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THE PROPRIOCEPTIVE SENSES: THEIR ROLES IN SIGNALING BODY SHAPE, BODY POSITION AND MOVEMENT, AND MUSCLE FORCE

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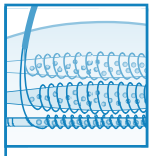


Proske U, Gandevia SC. The Proprioceptive Senses: Their Roles in Signaling Body Shape, Body Position and Movement, and Muscle Force. *Physiol Rev* 92: 1651–1697, 2012; doi:10.1152/physrev.00048.2011.—This is a review of the proprioceptive senses generated as a result of our own actions. They include the senses of position and movement of our limbs and trunk, the sense of effort, the sense of force, and the sense of heaviness. Receptors involved in proprioception are located in skin, muscles, and joints. Information about limb position and movement is not generated by individual receptors, but by populations of afferents. Afferent signals generated during a movement are processed to code for endpoint position of a limb. The afferent input is referred to a central body map to determine the location of the limbs in space. Experimental phantom limbs, produced by blocking peripheral nerves, have shown that motor areas in the brain are able to generate conscious sensations of limb displacement and movement in the absence of any sensory input. In the normal limb tendon organs and possibly also muscle spindles contribute to the senses of force and heaviness. Exercise can disturb proprioception, and this has implications for musculoskeletal injuries. Proprioceptive senses, particularly of limb position and movement, deteriorate with age and are associated with an increased risk of falls in the elderly. The more recent information available on proprioception has given a better understanding of the mechanisms underlying these senses as well as providing new insight into a range of clinical conditions.

> It is useful and justifiable for level of investigation to have its own language but we must expect that with a greater advancement of our knowledge it will be easy to translate one such language into another. Until such a time, each field must develop along its own lines, unhindered by the many possibilities for misinterpretation. E. von Holst (1954)

I. INTRODUCTION AND HISTORICAL BACKGROUND

A. Introduction

In everyday activities we depend on signals coming from our moving bodies to be able to respond to the space around us and react rapidly in changing circumstances. Much of this knowledge about position and movement of the limbs and trunk is provided by sensations arising in proprioceptors. The information they provide allows us to maneuver our way around obstacles in the dark and be able to manipulate objects out of view.

The term *proprioception* was passed down to us by Sherrington (356). He stated, "In muscular receptivity we see the body itself acting as a stimulus to its own receptors—the proprioceptors." In a strict interpretation of that definition, our bodies are supplied by many types of proprioceptors, not just those concerned with muscular sensibility. For example, we have receptors signaling distension of arteries, lungs, and the gut. Traditionally, however, the term *proprioceptor* has been restricted to receptors concerned with conscious sensations, and these include the senses of limb position and movement, the sense of tension or force, the sense of effort, and the sense of balance. Kinesthesia, a term introduced by Bastian (17), is used here to refer to sensations of limb position and movement. In this review we have not discussed the sense of balance. However, like the proprioceptive system, the vestibular system contributes to a range of conscious sensations as well as the guidance of movement and posture (for review, see Refs. 10, 87, 88).

Proprioceptive sensations are mysterious because we are largely unaware of them. They are distinguishable from

exteroceptors such as the eye and the ear in that they are not associated with specific, recognizable sensations. Yet, when we are not actually looking at our limbs, we are able to indicate with reasonable accuracy their positions and whether they are moving. Part of the explanation for this lack of identifiable sensations relates to the predictability of proprioceptive signals. We are aware that we are making a willed movement and so anticipate the sensory input that it generates. A general concept in sensory physiology is that what we feel commonly represents the difference between what is expected and what has actually occurred (e.g., Refs. 19, 86, 423). On that basis, if a movement goes to plan and there is no mismatch between the expected signals and those actually generated, no definable sensation is produced, yet the subject knows precisely the location of their limb. It is possible to generate an artificial proprioceptive signal using muscle vibration (159). Vibration produces sensations of limb displacement and movement, leading the subject to express astonishment at the unwilled nature of the sensations. This suggests that the will to move and the subsequent proprioceptive sensations are intimately linked.

