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Current Opinion in Physiology

Proprioception: clinical relevance and neurophysiology

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This review is intended for clinicians, therapists and researchers interested in proprioception and its role in kinesthesia and the control of movement. First, the neurophysiological basis of proprioception is summarized, identifying the sensory receptors involved and how their signals mediate the perception and control of bodily movement. Past and present hypotheses and the continuing uncertainties and controversies that surround them are outlined. Psychophysical experiments that have helped identify the contribution of proprioceptive receptors to kinesthesia in humans are briefly reviewed. The article then discusses proprioceptive deficits, what causes them, how they are treated and how proprioceptive acuity is assessed.

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Current Opinion in Physiology 2021, **21**:100440

This review comes from a themed issue on **Proprioception**

Edited by **Tim Cope** and **Leah Bent**

https://doi.org/10.1016/j.cophys.2021.05.003

INTRODUCTION

This article starts with an outline of the neurophysiology of proprioception as it relates to kinesthesia and sensorimotor control. It then covers aspects of proprioception of interest to clinicians, therapists and sports medicine practitioners. Busy clinicians may prefer to start with the clinical section, referring back to the basic neurophysiology when necessary.

THE NEUROPHYSIOLOGY OF PROPRIOCEPTION

Origins and definitions

In 1821 Charles Bell proposed that muscles contained sensory elements that contributed both to conscious sensation ("muscle sense") and to the subconscious, reflexive control of movement [1]. In 1907 Sherrington distinguished between outward-facing *extero-ceptive* receptors, such as cutaneous and visual receptors, that signaled stimuli exerted on the body by the environment, and inward-facing *intero-ceptive* receptors that sensed the organism's own internal actions. He coined the term "*proprio-ceptors*" for intero-ceptive receptors that sensed movement and position of body segments [2]. In the intervening years, it has become accepted that proprioception has both conscious and subconscious components, the latter mediating reflexive movements, as proposed by Bell. The conscious sense of *movement* is called kinesthesia [3,4••]. There is no specific word for the conscious sense of *position*, so position sense is sometimes included in the term kinesthesia. Similarly, there is no specific word for the conscious perception of force.

Conscious sensation: a moving target

Differentiating between conscious and subconscious movements, and deciding whether a movement is voluntary or involuntary, is not as straightforward as it may seem [5•]. An internal **"searchlight of attention"** has been proposed that determines whether something is, or is not, perceived [6,7]. Attention has been defined as the process of *selection* of the searchlight's target and consciousness as the ability to *report on* the target [8]. The reader can easily confirm the importance of attention in relation to proprioception simply by reaching forward. The arm movement is clearly voluntary and consciously perceived. Now reach forward but focus on sensations in your lower back and legs. Movements and forces are now perceived there, but whether to call them voluntary or involuntary may not be so obvious. In fact, anticipatory electromyographic activity starts in the back muscles before it does in the arm muscles. People with paralyzed back muscles often hook one arm behind their wheelchair before reaching out with the other arm, to prevent themselves from falling forward. This replaces the preparatory activation of their back muscles.

Proprioceptors: numbers and types

Receptors in the vestibular apparatus sense head movement and inclination, and by extension, body sway. Sherrington proposed that the vestibular apparatus was the leading segment of the proprioceptive system and the cerebellum was its "head ganglion" [2]. The proprioceptive role of the vestibular system is a large topic in itself, and beyond the scope of this article. Here we will focus on proprioception in the limbs, trunk and neck.

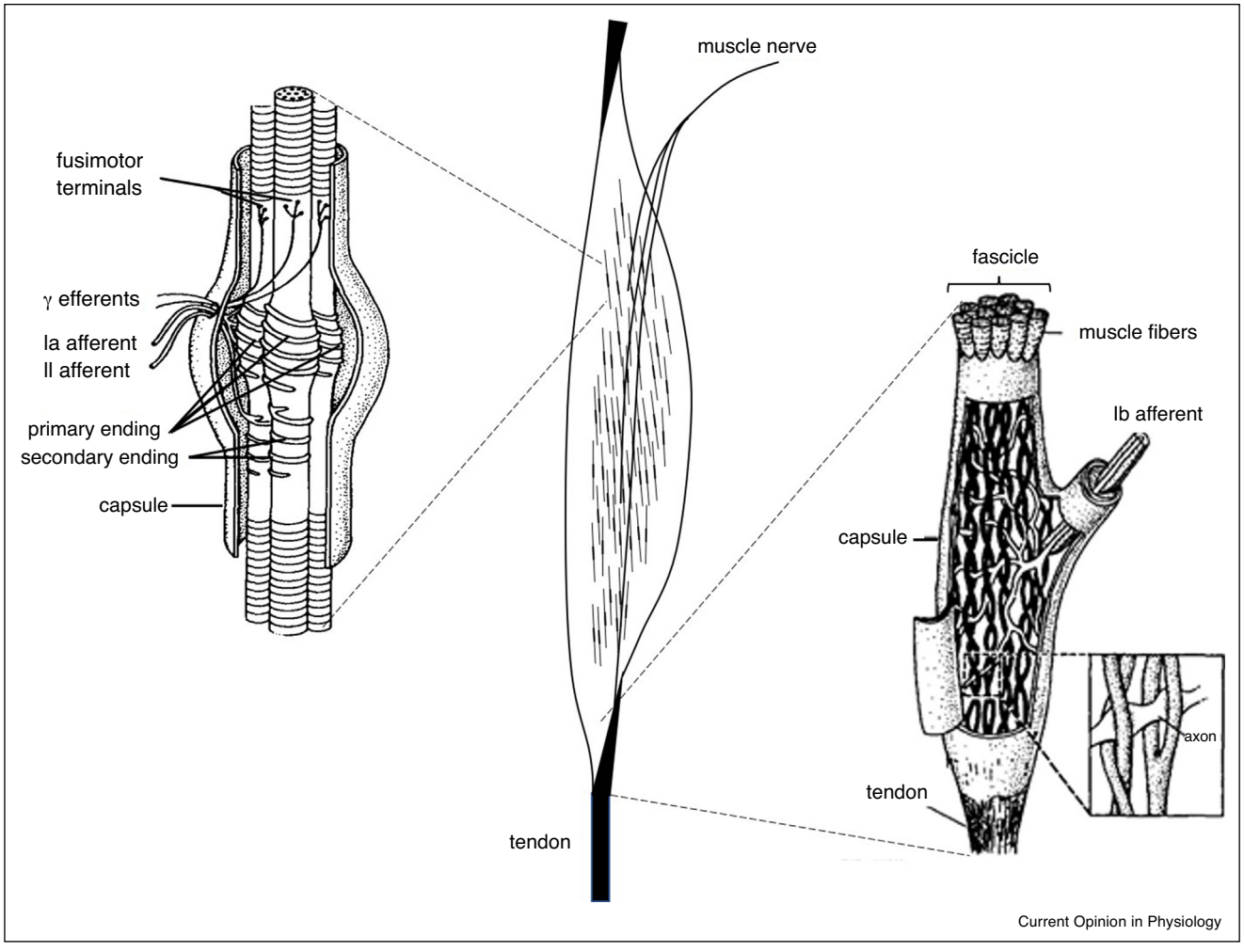
Stretch receptors in muscle, tendon and skin are the main candidates for the mediation of the sense of movement, position and force in the limbs, as evidenced by their response properties, the projections of their afferents in the CNS and by psychophysical experiments. Cutaneous

