REVIEW | *50 Years of Microneurography: Insights into Neural Mechanisms in Humans*

Functional properties of human muscle spindles

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Macefield VG, Knellwolf TP. Functional properties of human muscle spindles. *J Neurophysiol* 120: 452–467, 2018. First published April 18, 2018; doi:10.1152/jn.00071.2018.—Muscle spindles are ubiquitous encapsulated mechanoreceptors found in most mammalian muscles. There are two types of endings, primary and secondary, and both are sensitive to changes in muscle length and velocity, with the primary endings having a greater dynamic sensitivity. Unlike other mechanoreceptors in the somatosensory system, muscle spindles are unique in possessing motor innervation, via γ-motoneurons (fusimotor neurons), that control their sensitivity to stretch. Much of what we know about human muscles spindles comes from studying the behavior of their afferents via intraneural microelectrodes (microneurography) inserted into accessible peripheral nerves. We review the functional properties of human muscle spindles, comparing and contrasting with what we know about the functions of muscle spindles studied in experimental animals. As in the cat, many human muscle spindles possess a background discharge that is related to the degree of muscle stretch, but mean firing rates are much lower (~10 Hz). They can faithfully encode changes in muscle fascicle length in passive conditions, but higher level extraction of information is required by the central nervous system to measure changes in muscle length during muscle contraction. Moreover, although there is some evidence supporting independent control of human muscle spindles via fusimotor neurons, any effects are modest compared with the clearly independent control of fusimotor neurons observed in the cat.

α-γ coactivation; fusimotor neurons; γ-motoneurons; stretch reflexes

INTRODUCTION

Proprioception ("proprio" = self) is the sense of position and movement of parts of the body relative to one another, and the sense of force and effort associated with muscle contraction; kinesthesia is also used to describe this, but strictly speaking it only refers to the sense of movement. It is also clear that the sense of balance, although primarily subserved by the vestibular apparatus, requires input from the somatosensory system to allow head position relative to the body to be determined (Lackner and DiZio 2005). Proprioception is achieved through a summation of peripheral sensory input describing the degree of, and changes in, muscle length and tension, joint angle, and stretch of skin (Proske and Gandevia 2009, 2012). This sensory input originates from a number of sources. It is known that low-threshold mechanoreceptive units in the glabrous skin of the hand respond to isotonic movements without incidental excitation via direct touch (Hulliger et al.

1979). The sense of muscle tension has been largely attributed to Golgi tendon organs, responding to force generated by the muscle (Houk and Henneman 1967). Although joint receptors were initially viewed as important contributors to joint position sense at all angles (Mountcastle and Powell 1959), it has since been shown that their contribution to kinesthesia only extends to that of being limit detectors, detecting only extreme positions within the normal range in both the cat (Burgess and Clark 1969; Clark and Burgess 1975) and humans (Burke et al. 1988; Macefield et al. 1990). The most important contribution to proprioception is made by muscle spindles, stretch-sensitive mechanoreceptors found in virtually all skeletal muscles. Interestingly, they are particularly dense in muscles where accurate proprioception is important. For instance, in the intrinsic muscles of hands of the bonnet monkey, which are responsible for fine manipulative tasks, up to 42.3 spindles per gram (wet weight) were identified (Devanandan et al. 1983). They are also abundant in the neck of the cat (Richmond and Abrahams 1975) and human (Cooper and Daniel 1963), where they play important roles in integrating information on the position of the

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head with respect to the body. It is beyond the scope of the present review to deal with the many psychophysical studies on human proprioception and the relative roles of muscle spindles and cutaneous afferents in proprioception, and the reader is directed to two excellent reviews on proprioception, referred to above (Proske and Gandevia 2009, 2012). Although the aim is to provide the reader with an up-to-date appraisal of how human muscle spindles operate, where necessary we refer to data obtained in experimental animals. Accordingly, to set the stage, we shall commence with a brief review of the structural and functional properties of the mammalian muscle spindle, as studied primarily in the cat.

STRUCTURE OF THE MAMMALIAN MUSCLE SPINDLE

Much of what we have learnt about the structure of the mammalian muscle spindle comes from detailed observations made in the cat (Barker 1948; Boyd 1962; Hulliger 1984). The spindle's function as a length sensor arises essentially from its anatomical relationship with its parent muscle. It consists of a bundle of specialized, striated, intrafusal ("fusiform" = spindle shaped) muscle fibers lying in parallel with the fascicles of the regular, force-producing, extrafusal (skeletomotor) muscle fibers. Any length changes in the muscle therefore result in stretch of intrafusal fibers that is then detected by sensory receptors located on the equatorial and polar regions of the muscle spindle. For a detailed treatise on how muscle spindles transduce stretch into action potentials, the reader is referred to a recent review by Bewick and Banks (2015). Whereas the majority of each intrafusal fiber is contractile, the equatorial regions are less so. This divides the spindles into two, independently acting, polar regions. The small cross-sectional area of the intrafusal fibers in the adult means that their contraction makes an insignificant contribution to the total external force of the muscle while being sufficient to deform the sensory terminals (Kuffler et al. 1951). It is by this means that, through the motor innervation normally supplied to both polar regions of the spindle, via γ-motoneurons (fusimotor neurons), the central nervous system is able to actively modulate the muscle spindle's stretch sensitivity. Figure 1 shows a transverse section of a cat muscle spindle, illustrating the relationships between the primary afferent, the intrafusal muscle fibers, and capsular elements.

Detailed anatomical studies of human muscle spindles were first performed on excised human intercostal muscles, largely corroborating what has been documented in the cat (Kennedy 1970). However, human primary endings appear not to possess an annulospiral structure, and the secondary ending innervates nuclear bag as well as nuclear chain muscle fibers. An example is shown in Fig. 2. Detailed investigations of spindle structure also have been made from intrinsic and extrinsic finger muscles (Sahinen and Kennedy 1972; Van Gorp and Kennedy 1974).

Subdivision of intrafusal muscle fibers. The muscle fibers of the spindle are subdivided both structurally and functionally. The fibers were first distinguished histologically in the cat, into nuclear bag fibers and nuclear chain fibers, by the arrangement of nuclei in the equatorial cross section: bag fibers reveal multiple visible nuclei, whereas chain fibers would consistently have only one, due to the fact that chain fiber nuclei would be arranged in a single-file "chain" (Barker 1948). Bag fibers are of appreciably greater diameter and length than chain fibers, often extending beyond the spindle capsule (Boyd 1962; Cooper and Daniel 1963). Additionally, the fibers have been distinguished by the band structure of their myofilaments (Adal 1969; Corvaja et al. 1969) and through histochemical testing (James 1968; Spiro and Beilin 1969). Later studies further subdivided bag fibers into bag_1 and bag_2 types, based on variations in their ultrastructure and histochemical response profile (Banks et al. 1977; Ovalle and Smith 1972). An important observation was the variability between all three fibers in their reaction to staining for myofibrillar ATPase. Indeed, the structural differences between the fibers are enough to suggest some functional differences. Typically, bag_1 fibers have the slowest contraction rates, followed by bag_2 and, finally, chain fibers. These differences in response at different frequencies were explored in depth by Boyd (1976). Human muscle spindle fibers were later histochemically distinguished by the presence of variants of myosin heavy chains and M-band proteins (Eriksson et al. 1988). For more detail on the specific delineations and techniques used, the recent review by Thornell et al. (2015) should be observed.

The suggestion of functional duality is supported by the variations in afferent and efferent innervation, the properties of which will be discussed below. In terms of afferent innervation, primary afferents fibers innervate all three fiber types, whereas secondary fibers supply only bag_2 and chain fibers. Static fusimotor fibers also only supply bag_2 and chain fibers, whereas dynamic fusimotor axons innervate bag_1 fibers exclusively (Boyd et al. 1977; Proske 1997). When the significant
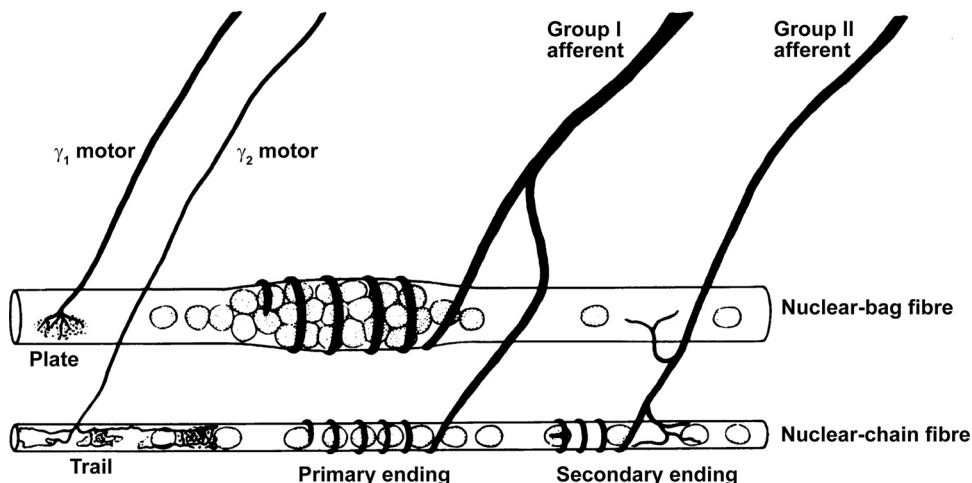
Fig. 1. Simplified diagram of the central region of a muscle spindle in the cat, showing a single "bag" intrafusal muscle fiber and a single "chain" intrafusal muscle fiber. Typically, muscle spindles in the cat contain 2 or 3 bag fibers, 4–6 chain fibers, and a complex motor innervation. Reproduced with permission from Matthews (1964).

Fig. 2. Drawing from a histological specimen of a human muscle spindle, sampled from an intercostal muscle. Only 2 bag and 2 chain intrafusal muscle fibers are represented. The number of entering nerves, particularly the degree of branching and number of endings, has been limited to a few of each type for clarity. Reproduced with permission from Kennedy (1970).
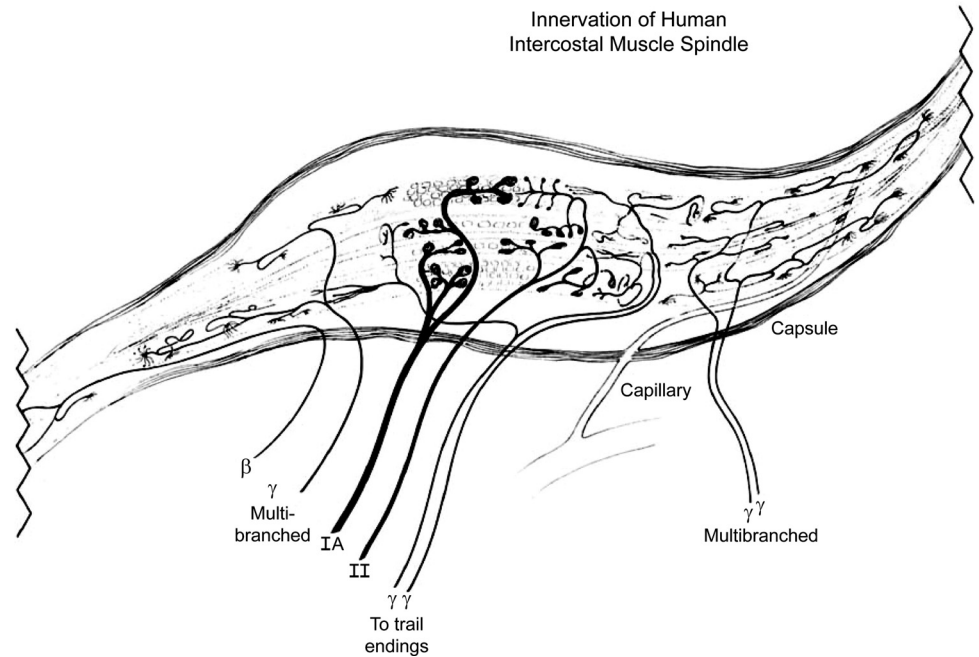
functional differences between these γ-motoneurons are considered (see below), it can be appreciated that the subdivisions of intrafusal fiber types work largely independently of one another.

Sensory innervation of the muscle spindle. There are two types of afferents that innervate muscle spindles. They are, like intrafusal fiber types, distinguished by structure and function into primary (type Ia) and secondary (type II) endings. As documented in the cat, primary endings have a larger diameter than secondary fibers (12–20 and 4–12 μm, respectively; Eccles and Sherrington 1930) as well as a faster conduction velocity (Hunt 1954). Our understanding of the anatomical differences comes largely from the work of Boyd (1962). Each spindle has only one primary sensory nerve ending (group Ia afferent). The ending consists of number of spirals, supplying all of the intrafusal fibers in the spindle at the equatorial region, with one spiral per fiber. It is deformations of this ending that allow the detection of changes in length of the parent muscle. The number of secondary (group II) afferent endings in a spindle varies from zero to five, and they often supply one fiber each. They predominately terminate on nuclear chain intrafusal fibers. The endings consist of smaller spirals than primary endings that terminate on the polar ends of the spindle.