The study of proprioception has always attracted widespread interest. Part of the reason is the important role played by proprioception in motor control. We are unable to move towards a target without ongoing visual and proprioceptive feedback. In addition, proprioception is appealing because it promises a better understanding of our everyday sensory experiences. In recent years, the topic has received additional impetus from developments in neuroimaging, in particular, magnetic resonance imaging (MRI). It has allowed study of the central activity patterns produced by proprioceptive stimuli. That, in turn, has led to recognition of the importance of integration of proprioceptive inputs with inputs from other senses such as vision and touch and identification of central areas likely to be involved in the integration. We are beginning to understand how some proprioceptive sensations arise and how they are used to create a body image. In designing experiments to test these ideas, it has also proven useful to resort to modern methods of generating virtual realities (341).

The subject of proprioception lies at the boundary between neurophysiology and neuropsychology. In this review we have taken a more physiological view and restricted ourselves to a discussion of aspects of the physiology of proprioceptors, their central projection patterns, and the generated sensations. An expanding field concerns the interactions between proprioception, vision, and vestibular inputs. While we discuss some of this, we have not reviewed the area exhaustively. The same applies at the more psychological end of the subject, for example, sensorimotor integration in the generation of concepts of "wellness," emotions, and social interactions. We have chosen not to review the extensive literature on eye movements, although some reference will be made to it. For comprehensive reviews, see, e.g., References 95, 216.

The topic of proprioception, as we have approached it, has been reviewed before (136, 244, 300, 303, 304). However, it is notable that some major textbooks claiming to cover all aspects of neuroscience (e.g., Ref. 286) and a even multivolume "comprehensive" handbook on the senses (49) have failed to include any detailed discussion of proprioception. Such omissions plus the many new developments in the field highlight the need for a reassessment of the topic and, hopefully, it will remind students, teachers, and others of the importance of the material. In this review we have tried to focus on recent developments, the role of motor commands in the generation of proprioceptive sensations, the ensemble signaling properties of proprioceptive afferents, and the information, based on MRI studies, of the central structures identified as playing a role in the generation of proprioceptive sensations.

B. Historical Background

The history of proprioception has been the subject of discussion for hundreds of years, with ideas emerging, their rejection, and subsequent reemergence as scientific progress takes its tortuous path. In reading some of the 19th century accounts, the sophistication of the ideas and clarity of expression are astonishing. An account of early speculations and the rise of a proposal for a "sixth sense" is provided by Wade (395). (Other articles with historical perspectives include References 95, 159, and 244.)

Aristotle firmly believed that there were only five senses: sight, hearing, smell, taste, and touch. He specifically excluded the existence of a sixth sense (see 339). Speculations about a muscle sense date back at least to the 17th century. William Harvey (181) speculated about the fact that muscles which move the fingers lie in the forearm. "Thus we perceive and so feel the fingers to move, but truly we neither perceive nor feel the movement of the muscles, which are in the elbow". Discovery of the sixth sense, the muscle sense, is attributed to Bell (20). He posed the question, "(do) muscles have any other purpose to serve than merely to contract under the impulse of their motor nerves?" He concluded, "We are sensible of the most minute changes of muscular exertion, by which we know the position of the body and limbs, when there is no other means of knowledge open to us." Bell also speculated about whether the signals were of central or peripheral origin.

The idea of a muscle sense was debated repeatedly during the 19th century. German physiologists talked about the "Muskelsinn." What was meant here was not a sensation originating in the muscles themselves, but in the brain. It was also referred to as a "sensation of innervation" (184, 268). The idea was that whenever we willed a movement,

this gave rise centrally to sensations of muscular activity and movement. Sherrington (355) in his influential textbook chapter on "The muscular sense" rejected these ideas, largely based on the observation that in the absence of motor commands, when our limbs lie relaxed, we still know where they are, even if we are not looking at them. Sherrington stated, "An objection to this hypothesis (sensation of innervation) is that it sunders sharply the sensations of passive from those of active movement, whereas there is strong ground for believing the two intimately allied." So there were two schools of thought, one claiming that the muscle sense had an entirely central origin, and the other believing that a peripheral signal was principally responsible. Bastian (17), who coined the term *kinesthesis*, was the only one at the time who contemplated a hybrid theory, comprising both central and peripheral components (see also Ref. 95). He later abandoned this idea in favor of a purely peripheral mechanism [for details, see Jones (204)]. Sherrington's views prevailed, and for the first half of the 20th century the subject of proprioception was largely founded on muscular sensations, although some counter views were proposed by the psychologist Lashley (222).

