., 1980) indicated that an axon that increased secondary position sensitivity supplied most or all of the chain fibres in one or both poles, sometimes with the bag_2 also, whereas one that did not increase the sensitivity supplied the bag_2, usually alone, in one or both poles.

The equatorial location of the primary ensures that intrafusal-fibre activation in either pole will affect the stretch response of the ending; but the juxta-equatorial location of any secondary necessarily entails an asymmetrical relationship with the adjacent and opposite poles. If, as is often the case (Banks, 1994), the poles receive separate fusimotor inputs, the effects on a secondary of experimental activation of a fusimotor axon in isolation might be expected to be very different according to whether the secondary is in the same or opposite

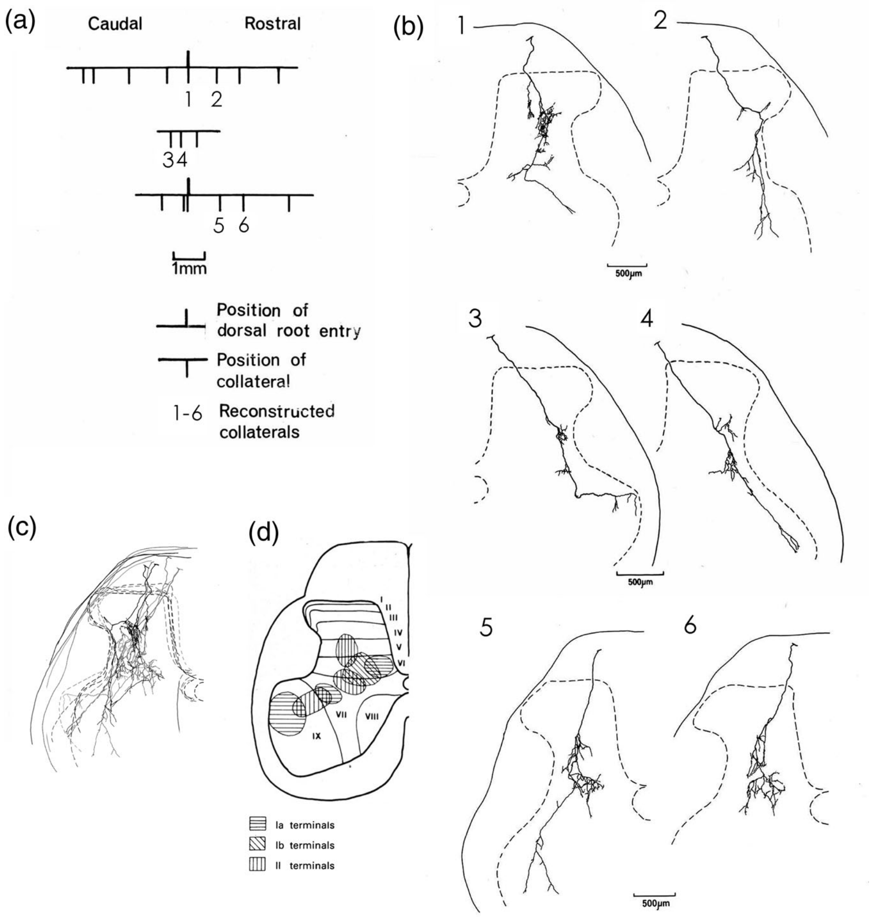


FIGURE 6 Central distribution of group II afferents. Intraspinal distributions of group II afferents from cat lateral gastrocnemius–soleus muscle spindles, labelled intra-axonally with horseradish peroxidase. (a) Diagrams of labelled axons within dorsal columns. Collaterals branch at intervals of ~0.8 mm on average. (b) Detailed reconstructions of collaterals 1–6 in (a), projected onto single transverse planes. (c) Collaterals of (b) superimposed; terminal branches are especially dense in layers V and VI. (d) Diagram showing the distribution of muscle-afferent terminals of groups Ia, Ib and II. Modified from Fyffe (1981) and reproduced by kind permission of Robert Fyffe

pole. Boyd (1981), using an isolated spindle preparation from cat tenuissimus with intact nerve and blood supplies, confirmed the conclusion of Jami et al. (1980) that increased position sensitivity in secondaries requires chain-fibre activation, and he also showed that the secondary had to be in the activated pole. The rare inhibitory action described by Bessou and Laporte (1962; see above) is now attributable to bag$_2$-fibre contraction, unloading separately innervated chain fibres in the same pole (Gioux et al., 1990), with a clear example being given by Poppele and Quick (1985; their figure 3).

The in-series arrangement of primary ending–secondary ending(s)–activated chain fibres requires further consideration of the mechanosensory transduction process and why the secondary response is less variable than that of the primary. The difference seems to be closely linked to the ability of the primary to be driven 1:1 by chain-fibre activation at constant stimulation rates, whereas secondaries are only rarely driven in this way (Celichowski et al., 1994). The driving response of the primary is thought to be caused by the high fusion frequency of chain-fibre contraction (Bessou & Pagès, 1969). If so, any high-frequency stress in the chain fibres is, presumably, transmitted via the secondary, yet the ending is insensitive to it. The electrotonically compact nature of secondaries noted above might be responsible for this behaviour, but there might also be important differences in ion-channel expression, such as voltage-regulated K$^+$ channels (Oliver et al., 2021).

7 | STRUCTURAL STUDIES ON THE CENTRAL DISTRIBUTION OF INDIVIDUAL GROUP II AFFERENTS

Of the topics covered in our review, none, perhaps, demonstrates the paucity of information concerning secondary-ending biology better than this. Intracellular labelling with horseradish peroxidase, introduced by Snow et al. (1976), was rapidly exploited in studies of the spinal cord, as reviewed by A. G. Brown (1981). The technique reveals not only intraspinal trajectories of axons and collaterals, but also the numbers and distribution of presynaptic boutons. These can be correlated with cytoarchitectonic and physiological data, such as potential postsynaptic neurons and the amplitude and duration of postsynaptic potentials. Early results included 46 group Ia and 13 group Ib afferents (for references, see A. G. Brown, 1981); however, only three group II muscle afferents were also described at this time, at least in part because of the technical difficulties involved, and of these, only two included the intraspinal axonal bifurcation into ascending and descending branches (Fyffe, 1981; Figure 6). Fyffe (1981) reconstructed two collateral branches from each of the axons, showing the most extensive terminal branching in the deep dorsal horn, predominantly laminae V and VI, but with some terminals extending into laminae VII and IX of the ventral horn (Figure 6). Hongo (1992) presented similar results for five collateral branches of cat plantaris group II afferents. All these afferents innervated cat hindlimb muscle; their central terminals were distributed mainly in lumbosacral segments L6–S1. In a recent study using neurobiotin labelling of rat triceps surae afferents, Vincent et al. (2017) carried out a quantitative analysis of central terminals of three examples of each of groups Ia, Ib and II, which showed a broadly similar laminar distribution of terminal varicosities to the terminal branches reconstructed by Fyffe (1981). The dense innervation of laminae V and VI by group II afferents, identified physiologically as derived from secondaries, is apparent in both the rat and the cat, though it is possible that in the rat they have a greater representation in lamina IX than in the cat. Among the interneurons that receive monosynaptic input from group II afferents, there is probably no class that is exclusive to that input. The interneurons include glutamatergic excitatory propriospinal and spinocerebellar neurons, and GABA- and glycinergic propriospinal neurons. Further details, which are beyond the scope of this review, may be found in the studies by Jankowska (2001), Jankowska and Edgeley (2010) and Shakya Shrestha et al. (2012). Analogous results to those of the lumbosacral region of the rat and cat have been described for physiologically identified primaries and secondaries in jaw-closing muscles of the cat by Kishimoto et al. (1998). Both groups of afferents terminated mainly in the dorsolateral subdivision of the trigeminal motor nucleus and in the supratrigeminal nucleus, but terminals of primary-ending afferents were more abundant than those of secondary endings in the dorsolateral subdivision of the trigeminal motor nucleus, whereas the converse was true for supratrigeminal nucleus.

The trigeminal nuclei and the lumbosacral region are at opposite ends of the neuraxis, but to what extent can results obtained from them be generalized to other regions with different functions, particularly cervical, controlling neck and forelimb movements, and thoracic, with its role in respiration? The relative abundance of spindles in dorsal neck muscles (Banks, 2006) and the preponderance of secondary endings in those that have been described so far (see above, and Banks et al., 2009) make this an especially interesting system for maintaining a stable platform for the head and for integration of spatial positioning information from the vestibular system with the position of the rest of the body in relationship to the head (Berthoz et al., 1992). Despite the abundance of spindles in neck muscles, such as complexus, they do not display strong monosynaptic reflexes, and this is reflected in the distribution of central terminals of group Ia afferents (Keirstead & Rose, 1988a, 1988b). There is, therefore, a difference in the central organization of muscle-afferent connections between cervical and lumbosacral regions of the spinal cord, but nothing is known about the microanatomy of central terminals of other groups of afferents from these muscles of the neck.

8 | CONCLUSIONS ON THE STRUCTURE AND FUNCTION OF SECONDARY ENDINGS AND GROUP II AFFERENTS

Before turning to the information provided by secondary endings to the CNS and the use made of that information by the CNS, it may be helpful to summarize key points from the above sections.