Muscle spindle afferents have been contrasted functionally by examining the response of mean firing rate to various changes in muscle length, commonly involving ramp-and-hold tests. This involves a muscle being held at a constant length (static component) before being stretched at a constant velocity (dynamic component) to a new length, at which it is again held constant. Primary afferents are sensitive to dynamic stretch, demonstrate an irregular spontaneous or volitionally maintained discharge, and exhibit an off-response at the point of relaxation (i.e., muscle stretch) following a slow ramping isometric contraction. They are silenced during rapid voluntary contraction when the fusimotor drive (discussed below) is insufficient to overcome the unloading effects of the extrafusal contractions. Secondary afferents generally exhibit a regular tonic discharge tonic discharge, decelerate during an unloading contraction, and do not exhibit an off-response at the termination of a voluntary ramp-and-hold contraction (Edin and Vallbo 1990a).

Motor innervation of the muscle spindle. Muscle spindles are unique among proprioceptors for possessing their own motor supply in addition to afferent innervation. This motor innervation may originate from small-diameter (4–8 μm), myelinated γ-motoneurons, also referred to as fusimotor fibers, or from axons branching from larger fibers that also supply extrafusal muscle, known as β- or skeletofusimotor fibers. These fibers supply both intrafusal fibers via trail endings at the polar ends. Similarly, in humans, extensively branched small-diameter axons were found to innervate the intrafusal fibers at the poles of the muscle spindle (Kennedy 1970). Stimulation of γ-motoneurons produces no overt tension in the muscle but does result in considerable excitation of both primary and secondary spindle afferents. It is known from the cat that stimulation of motoneurons supplying regular, extrafusal fiber, known as α-motoneurons, results in coactivation of γ-motoneurons (Severin et al. 1967). Hunt and Kuffler (1951) outlined the role of fusimotor drive for spindle function. During extrafusal muscle contraction the muscle shortens, leading to an unloading of the spindles, which reduces their spontaneous discharge. As stated above, γ-motoneuron activity is coactivated. This results in contraction of the polar ends of the intrafusal fibers, restoring tension and therefore sensitivity of the spindle to stretch. Thus it can be said that γ-motoneuron function is essential for controlling the sensitivity of muscle spindle afferents as length detectors.

Fusimotor motoneurons have been differentiated into static and dynamic fusimotor axons from ramp-and-hold experiments performed by Matthews (1962). Dynamic axons have a weak effect on primary afferent firing in muscles held at a constant length but are markedly sensitized to dynamic stretch, resulting in bursts at the beginning and end of the dynamic phase. Conversely, static axons are largely ineffective during the

dynamic phase but create a powerful excitatory action while the muscle is at constant length, increasing the overall response to a change in length. Static axons have a great influence on both primary and secondary fibers, whereas dynamic axons show little to no effect on secondary endings, even if a primary ending of the same fiber is stimulated (Appelberg et al. 1966). In the decerebrate cat there is significant resting fusimotor outflow, primarily in static γ-motoneurons (Matthews and Stein 1969a).

FUNCTIONAL PROPERTIES OF HUMAN MUSCLE SPINDLES

The first neurophysiological recordings from human muscle spindle afferents were made in vitro, again from excised intercostal muscles, and appeared in a brief report (Davis 1973); more detailed investigations of excised human spindles were undertaken by Kennedy and colleagues (Kennedy et al. 1974; Poppele and Kennedy 1974). As expected, human spindle afferents responded to direct passive stretch of the organ with a velocity-dependent increase in firing rate, their behavior largely paralleling that observed in the anaesthetized cat. However, it was not until the development of microneurography, by Karl-Erik Hagbarth and Åke Vallbo at the Academic Hospital in Uppsala, Sweden, in the mid-1960s, that it became possible to study the functional properties of human muscle spindles in vivo, and during active contractions as well as passive conditions. Indeed, the primary motivation of Hagbarth and Vallbo to use metal microelectrodes to record from peripheral nerves in awake human subjects was to study muscle spindles during voluntary contractions, to examine their potential role in the servo-loop model of motor control, postulated by Merton (1953).

Microneurography allows one to record from single myelinated axons, both afferent and efferent, applying reductionist principles (single-unit analyses of type-identified neurons) in a holistic fashion (intact nervous system, no anesthesia); one can also record from single unmyelinated sensory and motor (sympathetic) axons, both afferent and efferent. However, it is worth pointing out that microneurography is limited to peripheral nerves that are accessible via insertion through the skin and are not too deep, such as the median and ulnar nerves at the wrist or upper arm, the radial nerve in the upper arm, and the tibial and common peroneal nerves in the lower limb. In the context of the present review, this also limits the muscles that can be accessed; whereas distal muscles in the forearm and hand, and the lower leg and foot, can be examined, proximal and axial muscles are out of reach. Moreover, the types of active movements that can be studied are also limited, because of the risk of losing the recording site during brisk and/or forceful movements, a criticism that has been raised when data from conscious cats and conscious humans are compared (e.g., Prochazka 1989). The microneurographic approach is shown in Fig. 3. Myelinated axons generate positive-going spikes when the tip of the microelectrode is located close to (or embedded within) the myelin sheath of an axon, whereas those of C-fibers are negative-going because the action potentials are recorded from the exposed axolemma. Accordingly, one would think it would be possible to record directly from fusimotor neurons in humans, given that they have a larger diameter than C-fibers. Indeed, γ-motoneurons are myelinated, so they should, like other myelinated axons, generate positive-going spikes. How-

ever, surprisingly little is known about them in humans, and only one study claims to have recorded from γ-motoneurons directly, identifying them as "motor" because they did not respond to vibration and their activity could be modified according to criteria established in experimental animals (Ribot et al. 1986). Nevertheless, changes in fusimotor drive can be reliably inferred from changes in the firing of muscle spindle afferents, from which single-unit recordings can readily be obtained in awake humans. This will be considered further below.

Identification of muscle spindles. Muscle spindle afferents are found in muscle fascicles of peripheral nerves and supply a specific muscle. Identification is based on behavioral properties, similar to those used in studies in experimental animals. Many are spontaneously active at rest, with the mean frequency of the tonic discharge increasing during stretch of the receptor-bearing muscle and decreasing during passive shortening (unloading) of the parent muscle. These spontaneously active spindles are further subdivided into presumed primary or secondary endings: primary endings show a characteristic silent period following release of the stretch (passive shortening) and have a high dynamic sensitivity to passive stretch. Conversely, secondary endings typically decelerate, without ceasing completely, when the stretched muscle is returned to its resting length. In addition, Ia afferents typically show an increase in firing (off-discharge) during the relaxation phase of a volitionally generated ramping contraction and brisk relaxation; this off-discharge is absent for II afferents (Edin and Vallbo 1990a, 1990c). For example, for recordings from the common peroneal nerve, silent spindle endings are discovered by passively stretching the receptor-bearing muscle by plantarflexion of the ankle (for muscle spindles in tibialis anterior) or toes (extensor hallucis longus or extensor digitorum longus) or by inversion of the foot (for spindles in the peronei muscles). Subjects are asked to intermittently dorsiflex the foot or toes during the search procedure to facilitate the isolation of fusimotor-driven spindle afferents.

Initially, human muscle spindles were only classified as such if they were silenced during an electrically evoked brief contraction (twitch) of the parent muscle (in which the intrafusal muscle fibers are unloaded) and increased their background discharge (or were recruited) during the subsequent relaxation phase of the twitch. Although the "twitch-test" is considered the gold standard for identification of human muscle spindles, it is now not used routinely. It does require an amplifier that allows intraneural stimulation to be delivered without interrupting the recording (Burke 1997), although transcutaneous electrical stimulation over the muscle is also effective at inducing muscle twitches without disturbing the spindle afferent recording (Edin and Vallbo 1987). However, although muscle spindles respond during the relaxation (stretch) phase of the twitch, and Golgi tendon organ (Ib) afferents respond during the contraction phase, some muscle spindles do behave in an in-series fashion (i.e., like Golgi tendon organs) during a twitch contraction (Burke et al. 1987), and some α motoneurons may be reflexly recruited during the twitch (Inglis et al. 1995). As will be discussed below, many spindles are active during a voluntary contraction, which also recruits Golgi tendon organ afferents and, of course, motor axons. Spike-triggered averaging of surface electromyography (EMG) has been used to differentiate between Ib sensory and α-motor axons

**microneurographic recording from
muscle spindle afferents and
muscle sympathetic postganglionic
axons in awake human subjects**

via tungsten microelectrodes inserted
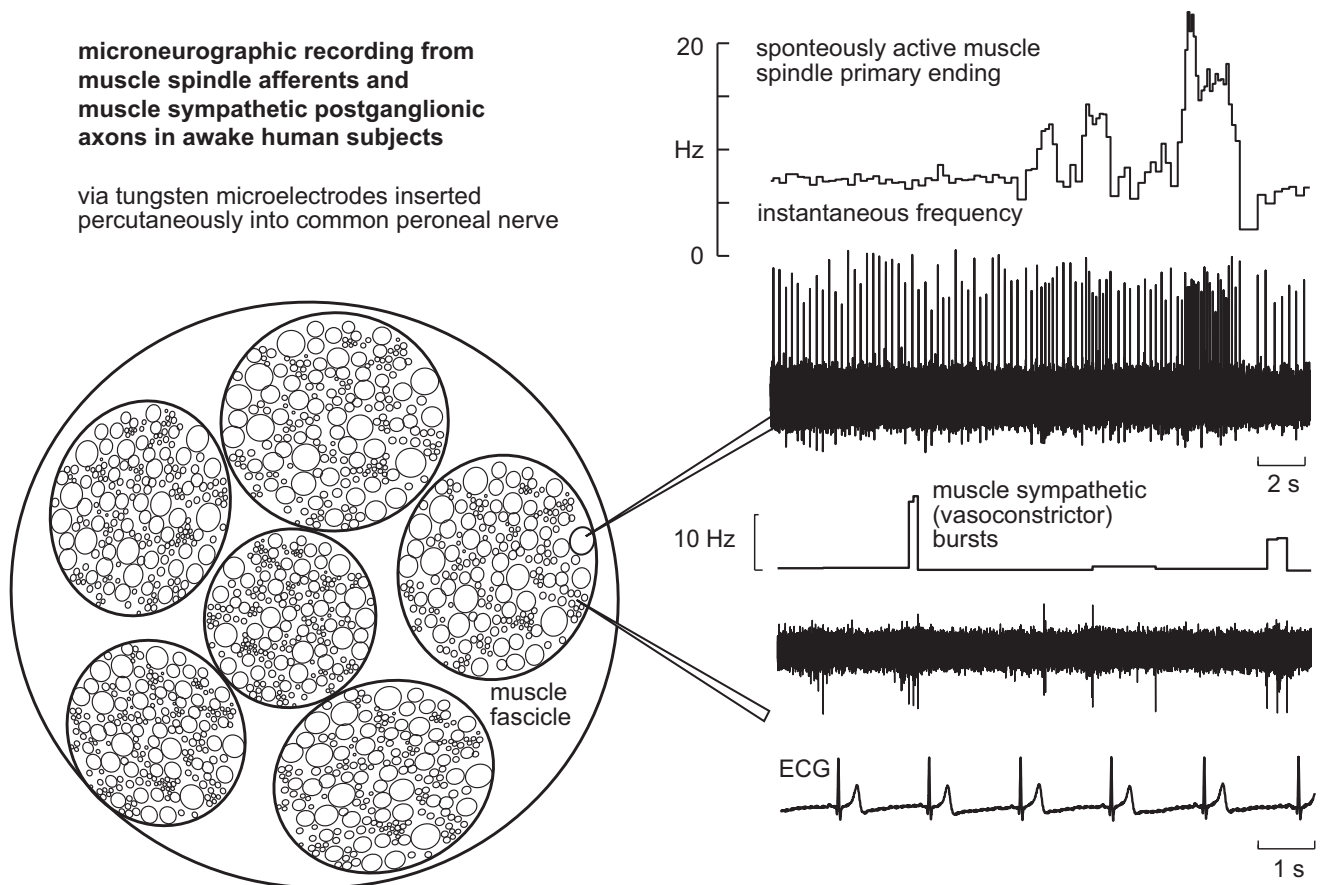percutaneously into common peroneal nerve

Fig. 3. Schematic representation of a cross section of a human peripheral nerve. The nerve is composed of distinct bundles of nerve fibers, some innervating muscle (motor fascicles) and others supplying skin (cutaneous fascicles). Within each fascicle are large- and small-diameter sensory fibers (afferents) and small-diameter (unmyelinated) postganglionic sympathetic fibers. Motor fascicles also contain large-diameter (α) motor axons supplying muscle fibers and smaller diameter (γ) fibers to the muscle spindles. At *top right* is an example of a recording from a spontaneously active muscle spindle afferent located in extensor digitorum longus responding to passive plantarflexion of the toes. At *bottom right* is a unitary recording from a postganglionic muscle sympathetic axon and concurrently recorded electrocardiographic activity (ECG). Reproduced with permission from Macefield (2005).

during active contractions, with motor axons being defined as such if the spike-triggered average EMG shows a clear time-locked response that follows the spike; conversely, Ib afferents either exhibit no time-locked EMG response or the EMG response precedes the spike (Fallon and Macefield 2007).