In his account of the muscle senses, Sherrington passed without comment from the role of muscle receptors in "active movement" to their contribution to spinal reflex action. This brushes over the two remarkably different roles of muscle receptors, their contribution to conscious sensation as proprioceptors, and their unconscious, automatic reflex action. This dichotomy of action led Merton (257) to declare, "Everyone agrees that the muscle spindles are the receptors for the stretch reflex and the mechanisms based on it, but it is also held at the same time that the muscle spindles give information about the length of the muscles to be used in our conscious judgements of limb position. Until the underlying incompatibility of these two notions is felt, one cannot properly appreciate the character of the problems that face us in this field." Here it is worth reflecting on the strategy of assigning to one class of receptors such diverse roles and what this means for central integrative processes. In the present review we have limited the meaning of "proprioceptor" to a receptor that gives rise to conscious sensations (300). In doing so, we are aware that receptors such as muscle spindles and tendon organs also play important roles in the unconscious, reflex control of movements.

When we think about limb position sense, an obvious place to look for receptors signaling position is in the joint about which the limb moves. That, indeed, was the prevailing view for much of the 20th century. Kinesthetic sensations were thought to arise exclusively in the joints. Sherrington himself was cautious, "The individual contributions toward muscular sense of these different sets of end-organs can only be conjectured" (355). In any case, as single afferent recording techniques were introduced, the view arose that the principal source of kinesthetic information lay in the joints themselves. The experimental basis for this view was provided by Boyd and Roberts (33) and Skoglund (362) [see also Skoglund (363), Mountcastle and Powell (267), and Jones (204)]. Today we know that this is not the case and that muscle receptors are the principal kinesthetic receptors. In an influential series of animal studies which challenged the view of joint receptors as the principal kinesthetic sensors, Burgess and colleagues (42, 43) showed that slowly adapting receptors in the knee joint of the cat provided ambiguous positional information because they increased their rate of discharge at both extremes of joint position. Here there was an interesting twist to the story. It was claimed that in the cat posterior articular nerve supplying the knee joint there were afferents which discharged across the mid range of knee position (33, 115, 362). These afferents changed their discharge rate monotonically with changes in joint angle, as would be expected from a receptor signaling joint position. Subsequently, however, these discharges were shown to come from muscle spindles in the popliteus muscle whose afferents had taken an aberrant course in the posterior articular nerve (250).

The modern view has muscle spindles as the principal proprioceptors. Here it is interesting to reflect on the tortuous path taken by progress in the field. Early, quite sophisticated ideas on a sensation of innervations were replaced by a view that focussed entirely on peripheral receptors. But this was still wrong, since the main receptor type was considered to be joint receptors, not muscle receptors. Nowadays, while we are aware of the importance of peripheral signals for passive proprioception, we have revived some of the old ideas on a sensation of innervations, to give "outflow" signals a bigger role, especially in active proprioception, where the generation of peripheral signals is accompanied by voluntary motor activity.

II. THE KINESTHETIC SENSORS

A. Introduction

During limb movement and changes in position, the tissues around the relevant joints will be deformed, including skin, muscles, tendons, fascia, joint capsules, and ligaments (e.g., Refs. 1, 169). All these tissues are innervated by mechanically sensitive receptors, and their density varies across muscles and regions of the body (e.g., Ref. 16). The question arises, which are the principal kinesthetic receptors? In this review the view is argued that muscle spindles play the major role in kinesthesia, with some skin receptors providing additional information. Emerging views suggest that Golgi tendon organs contribute to proprioception, including the senses of force and heaviness. Here the evidence remains indirect, the problem being that it is difficult to activate a population of tendon organs selectively. The major features of the muscle spindle and tendon organ are depicted in **FIGURES 1** and **2**, respectively. Joint receptors