receptors were designated extero-ceptors by Sherrington, but experiments have shown that cutaneous receptors over and around joints respond to skin stretch during self-generated movement and stimulating them mechanically or electrically evokes movement sensations [9–11]. Consequently, it has become accepted that they have a significant role in proprioception. Stretch receptors within the muscle belly called muscle spindles are the prime candidates for mediating the conscious perception of limb movement and position [4••]. The ensemble of Golgi tendon organs (GTOs) innervating a muscle's tendon signals the force the muscle exerts [12,13]. Figure 1 shows schematics of a muscle, with details of its spindles and GTOs. Some receptors in joints, ligaments and deep fascia respond to limb movement and probably contribute to proprioception, but it is unclear to what extent [14–16]. Visual and cutaneous sensation can provide information on the position and movement of body parts both relative to each other and relative to surrounding objects (extra-personal space). On the above definitions, these are examples of extero-ception.

The human body contains about 30,000 muscle spindles [17] and, extrapolating from animal studies, nearly as many GTOs [18,19–21]. The sensory axons from muscle spindles are myelinated and rapidly conducting (group I and II: 30-120 m/s in cats, about half this in humans). Cutaneous receptors are more numerous: the human hand alone has about 17,000 myelinated cutaneous afferents [22].

Much of the work on the anatomy and functional properties of proprioceptors has been done in rats, cats and non-human primates. Comparative studies have indicated that broadly speaking, human proprioceptors are similar in structure, numbers and response properties

Figure 1



Middle: schematic of a cat soleus muscle with approximate positions of its spindles (based on data from [222]). Left: details of the capsular region of a muscle spindle (adapted from [223]). Right: details of a Golgi tendon organ, (adapted from Refs. [223,225]).

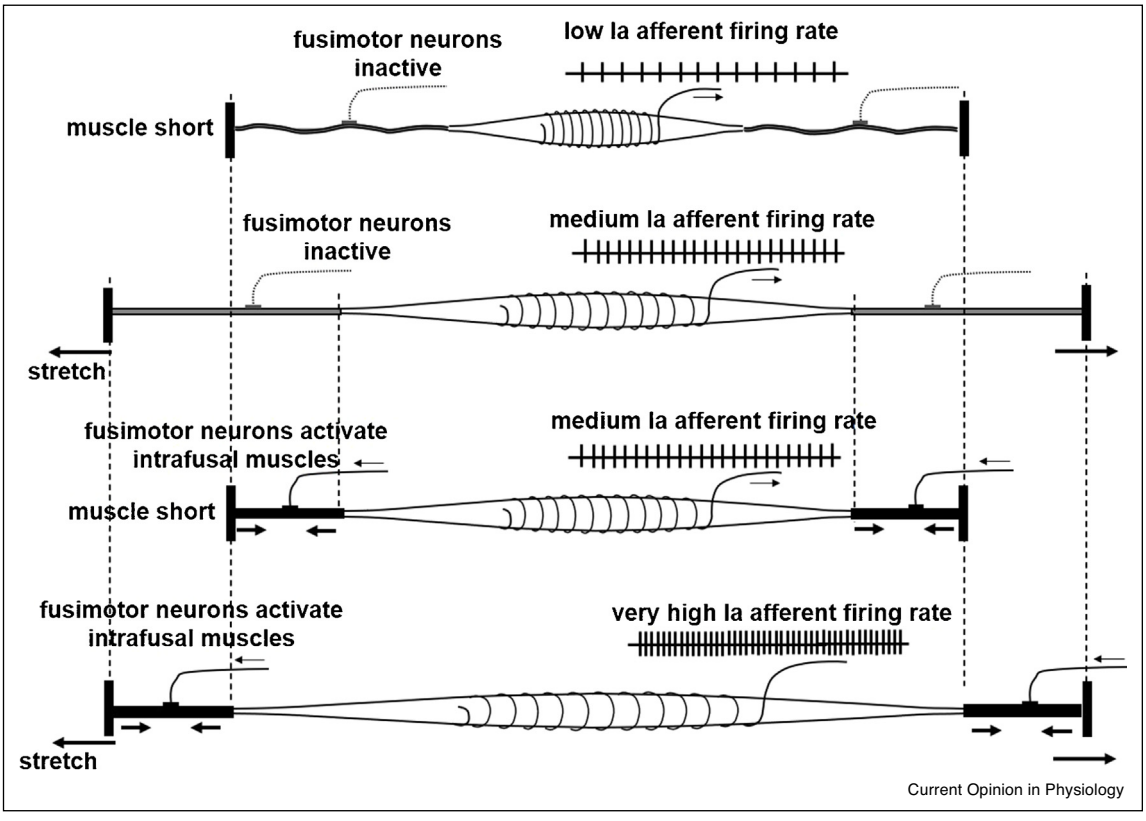
[23,24,25••,26,27]. The muscles in a cat contain a total of at least 30,000 nerve endings with slowly conducting myelinated afferents (Group III: <30 m/s) and over 60,000 unmyelinated afferents (group IV: <2.5 m/s) [28–30]. The group III and IV afferents include mechanoreceptors, nociceptors and thermoreceptors [31], most of which are unlikely to contribute directly to proprioception, though some joint receptors may do so directly [32], or indirectly through reflexive fusimotor drive to muscle spindles [33] (see below).