Sensitivity of muscle spindles to stretch. Spindle primary endings in the cat are exquisitely sensitive to small changes in length of their parent muscle (Brown et al. 1967); some endings can be driven up to 500 Hz with vibrations as small as 5 μm in peak-to-peak amplitude. Given their high dynamic sensitivity, Ia afferents in the cat respond ~90° in advance of the peak of the vibration cycle, which fits with their role as velocity receptors (Matthews and Stein 1969b); the same has been shown for human primary afferents (Kakuda 2000; Roll and Vedel 1982). Accordingly, many argue that Ia afferents primarily encode changes in relative muscle length, with the II afferents serving as absolute length detectors because of their lower sensitivity to small-amplitude, high-frequency vibration. However, we know that there is considerable overlap between the two types of spindle endings when the muscles are relaxed, and especially when the muscles are contracting (Burke et al. 1976a, 1976b; Fallon and Macefield 2007). Indeed, when muscles are active, the Golgi tendon organs, which are insensitive to length changes in the passive state but respond to the increase in muscle force, now become very sensitive to low-

amplitude vibration (Fallon and Macefield 2007). A recording from a primary afferent located in the extensor hallucis longus (EHL) muscle is shown in Fig. 4. It can be seen that the ending exhibits a high dynamic sensitivity to brisk stretch of the muscle, produced by passive plantarflexion of the big toe at the metatarsophalangeal joint (Fig. 4*A*). Moreover, applying vibration to the toe nail showed that the ending was sensitive to the small-amplitude vibrations transmitted through the tendon to its location within the muscle belly (Fig. 4*C*), although it was only partially entrained to the vibration cycle. Depending on their location in the muscle, spontaneously active muscle spindles, both primaries and secondaries, may exhibit a modulation of their discharge that is related to the pulsation of blood vessels in their immediate vicinity (Birznieks et al. 2012; McKeon and Burke 1981); some primary endings can even be driven or phase-locked to the pulse, generating one or two spikes that are time-locked to the heart beat (Birznieks et al. 2012).

All muscle spindles in humans, regardless of their identity as primary or secondary endings, are dynamically sensitive to imposed stretch of the parent muscle, usually produced by rotation about the joint on which the muscle acts. Muscle spindles faithfully encode joint angle when the muscles are relaxed, there being a linear relationship between joint angle and firing rate (Cordo et al. 2002; Day et al. 2017; Edin and
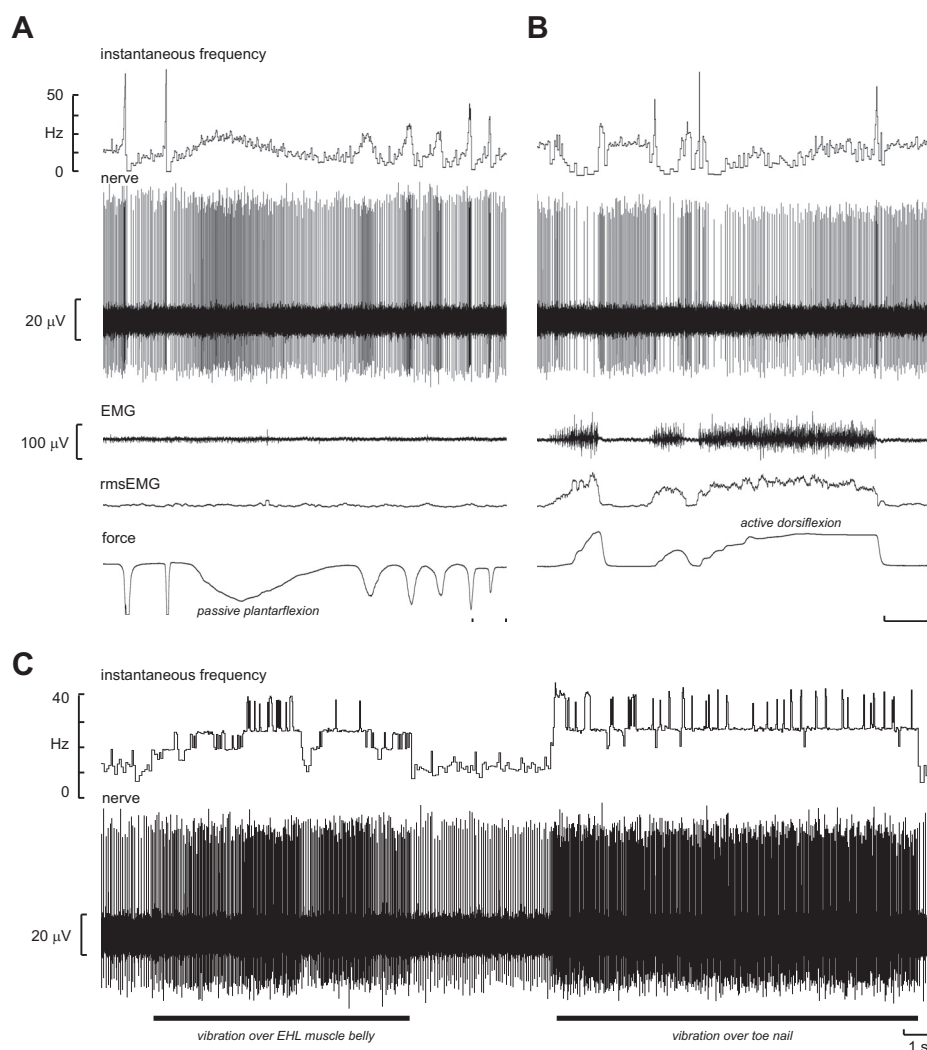
Fig. 4. Microelectrode recording from a spontaneously active muscle spindle primary ending located in the extensor hallucis longus (EHL) muscle. *A*: the afferent increased its firing during stretch of the receptor-bearing muscle induced by passive plantarflexion of the digit at the metatarsophalangeal joint. *B*: during a weak voluntary contraction, the spindle was unloaded during the first 2 contractions but overcame this unloading during the third contraction. *C*: the spindle responded to vibration (~90 Hz) applied via a handheld stimulator over the receptive field within the muscle belly (*left*) as well as over the toe nail (*right*); the latter indicates that the vibratory stimulus was transmitted adequately through the digit and, via the tendon, to the muscle. Reproduced with permission from Macefield (2005). EMG, electromyography; rmsEMG, root-mean-square electromyography.

Vallbo 1990a; Kakuda 2000; Peters et al. 2017), as well as between joint angle velocity and firing rate (Grill and Hallett 1995), but there are no such relationships when the parent muscles are actively holding a joint position (Hulliger et al. 1982, 1985; Vallbo et al. 1981). It was recently argued that muscle spindles also can encode, to a certain extent, force within the muscle. Blum et al. (2017) showed that the initial burst response of muscle spindles in the cat to an imposed passive stretch followed changes in the rate of rise in force (dF/dt) as well as acceleration, although later components correlated better to dF/dt. They conclude that the transient increase in dF/dt at the onset of lengthening reflects an increase in short-range stiffness due to actin-myosin cross-bridge dynamics. However, it should be pointed out that, like most investigations of muscle spindles, changes in muscle fascicle length were not recorded directly in this study and had to be estimated from changes in joint angle.

Recently, ultrasonography was used to monitor changes in muscle fascicle length of the tibialis anterior muscle during passive sinusoidal rotations of the ankle joint in humans (Day et al. 2017). An example of stretch-evoked firing of a primary ending is shown in Fig. 5. It can be seen that the spindle discharge approximated the sinusoidal changes in joint angle and muscle fascicle length and velocity. Across all spindles examined, the firing of the spindle could be approximated by a sine wave that had the same characteristics of the underlying fascicle length changes, regardless of the amplitude or velocity of stretch imposed by sinusoidal rotation of the ankle. Although this had been observed directly in the cat (Hasan and Houk 1975a; 1975b; Matthews and Stein 1969b; Poppele and Bowman 1970) and in human spindles studied in vitro (Poppele and Kennedy 1974), as well as inferred from studies that estimated muscle length from joint angle in humans (Kakuda 2000), it had never been directly measured in humans until this recent study using ultrasonography. During passive rotations of the ankle, the firing of muscle spindles in tibialis anterior muscle is highly correlated with changes in fascicle length, occurring at relatively small, physiological changes in muscle length and being independent of changes in the muscle-tendon unit. Given that the tibialis anterior muscle is essentially quiescent during standing, muscle spindles in this muscle would serve as ideal proprioceptors, given that they are signaling changes in length of passive muscle (Day et al. 2017). Muscle spindles in the calf muscles, which are actively engaged in keeping us upright when standing without support, also have been shown to be sensitive to the types of low-frequency, low-amplitude angular excursions associated with standing (Peters et al. 2017).
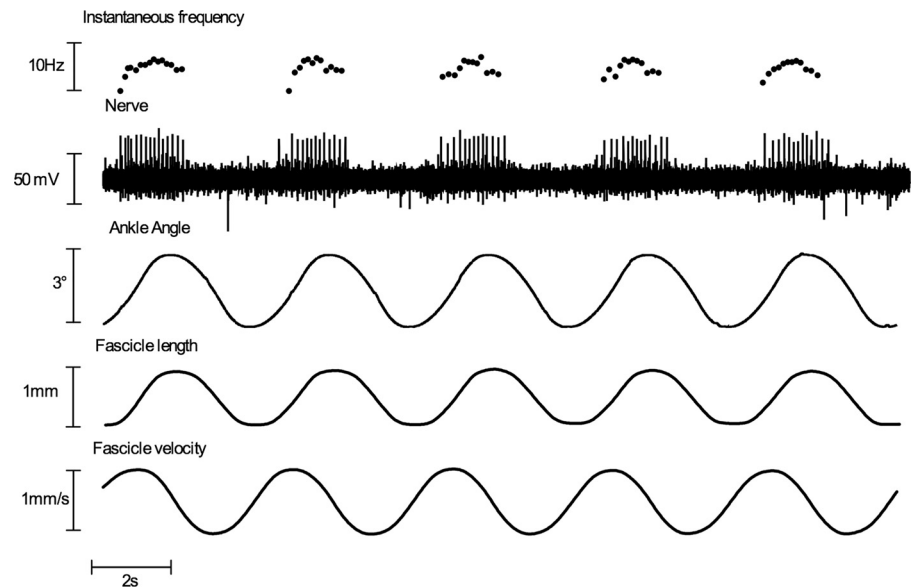
Fig. 5. Representative tibialis anterior spindle and fascicle behavior during passive rotations of the ankle. Recording is from a spontaneously active primary muscle spindle ending from the tibialis anterior during 5 passive rotations of the ankle. The instantaneous firing rate of the identified unit is shown along with ankle angle and fascicle length and velocity of a tracked muscle fascicle from the same tibialis anterior. Reproduced with permission from Day et al. (2017).

Muscle spindles, unlike cutaneous and joint receptors, respond in only one axis of joint rotation (Burke et al. 1987), that which causes stretch of the receptor-bearing muscle. Individual muscle spindles possess a directional sensitivity that allows them to encode changes in muscle length even during active contractions (Jones et al. 2001b). Moreover, fitting the firing of human muscle spindle afferents to various models demonstrated that the information content in the velocity signal was ~10 times higher than that of the displacement signal (Malik et al. 2016). Indeed, it has been argued that, given that the discharge of human primary endings precedes the rate of change in muscle length, they essentially act in the capacity of a "forward sensory model," influenced both by fusimotor drive during a contraction and future kinematics of the muscle (Dimitriou and Edin 2010). As a population, muscle spindles in the different muscles acting about the wrist joint, each of which has a preferred directional sensitivity, are able to encode multidirectional changes in joint angle (Jones et al. 2001b). The same is true for the ankle joint (Bergenheim et al. 2000; Ribot-Ciscar et al. 2002, 2003; Roll et al. 2000, 2004). This is shown for the ankle joint in Fig. 6, in which mean spindle firing in each muscle was fitted to a cosine (*A*) and the individual vectors for each muscle computed (*B* and *C*). Moreover, muscle spindles in these muscles can faithfully encode complex movements (Roll et al. 2000), including those emulating cursive writing (Albert et al. 2005; Roll et al. 2004).

Effects of immediate history on spindle discharge. It is well established that the discharge of muscle spindle endings is affected by previous stretch of the receptor bearing muscle (Edin and Vallbo 1990c) and by previous fusimotor activation during a voluntary contraction (Macefield et al. 1991; Proske et al. 2000; Ribot-Ciscar et al. 1991; Wilson et al. 1997. Muscle spindle discharge can remain elevated for long after a voluntary contraction (Wilson et al. 1997). This is not evidence of ongoing fusimotor drive but of "thixotropy," the persistence of actin-myosin bonds formed in intrafusal fibers by the fusimotor activity that accompanied the contraction but ceased with it. As noted above, persistence of actin-myosin bonds may allow muscle spindles to encode the rate of change of intramuscular force (Blum et al. 2017). Muscle thixotropy has been shown to

have significant effects on proprioception, with knowledge of joint position being affected by whether the muscle had previously contracted or was passively held in a lengthened or shortened position (Proske et al. 2000; Proske and Gandevia 2009, 2012). Sustained vibration applied to the muscle tendon has been shown to decrease resting spindle firing rate as well as reduce sensitivity to passive stretch immediately after the cessation of vibration (Ribot-Ciscar et al. 1998). This phenomenon lasted up to 40 s before there was a complete recovery. It was posited that the changes in spindle activity observed account for the kinesthetic illusions observed following vibratory stimuli (Roll and Vedel 1982).