1. Although muscle spindles occur throughout the tetrapods, mammalian spindles with a full complement of intrafusal fibres (b_1b_2c) might be the only ones to contain both phasically (primary) and tonically (secondary) responsive endings.
2. Numbers and distributions of the several components of skeletal muscle sensory innervation, in particular tendon organs and primary and secondary endings of spindles, vary independently and characteristically in different muscles.
3. The most complete information on sensory complements has been obtained from the cat, especially the hindlimb. Secondary endings compose from ~31% of all b_1b_2c-spindle sensory endings in calcaneometatarsalis, an intrinsic muscle of the foot, to 79% in rectus capitis posterior, an axial muscle concerned with head position.
4. The proportion of secondary endings is less in homologous muscles of the rat compared with the cat. If this is a function of body size, human spindles would be expected to have an even greater proportion of secondary endings than the cat, although direct comparisons are lacking.
5. On average, secondary endings have a higher threshold to stretch than primary endings; their output is less variable, but they have higher length sensitivity to maintained stretch.
6. Secondary endings occur predominantly on chain fibres and are therefore rarely influenced by dynamic fusimotor input.
7. In the lumbosacral region of the spinal cord, the central terminals of secondary-ending (or group II) afferents are distributed mainly to layers V–VII and show little overlap with the terminals of Ia or Ib afferents.

9 | WHAT DO MUSCLE SPINDLE AFFERENTS SIGNAL TO THE CNS?

As discussed above, the dynamic (velocity) component of response of spindle primaries to length changes is several times that in secondaries, and the static component in secondaries is greater than that in primaries (Botterman & Eldred, 1982). Dynamic fusimotor stimulation increases both the dynamic and static components of response in primaries, whereas static fusimotor stimulation increases the static component of response in both primaries and secondaries, while reducing the dynamic component in primaries. Static fusimotor action increases the background firing rate ('bias' or 'offset') of both types of endings. Individual fusimotor neurons range from having purely static to purely dynamic actions (Emonet-Dénand et al., 1977). These differences suggested that spindle secondary afferents were more suited to signalling maintained changes in length (position) than spindle primaries (P. B. C. Matthews, 1972).

Given that the responses of muscle spindle afferents to variations in muscle length are so strongly influenced by γ-fusimotor action, questions arise. How does the CNS use this modulatory influence during activities of daily life? What is the effect on the signals supplied to the CNS by the spindle afferents? In theory, if static and dynamic γ drive were always set to constant levels, the afferent signal would be an unvarying function of muscle length. On the contrary, if γ drive were rapidly and deeply modulated, the signal would be a more complicated function of muscle length and γ activity. In this situation, how would the CNS extract the length information needed for kinaesthesia and movement control?

9.1 | Early studies of movement-related recordings

To tackle these questions, the next step was to record the activity of spindle afferents and α- and γ-motoneurons during self-generated movement. In a pioneering study in decerebrate cats, Hunt (1951) found that the majority of γ-motoneurons fired tonically in the resting limb. They increased their firing rate immediately before and during α-motoneuronal activity in involuntary movements. This led to the proposal that γ-motoneurons were co-activated with α-motoneurons to keep spindle afferents firing during active muscle shortening (Kuffler & Hunt, 1952). In this view, the higher centres adjusted the γ drive according to the velocity of shortening 'expected', with the result that spindle firing remained roughly constant unless the shortening deviated from that 'intended' (Eldred et al., 1953; P. B. C. Matthews, 1964; Phillips, 1969).

Confirmatory evidence for both tonic and α-linked γ activity was subsequently obtained in other laboratories. As Hunt had found, γ-motoneurons generally fired at much higher rates than α-motoneurons ($\leq$ 150 impulses/s compared with $<$ 40 impulses/s, respectively) and, unlike α-motoneurons, they could be very responsive to innocuous stimuli applied to the skin, often far from the muscles they innervated (Eklund et al., 1964; Granit et al., 1953). In recordings from intercostal nerves, some γ-motoneurons were co-activated with α-motoneurons and others fired tonically throughout the respiratory cycle (Eklund et al., 1964; Sears, 1964).

An approach to establishing with more certainty the nature of fusimotor action during functional movements is to make recordings in premammillary decerebrate cats that walk spontaneously when suspended with feet placed on a moving belt (Hinsey et al., 1930). The advantage of this method is that it has been possible to record from several afferents simultaneously and from identified static and dynamic γ-motoneurons. In the first of such studies (Perret & Berthoz, 1973; Perret & Buser, 1972; Severin, 1970), it was clear that spindle discharges were markedly influenced by γ efferent discharge. There was evidence of both α–γ co-activation and α-independent γ activation (Cabelguen et al., 1984). More recent results of this type are discussed below.

9.2 | Human microneurography

In 1967, Hagbarth and Vallbo succeeded in recording from human muscle afferents by inserting microelectrodes percutaneously into peripheral nerves. The electrodes could easily be dislodged; therefore, initially, most of the data involved weak isometric contractions of the receptor-bearing muscles. As the technique evolved, it became possible to 'hold' single units during slow voluntary movements. In isometric contractions, the firing rates of spindle afferents increased with EMG activity, which indicated α-linked fusimotor action (Hagbarth & Vallbo, 1967; Vallbo, 1970). Reviewing the available data in 1979, Vallbo et al. (1979) stated that: '…the balance of evidence seems to be against the view that there is a significant fusimotor tone in healthy subjects when the muscles are relaxed and also against the view that the subject can induce fusimotor activation of his spindle endings by any volitional manoeuvre without contracting the receptor-bearing muscle.' In fact, such evidence was already available in humans (Burg et al., 1973), and further evidence was soon to come from chronic animal recordings.

9.3 | Awake animal spindle afferent recordings

In the 1970s, techniques were developed to record from single sensory afferents in normally behaving animals. In cats and monkeys with heads stabilized in a frame, the firing of jaw muscle spindle afferents was recorded from the midbrain trigeminal nucleus during chewing and lapping (Goodwin & Luschei, 1975; Taylor & Cody, 1974; Figure 7). From the outset, it was clear that spindle afferent firing rates were deeply modulated during cyclical movements, generally increasing during muscle lengthening and decreasing during shortening. As before, there was evidence for both α-linked and α-independent fusimotor activity. There was also evidence that fusimotor drive could wax and wane according to behavioural state, independently of α-motoneuronal activity. Here, it is worth mentioning some uncertainties regarding afferent identification. In the human neurography and animal jaw-muscle studies, some key tests that help to distinguish between spindle primaries and secondaries were not always applied. These tests include eliciting muscle twitches electrically, measuring afferent conduction velocities, vibrating the receptor-bearing muscle and, most importantly, administering suxamethonium during deep anaesthesia. The resulting uncertainty was acknowledged in some of the reports (Cody et al., 1972, 1975; Flament et al., 1992; Goodwin & Luschei, 1975) and became the subject of much discussion later (Edin & Vallbo, 1990; Prochazka & Hulliger, 1983).

In the mid-1970s, methods were developed to record afferent activity in awake cats from microwire electrodes chronically implanted in spinal dorsal roots (Loeb et al., 1977; Prochazka et al., 1976). In one of the methods, telemetry allowed the animals freedom of movement around the laboratory. Identification tests were carried out during subsequent periods of surgical anaesthesia, which allowed the above tests to be performed. Most of the recordings were from spindle primaries, Golgi tendon organs or cutaneous afferents. Relatively few were from spindle secondaries, but as in the jaw-muscle studies, their firing rates were closely related to the changes in length of the receptor-bearing muscles. They fired with less interspike variability than primaries and less evidence of fluctuating fusimotor drive. Figure 8 shows the

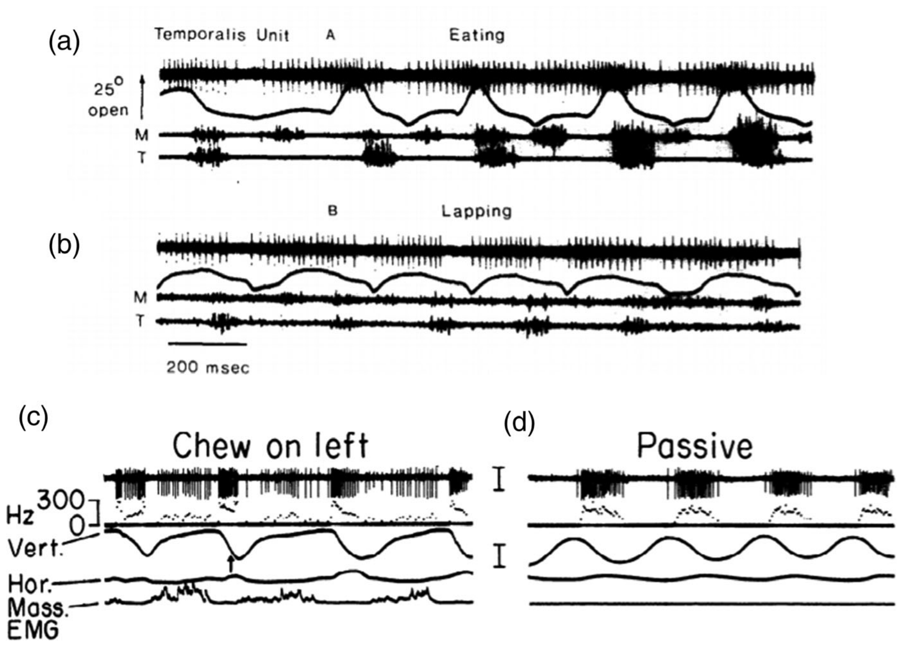


FIGURE 7 Recordings from spindle afferent neurons in the trigeminal nucleus in awake animals. (a,b) Recordings in the cat during eating and lapping (reprinted from Taylor & Cody, 1974, copyright 1974 with permission from Elsevier). (c,d) Recordings in the monkey: (c) during chewing; and (d) during movements imposed when the monkey was anaesthetized, inhibiting fusimotor activity (Goodwin & Luschei, 1975). Traces from top down: (a,b) cat temporalis spindle afferent action potentials, jaw aperture (muscle lengthening upward), masseter EMG (M) and temporalis EMG (T); (c,d) monkey masseter spindle afferent action potentials, instantaneous firing rate, vertical mandible position (muscle lengthening downward), horizontal mandible position and masseter EMG. The firing rates in all cases are deeply modulated, increasing during muscle lengthening and decreasing during shortening. The tests used to identify afferents in these studies were insufficient to separate spindle secondary afferents from spindle primary afferents with certainty. However, the relatively low firing rates in (a) and (b) and the low interspike interval variability in both afferents are consistent with them being spindle secondary afferents (see discussion in the text on afferent identification)