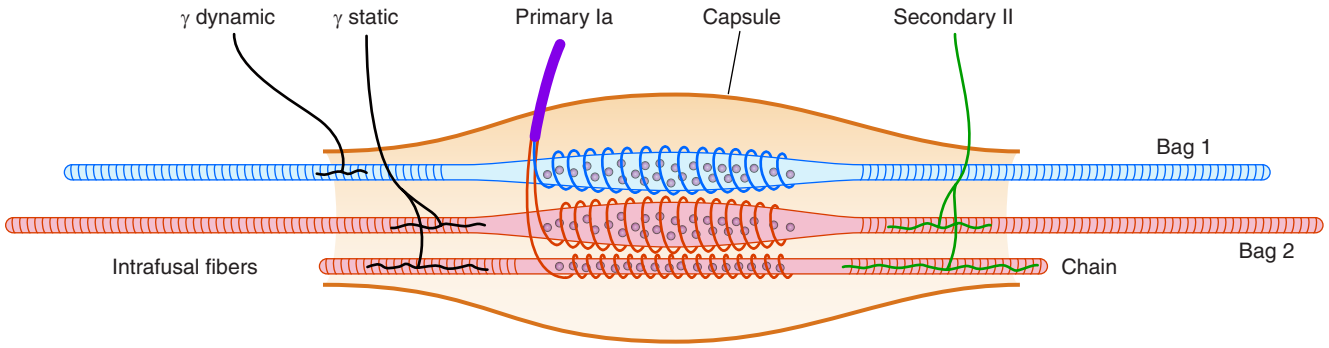


FIGURE 1. Diagrammatic representation of the mammalian muscle spindle. The intrafusal fibers include the large nuclear bag 1 and bag 2 fibers together with the smaller nuclear chain fibers. Ends of the bag fibers extend beyond the capsule while chain fibers lie within the limits of the capsule. Large, group Ia afferent fibers terminate as primary endings, making spiral terminations around the nucleated portions of all three intrafusal fiber types. Smaller, group II afferent fibers terminate as secondary endings, lying to one side of the primary endings and supplying bag 2 and chain fibers. Gamma dynamic (γ dynamic) fusimotor fibers innervate bag 1 fibers, while gamma static (γ static) fusimotor fibers innervate bag 2 and chain fibers. [Rredrawn from Proske (301).]

probably play only a minor role at most joints, acting as limit detectors. However, there is evidence of a contribution by joint receptors in the mid-range of movements at the finger joints (69, 116). Here we have considered the evidence for the contributions from each kind of mechanoreceptor and their relevant importance.

B. Evidence for Muscle Spindles as Major Kinesthetic Sensors

This is a summary of the evidence in support of the view that muscle spindles are major kinesthetic sensors. If kinesthetic information can come equally well from skin and joint receptors, what is the evidence that at many joints it is the muscle spindles that play the dominant role? The first pointer and perhaps the intuitively most appealing one comes from observations of persistent senses of position and movement after joint replacement.

1. Joint replacement surgery

In patients who have had a total hip replacement involving removal of all capsular and ligamentous components, both position and movement sense remained intact (170). The ability to detect passive movements and to duplicate positions of the hip was retained shortly after recovery from the operation and persisted unaltered over the subsequent period of several months. The authors concluded that the ability to detect joint position did not depend on stimuli arising in the joint capsule or on the surfaces of the hip joint. This view was supported by observations on local anesthesia within the knee joint (70). The evidence therefore suggests that, at least at some joints, joint receptors do not play a significant role in kinesthesia. Further studies of joint replacement and ligament repair have yielded somewhat variable results, some even suggesting the performance is improved post surgery (for review, see Ref. 316). This variation probably depends on the local pathology, its duration, associated changes in contralateral joints, as well as the methods of testing for deficits.