Muscle spindles

Human biceps and triceps brachii contain 320 and 520 muscle spindles respectively [25••]. With the caveat that muscles vary tremendously in muscle spindle density, on average, cat muscles contain 38*[cube root of mass in grams] spindles [34]. Thus, a 125-g muscle contains roughly 200 spindles. A typical muscle spindle (Latin: fusus) is 0.5-10 mm long and consists of 6 to 10 delicate *intrafusal* muscle fibres attached at each end to the surrounding force-producing *extrafusal* muscle fibres so as to be in parallel to them [20]. Intrafusal muscle contractions don't contribute measurably to the force produced by the extrafusal muscle. Rather, they modulate the sensitivity of the sensory endings.

A central, non-contractile region of the spindle, enclosed in a capsule, is innervated by 1 or 2 rapidly conducting (group Ia: 70-120 m/s in cats) axons terminating in *primary* sensory endings and 1 to 3 group II (30-70 m/s) axons terminating in *secondary* endings. The intrafusal muscle fibres are innervated by 10 to 12 small-diameter fusimotor neurons (Aγ conduction velocities: 15-55 m/s in cats compared to Aα motoneurons innervating extrafusal fibers: 50-100 m/s) [20]. In addition, intrafusal fibres in about one in three spindles are innervated by branches of α-motoneurons. In relation to proprioception, these α-motoneurons are called β-motoneurons, or skeletofusimotor neurons [35]. Most spindles contain three types of intrafusal muscle fibre. Broadly speaking, one type, activated by *dynamic* fusimotor neurons, greatly increases the stretch sensitivity of group Ia afferents [36,37], while

Figure 2



Effect of muscle stretch and fusimotor action on the firing of a muscle spindle primary (group Ia) afferent. A: spindle is short, intrafusal fibers are slack, sensory region is short, Ia firing rate is low. B: spindle is stretched, taking up intrafusal slack, sensory region elongates, so Ia firing increases. C: spindle is short, but fusimotor activity causes intrafusal muscle fibers to contract, stretching the sensory region, so Ia firing is similar to that in B. D: spindle is stretched as in B and fusimotor activity contracts intrafusal muscle fibers as in C. As a result, the sensory region is now stretched more than in A, B or C, so Ia firing is highest.

the other two types, activated by *static* fusimotor neurons, do this to a lesser extent, but they significantly increase the baseline firing rates of both group Ia *and* II afferents [29,38,39]. *Thus, in common with many other sensory systems, the CNS is able to adjust the responses of these proprioceptors, in this case by activating fusimotor neurons.*

What do spindle afferents signal?

Because a muscle spindle is attached in parallel to a short section of extrafusal muscle and is relatively very compliant, its length is determined by the length of the extrafusal muscle to which it is attached. In the absence of intrafusal muscle contraction, group Ia and II afferents respond to both length and its time derivative (velocity) of the extrafusal muscle. In this respect it could be likened to a small strain gauge that responds to strain in a metal surface. Velocity sensitivity is low in the smallest group II afferents and increases progressively to a maximum in the largest group Ia afferents [20,40]. Group Ia and II muscle spindle endings only "see" the length of the noncontractile section of the intrafusal fibre they innervate. The length of this section depends on the intrafusal tensile force [41•]. Stimulating a single static fusimotor neuron causes its intrafusal fibres to contract and shorten, thereby stretching the non-contractile region of the spindle and increasing the firing of the sensory endings [42]. In an extrafusal shortening contraction, static fusimotor drive can actively shorten intrafusal fibers, maintaining the length of the non-contractile region and thereby maintaining firing of the sensory endings [43]. Stimulating a dynamic fusimotor neuron stiffens its intrafusal muscle fibre so that when the spindle is stretched, much more of the length change is "seen" by the spindle primary ending [36,37]. Thus, through fusimotor action, the CNS can control both the background firing rate (also called "bias" or "offset") and the stretch sensitivity of spindle afferents. The schematic in Figure 2 shows how fusimotor drive activates intrafusal muscle fibers and changes the firing of the sensory afferents.

These properties were elucidated in detail in cats and primates [44,45]. Human muscle spindle afferents have a very similar anatomical structure, innervation and response properties, with the exception that the conduction velocities of their afferents are about half those in cats [26,27,46].

Fusimotor control in voluntary movement

It has proven very difficult to record from γ-fusimotor neurons in conscious animals and humans because of their small size. Hypotheses regarding fusimotor control have therefore relied either on recordings in decerebrate animals or inferences from spindle afferent firing. Several hypotheses emerged, starting with the *follow-up length servo hypothesis* [47]. This was soon replaced by the *servo-assistance hypothesis* (Matthews, 1970; Figure 2B). Here, it was posited that γ-fusimotor neurons were co-activated with α-motoneurons (*α–γ co-activation)* to maintain spindle afferent firing during shortening muscle contractions, as described above. It was further suggested that the fusimotor action might exactly compensate for the extrafusal shortening, except when this was impeded [29,48]. On this view, spindle afferents were misalignment detectors, only changing their firing rate when there was a disparity between expected and actual muscle length changes.