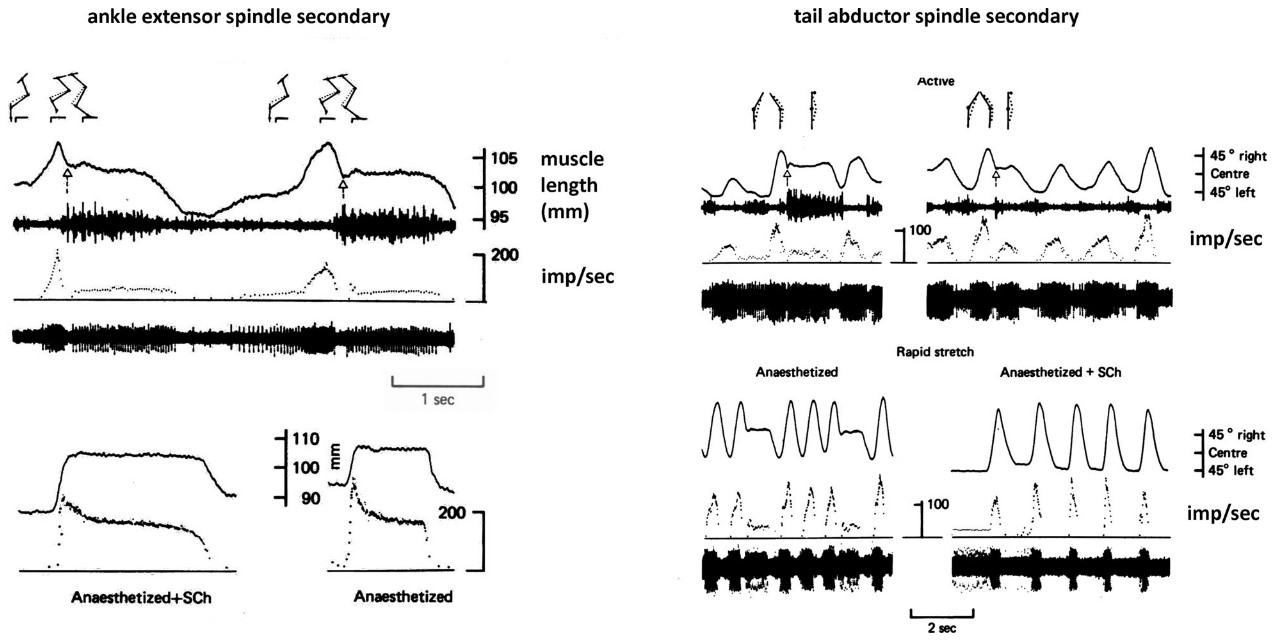


FIGURE 8 Recordings from spindle secondary afferents in an ankle extensor muscle (left) and a tail abductor muscle (right). Upper traces, voluntary movements; lower traces, movements imposed during brief periods of deep anaesthesia [the lack of a significantly increased dynamic response to stretch after i.v. succinylcholine chloride (SCh) was the main evidence that the afferents were muscle spindle secondaries and not primaries]. In both trials, spindle secondary firing closely followed the variations in muscle length, even after muscle shortening came to a halt upon contact with an external surface. Reproduced with permission from Prochazka et al. (1979), copyright 1979 the Physiological Society

firing of two spindle secondaries in awake cats. In both cases, the firing rates followed the variations in muscle length, independently of fluctuating EMG (i.e., α-motoneuronal) activity. This suggested that any α-linked fusimotor drive was relatively weak. Analysis with a simple mathematical model indicated that the length sensitivity of the secondary afferent was slightly higher when the animal was awake than when it was deeply anaesthetized, consistent with a steady level of static fusimotor drive in the awake state (Prochazka & Wand, 1981a).

9.4 | Fusimotor set

Spindle primary afferents showed large variations in background firing and stretch sensitivity in different behaviours and contexts, often uncorrelated with EMG activity. Taken together, these observations in awake animals led to the concept of task-dependent 'fusimotor set' (Prochazka et al., 1985). Evidence of fusimotor set has also been cited in humans, although the effects have been modest (Dimitriou, 2016; Horslen et al., 2018; Ribot-Ciscar & Ackerley, 2021; Ribot-Ciscar et al., 2009). Other human neurography groups have sought but failed to find such evidence. It was argued that the low firing rates of human spindles and the modest fusimotor effects compared with those in cats and monkeys represented a fundamental species difference. However, the response properties of human muscle spindles studied in vitro were virtually identical to those in cats (Newsom Davis, 1975; Poppele & Kennedy, 1974). The more likely explanation is that the range of movements in human neurography is greatly restricted. Muscle velocities have been far lower in the human data, generally, < 0.2 rest lengths/s, a range in which fusimotor action can maintain or even increase muscle-spindle afferent firing during muscle shortening. Another factor is that cats brought into an unfamiliar laboratory setting might be more wary and vigilant than human subjects, increasing the likelihood of large, behaviourally related fusimotor modulations. According to personal discussions with Drs Erich Luschei and Eberhard Fetz, this did not apply to the monkeys in the studies referred to above because they were highly adapted to the laboratory environment. To compare like with like, human muscle-spindle firing would have to be studied in tasks and contexts involving higher levels of uncertainty, speed and difficulty than has been possible so far.

Behaviourally related, α-independent changes in fusimotor drive have not been described in spindle secondaries in awake humans or animals. This could be attributable to: (1) such changes being the province of dynamic fusimotor neurons only; (2) spindle secondaries being less influenced by fusimotor action than primaries; or (3) the lack of data on spindle secondary firing in different behavioural contexts.

9.5 | Spindle afferent and γ-motoneuron recordings in reduced animal preparations

Results from the early studies on reduced preparations compared with those in freely moving animals have not secured a consensus of agreement on spindle discharge during locomotion. Taylor et al. (2000a) compared the behaviour of primary and secondary spindle afferents during active locomotion in high-decerebrate cats with that of the same afferents when the movements were reproduced passively under deep anaesthesia to block fusimotor drive. A strong fusimotor drive during locomotion was indicated by a relatively high rate of spindle discharge compared with discharges recorded during passive movements. Clear departures from length sensitivity were apparent. When the firing rates of secondary afferents during passive movements were subtracted from those during active movements, the difference records showed increases in firing rate as the muscle shortened and decreases as it lengthened. This was the case for both ankle flexor and extensor muscles, but with some phase advance for the extensors (Figure 9). The difference records were rather poorly related to EMG, which argued against α–γ co-activation. The behaviour of secondary afferents compared with that in freely moving cats (Loeb et al., 1985; Prochazka & Gorassini, 1998; Taylor & Cody, 1974) indicated a powerful, modulated drive by static fusimotor neurons. The firing of primary endings in ankle flexor and extensor muscles, using the same procedure (active minus passive discharge), revealed a burst of activity at the start of muscle lengthening, most probably resulting from increased dynamic fusimotor drive (Taylor et al., 2000a).

The first direct recordings from a population ($n = 32$) of γ-motoneurons in 11 locomoting decerebrate cats (Murphy et al., 1984) revealed two different patterns, one highly modulated and the other essentially tonic. Indirect reasoning suggested that these patterns represented discharge separately in dynamic and static γ-motoneurons. Taylor et al. (2000b) recorded the discharges of 50 γ-motoneurons and 68 spindle afferents in nine cats. They identified 13 dynamic and 28 static γ-motoneurons positively through observation of simultaneous recordings of spindle afferents during stimulation of the mesencephalic locomotor region. Essentially, three patterns of γ-motoneuron activity could be distinguished. All static γ efferents discharged continuously and were modulated in a time-dependent fashion with the locomotor cycle, but with two distinct patterns. Approximately two-thirds showed a marked increase in firing rate during active muscle shortening and a decrease during muscle lengthening (Taylor et al., 2000b, 2006), matching the pattern of the spindle secondary afferents (Taylor et al., 2000a). Other static γ-motoneurons showed more modest fluctuations in firing rate during the locomotor cycle that increased smoothly during muscle stretch. These two patterns of static fusimotor discharge (Figure 9) might support limited separate control over the bag$_2$ and chain intrafusal muscle fibres (Banks, 1991), a contingency that could be exploited by the CNS (see Gladden, 1981).