2. Dorsal column lesions

If sensory receptors contribute to conscious sensation, their afferents must project to the cerebral cortex. It is now well established from studies on animals that afferents from

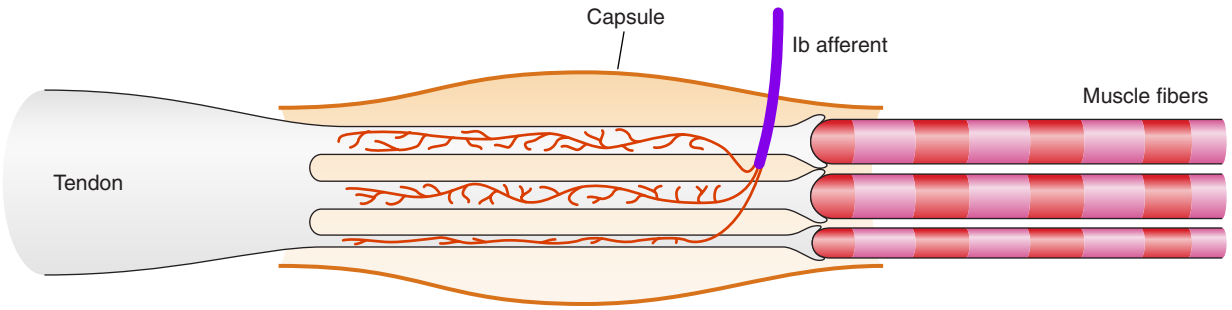


FIGURE 2. Diagrammatic representation of the mammalian Golgi tendon organ. The Group Ib axon penetrates the receptor capsule and branches, each branch terminating on a tendon strand that is attached to a muscle fiber. A typical tendon organ has 10 or more muscle fibers attached to it, each fiber belonging to a different motor unit. Contraction of a motor unit supplying a tendon organ stretches the tendon strand to which its muscle fiber is attached, generating activity in the Ib axon. [Redrawn in part from Proske (302).]

muscle spindles and tendon organs, as well as those from skin and joint project to the cortex (221, 247, 248, 278). The pathway taken by skin and joint afferents is via the dorsal (posterior) columns, gracile and cuneate nuclei, medial lemniscus, and thalamus. Muscle afferents from the forelimb also project centrally via the dorsal columns (336). However, for the hindlimbs, muscle afferents, unlike skin and joint afferents, leave the dorsal column in the upper lumbar region, synapse in Clarke's column, and project centrally in the dorsolateral funiculus as the dorsal spinocerebellar tract (for more detail, see Refs. 27, 220).

There is some evidence that the central projection pathways for skin and muscle afferents in humans are similar to that in mammals. Posterior column section at a thoracic level in humans leads to extensive loss of skin and joint sensation in the legs, but the central projection pathway for muscle afferents remains intact, indicated by preservation of the senses of position and movement. The evidence comes from a limited number of well-described patients with partial or total sections of their dorsal columns (396; see also Ref. 338). In a patient with thoracic cord injury, including total section of both dorsal columns, but only limited damage to the underlying cord, sensation of joint movement and direction of movement of the legs was close to normal. This finding was corroborated in two other patients. Overall, these data indicate that destruction of dorsal columns in the thoracic region does not impair kinesthesia in the lower limbs. By implication, skin and joint input is not essential for qualitatively normal kinesthesia in the legs.

3. Muscle thixotropy

Discussions of muscle thixotropy have often been missing from reviews of proprioception, yet the thixotropic behavior of muscle spindles frequently leads to errors in the interpretation of experimental data on kinesthesia. In addition, intrafusal thixotropy provides important evidence in support of muscle spindles as the principal kinesthetic sensors.

Thixotropy is the dependence of a muscle's passive mechanical property on its previous history of contraction and length changes. It arises from the presence of long-lasting stable cross-bridges between actin and myosin in the sarcomeres of resting muscle, including both extrafusal and intrafusal muscle fibers (308). The presence of these bridges is indicated by a frictional stiffness of the muscle at the start of a stretch, the short-range elastic component (SREC) (188). Accompanying the SREC is a sustained rise in resting tension, called filament resting tension (FRT) by Hill. When a muscle relaxes after a contraction, stable crossbridges form in the fibers at that length to give them their SREC (219, 266). If the muscle is then shortened, the compressive forces acting on sarcomeres which have been stiffened by the presence of the bridges are insufficient to detach the majority of bridges so that the muscle fiber is unable to fully take up the shorter length and falls slack. Such thixotropic states can persist for long periods provided the muscle is left undisturbed (311).