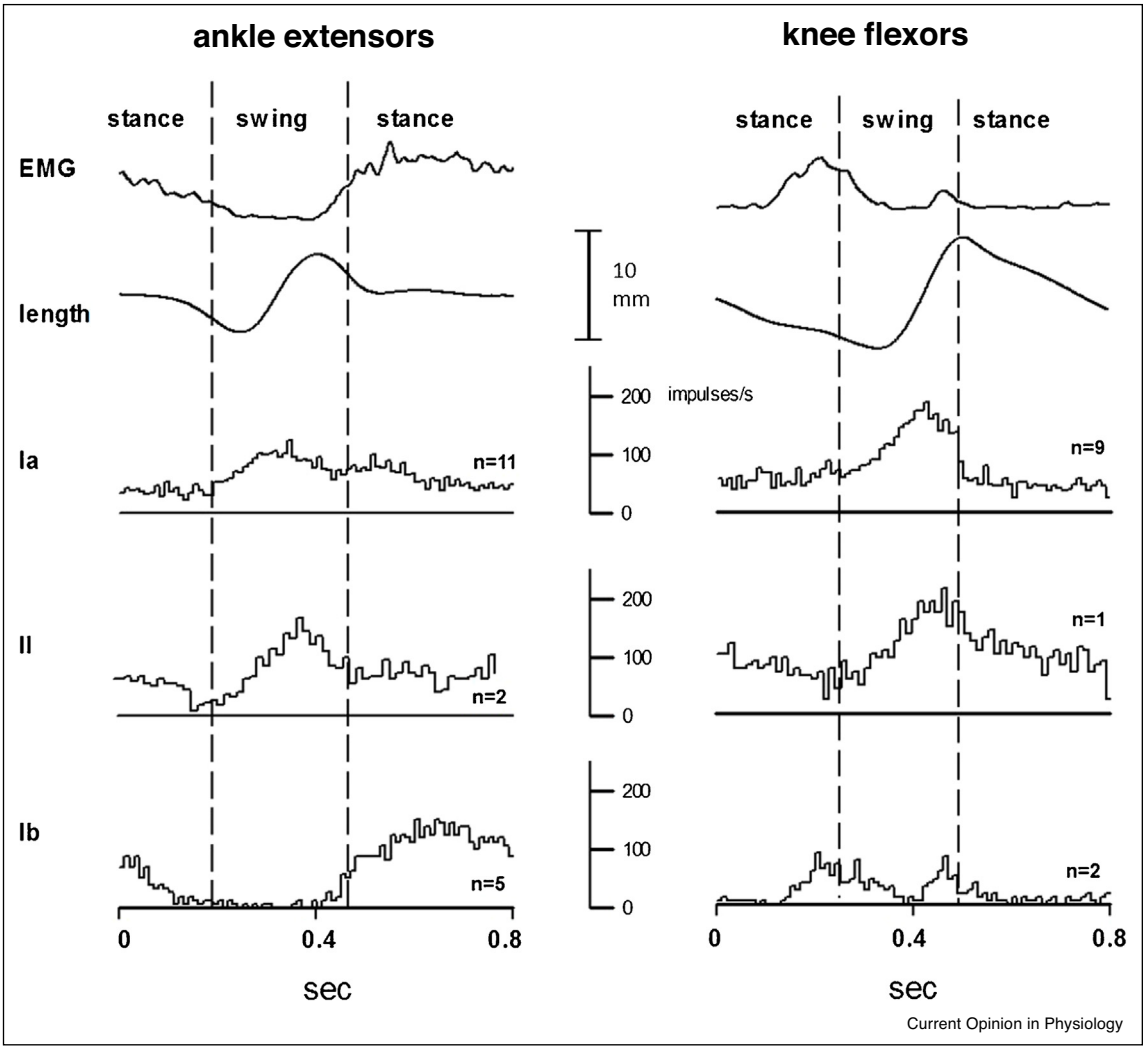
It should be mentioned that β-skeleto-fusimotor neurons, which innervate about one in three spindles, are α-motoneurons, and so their fusimotor action is linked to the activation of extrafusal muscle. α-motoneurons rarely fire above 30/s, compared to γ-motoneuronal firing rates of up to 200/s or more, so it is reasonable to assume that the effect on spindle afferent firing of β-skeleto-fusimotor neuron activity is relatively weak.

In the late 1960s the technique of human neurography was developed [49]. Semi-microelectrodes inserted through the skin into peripheral nerves of volunteers enabled the firing of individual sensory afferents to be recorded. The electrodes could be easily dislodged, so initially, only weak isometric contractions were studied. The firing of muscle spindle afferents always increased during such contractions, which lent strong support to the idea that the role of the fusimotor system was to maintain spindle afferent firing during extrafusal muscle shortening as outlined above.

However, with the advent of afferent recordings in awake animals performing a variety of unconstrained voluntary movements, it soon became apparent that spindle afferent firing was usually deeply modulated during muscle length changes [50–52]. Figure 3 shows the firing profiles of small ensembles of muscle spindle and Golgi tendon organ afferents during the locomotor step cycle. Spindle afferents did not usually fall silent during muscle shortening, indicating the presence of some co-activated fusimotor drive, but this was evidently weaker than the previous work had indicated. Furthermore, in movements that were novel or difficult, large increases in group Ia stretch-sensitivity were observed. This led to the hypothesis of *behavior-related fusimotor set*, whereby γ-motoneuronal drive was dialed up or down, independently of α–motoneuronal activity, according to the task and context [53]. In this regard it is worth noting that amphibia have muscle spindles whose only motor supply is in the form of β-skeleto-fusimotor neurons. γ-motoneurons evolved in mammals, which suggests that their function and modes of activation may differ from those of β-skeleto-fusimotor neurons and non-fusimotor α-motoneurons.

With increased vigilance, or when an animal prepared to make a series of movements, spindle afferent firing

Figure 3



Responses of small ensembles of muscle spindle group Ia and II afferents and Golgi tendon organ (GTO) afferents during normal locomotion in cats. Left: ankle extensors, right: knee flexors. The muscle spindle responses were related to muscle length and velocity, with small additional components related to the electromyographic (EMG) activity of the receptor-bearing muscles, consistent with biasing by alpha-linked fusimotor action. The GTO responses were closely correlated with the EMG, consistent with the signaling of muscle force. From [224].

tended to wind up to a new level, even when there was no measurable change in length or electromyographic activity of the receptor-bearing muscle. On the same note, in spindle afferent recordings in humans, task-dependent fusimotor effects on spindle afferent firing in the absence of extrafusal activity have been seen in various behavioral contexts [54–59]. It was suggested that these could "prepare the body for responsive and appropriate action to a change in environment", as previously suggested in the hypothesis of fusimotor set [58]. The effects seen in humans have been much smaller than those in cats, but this may be due to the constraints on movement and context in human neurography studies.

There is still no real consensus on how deeply the activity of γ-motoneurons is modulated during normal movements, how strong and inevitable is α–γ coactivation and whether context-dependent fusimotor set is a significant factor in humans. New proposals regarding fusimotor control continue to appear, including a predictive role [60,61]. The matter will only really be resolved if and when it becomes possible to record from γ-motoneurons in a range of voluntary movements and contexts. In the meantime, it seems reasonable to adopt the view that in normal behaviours, some fusimotor drive is α-coactivated and some is set to steady levels depending on the task [62,63].

Golgi tendon organs

GTOs are encapsulated receptors usually located at musculotendinous junctions [64]. Their sensory endings, leading to group Ib afferent axons, are entwined with the tendinous fibres of 10–20 motor units, a given motor unit affecting 1–6 tendon organs [65,66]. GTOs do not have an equivalent of the fusimotor system. They signal the force generated by their handful of motor units [67,68]. Individual GTOs signal increasing muscle force with steps in firing rate as successive motor units are recruited, but the ensemble firing rate of several GTOs signals whole muscle force [69,70].