Identified dynamic γ efferents showed a very different discharge pattern from the two static patterns (Taylor et al., 2000b). The discharge was intermittent during locomotion, turning on abruptly at the onset of muscle shortening and continuing at a high rate until immediately after the start of muscle lengthening. Concurrent recordings from primary afferents suggested that the dynamic γ discharge is timed appropriately to support a burst of primary-afferent discharge, signalling the onset of muscle stretch.

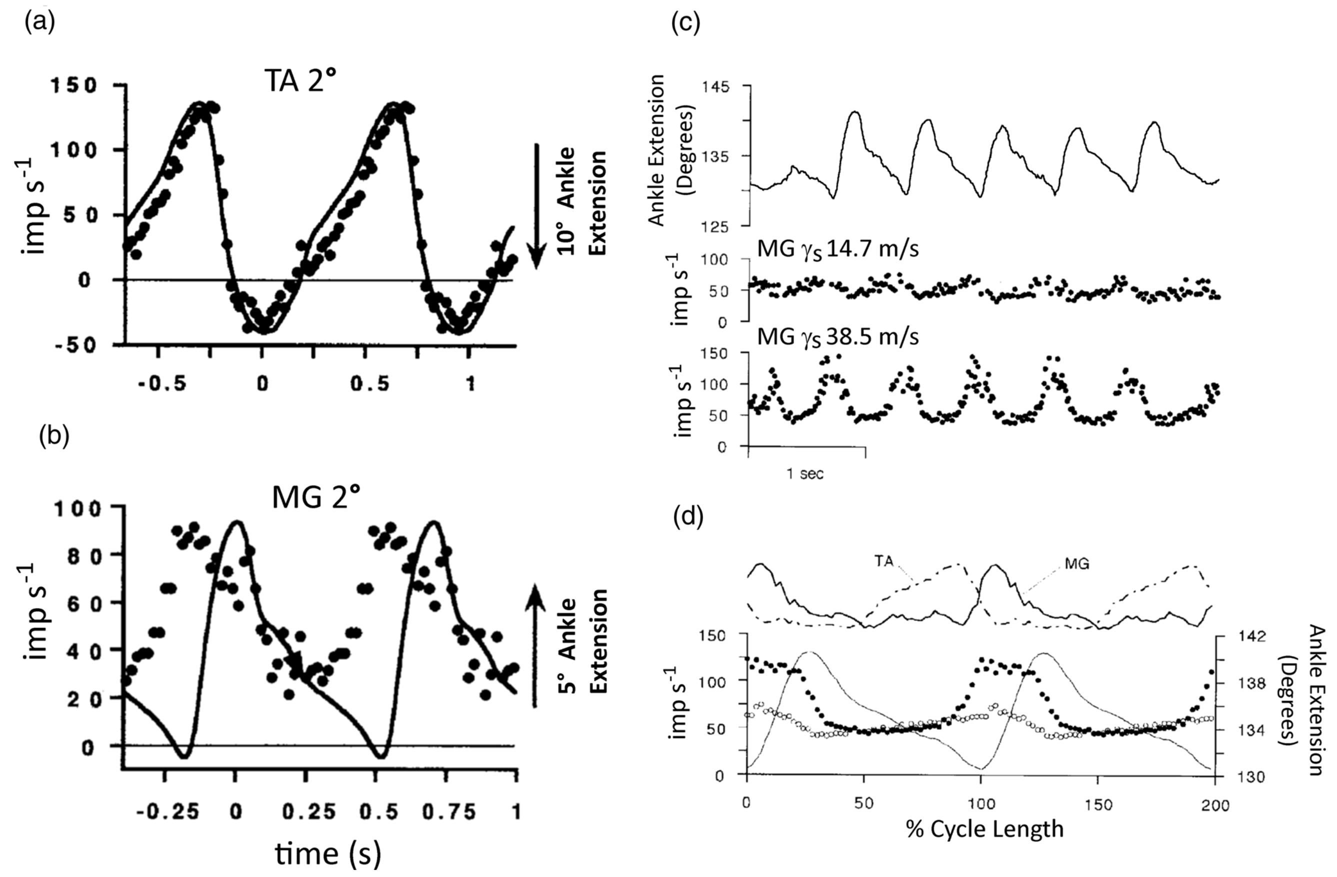


FIGURE 9 Muscle-spindle and γ efferent discharges recorded in decerebrate cats during treadmill locomotion. Three legs walked on the treadmill, while the left hindlimb was fixed and allowed to rotate only at the ankle. (a,b) The difference records, active minus passive discharges, for secondary spindle afferent firing for the tibialis anterior (TA) and gastrocnemius medialis (MG) muscles related to movement of the ankle. The solid dots represent 'difference' firing rates. Continuous lines are the angular rotation of the ankle, with arrowheads showing the direction of muscle lengthening. (c,d) Discharges of two γ-motoneurons of the gastrocnemius medialis muscle during active locomotion in a decerebrate cat. In (c), instantaneous firing rates (solid dots) and ankle angle (continuous line) are shown, with extension of the ankle (upward deflection) indicating shortening of the MG muscle. In (d), cycle averaged discharges are shown of the two γ efferents shown in (c). The top two traces show the smoothed rectified EMG signals from MG and TA. The lower three records are the smoothed discharges of the two γ efferents (showing distinctly different profiles; see main text) and averaged ankle angle (continuous line). The horizontal scale is normalized with respect to step cycle duration (average 0.65 s). (a,b) Adapted from figures 4 and 9 of Taylor et al. (2000a); (c,d) adapted from figure 3 of Taylor et al. (2000b) with permission, all copyright 2000 the Physiological Society

In conclusion, the findings in the decerebrate locomotor preparation argue for a mainly independent activation of α- and γ-motoneurons. The dynamic γ fusimotor action would enhance detection of phase transitions in length. The less modulated type of static γ fusimotor discharge would support length detection of the muscle, and the highly modulated static γ action would support a strongly increasing secondary afferent discharge during muscle shortening that has not been seen in freely moving, intact animals.

9.6 | Summary

What limitations might account for the differences between spindle discharges seen in freely moving and decerebrated animals? In the awake animals, recordings from secondary afferents were few in number, and technical limitations in monitoring muscle length probably led to some imprecision. Given that the tendons in series with muscles have some compliance, the monitored changes in length of muscles might differ from those of the muscle fibres (Griffiths, 1987, 1991; Hoffer et al., 1989). This might have led to errors in inferring the underlying fusimotor action. Simulations indicated that this discrepancy might be relatively small in the muscles studied (Elek et al., 1990). Although the locomotion of the animals appeared normal, lingering discomfort from the implantation surgery and the noisy and unfamiliar laboratory context might have affected behaviour. In the decerebrate cats, extensive denervation, open wounds and fixation of the head and hindlimb could have resulted in elevated nociceptive input during locomotion, likely to cause reflex drive to fusimotor neurons (Appelberg et al., 1983c). Additionally, there was significantly reduced load-bearing, particularly for the limb suspended above the treadmill for recording purposes. Thus, the differences in secondary afferent discharge observed between preparations remain unexplained but raise the possibility of optional adaptive neural control of locomotion.

10 | SPINDLE SECONDARY CONTRIBUTIONS TO THE CONTROL OF MOVEMENT

10.1 | Load compensation

Studies in animals and humans with deafferented limbs have shown the crucial importance of sensory input for the control of movement (Bell, 1834; J. D. Cole & Sedgwick, 1992; Lajoie et al., 1996). Many experiments have been performed to identify the roles of muscle and cutaneous afferents in this regard. A common strategy has been to apply rapid perturbations to body segments and analyse the time course of EMG response. A brief muscle stretch produced by tapping a tendon elicits a short-latency, reflexive EMG response resulting from a volley of action potentials in spindle primary afferents, monosynaptically activating α-motoneurons of the receptor-bearing muscle, causing it briefly to contract (the tendon jerk). Such stimulation is unlikely to provide significant reflex excitation of γ-motoneurons (Appelberg et al., 1983a; Ellaway & Trott, 1978; Fromm & Noth, 1976).

Longer-lasting stretches elicit this short-latency reflex in addition to medium- and long-latency responses (Hammond et al., 1956; Lee & Tatton, 1975; Marsden et al., 1976). The long-latency response is under volitional control and involves transcortical pathways from spindle afferents to the brain and back (Capaday et al., 1991; P. B. C. Matthews, 1991). There has been much debate about the medium-latency response. It could be a monosynaptic response to segmented discharge of spindle primaries (Eklund et al., 1982; Hagbarth et al., 1981; Prochazka & Wand, 1981b; Schuurmans et al., 2009) or to spindle secondary activity, arriving at the spinal cord after the initial group Ia volley (P. B. C. Matthews, 1969). Spindle group II afferents terminate on interneurons in intermediate layers V and VI of the grey matter (see Figure 5). Some of these interneurons synaptically activate homonymous α-motoneurons, providing an anatomical basis for a group II-mediated contribution (Soteropoulos & Baker, 2020). There is also the possibility that weak reflex connections to γ-motoneurons from group II afferents might contribute indirectly to longer-latency stretch reflexes by increasing spindle afferent responses (Appelberg et al., 1983b; Gladden et al., 1998; Noth & Thilmann, 1980).