Resting fusimotor outflow to human muscle spindles. Because many muscle spindles are active at rest, due to the prevailing degree of muscle stretch in the receptor-bearing muscle, a fall in firing rate during a voluntary contraction is interpreted as unloading of the spindle by shortening of the extrafusal muscle. Conversely, if the firing rate is maintained or increases (or a muscle spindle is recruited) during a voluntary contraction, it can be concluded that fusimotor neurons have been activated. In addition to firing rate, discharge variability is a useful measure of the effects of fusimotor drive on muscle spindles. In the decerebrate cat there is significant resting fusimotor outflow, primarily in static γ-motoneurons, that causes an increase in discharge variability of both primary (25%) and secondary (6.4%) endings; when the ventral roots have been cut, and hence fusimotor outflow interrupted, discharge variability decreases to 5.8% and 2.0%, respectively (Matthews and Stein 1969a). As in the cat, discharge variability is higher for the primary than for the secondary endings in humans, but there is overlap (Burke et al. 1979b; Nordh et al. 1983); mean variability is 3.6% and 8.3% for the secondary and primary spindle endings, respectively (Nordh et al. 1983). Matthews and Stein (1969a) noted that there is little difference between the discharge variability of deefferented muscle spindles in decerebrate cats and that in humans, suggesting that resting fusimotor drive to spindles is absent in relaxed human muscles (Burke et al. 1979a, 1981; Nordh et al. 1983). Muscle spindle discharge and the response to stretch do not change significantly following complete nerve block (Burke et al.
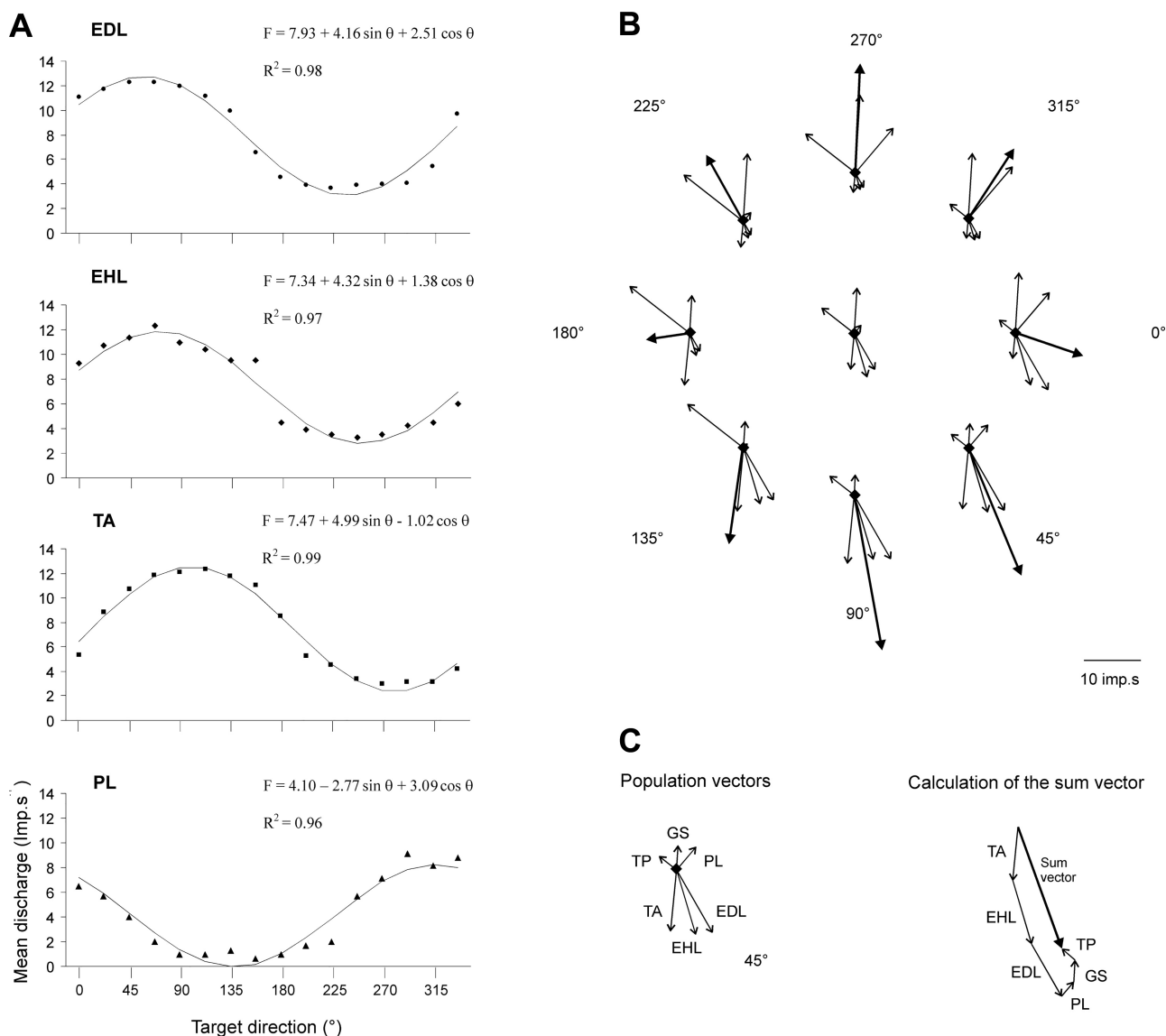
Fig. 6. *A*: mean discharge frequency of the whole sample of muscle spindle afferents for each differently oriented and maintained target position and for each recorded muscle. The direction of the target relative to the home position is given on the abscissa. Each of the muscle spindle populations coded the different positions according to a cosine-tuned function whose equation and coefficient of determination are given above each graph. *B*: the neuronal population vector model. Each diagram gives the result in one maintained position. The origin point of the vectors represents the target. Thin lines correspond to the population vector of each muscle; i.e., the direction of each vector corresponds to the preferred sensory direction of the muscle, and the length corresponds to the mean firing rate of the population of afferents of that muscle. The sum vector of all 6 population vectors is shown in bold. The *center* diagram gives the mean activity of each muscle population at the home position (foot in neutral position). *C*: individual and sum population vectors for all muscles. EDL, extensor digitorum longus; EHL, extensor hallucis longus; TA, tibialis anterior; PL, peroneus lateralis; GS, gastrocnemius soleus; TP, tibialis posterior. Combined from Figs. 3 and 4 of Ribot-Ciscar et al. (2003) and reproduced with permission.

1979a, 1981). There is some evidence of resting activity in dynamic γ-efferents, which may be increased by reflex action of cutaneous afferents (Aniss et al. 1990; Gandevia et al. 1994). However, the spontaneous firing rates of muscle spindles recorded from paralyzed leg muscles in people with spinal cord injury (~10 Hz) were no different from those recorded from intact individuals; the same was true for discharge variability (~7%; Macefield 2013). Again, this supports the conclusion that there is negligible fusimotor drive to human muscle spindles at rest. Whether this can be changed in a task-dependent manner will be discussed below.

Muscle spindle behavior during voluntary contractions. During a nerve block that preferentially affects α-motor axons,

a greater central drive (effort) is required to contract the paralyzed muscle; this increases the discharge of spindle endings, presumably because it activates γ-efferents (which are intact during the selective block) directed to the paralyzed muscle (Burke et al. 1979a). This supports the idea that static γ-motoneurons are activated when subjects volitionally contract a muscle (Vallbo 1974; Vallbo and al-Falahe 1990; Vallbo et al. 1979). When the contraction is isometric, the fusimotor activation is usually sufficient to enhance the background firing of spontaneously active spindles, increase their discharge variability, increase their static response to stretch, and reduce the pause in discharge that occurs on muscle shortening (Burke et al. 1979b; Vallbo 1971, 1973, 1974).

There is also a suggestion that voluntary effort also activates dynamic γ-efferents (Kakuda and Nagaoka 1998), and some indirect evidence that β (skeletofusimotor)-efferents can be activated both by voluntary effort (Aniss et al. 1988) as well as during transcranial stimulation of the motor cortex (Rothwell et al. 1990).

When voluntary contractions produce muscle shortening, the enhanced fusimotor drive can be sufficient to maintain or even increase spindle discharge, but this occurs only if the movement is slow or if the muscle is contracting against a load (Burke et al. 1978a, 1978b). This can be seen in Fig. 4B, in which the muscle spindle is unloaded during the slow contraction on the left but maintains its discharge during the longer contraction on the right. The increase in spindle discharge usually occurs after the onset of EMG activity in the contracting muscle, at a latency of some 20–50 ms when the contractions are rapid and phasic (Hagbarth et al. 1975; Vallbo 1971). The latency of spindle acceleration can vary with contraction speed and is consistent if the contraction is performed precisely the same way each time (Burke et al. 1978c, 1980; Wilson et al. 1997). In slow ramp contractions, it is likely that most spindle endings activated in the contraction will increase their discharge relatively early in the contraction (Edin and Vallbo 1990b; Wilson et al. 1997). This implies that at least some of the fusimotor neurons innervating a spindle are recruited early in the contraction. In isometric contractions, spindle discharge increases in proportion to contraction strength (Vallbo 1974), largely because the discharge rates of the activated spindles increase with contraction strength. Although there has been clear evidence of α-γ coactivation in all voluntary contractions examined so far, there has been some evidence that the balance between the α and γ drives can be varied (Burke et al. 1980; Hulliger et al. 1985). This would be expected given that different descending pathways have quantitatively different effects on α- and γ-motoneurons, and many peripheral afferent inputs have different reflex effects on α- and γ-motoneurons (Aniss et al. 1990; Gandevia et al. 1994). However, one thing is clear: there is no evidence of spindles being recruited, or increasing their background discharge, before the onset of EMG, a pattern that would be expected from the servo-control theory of Merton (1953). Indeed, it was the seminal work of Vallbo (1971) that conclusively demonstrated that spindle discharge lags behind the activation of α-motoneurons, as evidenced from the latency of firing from the onset of EMG in the contracting muscle.

As noted above, in passive conditions, human muscle spindles can faithfully encode angular position. However, during voluntary contractions, this sensitivity to length changes is essentially lost, particularly during movements that cause shortening of the muscle but even during lengthening movements (Jahnke and Struppler 1989). When subjects are asked to actively hold a constant position, there is no relationship between joint angle and spindle firing (Hulliger et al. 1982; Vallbo et al. 1981), with spindle firing being better related to load rather than angular position (Vallbo et al. 1981). Moreover, during fast voluntary movements, most spindles are silenced during shortening contractions, although some exhibit an increase in firing that reflects an increase in fusimotor drive as force is built up in the contracting muscle (al-Falahe et al. 1990a, 1991). Nevertheless, whereas muscle spindles in the agonist muscle may be poor at encoding position during

contraction, those in the antagonist muscle are not: as the agonist muscle shortens, the antagonist lengthens, providing spindles in the stretched muscle with length and velocity information that they can faithfully encode (Dimitriou 2014; Ribot-Ciscar and Roll 1998). When the agonist and antagonist co-contract, however, spindle firing is higher; this may possibly reflect the smaller length changes (to which muscle spindles are more sensitive) in this condition (Nielsen et al. 1994).

Muscle spindle behavior during complex motor tasks. Although most studies of human muscle spindles have used simple, and usually isometric, contractions of the receptor-bearing muscle, there have been some studies in which more complex volitional movements have been examined. When subjects were asked to grip an instrumented manipulandum between finger and thumb using the precision grip, randomly occurring increases in tangential force at difference amplitudes and rates generated automatic long-latency increases in grip force that prevent slip and loss of grip of the manipulandum: this caused increases in muscle spindle firing in the finger flexor muscles during the evoked increases in grip force, increases that reflected the rate of rise in grip force, but there was no evidence of an increase in spindle firing in anticipation of the movement and no increases in spindle firing because the imposed tangential load increased before the generation of the grip response (Macefield and Johansson 1996). When subjects were asked to reach, grasp, and lift objects (blocks of different size), both primary and secondary muscle spindle endings in the finger extensor muscles increased their activity in a manner that reflected the velocity of the finger kinematics, with primary afferents also signaling acceleration, but neither class of spindle encoded the changes in muscle length or provided information on the size of the grasped object (Dimitriou and Edin 2008a).