Cutaneous Receptors

Slowly adapting (SA) cutaneous receptors over and around limb joints respond to skin stretch, with firing rates that are a function of joint angle and joint angular velocity [11,71–74]. Those best suited to signal joint angle are SA type II receptors (SAII). SA type I receptors (SAI) respond more locally, fire less regularly and adapt more rapidly. In addition, there are at least four kinds of hair follicle and glabrous skin receptors which respond to hair deflection or skin stretch [75]. The location and orientation of cutaneous receptors determine their "preferred direction of firing" i.e. the direction of joint movement to which they respond best [71,76]. Stimulating cutaneous afferents mechanically or electrically can produce movement illusions [9,11]. Anesthetizing them reduces kinesthetic acuity [77].

Joint receptors

Most joint receptor afferents signal the extremes of joint angle [78,79]. Some may signal in the mid-range [32,80–84] but it has been argued that these afferents are actually muscle receptors near the joints [85–87]. Loading of the joint capsule may be necessary for mid-range responsiveness [88]. Most joint afferents have weak polysynaptic connections with alpha motoneurons [33], their role possibly being to inhibit motoneurons when joints are damaged [89].

Mathematical models

Numerous models of the response properties of mechanoreceptors have been published (reviewed in: [41•,62]). They range from simple transfer functions with one or two free parameters, to neuromechanically-based models with 20 or more parameters. The choice of which model to use depends on the purpose. If the aim is to predict the responses of individual receptors, including nonlinearities such as stochastic variability in firing and initial bursts, complex models are likely to be more accurate. If the aim is to predict ensemble afferent input to the CNS from a population of receptors, modelling such nonlinearities can actually be counter-productive. This is because CNS neurons integrate the inputs from many receptors. This "washes out" variability and asynchronous responses of individual receptors. Simpler models may therefore paradoxically be more accurate for such applications. Given the complexities, the reported r^2 values of fits to experimental data for most of the models have been surprisingly good, generally exceeding 0.8 and in some cases 0.9 [62].

How does one decide on the accuracy required? Again, this depends on the purpose. For example, the gain of length and force feedback in spinal stretch reflexes is probably quite low because of the sluggish responses of load-moving muscles [90,91]. These reflexes therefore probably contribute quite modestly to load compensation [92] and r^2 values of 0.9 in predicting ensemble afferent signals may suffice (i.e. a higher accuracy would make little difference to predictions of load compensation). On the other hand, the timing of locomotor phase transitions may rely on precise information on the position and velocity of a limb [93,94], so a higher accuracy in predicting afferent input may be needed.

Regarding muscle spindle models in particular, the major issue is the lack of consensus to this day on the way fusimotor activity is modulated during normal movement. If fusimotor drive remains fairly constant during movements [53], or if a component of fusimotor drive is co-activated with α-motoneuronal activity, the fusimotor contribution to spindle afferent firing can be modelled by adjusting one or two parameters in the simpler models [63]. If fusimotor activity is highly modulated but well characterized, as is possible in decerebrate locomotor experiments [61,95], the more complex models may be more reliable, at least for single receptors (e.g. [41•,96]). At this point the jury is out as to whether fusimotor activity is indeed deeply modulated or relatively steady in conscious, normally behaving animals, including humans. Regarding the role of GTOs, recent modelling has indicated that a combination of spindle and GTO afferent input could provide an estimate of muscle-tendon length, for low-level feedback during postural and movement tasks [97].

Psychophysics

Numerous innovative psychophysical studies of proprioception have been performed since the 1970s. There are several excellent recent reviews of these studies [4••,15,98•,99••]. The following is a list of the key conclusions and hypotheses.

1 Muscle spindles and cutaneous receptors are largely responsible for human kinesthesia and position sense [100].
2 The contribution of joint receptors remains controversial. They may signal position near the limits of joint movement [98•,101,102].
3 There is some evidence that both muscle spindles and GTOs mediate the perception of force and effort [103].

4 Copies of motor commands may be combined in supraspinal areas with signals from proprioceptors to generate the consciously perceived sense of position and movement [99••].
5 Proprioception can be disturbed by exercise and fatigue [98•].
6 Proprioceptive acuity declines with age [99••], though the amount of decline may not be as large as previously suggested [104]
7 Proprioception is concerned with both the relative positions of the body and its parts and the position of the body and limbs in external space [105].

Two interesting properties of muscle spindles have been useful in identify their contribution to proprioception in humans [4••]. The first is the selective sensitivity of muscle spindle group Ia afferents to **vibration** [106]. Pioneering experiments fifty years ago showed that tendon vibration elicited kinesthetic illusions [107•,108]. This reinstated muscle spindles as contributors to kinesthesia. Vibration has been used ever since in psychophysical studies of proprioception.

The second property, which is common to both intrafusal and extrafusal muscle, is ***"thixotropy"***, also known as "*stiction*" [109]. Stable cross-bridges develop in resting intrafusal muscles, which stiffens their contractile regions on either side of the central non-contractile sensory region. When the spindle is first stretched, the sensory region briefly "sees" more of the stretch and this causes a brief initial burst of Ia afferent firing [40]. Continued stretch or fusimotor drive releases the "stuck" cross-bridges [110], so in daily life the effect is probably restricted to the first movement after a period of complete rest. However, thixotropy is important, not only because it has provided convincing evidence that spindles contribute to proprioception, but also because it affects clinical tests of proprioceptive acuity (see above).

There are two unresolved problems regarding the spindle contribution to kinesthesia. First, there is evidence that during normal movement, tendons of phasically contracting muscles can absorb some of the origin-to-insertion length change. This can distort the relationship between muscle length and spindle afferent firing [111–115].

Second, modulations in fusimotor drive interact with muscle length changes to modulate spindle afferent firing. This means that spindle afferents signal some combination of movement ***and*** fusimotor drive. How does the CNS extract just the movement and position components it needs for kinesthesia? This has bothered neurophysiologists for many years. One suggestion is that the fusimotor command is sent as an efference copy signal to the cerebellum where it is subtracted from the incoming afferent signal [99••,116,117]. It was acknowledged that this would not be a straightforward process, given the complex nonlinearities involved. Artificial neural networks that "learn" to associate multiple inputs with multiple outputs may provide a further clue [118]. It is conceivable that over hundreds of the thousands of movements that take place during the acquisition of motor skills, the cerebellum "learns" to separate the kinesthetic components of spindle afferent input from the fusimotor components, either with or without explicit efference copy. Another idea, that would ignore fusimotor action co-activated with α-motoneuronal activity, is that only the signals from the inactive antagonist muscle reach consciousness [119••].