A spindle secondary contribution to medium- and long-latency stretch reflexes has been tested in many different ways, with contradictory results. Studies in humans and decerebrate cats supported a spindle group II contribution (P. B. C. Matthews, 1969, 1984), but this was refuted in a follow-up study in humans, in which limb cooling was used to cause differing conduction delays in group Ia and II axons (P. B. C. Matthews, 1989). A promising line of investigation opened with the demonstration in chloralose-anaesthetized cats that the α_2-adrenergic agonist tizanidine strongly depressed group II-evoked field potentials of interneurons in the intermediate layers mentioned above (Bras et al., 1990; Skoog, 1996). In human subjects walking on a treadmill, stretches were applied about the ankle before and after oral doses of tizanidine, resulting in a 50% reduction in the medium-latency stretch reflex in the soleus muscle (Grey et al., 2001). Four other interventions in the same study corroborated the result, leading to the conclusion that group II muscle afferents contributed to the medium-latency stretch reflex.

Experiments in other laboratories on the effect of tizanidine on medium-latency reflexes in the human upper extremity supported this conclusion (Lourenço et al., 2006; Meskers et al., 2010), but in a more recent human study involving both upper and lower extremity muscles, the medium-latency reflex was not significantly reduced after tizanidine was taken (Kurtzer et al., 2018). It remains possible that the differences between these studies was attributable to slight differences in protocols and tasks (Marchand-Pauvert et al., 2005).

What can be concluded about the role of spindle secondaries in load-compensation responses? Essentially, the question remains open. There is good evidence for a closed-loop pathway from group II afferents to spinal cord intermediate-layer interneurons that activate homonymous and heteronymous α-motoneurons monosynaptically. There is conflicting evidence that inhibition of the intermediate-layer interneurons by tizanidine reduces medium-latency and long-latency reflexes. There is electrophysiological evidence that spindle secondary afferents contribute to medium-latency reflexes and that such responses depend on task.

10.2 | Phase switching in the locomotor step cycle

Load compensation responses provide continuous feedback control of muscle activation, whereas the transitions between flexion and extension in the locomotor step cycle are switch-like events. Sensory input has long been implicated in these transitions (Freusberg, 1874). Regarding spindle afferents, it is not known whether primary or secondary afferents, or both, are involved. Theoretically, positional information from secondaries could provide the basis for triggering phase transitions. The phase advance conferred by the dynamic response of spindle primary afferents could adjust the timing according to locomotor speed.

This discussion has so far largely ignored the reflex control of γ-motoneurons in the sensitization of spindle afferents. A comprehensive review has been provided by Hulliger (1984). The consensus from a large number of studies is that group I and II muscle inputs, and joint afferents, provide only weak actions, with inconsistent organization. The case for substantial inputs from group III muscle afferents (Appelberg et al., 1983c; Ellaway et al., 1982; Noth & Thilmann, 1980) and from cutaneous receptors (Appelberg et al., 1977; Bessou et al., 1981; Johansson & Sojka, 1985) is stronger, with a degree of specificity and organization with respect to both group III muscle-afferent (Ellaway et al., 1982) and skin (Davey & Ellaway, 1989a, b; Ellaway et al., 1997) inputs. However, there are serious limitations to drawing conclusions from the work on reflex effects on γ-motoneurons owing to the differences in the preparations studied and because static and dynamic fusimotor neurons have not been identified reliably. Additionally, the extent to which reflex effects on γ-motoneurons are controlled by supraspinal centres

(Appelberg et al., 1983d; Fromm & Noth, 1976; Gladden et al., 1998) has not been established and would be relevant in the case of even a weak group II excitatory action to manage the consequences of positive feedback.

11 | CONCLUSIONS ON SPINDLE SECONDARY CONTRIBUTIONS TO SENSORY SIGNALLING AND MOTOR CONTROL

The firing of muscle spindle afferents is determined not only by the length of the extrafusal muscles to which they are attached, but also by fusimotor input. It was recently claimed that muscle-spindle primary afferents in passive muscle signal muscle force and its derivative rather than length-related variables (Blum et al., 2017). The correspondence to force is not surprising, because in the absence of extrafusal contraction, force and length are very similar. However, in the ascending phase of a maximal muscle twitch, as force rises and length declines, spindle afferent firing declines. In fact, this classical test distinguishes spindle afferents from Golgi tendon organ afferents, which do signal muscle force. The claim has recently been modified (Blum et al., 2020).

As a result of the technical difficulties in recording from spindle afferents and, in particular, from γ-fusimotor neurons during voluntary movement, there remains much disagreement and conjecture on the precise nature of the signals conveyed by spindle afferents. At this point, although it might be simplistic, it is reasonable to view spindle secondaries as signalling extrafusal muscle-fibre length variations, with some fusimotor biasing and phasic modulation. This is in contrast to spindle primaries, whose signals are dominated by muscle velocity and whose sensitivity can vary up to 10-fold with the level of muscle activity, behavioural task and context. Notwithstanding the uncertainties, there is little doubt that spindle afferent input plays a crucial role in the reflex and voluntary control of movement. There is clear involvement in load compensation, interaction with the timing elements of the locomotor central pattern generator and the control of complex voluntary movements of the upper extremity.

12 | THE KINAESTHETIC SENSES

The group of sensations comprising proprioception includes the senses of position and movement, often referred to collectively as the kinaesthetic senses, the senses of effort, muscle force and heaviness and the sense of balance. Although the supporting evidence is limited, it is generally believed that the secondary endings of muscle spindles contribute to the sense of position of the body and its parts.

Here, it is proposed that muscle spindles play a role in limb position sense. There have been debates, in the past, about contributions from other sensory receptors in kinaesthesia, such as receptors in skin and joints. However, current evidence supports the view that in normal circumstances the predominant position signal comes from muscle spindles. For a review, see Proske and Gandevia (2012).

A muscle stretch receptor, designed to signal position of the body and its limbs, must be able to generate activity that is directly related to the length of a muscle, the angle of a joint. It is envisaged that the ability of muscle spindles to be able to maintain steady levels of discharge at a given length, where their discharge rate is proportional to length, is the signal responsible for providing the brain with positional information. However, it is unlikely that the stretch receptor discharges are directly converted into estimates of limb position. The spindle signal might contribute to determination of body posture (i.e., position in postural space), but not in extrapersonal space. For information about the position of the body in its surroundings, further brain processing is required that involves knowledge about the lengths and shapes of body parts (Longo & Haggard, 2010).

Although the senses of both position and movement are attributed to signals coming from muscle spindles, and although both senses make important contributions to proprioception, it is argued here that, of the two, the sense of limb position is the more important. For a review of the evidence for the existence of a sense of position independent of the sense of movement, see P. B. C. Matthews (1988). In the rare cases of an acute loss of all large-diameter afferents from skin and muscle, initially the patient experiences a loss of self and feels disembodied, floating in mid-air (J. Cole, 1995). In these conditions, the importance of position sense becomes apparent, because it provides information about the position of the body and its parts in space. Position sense is therefore likely to play an important role in self-awareness.

The evidence supports secondary endings in addition to primary endings of spindles as contributing to position sense. Much has been written about primary endings; therefore, attention is focused here on secondaries, which have been somewhat neglected in the past. Based on the data published by Banks et al. (2009) and shown in Figure 2, it can be estimated that in hindlimb muscles of the cat there are, on average, ∼1.5 secondary endings for every primary ending. Clearly, therefore, simply on the basis of their widespread distribution, secondary endings are likely to subserve an important function. The argument that the sense of position is the more significant of the two kinaesthetic senses finds support in the massive sensory receptor machinery dedicated to it.

13 | MUSCLE SPINDLES AS POSITION SENSORS

The evidence for a role for muscle spindles in proprioception is largely based on the experiments of Goodwin et al. (1972). Blindfolded subjects were required to match the position of one arm by placement of the other. In the absence of vision, it was a proprioceptive sensation-matching task ('I place my arm where I feel the other arm is located'). Subjects managed to complete the task with reasonable accuracy. The evidence that pointed to the involvement of muscle spindles was based on kinaesthetic sensations generated by muscle vibration. At the time, it was already known from animal experiments that muscle spindles were sensitive to vibration (M. C. Brown et al., 1967). Goodwin and colleagues vibrated elbow flexors or extensors at a frequency of 100 Hz and an amplitude of 0.5–2.0 mm. Vibration of elbow flexors led predominantly to a sensation of forearm movement in the direction of extension, vibration of extensors of movement into flexion. But it was not only a sensation of movement. There was an accompanying sensation of displaced position. During vibration of elbow flexors, the subject believed their arm was in a more extended posture, the muscle longer than its real length. A joint was perceived to be in a position it would take up if the vibrated muscle was stretched. Goodwin et al. concluded that the primary endings of muscle spindles were largely responsible for these illusory sensations, because it was known that they were much more sensitive to vibration than secondary endings.

The thesis presented here is that secondary endings of spindles contribute to the sensation of position of the body and its limbs. The observations of Goodwin et al. make the point that the primary endings also contribute to position sense. In animal experiments, it had been shown earlier that secondary endings were unlikely to contribute to movement sensations because of their limited dynamic responsiveness. However, their ability to signal length changes was similar to that for primary endings (Jansen & Matthews, 1962). Nevertheless, a difficulty with assessment of the role of secondary endings in kinaesthesia remains the fact that there are few studies where sensations are directly attributable to secondary endings (McCloskey, 1973).