Likewise, primary spindle endings in the wrist extensors encoded velocity and acceleration of the wrist kinematics during a key-pressing task, with secondary endings signaling velocity, but neither class of spindle afferent encoded changes in muscle length (Dimitriou and Edin 2008b). Mean data from 15 primary and 8 secondary spindle endings, located in the extensor carpi radialis muscle, are shown in Fig. 7. Subjects used their middle finger to press keys on a 3 × 3 keyboard, resulting in the parent muscle being either long or short during the task. For the key sequences shown, both acceleration and velocity influenced the primary afferents, but only velocity affected the secondary afferents. The authors suggested that for the central nervous system to estimate the length or velocity of a muscle from the firing of muscle spindles, additional information would be required not only about the central command to the extrafusal and intrafusal muscle fibers but also about the mechanical properties of the load, including muscle-tendon compliance on which the muscle acts. Indeed, volitional contraction of a finger against a viscous load revealed no specific signals in the spindle afferents that could encode the decrease in compliance (McNulty et al. 2008). Again, the central nervous system presumably disambiguates information on load by comparing the central command required to perform the movement with the resultant sensory feedback and the expected sensory feedback.
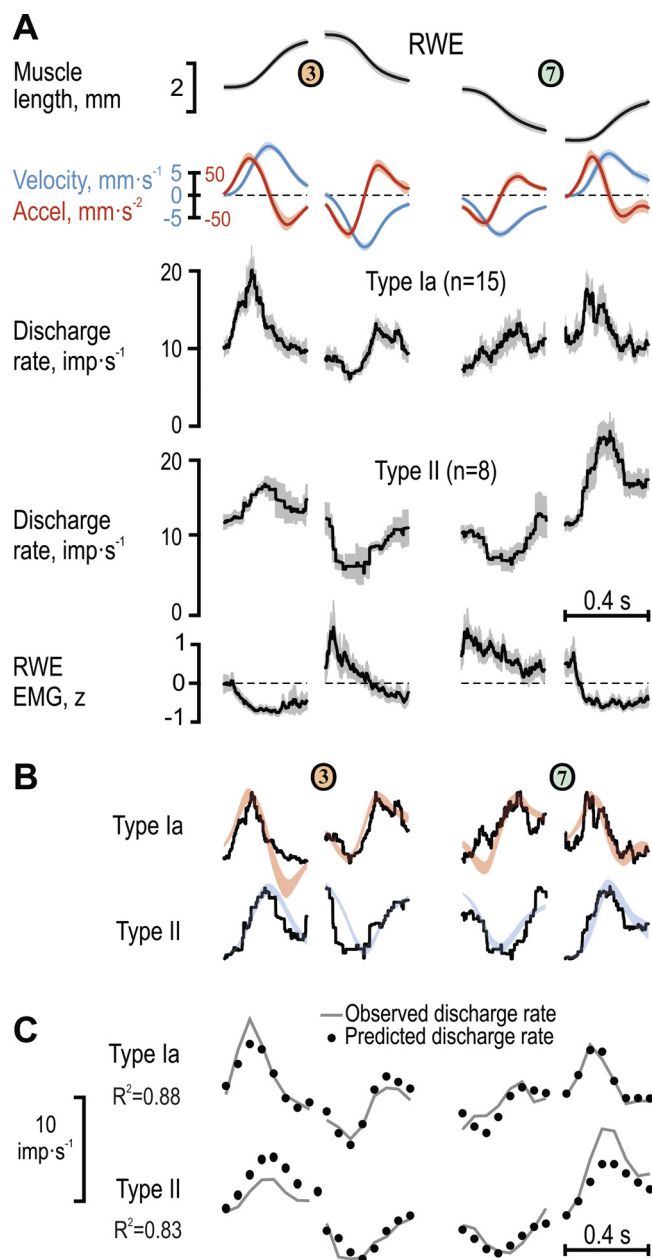
Fig. 7. Ensemble responses of muscle spindle afferents from the radial wrist extensor (RWE) muscle. *A*: averaged muscle length, velocity, acceleration (Accel), and EMG signals, along with the corresponding ensemble discharge rates (impulses/s) of type Ia (*n* = 15) and type II afferents (*n* = 8) from the RWE, for a "long" *key 3* and a "short" *key 7*. Shaded areas around means represent ± SD. *B*: qualitative comparisons of ensemble discharge profiles and acceleration (red) and velocity (blue). *C*: reconstructions of the observed ensemble discharge rates shown in *A*. Continuous lines represent the observed values, and circles represent the values predicted from linear regressions using the kinematics signals and RWE EMG as independent predictors. Reproduced with permission from Dimitriou and Edin (2008a).

INDEPENDENT CONTROL OF HUMAN FUSIMOTOR NEURONS

Despite the obvious links established in animal studies, including the elegant chronic recordings from muscle spindle afferents in awake behaving cats (Prochazka and Gorassini 1998a, 1998b), there are relatively few studies in humans that support significant independent modulation of spindle gain via the fusimotor system. Nevertheless, reflex connections of human fusimotor neurons with cutaneous and muscle afferents (Aniss et al. 1990; Gandevia et al. 1994), as well as visual inputs (Jones et al. 2001a), have indicated the potential substrate for such independent control to exist. Vestibular stimulation is a potent stimulus for fusimotor neurons in the hindlimbs of the cat (Carli et al. 1967; Diete-Spiff et al. 1967; Grillner et al. 1969, 1970; Lund and Pompeiano 1965; Rubin et al. 1977), but studies in relaxed (Bent et al. 2007; Gandevia et al. 1994; Ribot-Ciscar et al. 2000) and active (Aniss et al. 1990; Bent et al. 2013; Jones et al. 2001a; Nafati et al. 2004) muscles have yet to demonstrate independent fusimotor changes in response to vestibular stimulation. Even in the near-vertical position, in the presence of ongoing EMG in the leg muscles (and presumably an increase in vestibulospinal drive), no evidence of independent fusimotor-driven changes in spindle sensitivity has been found (Knellwolf et al. 2016), although whether the same will be true when subjects are standing freely and exposed to postural perturbations remains to be seen. Recently, a small change in dynamic sensitivity of muscle spindles in the leg to passive rotations about the ankle joint was found when subjects listened to emotionally charged but not emotionally neutral music (Ackerley et al. 2017). A recent immunohistochemical study provided morphological evidence for the presence of sympathetic innervation of human muscle spindles, identifying neuropeptide Y receptors on intrafusal fibers (Radovanovic et al. 2015). However, experimentally it has been shown that sustained increases in muscle sympathetic outflow have no effect on spindle firing rate or discharge variability (Macefield et al. 2003). There also have been investigations into the effect of noxious stimuli on fusimotor drive. A model for chronic musculoskeletal pain syndromes was established in anesthetized animals based on the reflex activation of fusimotor neurons by nociceptor response (Johansson and Sojka 1991). Unfortunately, following the same trend as other candidates for independent control, when this potential reflex excitation of fusimotor drive was investigated in awake human subjects, during the deep pain produced by injection or infusion of hypertonic saline into the tibialis anterior muscle, no net change in the spindle firing was seen (Birznieks et al. 2008; Fazalbhoy et al. 2013).

It is generally accepted that fusimotor and skeletomotor neurons are coactivated during voluntary contractions in humans, with little evidence of independent control of the two motor systems, a point first made by Vallbo (1971). Many studies have since shown that the γ- and α-motoneurons are coactivated (Al-Falahe et al. 1988; al-Falahe 1990a, 1990b; Kakuda et al. 1996; Wilson et al. 1997). However, it is reasonable to think that changes in the gain of human muscle spindles are likely to occur in a task-dependent manner. Indeed, there has been some evidence to suggest that fusimotor neurons can change the sensitivity of muscle spindles independently of changes in EMG, and hence the activity of α-motoneurons. When subjects perform a precision aiming task that had to be adapted to changes in visual feedback, the firing of muscle spindle afferents did not increase, but rather decreased, which the authors suggested allows the central nervous system to resolve the conflict between proprioceptive and visual feedback during the task (Jones et al. 2001a). Whereas some investigators have found no evidence of selective recruitment of fusimotor neurons (Gandevia and Burke 1985; Gandevia et al. 1997; Kakuda et al. 1996, 1997; Wessberg and Vallbo

1995), others have when attention to the task is required (Hospod et al. 2007; Ribot-Ciscar et al. 2000, 2009). Kakuda et al. (1996, 1997) found that fusimotor activity was higher during a precision task involving the fingers but that the effect was not independent of the increase in skeletomotor activity. Conversely, Ribot-Ciscar and colleagues found evidence for an increase in spindle sensitivity during reinforcement maneuvers (Ribot-Ciscar et al. 2000) and as a function of task requirement (Ribot-Ciscar et al. 2009). Hospod et al. (2007) examined the effects of attending to either the movement or final position of an imposed ankle movement on spindle firing, showing that the balance of dynamic and static fusimotor drive to the spindle was shifted by directing one's attention to the foot. However, it must be emphasized that the observed changes that support

independent fusimotor drive were very small, and certainly not as impressive as those documented in the cat. There is evidence that human muscle spindles also receive β innervation, i.e., a common axon that supplies both extrafusal and intrafusal muscle fibers (Kakuda et al. 1998), a mechanism that ensures coactivation of α- and γ-motoneurons. Nevertheless, modeling does suggest that selective control of the dynamic and static γ-motoneurons is required to fully generate the repertoire of human movement and posture (Li et al. 2015). Indeed, most recently, Dimitriou (2016) showed that changes in spindle behavior during a visuomotor learning task cannot be fully explained by differences in muscle activity, but rather reflect an increase in fusimotor drive in the stage at which subjects have learnt (adapted) to the task.
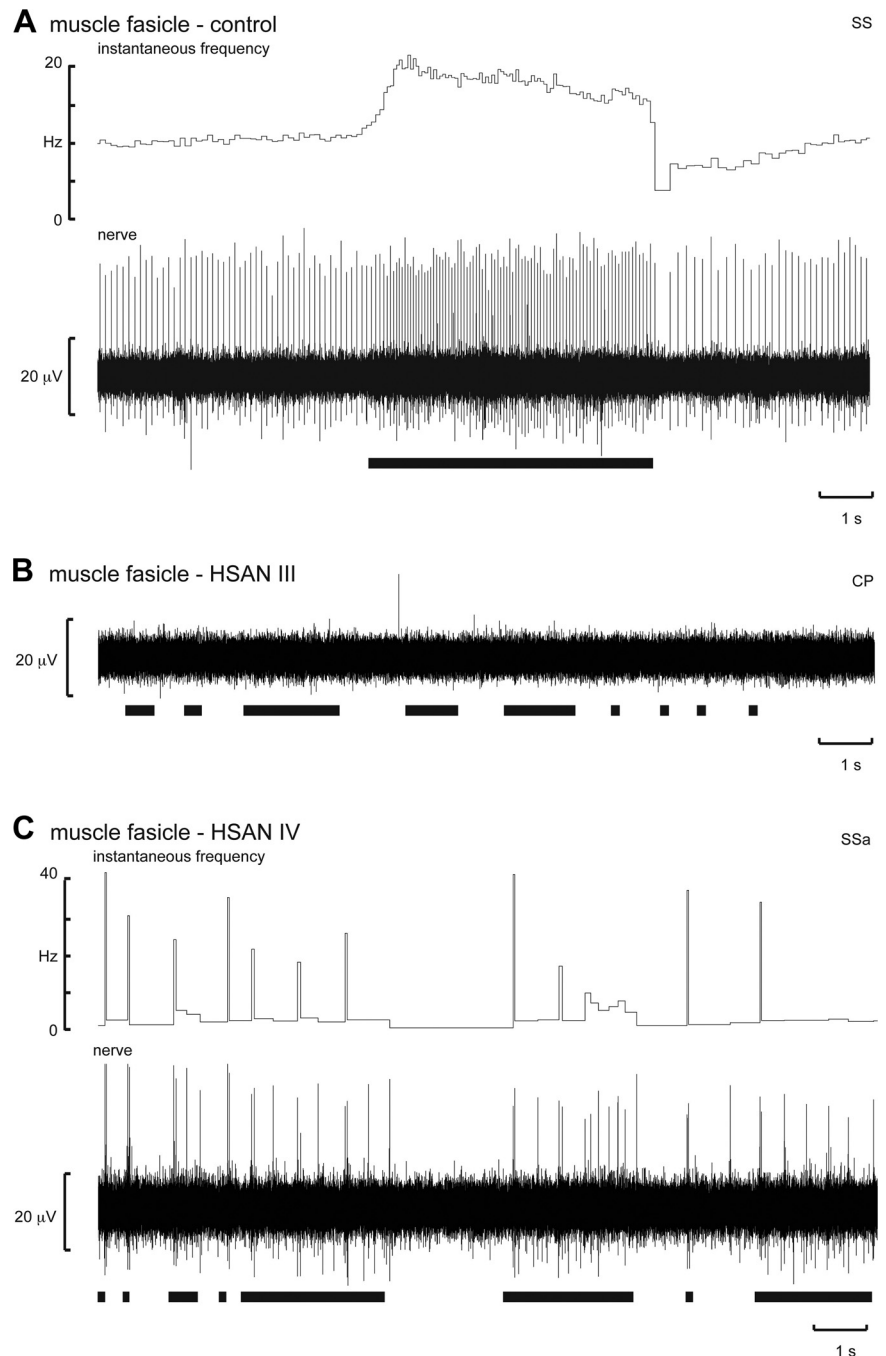

Fig. 8. Intraneural recordings from muscle fascicles of the common peroneal nerve (CP) during muscle stretch in a control subject (*A*), a patient with hereditary sensory and autonomic neuropathy type III (HSAN III; *B*), and a patient with HSAN IV (*C*). *A*: single-unit recording from a muscle spindle secondary ending located in the extensor hallucis longus muscle; the afferent responded during passive plantarflexions of the big toe. *B*: complete absence of muscle spindle afferent activity in the peronei fascicle during muscle stretch induced by passive inversion of the foot. *C*: recording from a muscle spindle primary ending located in the extensor digitorum longus muscle; the afferent responded dynamically during passive plantarflexions of the toes. In all traces, black horizontal bars indicate periods of passive stretch of the receptor-bearing muscle. Subject ID is represented by initials in top right corner of each panel. Reproduced with permission from Macefield et al. (2011).