At long lengths a resting muscle will lie taut, regardless of its contraction history, whereas at short lengths it becomes slack (158) and may even buckle (186). There are intermediate lengths where a muscle can be either slack or taut depending on its history of contraction and length changes. What is meant by slack is that the muscle is effectively longer than the distance between its two points of attachment, so it is obliged to lie slack. Slack can be introduced at any particular length, by contracting the muscle at a longer length, letting it relax for several seconds, and then shortening it to the original length. While the presence of slack in the whole muscle may not always be apparent, the muscle spindles with their compliant connections to adjacent extrafusal fibers are particularly prone to it (for review, see Ref. 310). The method used to condition muscle and its effects on spindle discharge rates are shown in **FIGURE 3**.

For the soleus muscle of the anesthetized cat, in which slack has been removed by a conditioning contraction, the spindle resting discharge rate of 40 pulses/s falls to 10 pulses/s when slack is introduced in the muscle **(FIGURE 3)**. It means that intrafusal tension falls, and therefore, the stress exerted by the intrafusal fibers on the spindle sensory endings is reduced. Thus spindle background discharge rate falls. If now the muscle is contracted voluntarily, to include both intrafusal and extrafusal contractions, the slack in spindles will be removed and the background discharge rates will rise. So simply by contracting and then relaxing a muscle, without changing its length, background discharge rates in spindles can be changed (164). This produces significant changes in perceived limb position **(FIGURE 4)**.

Thixotropic behavior is restricted to extrafusal muscle and muscle spindles. Its effects are prominent at short and intermediate muscle lengths, and it fades at long lengths, as a result of spontaneous detachment of stable crossbridges in the presence of the high passive tension (164). Because most tendon organs have a high threshold to passive stretch, the muscle has to be stretched to long lengths for tendon organs to generate maintained activity. At those lengths thixotropic effects are small, or absent (305). Skin and joint afferents, because of the viscoelasticity of the underlying tissue, will show some hysteresis in their responses to lengthening and shortening movements. However, these changes are independent of muscle contraction, and they do not persist after the movement has stopped, so they are not truly thixotropic, that is, dependent on the previous history.

If elbow flexors of one arm are conditioned to lie either slack or taut, this can lead to perceived changes in arm position of ~5° (165). If the two arms are conditioned in opposite ways so that elbow flexors on one side lie slack while on the other side they are taut, it can lead to mean