It should, perhaps, be mentioned at this point that there is evidence for position signalling in the complete absence of any sensory input. In these experiments, all nerves to the hand were blocked (the phantom hand) and a 30% of maximal effort produced significant illusory sensations of displacement of the position of the hand (Gandevia et al., 2006). In a subsequent study (Smith et al., 2009), it was shown that in a normal hand with an intact and functioning nerve supply, during an isometric effort, position illusions could also be generated. The conclusion was that in evaluating the central processing of proprioceptive information, it had to be considered that motor commands, by themselves, were able to generate positional information. What role a position signal, generated by a 30% effort, plays in proprioceptive sensorimotor control, remains uncertain. In addition, although the contribution of central command signals to position sense has been demonstrated for the wrist, similar evidence for position sense at the forearm is currently lacking (Walsh et al., 2013). Finally, as described below, it is possible in the complete absence of any motor commands to indicate, with reasonable accuracy, the position of a hidden arm (Chen et al., 2021). It seems that some proprioceptive mechanisms are able to operate independently of the motor system.

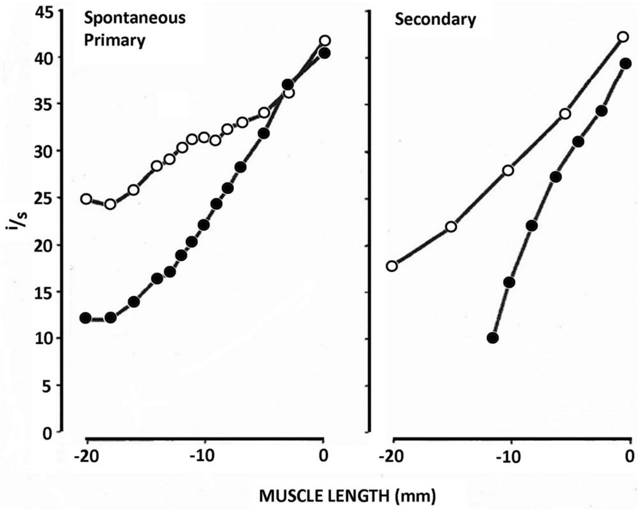


FIGURE 10 Plots of resting discharge, in impulses per second (i/s), for two spindle endings recorded in the soleus muscle of the anaesthetized cat, showing the effects of thixotropy in both primary and secondary. The 'spontaneous' primary ending was an example of an ending that maintained some activity down to short muscle lengths, regardless of the form of conditioning (Gregory et al., 1991). Muscle length is given as millimetres below maximal muscle length (L_m), which was the length measured at the start of the experiment when the ankle joint was maximally dorsiflexed. At $L_m - 20$ mm, the muscle lay slack. For each ending, the resting discharge was measured after the muscle had been conditioned with a 1-s-duration tetanic contraction at 100 pulses/s, at fusimotor strength, given at $L_m - 20$ mm. The upper graph for each ending (open circles), was obtained by plotting the average discharge rate for the ending when the muscle was stretched at 1–2 mm increments up to L_m, immediately after the contraction. For the lower plot (filled circles), after the contraction the passive muscle was stretched to L_m, held there briefly and then returned to $L_m - 20$ mm, and the incremental measurements were recommenced. This meant that the muscle had undergone a 20 mm lengthening and shortening before remeasurement of resting rates. At each length, mean resting rates for the two spindle endings were measured over 10 s of recording. It can be seen that when no slack was present (contraction only), both primary and secondary endings were able to respond to progressive increases in muscle length over the full working range of the muscle. Furthermore, when slack was present (after the 20 mm stretch–shortening movement) for both endings, the slope of the line, representing the position sensitivity, became steeper. For the primary ending, position sensitivity increased from 1.0 to 1.8 i/s/mm; for the secondary ending, the increase was from 1.2 to 2.0 i/s/mm. In the presence of slack, the secondary ending remained silent until the muscle had been stretched to $L_m - 12$ mm. Redrawn from Proske et al. (1993), copyright 1993 with permission from Elsevier

14 | THE DISCHARGE FREQUENCY–MUSCLE LENGTH RELATIONSHIP

The plot of the frequency of steady (adapted) firing against muscle length, for a spindle ending over a range of muscle lengths, shows an approximately linear relationship (Figure 10). The slope of the line is called the position sensitivity. Values for position sensitivity are usually approximately the same for primary and secondary endings (Harvey & Matthews, 1961), but have been cited as higher for secondary endings by a factor of 1.5 (Hulliger, 1984).

Examples of primary and secondary ending discharges at a series of lengths, over the full physiological range of muscle lengths (soleus muscle of the anaesthetized cat), are shown in Figure 10. Here, at each muscle length the adapted rates of ending discharges were averaged over 10 s. The two points that were made in this figure were that the slopes of the relationship between length and firing rate were similar for the 'spontaneous' primary ending (Gregory et al., 1991) and the secondary ending and that for both endings the value of the slope, that is the position sensitivity, depended on the immediate previous history of contraction and length changes of the muscle (Proske et al., 1993).

To conclude, based on the observations made with high-frequency, small-amplitude vibration, spindle primaries are considered exclusively responsible for the sense of movement, whereas both primaries and secondaries contribute to the sense of position. Given a similar length sensitivity for the two types of endings, it will be argued that because in spindles of most muscles there is a larger number of secondaries than primaries, the predominant source of position information in the body's musculature comes from spindle secondaries.

15 | SECONDARY ENDINGS OF SPINDLES AS POSITION SENSORS

There is, in fact, relatively little direct evidence linking secondary endings of spindles with the sense of limb position. McCloskey (1973) extended the vibration study of Goodwin et al. (1972) to include a wider range of vibration frequencies and amplitudes. Initially, he confirmed the generation of a movement sensation in response to application of a physiotherapy vibrator to the arm, using a vibration frequency of 100 Hz and 1 mm amplitude. He observed movement sensations over the range 7–30°/s. He then generated lower-frequency, larger-amplitude vibrations by fitting a jig-saw attachment to an electric drill. By altering the driving voltage of the drill, the vibration frequency of the probe could be lowered from 48 to 2–3 Hz at an amplitude of 15 mm, reducing to 5 mm when in contact with the muscle tendon.

With 100 Hz vibration, using the physiotherapy vibrator, McCloskey observed the expected illusions of movement and displaced position. When the jig-saw was used, vibration at 48 Hz led subjects to experience an illusion of movement. Lowering the jig-saw frequency, a point could be reached where subjects no longer perceived any movement, but the joint was perceived to be in a position it would take up if the vibrated muscle was stretched. Here, the error was usually greater than the same subject made when 100 Hz vibration was used. For vibration of the biceps, the arm felt to be more extended than its true position; for vibration of the triceps, it felt more flexed.

The jig-saw frequency could be adjusted to give a movement illusion comparable to that induced by 100 Hz. However, the position error generated in these conditions was much greater than with 100 Hz. It implied that the 100 Hz vibration at 1 mm amplitude was likely to be restricted largely to excitation of spindle primary endings. Engaging spindle primary endings to a similar extent with the jig-saw was likely, at the same time, to recruit large numbers of secondary endings, given that the jig-saw was driven at a five-times greater amplitude than the physiotherapy vibrator. In addition, with the lower frequencies used with the jig-saw, it was likely that the primary endings became locked to the stimulus, in a 1:1 relationship, representing a relatively low rate of discharge, such that their contribution to the evoked sensation remained relatively low (see also Cordo et al., 1995; Roll et al., 1989). McCloskey concluded that the subjective judgements of static limb position and of limb movement were derived from separate lines of central processing.

The bigger position illusions generated with the jig-saw implied that it was necessary to use large-amplitude vibration to engage secondary endings, implying that secondary endings had higher stretch thresholds than primary endings. There is some evidence for this (see *Recognition of the secondary ending* above, and Hunt, 1954). In a study on soleus, Gregory et al. (1977) found that for secondary endings the minimum passive tension required to generate a maintained resting discharge was 9–55 g (or ~88–539 mN), and at threshold the firing rate was in the range 7–12 impulses/s. For primary endings, threshold tension was 8–35 g (or ~78–343 mN) and threshold firing rate 1–14 impulses/s. Secondary endings, because of their low discharge variability and their tendency to stop firing at low rates (Gregory et al., 1977), will be able to transmit positional information more rapidly to the CNS than primary endings, but their signalling capacity will be limited to a smaller range of firing rates. It remains uncertain what implications this has for the fidelity of the position signal generated by the two types of endings.

A number of other investigators have described vibration responses of secondary endings in human muscle. Here, amplitudes of vibration of 1.5 mm or less were used (Burke et al., 1976; Fallon & Macefield, 2007; Roll et al., 1989), making it likely that only a limited number of secondary endings would have been recruited. The general picture that emerged was similar to that described by McCloskey (1973). To conclude, it would be well worth repeating some of the vibration experiments, but using vibrators able to deliver stimuli over a wide range of amplitudes and frequencies. That would make it possible to examine in more detail the interplay of the senses of position and movement attributable to the two types of spindle endings.

16 | THIXOTROPY

All striated muscle exhibits thixotropy; it is a fundamental property. At the end of a contraction, as the muscle relaxes, cross-bridges between actin and myosin detach. However, a few cross-bridges spontaneously re-form, but once attached do not go through their power stroke to produce force. If the muscle is left undisturbed, these bridges will remain attached for long periods. Their presence is indicated by an initial stiffness at the onset of a stretch of the passive muscle (Hill, 1968). The stretch detaches the bridges, which promptly re-form at the longer length. If the muscle is shortened, the presence of stable cross-bridges acts like a splint; the compressive forces acting on the shortening muscle are typically insufficient for the bridges to detach and, stiffened by their presence, the fibres fall slack; they may even kink. Indeed, such kinking in intrafusal fibres has been observed (Gladden, 1976). All of this means that the passive mechanical properties of muscle are dependent on the previous history of contraction and length changes. The associated passive forces are typically small. However, given that the intrafusal fibres of muscle spindles exhibit thixotropic behaviour, these forces are sufficient to produce significant modulation of spindle discharge rates. Thixotropy-dependent changes in discharges of muscle spindles have been shown to be correlated with errors in human limb position sense (Gregory et al., 1988).