EFFECTS OF MUSCLE SPINDLE ACTIVITY ON MOTOR ACTIVITY

It is well known that muscle spindles exert short-latency positive feedback onto α-motoneurons in the spinal cord, although the synaptic strength of individual muscle spindles is weak; the same is true for individual muscle spindles in humans, as assessed using spike-triggered averaging of EMG, whereas the synaptic coupling of tactile afferents to motoneurons is strong (Fallon et al. 2005; McNulty and Macefield 2001, 2002). In long, fatiguing contractions, muscle spindle discharge is maximal initially at the beginning of a contraction and then decreases by about one-third at the end, which implies that feedback support to the contraction is initially maximal but subsequently falls (Macefield et al. 1991). A further implication is that, contrary to initial views, the γ-efferent system is not mobilized to compensate for fatigue. When a motor nerve is blocked distal to the recording site, recordings can be made from α-motoneurons deprived of feedback support from endings in the now-paralyzed muscle (Gandevia et al. 1990, 1993; Macefield et al. 1993). The discharge rates of motor axons reach roughly two-thirds of those of normally intact motor units, a finding that suggests significant feedback support to the contracting motoneuron pool. However, whether this occurs through segmental, suprasegmental, or cerebral pathways (or all) is not known. Nevertheless, despite it being more difficult to maintain motor unit firing in the absence of muscle afferents feedback, subjects can still recruit and de-recruit motoneurons and modulate their firing rates given only knowledge of the central command (effort) that they are sending to the muscle.

What happens to motor control when spindle input is absent? Patients with complete large-fiber sensory neuropathy are critically dependent on vision to control the positions of their limbs in space, having lost input from large-diameter afferents originating in both muscle and skin (Cole and Sedgwick, 1992; Lajoie et al. 1996; Rothwell et al. 1982). It was recently shown that patients with hereditary sensory and autonomic neuropathy type III (HSAN III), also known as familial dysautonomia or Riley-Day syndrome, are devoid of functional muscle spindles in the legs, which fits with the loss of tendon and H-reflexes in these individuals (Macefield et al. 2011). They also have greatly elevated pain thresholds. Conversely, patients with another congenital sensory and autonomic neuropathy (HSAN IV), also known as congenital insensitivity to pain with anhidrosis (CIPA), have intact muscle spindles, as shown in Fig. 8. Unlike individuals with large-fiber sensory neuropathy, those with HSAN III and HSAN IV have preserved large-diameter cutaneous afferents, although small-diameter cutaneous afferents are greatly reduced (Macefield et al. 2011). Nevertheless, their proprioception is greatly affected in these individuals, as is their gait and capacity to point at a target (Macefield et al. 2013), arguing for an important role of muscle spindles in many aspects of human motor control.

CONCLUDING REMARKS

Microneurographic studies of muscle spindle behavior in awake human subjects have contributed much information that corroborates what we know from studies in experimental animals. Muscle spindles provide length and velocity information in passive conditions, but this is largely lost in active conditions, suggesting that the central nervous system must disambiguate the sensory feedback provided by muscles spindles (and Golgi tendon organs) and central command during a voluntary contraction. Whether there is independent control of fusimotor neurons in humans is still debated, and it is highly likely that such independence is critically dependent on the task and on the muscles being investigated. Indeed, one would expect motor control strategies in the hand, involved in precise movements, to differ from those in the leg, engaged in postural and locomotor activities. Nevertheless, when evidence has been provided, the independence of fusimotor and skeletomotor outflows has been shown to be much weaker than that in the cat.

DISCLOSURES

AUTHOR CONTRIBUTIONS

V.G.M. conceived and designed research; V.G.M. and T.P.K. drafted manuscript; V.G.M. and T.P.K. edited and revised manuscript; V.G.M. and T.P.K. approved final version of manuscript.

REFERENCES

Ackerley R, Aimonetti JM, Ribot-Ciscar E. Emotions alter muscle proprioceptive coding of movements in humans. *Sci Rep* 7: 8465, 2017. doi:10.1038/s41598-017-08721-4.

Adal MN. The fine structure of the sensory region of cat muscle spindles. *J Ultrastruct Res* 26: 332–353, 1969. doi:10.1016/S0022-5320(69)80011-0.

al-Falahe NA, Nagaoka M, Vallbo AB. Response profiles of human muscle afferents during active finger movements. *Brain* 113: 325–346, 1990a. doi:10.1093/brain/113.2.325.

al-Falahe NA, Nagaoka M, Vallbo AB. Lack of fusimotor modulation in a motor adaptation task in man. *Acta Physiol Scand* 140: 23–30, 1990b. doi:10.1111/j.1748-1716.1990.tb08972.x.

al-Falahe NA, Nagaoka M, Vallbo AB. Dual response from human muscle spindles in fast voluntary movements. *Acta Physiol Scand* 141: 363–371, 1991. doi:10.1111/j.1748-1716.1991.tb09092.x.

Al-Falahe NA, Vallbo AB. Role of the human fusimotor system in a motor adaptation task. *J Physiol* 401: 77–95, 1988. doi:10.1113/jphysiol.1988.sp017152.

Albert F, Ribot-Ciscar E, Fiocchi M, Bergenheim M, Roll JP. Proprioceptive feedback in humans expresses motor invariants during writing. *Exp Brain Res* 164: 242–249, 2005. doi:10.1007/s00221-005-2246-5.

Aniss AM, Diener HC, Hore J, Burke D, Gandevia SC. Reflex activation of muscle spindles in human pretibial muscles during standing. *J Neurophysiol* 64: 671–679, 1990. doi:10.1152/jn.1990.64.2.671.

Aniss AM, Gandevia SC, Burke D. Reflex changes in muscle spindle discharge during a voluntary contraction. *J Neurophysiol* 59: 908–921, 1988. doi:10.1152/jn.1988.59.3.908.

Appelberg B, Bessou P, Laporte Y. Action of static and dynamic fusimotor fibres on secondary endings of cat's spindles. *J Physiol* 185: 160–171, 1966. doi:10.1113/jphysiol.1966.sp007978.

Banks RW, Harker DW, Stacey MJ. A study of mammalian intrafusal muscle fibres using a combined histochemical and ultrastructural technique. *J Anat* 123: 783–796, 1977.

Barker D. The innervation of the muscle-spindle. *Q J Microsc Sci* 89: 143–186, 1948.

Bent LR, Bolton PS, Macefield VG. Vestibular inputs do not influence the fusimotor system in relaxed muscles of the human leg. *Exp Brain Res* 180: 97–103, 2007. doi:10.1007/s00221-006-0836-5.

Bent LR, Sander M, Bolton PS, Macefield VG. The vestibular system does not modulate fusimotor drive to muscle spindles in contracting leg muscles of seated subjects. *Exp Brain Res* 227: 175–183, 2013. doi:10.1007/s00221-013-3497-1.

Bergenheim M, Ribot-Ciscar E, Roll JP. Proprioceptive population coding of two-dimensional limb movements in humans: I. Muscle spindle feedback during spatially oriented movements. *Exp Brain Res* 134: 301–310, 2000. doi:10.1007/s002210000471.

Bewick GS, Banks RW. Mechanotransduction in the muscle spindle. *Pflugers Arch* 467: 175–190, 2015. doi:10.1007/s00424-014-1536-9.

Birznieks I, Boonstra TW, Macefield VG. Modulation of human muscle spindle discharge by arterial pulsations–functional effects and consequences. *PLoS One* 7: e35091, 2012. doi:10.1371/journal.pone.0035091.

Birznieks I, Burton AR, Macefield VG. The effects of experimental muscle and skin pain on the static stretch sensitivity of human muscle spindles in relaxed leg muscles. *J Physiol* 586: 2713–2723, 2008. doi:10.1113/jphysiol.2008.151746.

Blum KP, Lamotte D'Incamps B, Zytnicki D, Ting LH. Force encoding in muscle spindles during stretch of passive muscle. *PLoS Comput Biol* 13: e1005767, 2017. doi:10.1371/journal.pcbi.1005767.

Boyd IA. The structure and innervation of the nuclear bag muscle fibre system and the nuclear chain muscle fibre system in mammalian muscle spindles. *Philos Trans R Soc Lond B Biol Sci* 245: 81–136, 1962. doi:10.1098/rstb.1962.0007.

Boyd IA. The response of fast and slow nuclear bag fibres and nuclear chain fibres in isolated cat muscle spindles to fusimotor stimulation, and the effect of intrafusal contraction on the sensory endings. *Q J Exp Physiol Cogn Med Sci* 61: 203–254, 1976.

Boyd IA, Gladden MH, McWilliam PN, Ward J. Control of dynamic and static nuclear bag fibres and nuclear chain fibres by gamma and beta axons in isolated cat muscle spindels. *J Physiol* 265: 133–162, 1977. doi:10.1113/jphysiol.1977.sp011709.

Brown MC, Engberg I, Matthews PBC. The relative sensitivity to vibration of muscle receptors of the cat. *J Physiol* 192: 773–800, 1967. doi:10.1113/jphysiol.1967.sp008330.

Burgess PR, Clark FJ. Characteristics of knee joint receptors in the cat. *J Physiol* 203: 317–335, 1969. doi:10.1113/jphysiol.1969.sp008866.

Burke D. The activity of human muscle spindle endings in normal motor behavior. *Int Rev Physiol* 25: 91–126, 1981.

Burke D. Unit identification, sampling bias and technical issues in microneurographic recordings from muscle spindle afferents. *J Neurosci Methods* 74: 137–144, 1997. doi:10.1016/S0165-0270(97)02244-9.

Burke D, Aniss AM, Gandevia SC. In-parallel and in-series behavior of human muscle spindle endings. *J Neurophysiol* 58: 417–426, 1987. doi:10.1152/jn.1987.58.2.417.

Burke D, Gandevia SC, Macefield G. Responses to passive movement of receptors in joint, skin and muscle of the human hand. *J Physiol* 402: 347–361, 1988. doi:10.1113/jphysiol.1988.sp017208.

Burke D, Hagbarth KE, Löfstedt L. Muscle spindle activity in man during shortening and lengthening contractions. *J Physiol* 277: 131–142, 1978a. doi:10.1113/jphysiol.1978.sp012265.

Burke D, Hagbarth KE, Löfstedt L. Muscle spindle responses in man to changes in load during accurate position maintenance. *J Physiol* 276: 159–164, 1978b. doi:10.1113/jphysiol.1978.sp012225.

Burke D, Hagbarth KE, Löfstedt L, Wallin BG. The responses of human muscle spindle endings to vibration of non-contracting muscles. *J Physiol* 261: 673–693, 1976a. doi:10.1113/jphysiol.1976.sp011580.

Burke D, Hagbarth KE, Löfstedt L, Wallin BG. The responses of human muscle spindle endings to vibration during isometric contraction. *J Physiol* 261: 695–711, 1976b. doi:10.1113/jphysiol.1976.sp011581.

Burke D, Hagbarth KE, Skuse NF. Recruitment order of human spindle endings in isometric voluntary contractions. *J Physiol* 285: 101–112, 1978c. doi:10.1113/jphysiol.1978.sp012560.

Burke D, Hagbarth KE, Skuse NF. Voluntary activation of spindle endings in human muscles temporarily paralysed by nerve pressure. *J Physiol* 287: 329–336, 1979a. doi:10.1113/jphysiol.1979.sp012662.

Burke D, McKeon B, Westerman RA. Induced changes in the thresholds for voluntary activation of human spindle endings. *J Physiol* 302: 171–181, 1980. doi:10.1113/jphysiol.1980.sp013236.

Burke D, Skuse NF, Stuart DG. The regularity of muscle spindle discharge in man. *J Physiol* 291: 277–290, 1979b. doi:10.1113/jphysiol.1979.sp012812.

Carli G, Diete-Spiff K, Pompeiano O. Responses of the muscle spindles and of the extrafusal fibres in an extensor muscle to stimulation of the lateral vestibular nucleus in the cat. *Arch Ital Biol* 105: 209–242, 1967.

Clark FJ, Burgess PR. Slowly adapting receptors in cat knee joint: can they signal joint angle? *J Neurophysiol* 38: 1448–1463, 1975. doi:10.1152/jn.1975.38.6.1448.

Cole JD, Sedgwick EM. The perceptions of force and of movement in a man without large myelinated sensory afferents below the neck. *J Physiol* 449: 503–515, 1992. doi:10.1113/jphysiol.1992.sp019099.

Cooper S, Daniel PM. Muscle spindles in man; their morphology in the lumbricals and the deep muscles of the neck. *Brain* 86: 563–586, 1963. doi:10.1093/brain/86.3.563.

Cordo PJ, Flores-Vieira C, Verschueren SM, Inglis JT, Gurfinkel V. Position sensitivity of human muscle spindles: single afferent and population representations. *J Neurophysiol* 87: 1186–1195, 2002. doi:10.1152/jn.00393.2001.

Corvaja N, Marinozzi V, Pompeiano O. Muscle spindles in the lumbrical muscle of the adult cat. Electron microscopic observations and functional considerations. *Arch Ital Biol* 107: 365–543, 1969.

Davis JN. Proceedings: discharge properties of primary and secondary endings in human intercostal muscle spindles studied in vitro. *J Physiol* 234: 30P–32P, 1973.

Day J, Bent LR, Birznieks I, Macefield VG, Cresswell AG. Muscle spindles in human tibialis anterior encode muscle fascicle length changes. *J Neurophysiol* 117: 1489–1498, 2017. doi:10.1152/jn.00374.2016.

Devanandan MS, Ghosh S, John KT. A quantitative study of muscle spindles and tendon organs in some intrinsic muscles of the hand in the bonnet monkey (*Macaca radiata*). *Anat Rec* 207: 263–266, 1983. doi:10.1002/ar.1092070204.