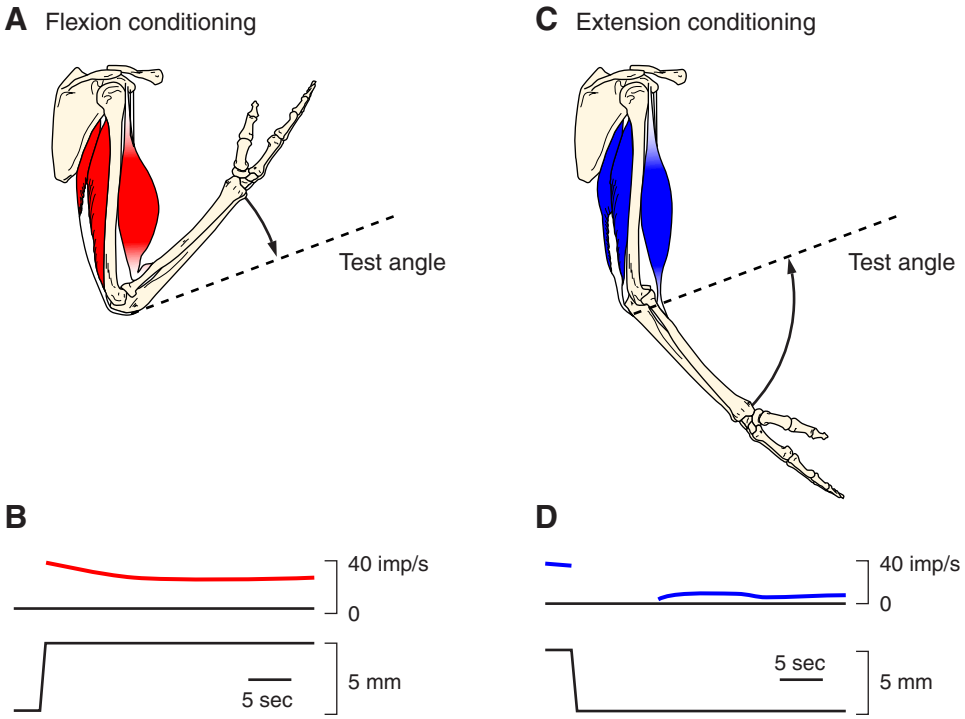


FIGURE 3. The method of conditioning muscle to put it into a defined state. In *A* and *B*, at the top is shown a diagrammatic human forearm with one flexor and one extensor muscle drawn in. During flexion conditioning (*A*, red) the forearm is flexed, elbow flexors are briefly contracted, and once the muscle has relaxed, the passive forearm is placed at the test angle. During extension conditioning (*C*, blue) the forearm is extended, elbow extensors are contracted, and on relaxation the relaxed forearm is placed at the test angle. *Traces B* and *D* below the forearm diagrams give schematic representations of firing rates of muscle spindles in the soleus muscle of the anesthetized cat after it had undergone two kinds of muscle conditioning comparable to those used at the human elbow joint. A conditioning contraction of soleus when it was shortened by 5 mm (*B*, red trace), on return to the test length led to a spindle resting discharge of 40 impulses/s. A conditioning contraction after soleus had been stretched by 5 mm (*D*, blue trace) led on return to the test length of a spindle rate of 10 impulses/s. [Redrawn in part from Wood et al. (425).]

matching errors of ~20°, representing a quarter of the total range of movement of the arm (5). Despite such large differences in arm position, on interrogation, the blindfolded subjects insist that their arms are accurately aligned. The fact that conditioning of the two arms in this way leads to such large errors suggests that the brain is listening to both arms and most probably is responding to the difference signal from them (412).

Since much of the early data were acquired without knowledge of thixotropy, the complication this introduces was overlooked. It has meant that sometimes uncertainty has remained about the significance of particular results. The frequently cited report that position sense is more accurate with active rather than passive movements (280) probably has as its basis muscle thixotropy. Thixotropy is a property of passive muscle so its influence on proprioception is especially important for position and movement sense in the passive limb. However, thixotropic influences can persist with voluntary contractions of 5–10% of maximum (168, 200).

The failure of many experiments concerned with limb position sense to place the test muscle in a defined state, has led to uncertainties in the interpretation of some of the data. So, for example, in a recent study of the perceived position of a passively moved arm (131), no conditioning contractions of elbow muscles were carried out. It was assumed that as subjects remained passive throughout the 0.5-h testing session, no change in muscle spindle activity was likely over this time. Nevertheless, any unintended movements would risk changing spindle sensitivity and alter the outcome. In addition, the thixotropic state of the subject's arm would depend on what the subject had been doing immediately before the experimental trial, risking bigger intersubject differences during the subsequent measurements. Similarly, if the aim of an experiment is to compare position sense in an unloaded limb, with that when the limb is supporting a load, the voluntary contraction used to support the load will remove any preexisting slack in spindles during the unloaded measurements and lead to position errors that have nothing to do with central effects of the load (419).

Thixotropy-dependent errors in position sense are typically present only in the passive limb, so the motor output generated by the CNS is not directly involved. The direction and distribution of the errors strongly imply that it is the