All primary endings, but not all secondary endings of muscle spindles exhibit thixotropic behaviour (Edin & Vallbo, 1988; Proske et al., 1992). In the study by Proske et al. (1992), 11 of 35 secondary endings did not show muscle history effects. Secondary endings supplied by larger afferent axons (conduction velocity 50–70 m/s) tended to supply bag$_2$ intrafusal fibres, chain fibres, or both (Taylor et al., 1994). Typically, such endings lie in the juxta-equatorial region of the intrafusal fibres, adjacent to the terminals of primary endings at the fibre equator. These endings exhibit thixotropy; a subset of secondary endings, supplied by smaller axons (conduction velocity 30–50 m/s), do not (Figure 11).

This second group was argued to innervate chain fibres only, and the receptor terminals lie further out from the equator, in the region of the capsular sleeve. If passive spindles are shortened, they fall slack, and some chain fibres have been observed to kink (Gladden, 1976). Descriptions of kinking have shown that this occurs toward the capsular sleeve. It has led to the proposal (Proske et al., 1992) that endings that do not show thixotropic behaviour lie directly over a region of kinking and, indeed, the nerve ending itself might become kinked. These endings are stimulated both during the uptake of slack, when the intrafusal fibres straighten out, and during stretch of the intrafusal fibres. Endings showing thixotropic behaviour typically remain silent during the uptake of slack. The data suggest that up to about one-half of secondary endings are thixotropy insensitive.

What is the relevance for position sense of the presence of some spindle endings that do not show thixotropic behaviour? The obvious answer is that they will respond more predictably to changes in muscle length, which could be considered a factor that impacts their suitability as position sensors; they will respond more reliably and predictably to changes in muscle length. Other factors are the lower discharge variability in these endings and the fact that, overall, there are more secondary endings than primary endings in most muscles. All of this argues for the generation of prompt and predictable position signals, something the primary endings are less able to do.

17 | MEASURING POSITION SENSE

Surprisingly, both the term proprioception and the method of its measurement are subject to widely discrepant interpretations (Han et al., 2016; Proske & Gandevia, 2012). In the present account, the view has been taken that use of the term should be based on the method first used to establish muscle spindles as proprioceptors (Goodwin et al., 1972). It is well and good to interpret the term proprioception in a variety of ways, but its study should always be guided by the experimental evidence. Goodwin et al. used a two-arm matching task in the vertical plane, where one arm was placed at a given angle, and the blindfolded subject had to match its position with their other arm. The evidence, based on vibration responses, is that muscle spindles are directly responsible for this sense. Additional supporting evidence

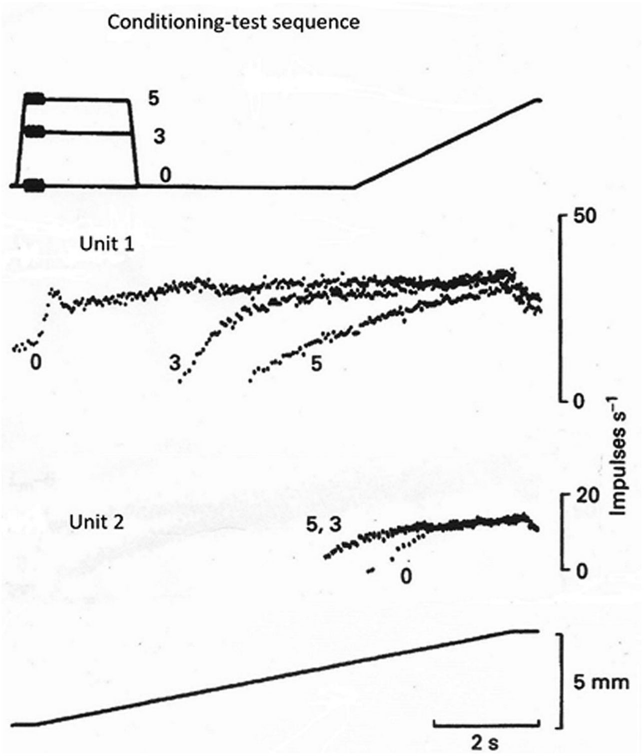


FIGURE 11 Discharges of two secondary endings of the soleus muscle of the anaesthetized cat recorded at maximal muscle length minus 14 mm (L_m − 14). Discharges have been displayed as instantaneous frequency (in impulses per second). At the top of the figure is shown, diagrammatically, the conditioning and test sequence applied to each ending. The endings were subjected to a slow stretch after they had been conditioned by three different conditioning step sizes. Conditioning consisted of a fusimotor-strength contraction of the muscle only (stimulated at 100 pulses/s; 0), a contraction after the muscle had been stretched by 3 mm; 3) and after it had been stretched by 5 mm (5). At the bottom of the figure is shown, on an expanded time scale, the change in length of the muscle during the test stretch and the afferent responses of the two secondary endings to the stretch. The ending in the upper frequency trace (Unit 1), with an afferent conduction velocity of 58 m/s, showed thixotropic behaviour, responding immediately at stretch onset when there was no conditioning length step (0, no slack) and delaying its response in proportion to the size of the conditioning length step (3 and 5 mm), which will determine the amount of slack introduced in the spindle. The ending illustrated in the lower frequency trace (Unit 2), which had an afferent conduction velocity of 46 m/s, appeared to be thixotropy insensitive. With no conditioning length step (0; i.e., without introducing any slack), there was an initial low spluttering discharge, with a more sustained response at longer lengths. When 3 or 5 mm length steps were inserted before the test stretch, the two discharge traces overlapped closely, demonstrating an insensitivity to the amount of slack introduced in the spindle before the test stretch. In fact, the discharge in the absence of slack started later than in the presence of slack, the opposite result to that predicted by the slack hypothesis. Redrawn from Proske et al. (1992), copyright 1992 the Physiological Society

comes from spindle thixotropy used as a tool for the study of position sense in a two-arm matching task. Muscle spindles are the only known mechanoreceptors that exhibit thixotropy. The reason is, of course, that spindle sensory endings lie on striated muscle, the intrafusal fibres. A feature of position sense measured in a two-arm matching task is that subjects are reasonably accurate in their matches, provided the muscle is appropriately conditioned beforehand. Errors of ±2° can be achieved (Allen et al., 2007).

In more recent times, not everyone has favoured this method of measurement because, it is claimed, in the brain the inter-hemispheric transfer of information from one arm to the other introduces errors (Goble, 2010). Therefore, a one-arm joint position reproduction task has been preferred. The disadvantage of this method is that it is based on memory. The subject is told to remember a particular limb position during a learning trial, and in the next trial they are asked to reproduce it from memory. Inevitably, at least part of the outcome using this method is dependent on the ability of the subject to remember, rather than from any changes in proprioceptive afferent input. We have preferred the two-arm test because it is simple, and there is evidence for a direct influence from muscle spindles on the measured outcome.

However, in everyday life one does not go around determining the position of an arm by aligning it with the other. Rather, if asked, 'Where is my arm, if I cannot see it?', we point to it. In fact, a similar experimental set-up to the one used with matching can be arranged for pointing tasks. One arm is hidden from view, and the other rotates a paddle that acts as a pointer. The subject is asked to move the pointer paddle into alignment with the perceived position of the hidden reference arm (figure 1 in Tsay et al., 2016b). A comparison of position errors between matching and pointing tasks reveals unexpected differences.

Firstly, as already mentioned, matching performance can be reasonably accurate. In pointing, on the other hand, for position-sense measurements at the forearm, systematic errors of ~10° are made in the direction of forearm extension (Chen et al., 2021). Secondly, matching errors are subject to the influences of thixotropic conditioning of arm muscles, whereas pointing errors remain unaffected. Thirdly, Velay et al. (1989), in making a similar comparison between matching and pointing tasks, showed that for blindfolded subjects the errors in pointing to an arm were subject to visual impressions of the spatial position of the arm acquired immediately before the test. For two-arm matching, in contrast, vision did not appear to play a role (Velay et al., 1989). In addition, for two-arm matching the outcome is similar whether the subject is fully blindfolded or if they are able to see their pointing arm (Tsay et al., 2016a). Hence, position sense measured in pointing and matching tasks shows a number of important differences, and our current view is that the neural pathways underlying the two methods are not the same. The distribution of errors in pointing suggests that here the position signal has been processed centrally, to become susceptible to visual inputs, whereas for matching the evidence suggests a direct conversion of muscle spindle discharges into a position signal.

More recently, Chen et al. (2021) have done the pointing task in a rather different way. Drawn on a screen, which blocked the view of the reference arm, was a series of trajectory lines indicating a range of possible positions of the arm (figure 1 in Chen et al., 2021). Each line was labelled, and the subject was asked to indicate verbally, for different arm positions, which line corresponded most closely to the perceived position of the hidden arm. During this task, subjects were asked to keep their other arm, unmoving, at their side. It turned out that subjects were as accurate in indicating the position of the hidden arm in the verbal task as in the pointing task. The implication of this result is that in a pointing task, motor activity accompanying movement of the pointer with the other arm does not play a role in the outcome.