In spite of these problems, the time course of limb joint angles during normal locomotion has been inferred reasonably accurately from the firing rates of a handful of muscle and cutaneous afferents using linear algebraic algorithms [120,121]. Analysis showed that muscle spindle afferents provided the most information in this regard. Recordings from spinocerebellar tract neurons suggest that they integrate inputs from limb proprioceptors to encode the movement and position of the endpoint of the whole limb, for example the paw or hand [122–124].

Before concluding this section, it is worth mentioning the interesting work in recent years on the centrally generated sense of effort, the sense of agency, the effects of exercise, fatigue and low gravity and the distortions in proprioception that can occur in phantom limbs. These issues are beyond the scope of this article and the reader is referred to recent excellent reviews [4••,98•,99••].

Proprioception in sensorimotor control

In the absence of sensory input to its motoneurons, a steadily activated muscle resists stretch [125]. This intrinsic property of muscles provides the first level of feedback control, or load compensation. At the next level, proprioceptive signals are fed back to spinal α- and γ-motoneurons, spinal interneurons and supraspinal centers for more complex, context-dependent control of movement. The shortest-latency and most direct reflex action is the monosynaptic excitation of α-motoneurons of their own muscle by group Ia afferents. In longer latency responses, spinal interneurons receiving input from spindle group Ia, II and GTO Ib afferents excite or inhibit α-motoneurons, depending on the muscles involved, task and context. Proprioceptive input to the brain results in long-latency responses, the early components being reflex-like "triggered reactions" [126] and the later components being more varied and "volitional" [127,128]. Thus, prior instruction to subjects either to resist an imposed movement applied to the arm or to "let go", has a large and functionally selective effect on these longer-latency EMG responses [129,130].

It is interesting that people with spastic hypertonus or Parkinson's disease exhibit long-latency reflexes, but are

often unable to adjust them voluntarily. This recalls Bernstein's [131] description of motor learning: " when someone who is a novice at a sport, at playing a musical instrument or at an industrial process, first attempts to master the new coordination, he is rigidly, spastically fixed and holds the limb involved, or even his whole body, in such a way as to reduce the number of kinematic degrees of freedom which he is required to control" [132].

The timing of flexion-extension phase transitions by the spinal central pattern generator for locomotion is influenced by proprioceptive input. The above spinally-mediated reactions are rapid and can proceed in the absence of supraspinal centers, so they are considered involuntary responses. Proprioceptive input to supraspinal centers contributes to the control of more complex movements, for example, task-related movements of the arms and hands.

For many years GTO input was thought reflexly to inhibit the receptor-bearing muscle. This is equivalent to negative feedback control of *force*. It was therefore a great surprise when experiments indicated that GTO input from extensor muscles synaptically *facilitated* homonymous motoneurons during fictive locomotion [133]. This is equivalent to *positive* force feedback, which is avoided by control systems engineers, as it is associated with instability. However, subsequent analysis showed that muscle length-tension properties act to keep the gain of positive force feedback below the level that causes instability [90]. GTO-mediated positive force feedback may play a major role in the control of the stance phase of the locomotor step cycle [134–136]. Here, the positive force feedback gain may briefly exceed the unstable level during each load-bearing stance phase, for example in sprints or hops.

Proprioceptive control of locomotion

There is evidence in quadrupeds for a central pattern generator (CPG) for locomotion in the spinal cord [137,138]. The CPG has been posited to comprise separate components controlling the timing of locomotor phase transitions and the activity of selected groups of muscles [139]. The CPG acting without sensory input would generate a fixed sequence of alternating stance and swing phases without adjusting to postural drift or changes in the terrain. This can quickly lead to falls, as shown in modeling studies [94,140]. The addition of stretch reflexes and rules that overrode the CPG-generated pattern by triggering phase transitions when the limb reached a specific point of extension, was indispensable for stable stepping in these models.

Long-loop reflexes

Long-latency components in electromyographic responses to muscle stretch have been ascribed to pathways to the motor cortex and back [127]. They are usually larger and of longer duration than short-latency stretch reflex responses, contributing more to load compensation. They are commonly referred to as long-loop stretch reflexes, but they can be suppressed voluntarily. A recent study concludes: 'Neural activity occurring within the period normally ascribed to the long-latency stretch reflex is highly adaptable to current task demands and possibly should be considered more intelligent than "reflexive"' [141].

Finally, it should be stressed that vestibular proprioceptive input plays a major role in posture and locomotion. Vestibular input combines with proprioceptive input from the limbs, trunk and neck to maintain stability in posture and perception [142•].

CLINICAL INTEREST IN PROPRIOCEPTION

Testing proprioception

In a common bedside neurological test of *consciously perceived* proprioception, the subject is asked, with eyes closed, to identify the direction of a movement applied to the index finger or big toe. Alternatively, the subject may be asked to match the imposed movement with a subsequent active movement of the same extremity or the corresponding contralateral extremity. If sensation is found to be absent at distal joints, a rigorous tester may then apply movements to more proximal joints where kinesthetic sensitivity is superior [99••,143–147].

It has been argued that the sense of *movement* differs from that of *static position* and that they should therefore be tested separately [148–150]). In practice, clinicians move the subject's extremity rapidly from one position to another and immediately ask the subject whether he or she sensed a change. This doesn't allow movement and position sense to be separated. Furthermore, the length and activity of muscles prior to testing influences detection thresholds because of *stiction* effects in muscle spindles (see below [99••]). Testing should only be performed after specific pre-conditioning, but this is not widely known or practiced [4••,143].

To test *proprioceptive control*, subjects may be asked to stand still for 30 seconds with eyes closed. Body sway is qualitatively rated, on the assumption that balance control under these circumstances relies heavily on proprioceptive input from the ankles and hips [151,152]. Other tests involve responses to imposed muscle stretch. The simplest is the tendon jerk, in which a rapid stretch is applied to muscles by tapping a tendon with a tendon hammer [153]. The stretch evokes a burst of activity in muscle spindle afferents that reflexly activates spinal α-motoneurons innervating the stretched muscles via the monosynaptic reflex arc mentioned above. Qualitative judgements of the size of tendon jerk responses are used in the diagnosis of a variety of neurological disorders [153].