Diete-Spiff K, Carli G, Pompeiano O. Spindle responses and extrafusal contraction on stimulation of the 8th cranial nerve or the vestibular nuclei in the cat. *Pflugers Arch Gesamte Physiol Menschen Tiere* 293: 276–280, 1967. doi:10.1007/BF00417125.

Dimitriou M. Enhanced muscle afferent signals during motor learning in humans. *Curr Biol* 26: 1062–1068, 2016. doi:10.1016/j.cub.2016.02.030.

Dimitriou M. Human muscle spindle sensitivity reflects the balance of activity between antagonistic muscles. *J Neurosci* 34: 13644–13655, 2014. doi:10.1523/JNEUROSCI.2611-14.2014.

Dimitriou M, Edin BB. Discharges in human muscle spindle afferents during a key-pressing task. *J Physiol* 586: 5455–5470, 2008a. doi:10.1113/jphysiol.2008.160036.

Dimitriou M, Edin BB. Discharges in human muscle receptor afferents during block grasping. *J Neurosci* 28: 12632–12642, 2008b. doi:10.1523/JNEUROSCI.3357-08.2008.

Dimitriou M, Edin BB. Human muscle spindles act as forward sensory models. *Curr Biol* 20: 1763–1767, 2010. doi:10.1016/j.cub.2010.08.049.

Eccles JC, Sherrington CS. Numbers and contraction-values of individual motor-units examined in some muscles of the limb. *Proc R Soc Lond B Biol Sci* 106: 326–357, 1930. doi:10.1098/rspb.1930.0032.

Edin BB, Vallbo AB. Twitch contraction for identification of human muscle afferents. *Acta Physiol Scand* 131: 129–138, 1987. doi:10.1111/j.1748-1716.1987.tb08214.x.

Edin BB, Vallbo AB. Dynamic response of human muscle spindle afferents to stretch. *J Neurophysiol* 63: 1297–1306, 1990a. doi:10.1152/jn.1990.63.6.1297.

Edin BB, Vallbo AB. Muscle afferent responses to isometric contractions and relaxations in humans. *J Neurophysiol* 63: 1307–1313, 1990b. doi:10.1152/jn.1990.63.6.1307.

Edin BB, Vallbo AB. Classification of human muscle stretch receptor afferents: a Bayesian approach. *J Neurophysiol* 63: 1314–1322, 1990c. doi:10.1152/jn.1990.63.6.1314.

Eriksson PO, Butler-Browne G, Fischman D, Grove BK, Schiaffino S, Virtanen I, Thornell LE. Myofibrillar and cytoskeletal proteins in human muscle spindles. In: *Mechanoreceptors: Development, Structure, and Function*, edited by Hník P, Soukup T, Vejsada R, Zelená J. Boston, MA: Springer, 1988, p. 273–274. doi:10.1007/978-1-4899-0812-4_51

Fallon JB, Bent LR, McNulty PA, Macefield VG. Evidence for strong synaptic coupling between single tactile afferents from the sole of the foot and motoneurons supplying leg muscles. *J Neurophysiol* 94: 3795–3804, 2005. doi:10.1152/jn.00359.2005.

Fallon JB, Macefield VG. Vibration sensitivity of human muscle spindles and Golgi tendon organs. *Muscle Nerve* 36: 21–29, 2007. doi:10.1002/mus.20796.

Fazalbhoy A, Macefield VG, Birznieks I. Tonic muscle pain does not increase fusimotor drive to human leg muscles: implications for chronic muscle pain. *Exp Physiol* 98: 1125–1132, 2013. doi:10.1113/expphysiol.2012.071670.

Gandevia SC, Burke D. Effect of training on voluntary activation of human fusimotor neurons. *J Neurophysiol* 54: 1422–1429, 1985. doi:10.1152/jn.1985.54.6.1422.

Gandevia SC, Macefield G, Burke D, McKenzie DK. Voluntary activation of human motor axons in the absence of muscle afferent feedback. The

control of the deafferented hand. *Brain* 113: 1563–1581, 1990. doi:10.1093/brain/113.5.1563.

Gandevia SC, Macefield VG, Bigland-Ritchie B, Gorman RB, Burke D. Motoneuronal output and gradation of effort in attempts to contract acutely paralysed leg muscles in man. *J Physiol* 471: 411–427, 1993. doi:10.1113/jphysiol.1993.sp019907.

Gandevia SC, Wilson L, Cordo PJ, Burke D. Fusimotor reflexes in relaxed forearm muscles produced by cutaneous afferents from the human hand. *J Physiol* 479: 499–508, 1994. doi:10.1113/jphysiol.1994.sp020313.

Gandevia SC, Wilson LR, Inglis JT, Burke D. Mental rehearsal of motor tasks recruits α-motoneurones but fails to recruit human fusimotor neurones selectively. *J Physiol* 505: 259–266, 1997. doi:10.1111/j.1469-7793.1997.259bc.x.

Grill SE, Hallett M. Velocity sensitivity of human muscle spindle afferents and slowly adapting type II cutaneous mechanoreceptors. *J Physiol* 489: 593–602, 1995. doi:10.1113/jphysiol.1995.sp021075.

Grillner S, Hongo T, Lund S. Descending monosynaptic and reflex control of γ-motoneurones. *Acta Physiol Scand* 75: 592–613, 1969. doi:10.1111/j.1748-1716.1969.tb04414.x.

Grillner S, Hongo T, Lund S. The vestibulospinal tract. Effects on alpha-motoneurones in the lumbosacral spinal cord in the cat. *Exp Brain Res* 10: 94–120, 1970. doi:10.1007/BF00340521.

Hagbarth KE, Wallen G, Löfstedt L. Muscle spindle activity in man during voluntary fast alternating movements. *J Neurol Neurosurg Psychiatry* 38: 625–635, 1975. doi:10.1136/jnnp.38.7.625.

Hasan Z, Houk JC. Analysis of response properties of deefferented mammalian spindle receptors based on frequency response. *J Neurophysiol* 38: 663–672, 1975a. doi:10.1152/jn.1975.38.3.663.

Hasan Z, Houk JC. Transition in sensitivity of spindle receptors that occurs when muscle is stretched more than a fraction of a millimeter. *J Neurophysiol* 38: 673–689, 1975b. doi:10.1152/jn.1975.38.3.673.

Hospod V, Aimonetti JM, Roll J-P, Ribot-Ciscar E. Changes in human muscle spindle sensitivity during a proprioceptive attention task. *J Neurosci* 27: 5172–5178, 2007. doi:10.1523/JNEUROSCI.0572-07.2007.

Houk J, Henneman E. Responses of Golgi tendon organs to active contractions of the soleus muscle of the cat. *J Neurophysiol* 30: 466–481, 1967. doi:10.1152/jn.1967.30.3.466.

Hulliger M. The mammalian muscle spindle and its central control. *Rev Physiol Biochem Pharmacol* 101: 1–110, 1984. doi:10.1007/BFb0027694.

Hulliger M, Nordh E, Thelin AE, Vallbo AB. The responses of afferent fibres from the glabrous skin of the hand during voluntary finger movements in man. *J Physiol* 291: 233–249, 1979. doi:10.1113/jphysiol.1979.sp012809.

Hulliger M, Nordh E, Vallbo AB. The absence of position response in spindle afferent units from human finger muscles during accurate position holding. *J Physiol* 322: 167–179, 1982. doi:10.1113/jphysiol.1982.sp014030.

Hulliger M, Nordh E, Vallbo AB. Discharge in muscle spindle afferents related to direction of slow precision movements in man. *J Physiol* 362: 437–453, 1985. doi:10.1113/jphysiol.1985.sp015687.

Hunt CC. Relation of function to diameter in afferent fibers of muscle nerves. *J Gen Physiol* 38: 117–131, 1954. doi:10.1085/jgp.38.1.117.

Hunt CC, Kuffler SW. Further study of efferent small-nerve fibers to mammalian muscle spindles; multiple spindle innervation and activity during contraction. *J Physiol* 113: 283–297, 1951. doi:10.1113/jphysiol.1951.sp004572.

Inglis JT, Wilson LR, Gandevia SC, Burke D. Efferent responses to twitch tests used in identifying human muscle afferents. *Neurosci Lett* 188: 97–100, 1995. doi:10.1016/0304-3940(95)11405-L.

Jahnke MT, Struppler A. Response of human muscle spindle afferents to abrupt load perturbations. *Brain Res* 501: 324–331, 1989. doi:10.1016/0006-8993(89)90649-5.

Jahnke MT, Struppler A. Responses of human muscle spindle afferents during isotonic position holding and active movements. *Brain Res* 515: 181–186, 1990. doi:10.1016/0006-8993(90)90594-2.

James NT. Histochemical demonstration of myoglobin in skeletal muscle fibres and muscle spindles. *Nature* 219: 1174–1175, 1968. doi:10.1038/2191174a0.

Johansson H, Sojka P. Pathophysiological mechanisms involved in genesis and spread of muscular tension in occupational muscle pain and in chronic musculoskeletal pain syndromes: a hypothesis. *Med Hypotheses* 35: 196–203, 1991. doi:10.1016/0306-9877(91)90233-O.

Jones KE, Wessberg J, Vallbo A. Proprioceptive feedback is reduced during adaptation to a visuomotor transformation: preliminary findings. *Neuroreport* 12: 4029–4033, 2001a. doi:10.1097/00001756-200112210-00035.

Jones KE, Wessberg J, Vallbo AB. Directional tuning of human forearm muscle afferents during voluntary wrist movements. *J Physiol* 536: 635–647, 2001b. doi:10.1111/j.1469-7793.2001.0635c.xd.

Kakuda N. Response of human muscle spindle afferents to sinusoidal stretching with a wide range of amplitudes. *J Physiol* 527: 397–404, 2000. doi:10.1111/j.1469-7793.2000.00397.x.

Kakuda N, Miwa T, Nagaoka M. Coupling between single muscle spindle afferent and EMG in human wrist extensor muscles: physiological evidence of skeletofusimotor (beta) innervation. *Electroencephalogr Clin Neurophysiol* 109: 360–363, 1998. doi:10.1016/S0924-980X(98)00030-7.

Kakuda N, Nagaoka M. Dynamic response of human muscle spindle afferents to stretch during voluntary contraction. *J Physiol* 513: 621–628, 1998. doi:10.1111/j.1469-7793.1998.621bb.x.

Kakuda N, Vallbo AB, Wessberg J. Fusimotor and skeletomotor activities are increased with precision finger movement in man. *J Physiol* 492: 921–929, 1996. doi:10.1113/jphysiol.1996.sp021358.

Kakuda N, Wessberg J, Vallbo AB. Is human muscle spindle afference dependent on perceived size of error in visual tracking? *Exp Brain Res* 114: 246–254, 1997. doi:10.1007/PL00005633.

Kennedy WR. Innervation of normal human muscle spindles. *Neurology* 20: 463–475, 1970. doi:10.1212/WNL.20.5.463.

Kennedy WR, Poppele RE, Webster HF. Human muscle spindles: isolation from biopsy, physiologic activity, and fine structure. *Trans Am Neurol Assoc* 99: 126–129, 1974.

Knellwolf TP, Hammam E, Macefield VG. The vestibular system does not modulate fusimotor drive to muscle spindles in relaxed leg muscles of subjects in a near-vertical position. *J Neurophysiol* 115: 2529–2535, 2016. doi:10.1152/jn.01125.2015.

Kuffler SW, Hunt CC, Quilliam JP. Function of medullated small-nerve fibers in mammalian ventral roots; efferent muscle spindle innervation. *J Neurophysiol* 14: 29–54, 1951. doi:10.1152/jn.1951.14.1.29.

Lackner JR, DiZio P. Vestibular, proprioceptive, and haptic contributions to spatial orientation. *Annu Rev Psychol* 56: 115–147, 2005. doi:10.1146/annurev.psych.55.090902.142023.

Lajoie Y, Teasdale N, Cole JD, Burnett M, Bard C, Fleury M, Forget R, Paillard J, Lamarre Y. Gait of a deafferented subject without large myelinated sensory fibers below the neck. *Neurology* 47: 109–115, 1996. doi:10.1212/WNL.47.1.109.

Li S, Zhuang C, Hao M, He X, Marquez JC, Niu CM, Lan N. Coordinated alpha and gamma control of muscles and spindles in movement and posture. *Front Comput Neurosci* 9: 122, 2015. doi:10.3389/fncom.2015.00122.

Lund S, Pompeiano O. Descending pathways with monosynaptic action on motoneurones. *Experientia* 21: 602–603, 1965. doi:10.1007/BF02151558.

Macefield G, Gandevia SC, Burke D. Perceptual responses to microstimulation of single afferents innervating joints, muscles and skin of the human hand. *J Physiol* 429: 113–129, 1990. doi:10.1113/jphysiol.1990.sp018247.

Macefield G, Hagbarth KE, Gorman R, Gandevia SC, Burke D. Decline in spindle support to alpha-motoneurones during sustained voluntary contractions. *J Physiol* 440: 497–512, 1991. doi:10.1113/jphysiol.1991.sp018721.

Macefield VG. Physiological characteristics of low-threshold mechanoreceptors in joints, muscle and skin in human subjects. *Clin Exp Pharmacol Physiol* 32: 135–144, 2005. doi:10.1111/j.1440-1681.2005.04143.x.

Macefield VG. Discharge rates and discharge variability of muscle spindle afferents in human chronic spinal cord injury. *Clin Neurophysiol* 124: 114–119, 2013. doi:10.1016/j.clinph.2012.05.015.