However, there are broader implications of this result. Firstly, it is possible to generate a consciously perceived position signal based purely on proprioceptive afferent input, without involving the motor system, other than making a verbal report. Secondly, the result suggests that subjects are continuously aware of the positions of their body and its limbs, without looking at them. One only has to think about where one's arms are and be able to indicate their position with reasonable accuracy. This could be the basis for our self-awareness. However, if we find ourselves in a visually distorted environment, this is likely to interfere with our ability to localize body parts accurately.

As has been argued, the dominant signal coming from muscle spindles is a position signal, and this is largely coming from secondary endings. It has been estimated that secondary endings have 1.5 times the position sensitivity of primary endings (Hulliger, 1984), and there are ~1.5 times as many secondary endings in spindles (Banks et al., 2009; see Figure 1). Putting those figures together, the position signal coming from secondary endings will be more than twice that of primary endings, in both size and fidelity. Such considerations highlight the importance of the contribution from spindle secondary endings to proprioception.

The idea that one has a constant awareness of the body and its parts also has implications for the outcome of measurements of position sense. When a two-arm matching task is used, to what extent are the positions of the reference and indicator arms determined directly by a spindle signal or, alternatively, by the more processed signal observed in pointing tasks? The conclusion must be that, without being aware of it, subjects are probably accessing more than one source of position information, selecting the more appropriate one depending on the demands of the task.

18 | TWO SENSES OF LIMB POSITION?

In a two-arm matching task, with chosen forms of conditioning of arm muscles, it is possible to maximize spindle discharge levels in elbow flexors of one arm and in elbow extensors of the other. In trying to achieve a satisfactory match after such conditioning, the subject makes large errors (±10°; Allen et al., 2007). Conditioning of the reference arm leaves its flexor spindles sensitized and maintaining high levels of resting activity. The indicator arm, on the contrary, has its extensors sensitized, with flexor spindles discharging at low levels. In making the match, the subject appears to ignore the larger indicator extensor signal and chooses to place their indicator in a position where its flexor activity matches that of the reference flexors. That position is too extended by 10° for an accurate match of arm positions.

The direction of the errors can be reversed by raising extensor spindle activity in the reference arm and flexor activity in the indicator. Importantly, subjects remain unaware of the discrepancy in their arm positions in making such matches (Allen et al., 2007). This is the case despite subjects being able to achieve accurate matches when muscles of both arms are conditioned identically. It leads to the conclusion that in two-arm matching the brain considers the arms aligned when arm positions have been adopted where the spindle discharges from the two arms are matched, and not when identical joint angles have been achieved. And the subject remains unaware of this. In making a match, what the subject interprets as a position signal is a spindle signal, not a joint-angle signal.

In a pointing task, the situation is different. Here, position sense involves only one arm at a time; vision plays a role but thixotropy does not, and subjects are constantly aware of this sense, which relates to the position of the arm, not the matching of proprioceptive signals. It has been speculated that in two-arm matching the goal is to bring the two hands together accurately, for the manipulation of objects and tools. The sense accessed in a pointing task has a more global function. Velay et al. (1989) postulated that two-arm matching provided information about the body in postural space, whereas one-arm pointing was concerned with the disposition of the body in extrapersonal space. It could be argued that for a role in postural space, precision of the proprioceptive signal is paramount. If so, then to have a contribution from spindle secondary endings that lack a thixotropic sensitivity would be an advantage, giving the system a degree of reproducibility, which it would otherwise not have.

More broadly, muscle spindles represent two sensory systems in one; the primary ending, which is dynamically sensitive, able to signal both movement and position, and the secondary ending, which signals position predominantly. The large volume of position-related information coming from spindles allows for the prompt and precise calibration of limb position. Unexpectedly, this is achieved in two different ways, probably involving distinct afferent projection pathways (Chen et al., 2021). It poses the question, why should such different mechanisms have evolved? Is it simply a matter of functional roles, internal postural signalling versus extrapersonal space perception? What all of this points out is that our understanding of proprioception and its central processing remain relatively primitive.

19 | CONCLUDING COMMENTS

When the topic of the role of secondary endings in kinaesthesia was chosen, it was not realized that there existed little supporting evidence for such a role. In fact, it was largely the experiments of McCloskey (1973) on vibration that provided the basis for claims that secondary endings contributed principally to limb position sense. It has been mentioned that there are reasons to believe that position sense is the most important of the proprioceptive senses, given its role in self-awareness (J. Cole, 1995). The problem with studying the role of secondary endings in position sense is that there is no identifiable sensation associated with a change in position sense. It is the sense without a sensation! In the experiments reported by Goodwin et al. (1972), the vibration-evoked activity in spindle primary endings could be associated with a clearly defined sensation, that of movement. The same was not true for the sense of position. Goodwin et al. stated, 'if at any point during the movement (generated by vibration), the blindfold was removed, the subject would invariably express surprise at the position in which he had put himself'. A new tool that has become available for the study of position sense is that of thixotropic conditioning. By altering the passive properties of intrafusal fibres, it has been possible to raise or lower spindle discharge rates and so manipulate position sense. The thixotropy tool has revealed, unexpectedly, that there is not only one position sense, but several, probably with different underlying mechanisms (Chen et al., 2021). If, in the future, a better understanding of the role of secondary endings in position sense is to be achieved, it will be necessary to incorporate the concept of more than one sense.

COMPETING INTERESTS

None declared.

AUTHOR CONTRIBUTIONS

All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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APPENDIX:

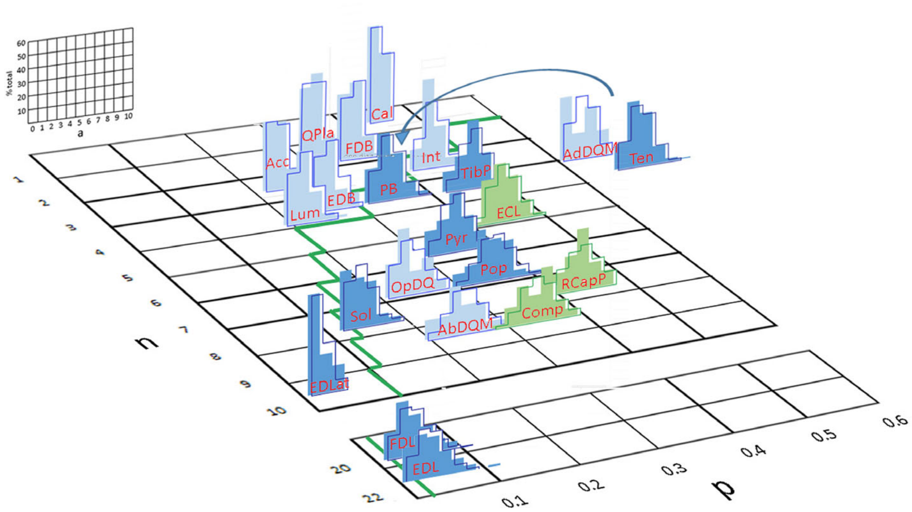

FIGURE A1 Four-dimensional plot of the frequency distributions of the sensory complements of muscle spindles from hindfoot (light blue), limb (dark blue) and axial (green) muscles of the cat. Only the spindle units (or capsules) with a full complement of intrafusal fibres (b_1b_2c units) are included. The observed (filled histograms) and best-fitting binomial distributions (outline histograms) are shown for each muscle, with values to be read from the small vertical calibration grid (percentage of total vs. a, where a = the numbers of sensory endings additional to a single primary ending). When a = 0, the unit has a primary only, and in almost all cases a = the number of secondary endings. Pairs of observed and theoretical histograms are positioned on the two-dimensional main grid according to their best-fitting binomial parameters, n and p, where mean(a) = np. The green line divides the grid into upper left, where mean(a) < 1 (on average, spindle units have fewer secondary than primary endings), and lower right, where mean(a) > 1 (on average, spindle units have more secondary than primary endings). Note that all the intrinsic muscles of the foot have b_1b_2c capsules with more primaries than secondaries, with the notable exception of the three muscles that control mediolateral positioning of the fifth digit. Apart from the forelimb extensor digitorum lateralis, all other muscles in the sample have b_1b_2c capsules with more secondaries than primaries; the three axial muscles, two of which are concerned with head positioning (rectus capitis posterior and complexus), all have particularly large proportions of secondaries (69–79% of all b_1b_2c afferents). Abbreviations: AbDQM, abductor digiti quinti medius; AdDQM, adductor digiti quinti medius; Acc, accessories (superficial lumbrical); Cal, calcaneometatarsalis; Comp, complexus; ECL, extensor caudae lateralis; EDB, extensor digitorum brevis; EDLat, extensor digitorum lateralis; EDL, extensor digitorum longus; FDB, flexor digitorum brevis; FDL, flexor digitorum longus; Int, interosseus; Lum, lumbricales (deep lumbricals); OpDQ, opponens digiti quinti; PB, peroneus brevis; Pop, popliteus; Pyr, pyriformis; QPla, quadratus plantae; RCapP, rectus capitis posterior; Sol, soleus; Ten, tenuissimus. To avoid overlaps, AdDQM and Ten are shown displaced from their grid location at n = 4, 0.3 < p < 0.4 (shared with PB). Based on Banks & Stacey (1988); with data from Banks, Hulliger, Saed & Stacey (2009)