In another approach, the resistance to movement applied about the ankle, knee, wrist or elbow joints is assessed. The responses are rated according to the Modified Ashworth Scale (MAS) [154] or the Tardieu scale [155,156] for spastic hypertonus and the Unified Parkinson's Disease Rating Scale (UPDRS) for parkinsonian rigidity [157]. MAS and UPDRS ratings are often used to guide treatment strategies, but their inter-rater and test-re-test reliability depend on how the tests are performed and the testers' training and experience [158,159••]. The correlation between such ratings and quantitatively measured mechanical variables is poor [160].

Devices have been designed in an attempt to quantify and standardize some of the above tests, but so far they have not been widely adopted [156,161,162]. What is needed are simple, hand-held devices that measure applied forces and movement and provide the clinician with one or two key indices of impairment. It would be crucial for standardization to provide clear instructions on testing protocols. To encourage clinical acceptance, it would be advisable to express these indices in terms of scales familiar to clinicians, such as the MAS and UPDRS, at least initially.

Deafferentation

In animals deprived of proprioceptive input from the legs, locomotion is initially completely uncoordinated [163]. Intense training can restore locomotion after chemical deafferentation, but adaptative responses to uneven terrain remain permanently absent [164]. Voluntary control of movement is severely impaired in humans who have lost limb proprioception but can improve with training and conscious attention [165]. If neck proprioception is also lost, locomotion becomes virtually impossible [166].

Spastic hypertonus

Motoneurons deprived of their descending input, e.g., after stroke or spinal cord injury, become increasingly sensitive to proprioceptive afferent input evoked by muscle stretch. This leads to spastic hypertonus which is characterized by tonic muscle activity, contractures and increased resistance to muscle stretch, resulting in a decreased range of motion and abnormal limb postures [167•,168]. Increased spindle stretch sensitivity through elevated fusimotor drive (see above) was implicated in hypertonus in the 1960s and this led to the clinical use of lidocaine or phenol to block fusimotor neurons in peripheral nerves. However, human neurography studies have failed to find evidence of increased fusimotor drive in people with spastic hypertonus [169–171] so this theory has been abandoned [172]. The more likely mechanisms of spastic hypertonus include the withdrawal of descending presynaptic inhibition of proprioceptive afferents [173], increased sensitivity of the motoneuronal membrane to synaptic input [174,175] and changes in the protein structure of muscle fibers, leading to contractures and increased stiffness [176••].Treatment of spastic hypertonus includes muscle stretching (see below), paralyzing muscles with Botox, or reducing synaptic drive to interneurons and α-motoneurons from proprioceptive afferents with antispastic drugs (diazepam, baclofen, tizanidine [177,178]). However, many people living with spastic hypertonus rely on the load compensation it provides to stand and walk [179]. Paradoxically, reducing hypertonus with drugs may therefore degrade some aspects of voluntary movement. Because of this, it has been suggested "that antispastic therapy should be given with care in patients with only mild to moderate spasticity and reasonably preserved functionality" [172].

Arthritis and ageing

A study of proprioceptive thresholds in the elderly concluded that: "Proprioception declines with age, and is further impaired in elderly patients with knee osteoarthritis. Poor proprioception may contribute to functional impairment in knee osteo-arthritis" [180,181]. A study in old rats showed that muscle spindle primary endings underwent drastic age-related morphological changes and their stretch-responses became indistinguishable from those of muscle spindle secondary endings [182]. Spindle secondary endings respond mainly to muscle length (*position*), while spindle primary endings respond to both muscle length and the rate of change of muscle length (*movement*) [183]. Taking these results together, one might conclude that the elderly have relatively greater deficits in the perception of movement than position. However, a recent study indicates that both movement and position sense in elderly, healthy humans, are surprisingly well preserved [104].

Tremor

The spinal and transcortical reflex loops mediated by muscle spindle afferents are feedback loops with delays and phase lags resulting from nerve conduction and muscle contraction. Delays and phase lags in feedback loops result in oscillatory instability when the loop gain exceeds a certain threshold [184]. Human tremors are oscillations that range from relatively high-frequency (8-12 Hz) "physiological tremor" to a wide variety of pathological tremors in the 2-8 Hz range, the most common being essential tremor, parkinsonian tremor and cerebellar tremor [185]. It is the prevailing view that whereas physiological tremor may be due to instability in the proprioceptive stretch reflex pathways [173,184], pathological tremors at the lower frequencies are generated largely from within the CNS [186]. However, 4-6 Hz tremor can be provoked in neurologically normal people by artificially increasing the proprioceptive reflex loop gain, suggesting that if a pathological disorder elevated the sensitivity of reflex pathways, they could cause or facilitate 4-6 Hz tremor [187]. A comprehensive review in 2000 discussed the known oscillatory loops within the CNS that might generate pathological tremor and the

possibility that peripheral reflex pathways, especially those with long delays, could facilitate these oscillations [188]. A recent study in people with Parkinson's disease supports this idea [189].

Muscle stretching and "proprioceptive neuromuscular facilitation"

It has been standard practice in motor rehabilitation for many years to apply slow and maintained ("static") stretch or rapid ("ballistic") stretch to muscles whose range of motion is reduced, for example, in spastic paralysis, or in healthy people in the course of yoga, or in preparation for sporting activity [190]. In the late 1940s, passive stretching was expanded to include voluntary contractions of the target muscles or their antagonists [191,192]. The premise, which was based on the available neurophysiology, was that this would activate proprioceptors in the target muscles as well as their antagonists, to reflexly inhibit the target muscles, making them more compliant. The method was named proprioceptive neuromuscular facilitation (PNF). Over the years, philosophical components were added and the method became widely taught and practiced [193]. Systematic reviews have evaluated the efficacy of static and ballistic stretching and PNF in health [144,195] and disease [193,196–199]. The reviews all commented on a lack of standardization in the studies surveyed but concluded that on balance, the evidence indicated that passive stretching and PNF can increase the range of motion of target muscles. PNF may improve flexibility more than passive stretching alone [198], but interestingly, it can reduce performance in athletes if performed shortly before explosive movements [194,195].

Four mechanisms have been proposed for the effects of PNF: autogenic and reciprocal inhibition, mechanical lengthening of the target muscles and tendons, and increased tolerance of the discomfort elicited by stretch [198]. When a muscle is stretched, this activates its spindle primary afferents, which reflexly excite the muscle's α-motoneurons (autogenic excitation). This can double the stiffness of the muscle, reducing its range of motion [200]. Autogenic and reciprocal inhibition, which act in opposite directions, were posited to reduce the net synaptic excitation of α-motoneurons of target muscles in PNF.