Macefield VG, Gandevia SC, Bigland-Ritchie B, Gorman RB, Burke D. The firing rates of human motoneurones voluntarily activated in the absence of muscle afferent feedback. *J Physiol* 471: 429–443, 1993. doi:10.1113/jphysiol.1993.sp019908.

Macefield VG, Johansson RS. Control of grip force during restraint of an object held between finger and thumb: responses of muscle and joint afferents from the digits. *Exp Brain Res* 108: 172–184, 1996.

Macefield VG, Norcliffe-Kaufmann L, Gutiérrez J, Axelrod FB, Kaufmann H. Can loss of muscle spindle afferents explain the ataxic gait in Riley-Day syndrome? *Brain* 134: 3198–3208, 2011. doi:10.1093/brain/awr168.

Macefield VG, Norcliffe-Kaufmann LJ, Axelrod FB, Kaufmann H. Relationship between proprioception at the knee joint and gait ataxia in HSAN III. *Mov Disord* 28: 823–827, 2013. doi:10.1002/mds.25482.

Macefield VG, Sverrisdottir YB, Wallin BG. Resting discharge of human muscle spindles is not modulated by increases in sympathetic drive. *J Physiol* 551: 1005–1011, 2003. doi:10.1113/jphysiol.2003.040196.

Malik P, Jabakhanji N, Jones KE. An assessment of six muscle spindle models for predicting sensory information during human wrist movements. *Front Comput Neurosci* 9: 154, 2016. doi:10.3389/fncom.2015.00154.

Matthews PB. Muscle spindles and their motor control. *Physiol Rev* 44: 219–288, 1964. doi:10.1152/physrev.1964.44.2.219.

Matthews PB. The differentiation of two types of fusimotor fibre by their effects on the dynamic response of muscle spindle primary endings. *Q J Exp Physiol Cogn Med Sci* 47: 324–333, 1962.

Matthews PB, Stein RB. The regularity of primary and secondary muscle spindle afferent discharges. *J Physiol* 202: 59–82, 1969a. doi:10.1113/jphysiol.1969.sp008795.

Matthews PB, Stein RB. The sensitivity of muscle spindle afferents to small sinusoidal changes of length. *J Physiol* 200: 723–743, 1969b. doi:10.1113/jphysiol.1969.sp008719.

McKeon B, Burke D. Component of muscle spindle discharge related to arterial pulse. *J Neurophysiol* 46: 788–796, 1981. doi:10.1152/jn.1981.46.4.788.

McNulty P, Macefield V. Reflexes in the hand: strong synaptic coupling between single tactile afferents and spinal motoneurones. In: *Sensorimotor Control of Movement and Posture. Advances in Experimental Medicine and Biology*, edited by Gandevia SC, Proske U, Stuart DG. Boston, MA: Springer, 2002, vol. 508, p. 39–45. doi:10.1007/978-1-4615-0713-0_6.

McNulty PA, Galea V, Fallon JB, Bent LR, Macefield V. Low-threshold afferent signalling of viscous loads during voluntary movements of the human digits. *Neuroreport* 19: 1049–1054, 2008. doi:10.1097/WNR.0b013e3283036ea0.

McNulty PA, Macefield VG. Modulation of ongoing EMG by different classes of low-threshold mechanoreceptors in the human hand. *J Physiol* 537: 1021–1032, 2001. doi:10.1113/jphysiol.2001.012664.

Merton PA. Speculations on the servo-control of movement. In: *Ciba Foundation Symposium: The Spinal Cord*, edited by Malcolm JA, Gray JA. London: Churchill, 1953, p. 247–260.

Mountcastle VB, Powell TP. Central nervous mechanisms subserving position sense and kinesthesis. *Bull Johns Hopkins Hosp* 105: 173–200, 1959.

Nafati G, Rossi-Durand C, Schmied A. Proprioceptive control of human wrist extensor motor units during an attention-demanding task. *Brain Res* 1018: 208–220, 2004. doi:10.1016/j.brainres.2004.05.066.

Nielsen J, Nagaoka M, Kagamihara Y, Kakuda N, Tanaka R. Discharge of muscle afferents during voluntary co-contraction of antagonistic ankle muscles in man. *Neurosci Lett* 170: 277–280, 1994. doi:10.1016/0304-3940(94)90337-9.

Nordh E, Hulliger M, Vallbo AB. The variability of inter-spike intervals of human spindle afferents in relaxed muscles. *Brain Res* 271: 89–99, 1983. doi:10.1016/0006-8993(83)91367-7.

Ovalle WK, Smith RS. Histochemical identification of three types of intrafusal muscle fibers in the cat and monkey based on the myosin ATPase reaction. *Can J Physiol Pharmacol* 50: 195–202, 1972. doi:10.1139/y72-030.

Peters RM, Dalton BH, Blouin JS, Inglis JT. Precise coding of ankle angle and velocity by human calf muscle spindles. *Neuroscience* 349: 98–105, 2017. doi:10.1016/j.neuroscience.2017.02.034.

Poppele RE, Bowman RJ. Quantitative description of linear behavior of mammalian muscle spindles. *J Neurophysiol* 33: 59–72, 1970. doi:10.1152/jn.1970.33.1.59.

Poppele RE, Kennedy WR. Comparison between behavior of human and cat muscle spindles recorded in vitro. *Brain Res* 75: 316–319, 1974. doi:10.1016/0006-8993(74)90753-7.

Prochazka A. Sensorimotor gain control: a basic strategy of motor systems? *Prog Neurobiol* 33: 281–307, 1989. doi:10.1016/0301-0082(89)90004-X.

Prochazka A, Gorassini M. Models of ensemble firing of muscle spindle afferents recorded during normal locomotion in cats. *J Physiol* 507: 277–291, 1998a. doi:10.1111/j.1469-7793.1998.277bu.x.

Prochazka A, Gorassini M. Ensemble firing of muscle afferents recorded during normal locomotion in cats. *J Physiol* 507: 293–304, 1998b. doi:10.1111/j.1469-7793.1998.293bu.x.

Proske U. The mammalian muscle spindle. *Physiology (Bethesda)* 12: 37–42, 1997. doi:10.1152/physiologyonline.1997.12.1.37.

Proske U, Gandevia SC. The kinaesthetic senses. *J Physiol* 587: 4139–4146, 2009. doi:10.1113/jphysiol.2009.175372.

Proske U, Gandevia SC. The proprioceptive senses: their roles in signaling body shape, body position and movement, and muscle force. *Physiol Rev* 92: 1651–1697, 2012. doi:10.1152/physrev.00048.2011.

Proske U, Wise AK, Gregory JE. The role of muscle receptors in the detection of movements. *Prog Neurobiol* 60: 85–96, 2000. doi:10.1016/S0301-0082(99)00022-2.

Radovanovic D, Peikert K, Lindström M, Domellöf FP. Sympathetic innervation of human muscle spindles. *J Anat* 226: 542–548, 2015. doi:10.1111/joa.12309.

Ribot E, Roll JP, Vedel JP. Efferent discharges recorded from single skeletomotor and fusimotor fibres in man. *J Physiol* 375: 251–268, 1986. doi:10.1113/jphysiol.1986.sp016115.

Ribot-Ciscar E, Bergenheim M, Albert F, Roll JP. Proprioceptive population coding of limb position in humans. *Exp Brain Res* 149: 512–519, 2003. doi:10.1007/s00221-003-1384-x.

Ribot-Ciscar E, Bergenheim M, Roll JP. The preferred sensory direction of muscle spindle primary endings influences the velocity coding of two-dimensional limb movements in humans. *Exp Brain Res* 145: 429–436, 2002. doi:10.1007/s00221-002-1135-4.

Ribot-Ciscar E, Hospod V, Roll JP, Aimonetti JM. Fusimotor drive may adjust muscle spindle feedback to task requirements in humans. *J Neurophysiol* 101: 633–640, 2009. doi:10.1152/jn.91041.2008.

Ribot-Ciscar E, Roll JP. Ago-antagonist muscle spindle inputs contribute together to joint movement coding in man. *Brain Res* 791: 167–176, 1998. doi:10.1016/S0006-8993(98)00092-4.

Ribot-Ciscar E, Rossi-Durand C, Roll JP. Muscle spindle activity following muscle tendon vibration in man. *Neurosci Lett* 258: 147–150, 1998. doi:10.1016/S0304-3940(98)00732-0.

Ribot-Ciscar E, Rossi-Durand C, Roll JP. Increased muscle spindle sensitivity to movement during reinforcement manoeuvres in relaxed human subjects. *J Physiol* 523: 271–282, 2000. doi:10.1111/j.1469-7793.2000.t01-1-00271.x.

Ribot-Ciscar E, Tardy-Gervet MF, Vedel JP, Roll JP. Post-contraction changes in human muscle spindle resting discharge and stretch sensitivity. *Exp Brain Res* 86: 673–678, 1991. doi:10.1007/BF00230541.

Richmond FJ, Abrahams VC. Morphology and distribution of muscle spindles in dorsal muscles of the cat neck. *J Neurophysiol* 38: 1322–1339, 1975. doi:10.1152/jn.1975.38.6.1322.

Roll JP, Albert F, Ribot-Ciscar E, Bergenheim M. "Proprioceptive signature" of cursive writing in humans: a multi-population coding. *Exp Brain Res* 157: 359–368, 2004. doi:10.1007/s00221-004-1853-x.

Roll JP, Bergenheim M, Ribot-Ciscar E. Proprioceptive population coding of two-dimensional limb movements in humans: II. Muscle-spindle feedback during "drawing-like" movements. *Exp Brain Res* 134: 311–321, 2000. doi:10.1007/s002210000472.

Roll JP, Vedel JP. Kinaesthetic role of muscle afferents in man, studied by tendon vibration and microneurography. *Exp Brain Res* 47: 177–190, 1982. doi:10.1007/BF00239377.

Rothwell JC, Gandevia SC, Burke D. Activation of fusimotor neurones by motor cortical stimulation in human subjects. *J Physiol* 431: 743–756, 1990. doi:10.1113/jphysiol.1990.sp018357.

Rothwell JC, Traub MM, Day BL, Obeso JA, Thomas PK, Marsden CD. Manual motor performance in a deafferented man. *Brain* 105: 515–542, 1982. doi:10.1093/brain/105.3.515.

Rubin AM, Liedgren SR, Milne AC, Young JA, Fredrickson JM. Vestibular and somatosensory interaction in the cat vestibular nuclei. *Pflugers Arch* 371: 155–160, 1977. doi:10.1007/BF00580784.

Sahinen FM, Kennedy WR. Distribution of muscle spindles in the human first dorsal interosseus. *Anat Rec* 173: 151–155, 1972. doi:10.1002/ar.1091730204.

Severin FV, Orlovskiĭ GN, Shik ML. [Work of muscle receptors during controlled locomotion]. *Biofizika* 12: 502–511, 1967.

Spiro AJ, Beilin RL. Histochemical duality of rabbit intrafusal fibers. *J Histochem Cytochem* 17: 348–349, 1969. doi:10.1177/17.5.348.

Thornell LE, Carlsson L, Eriksson PO, Liu JX, Österlund C, Stål P, Pedrosa-Domellöf F. Fibre typing of intrafusal fibres. *J Anat* 227: 136–156, 2015. doi:10.1111/joa.12338.

Vallbo ÅB. Muscle spindle response at the onset of isometric voluntary contractions in man. Time difference between fusimotor and skeletomotor effects. *J Physiol* 218: 405–431, 1971. doi:10.1113/jphysiol.1971.sp009625.

Vallbo ÅB. Muscle spindle afferent discharge from resting and contracting muscles in normal human subjects. In: *New Developments in Electromyograpy and Clinical Neurophysiology*, edited by Desmedt JE. Basel: Karger, 1973, vol. 3, p. 251–262.

Vallbo AB. Human muscle spindle discharge during isometric voluntary contractions. Amplitude relations between spindle frequency and torque. *Acta Physiol Scand* 90: 319–336, 1974. doi:10.1111/j.1748-1716.1974.tb05594.x.

Vallbo AB, al-Falahe NA. Human muscle spindle response in a motor learning task. *J Physiol* 421: 553–568, 1990. doi:10.1113/jphysiol.1990.sp017961.

Vallbo AB, Hagbarth KE, Torebjörk HE, Wallin BG. Somatosensory, proprioceptive, and sympathetic activity in human peripheral nerves. *Physiol Rev* 59: 919–957, 1979. doi:10.1152/physrev.1979.59.4.919.

Vallbo AB, Hulliger M, Nordh E. Do spindle afferents monitor joint position in man? A study with active position holding. *Brain Res* 204: 209–213, 1981. doi:10.1016/0006-8993(81)90666-1.

van Gorp PE, Kennedy WR. Localization of muscle spindles in the human extensor indicis muscle for biopsy purposes. *Anat Rec* 179: 447–452, 1974. doi:10.1002/ar.1091790404.

Wessberg J, Vallbo AB. Human muscle spindle afferent activity in relation to visual control in precision finger movements. *J Physiol* 482: 225–233, 1995. doi:10.1113/jphysiol.1995.sp020512.

Wilson LR, Gandevia SC, Burke D. Discharge of human muscle spindle afferents innervating ankle dorsiflexors during target isometric contractions. *J Physiol* 504: 221–232, 1997. doi:10.1111/j.1469-7793.1997.221bf.x.