Autogenic inhibition mediated by GTO afferents was proposed at a time when GTOs were thought to function as overload protectors, firing at the extremes of muscle stretch and synaptically inhibiting the α-motoneurons of the active muscle. It was later found that GTOs signal muscle force throughout the physiological range [67]. More importantly, GTO-mediated reflex inhibition of homonymous muscles turned out to be relatively weak [201] and could even reverse, to become excitation, at least during locomotion [135]. This makes GTO-mediated inhibition a questionable mechanism of PNF [198]. Mechanisms remaining in contention include reciprocal inhibition (mediated by spindle afferents from antagonist muscles), presynaptic inhibition (mediated by interneuronal and descending pathways [173]), mechanical sarcomere lengthening [190] and increased stretch tolerance [202].

Proprioceptive training

Deficits in proprioception resulting from pain, fatigue, intense exercise, swollen joints, musculoskeletal trauma and neuropathies are associated with deficits in motor control, increased co-morbidity and an elevated risk of injury [98•,143,147]. Proprioceptive training has become widely practiced and promoted by rehabilitation and sports medicine practitioners, on the assumption that proprioception can be improved by training, and this will in turn improve sensorimotor control. A recent systematic review provides qualified support for this view, while pointing out the wide variety of interventions, outcome measures and results in the studies evaluated [203]. The authors state that terminological clarity is "dearly needed" when it comes to the interpretation of what is meant by proprioceptive training. The following definition is proposed: "Proprioceptive training is an intervention that targets the improvement of proprioceptive function, focusing on the use of somatosensory signals such as (those from) proprioceptive or tactile afferents in the absence of information from other modalities such as vision. Its ultimate goal is to improve or restore sensory and/or sensorimotor function." The authors also addressed the question of mechanism, namely, does proprioceptive training induce actual changes in the peripheral or central nervous system that could account for the functional improvements? Of the few studies that have been done in this regard, most have been short-term, comparing measurements such as cortical evoked potentials or changes in brain images before and after training on the same day. What is clearly needed is well-designed studies comparing sensorimotor function before and after weeks or months of regular proprioceptive training in different groups of participants.

Pain management

Billion dollar industries have developed around transcutaneous electrical nerve stimulation (TENS), intramuscular stimulation (IMS) and spinal cord stimulation (SCS) to relieve pain [204••,205]. The mechanism usually proposed is the *Gate Theory of Pain*, namely the inhibition of transmission of nociceptive signals to the brain by intense activation of sensory afferents either around the painful site or at remote "trigger points" [206–209]. Muscle spindle and GTO afferents have the largest axons and lowest thresholds to electrical stimulation of any nerve fibers in the mammalian body, so it follows that proprioceptive input may partly mediate the effects of TENS, IMS and SCS. A common reaction to a painful event such

as hitting one's thumb with a hammer is to shake one's arm vigorously even before pain is felt. The shaking elicits proprioceptive signals which reach the spinal cord before the nociceptive activity. According to the Gate Theory, this activity would inhibit nociceptive transmission.

Massage has been used for centuries to relax and alleviate pain in tense or "knotted" muscles by applying strong pressure to them. The "knots" that melt away with massage are presumably parts of muscles that have been tense (tonically active) for some time. Muscle blood flow reduces at surprisingly low levels of sustained muscle contraction, causing a build-up of metabolites that in turn cause fatigue and pain [210]. The neurophysiological mechanism by which massage relaxes the "knots" and reduces pain is unclear. One possibility is that GTO afferents reflexly inhibit the tonically active α-motoneurons. However, this notion stemmed from the idea that GTOs only signaled extremes of muscle force, acting as overload protectors. In fact they signal force through the entire physiological range [67,211–213]. Muscle spindle afferents reflexly *facilitate* rather than inhibit the α-motoneurons of the receptor-bearing muscles. Furthermore, though muscle stretch and vibration, which are potent means of activating muscle spindle afferents, can increase flexibility and range of motion, as discussed above, they do not in general relax tensed muscles as effectively as massage. On the other hand, group III muscle receptors, many of which terminate in free nerve endings, respond to firm muscle squeezing and kneading [29,214]. Group III and IV muscle afferents have been implicated in the clasp-knife response, the sudden relaxation of active muscles in spastic hypertonus [28,215–218]. Though some group IV afferents respond to deep pressure, most signal painful stimuli, which elicit withdrawal responses rather than generalized inhibition of tonically-active muscles [219]. On balance therefore, of the various candidates, group III and some group IV mechanoreceptive afferents are the most likely to mediate the relaxing effect of massage, though input from proprioceptive afferents may facilitate the effect.

Acupuncture

It has been proposed that the twirling of a "dry" acupuncture needle within a tensed portion of muscle "catches" portions of the muscle and activates muscle spindles in the region; the spindle afferent input to the CNS then supposedly reflexly relaxes the muscle [220,221]. This explanation seems unlikely for several reasons. First, in the present author's experience, muscle spindle afferents respond weakly if at all to movements of an intramuscular needle. Second, electrical stimulation through an intramuscular needle activates extrafusal muscle, unloading spindles. This causes a *reduction* in firing in spindle afferents rather than an increase in firing [29]. Third, given the reflex actions described above, it seems unlikely that spindle afferent input could explain the relaxing effects of acupuncture. On balance it seems more likely that the effect is mediated by group III and IV afferents, including deep pressure and nociceptive afferents, which are activated by the acupuncture needle, whether it is twirled around, or whether it is used to deliver electrical stimuli (IMS).

CONCLUSIONS

Proprioception is crucial for the conscious perception of movement and position of the body segments. It is also crucial for the control of bodily movement. Proprioceptive deficits occur in a number of neurological disorders and after fatiguing exercise. To some extent these deficits can be rectified by exercises designed to challenge proprioceptive perception and motor control. The testing of proprioception remains largely qualitative and highly variable between examiners. What is needed is simple, hand-held devices that measure applied forces and movement and provide the clinician with one or two key indices of impairment. Much is known about the receptors that generate proprioceptive signals, but there remain some fundamental questions about how the CNS decodes these signals and how it integrates them into motor commands. Unresolved issues include the way the CNS controls fusimotor activity during normal movement, the way the CNS extracts the components of movement and position from muscle spindle signals that have been modulated by fusimotor action and the way proprioceptive input is used in CNS networks controlling movement.

Author's statement

The author has no competing interests. The work has not been published previously, it is not under consideration for publication elsewhere, and if accepted, it will not be published elsewhere in the same form.

The author did not receive financial support for the preparation of this review article

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

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