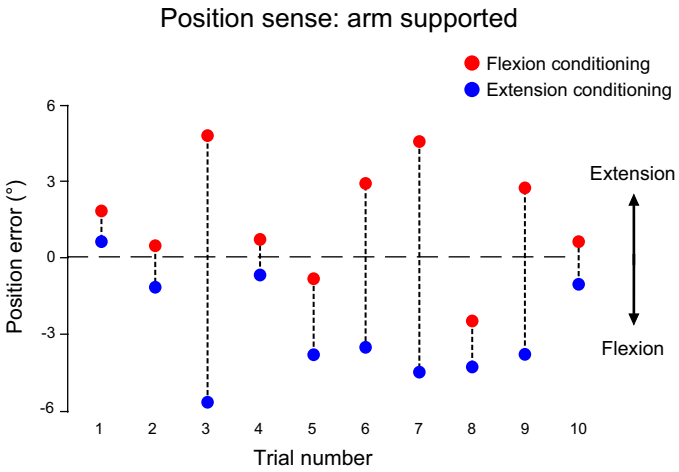


FIGURE 4. The effects of muscle conditioning on human position sense at the forearm measured in a two-arm matching task. Shown are 10 pairs of successive trials from one subject. Following a conditioning contraction of the reference arm, the relaxed arm was placed by the experimenter on a support at the test angle. To indicate its location, the subject then moved their other arm to a matching position. Errors were calculated as the difference in position of the two arms and were displayed using the convention, errors in the direction of extension as positive, errors in the direction of flexion as negative. Symbols in red, position errors after flexion conditioning; symbols in blue, errors after extension conditioning (see **FIGURE 3**). Trials were alternated between the two forms of conditioning, and each pair of measurements has been joined by a dotted line. The dashed line indicates zero error. Flexion conditioning leads errors to lie systematically in the direction of extension relative to the errors after extension conditioning. [Data from Winter et al. (419).]

resting activity of muscle spindles which generates a signal of limb position and that in a matching task the parameter measured by the brain is the difference in signals between the limbs. Such behavior raises the question of what is the reference point used to determine the starting position of the limb. Another issue is what happens in a contracting muscle (e.g., Ref. 6). During a voluntary contraction, some spindle impulses will be generated by fusimotor activity (e.g., Refs. 3, 47, 386, 416). It remains uncertain how position sense is generated under these conditions (e.g., Refs. 93, 242, 401). A speculative proposal about how the brain might distinguish between spindle impulses generated by stretch and fusimotor activity is put forward below **(FIGURE 16)**.

Thixotropy provides the only known method for manipulating position sense in the passive limb without the use of external stimuli such as vibration. No attempts have been made so far to grade thixotropic conditioning to see whether this produces progressive changes in position sense. What change in the ensemble rate of spindle discharge in a muscle is needed per degree of position sense change? Here there are potentially confounding effects from extrafusal fibers on muscle spindle discharge (e.g., Ref. 44). In addition, thixotropy represents a useful tool for the study of subjects who are suspected to have proprioceptive disturbances, such as Parkinsonian patients (240, 428) and the elderly (195).

4. Muscle vibration

Arguably the most influential evidence in support of muscle spindles as the principal kinesthetic receptors is the illusion of limb movement and displaced position produced by vibration over the tendon or muscle (111, 159). These observations, more than any others, swung prevailing opinion in the 1970s away from joint receptors, in favor of muscle receptors. Vibration of the tendon of biceps or triceps brachii at 100 Hz produced an illusion of movement and of changed position at the elbow in a direction that would elongate the vibrated muscle. Vibration over the elbow joint produced no illusion.

Simultaneous vibration of antagonist muscles at similar frequencies and amplitudes produced no movement sensation at all, suggesting that the difference in signal between agonists and antagonists is what is perceived centrally (325). Further details of the frequency dependence of the vibration illusion were provided by McCloskey (243). He showed that the velocity of the vibration illusion slowed in direct proportion to the load being supported by the vibrated muscle. When the muscle generated half-maximal contractions or more, vibration no longer produced any illusion, a result that has recently been confirmed (13). Furthermore, vibration at lower frequencies with larger amplitudes produced illusions of displaced position only.

The studies with vibration have since been repeated and extended many times under both passive conditions and during voluntary movements (e.g., Refs. 57, 82, 217, 391). Importantly, microneurography has revealed that the primary endings of spindles are largely responsible for the illusion and that the vibration frequency for an optimal response in human muscles is ~80 Hz (e.g., Refs. 205, 332, 333). While most observations have confirmed that it is principally the primary endings of spindles that are responsive to vibration in the relaxed muscle, it is well known that some Golgi tendon organs respond to tendon or muscle vibration (46), particularly if the subject is slightly tensing their muscles (113). This is a reflection of the fact that tendon organs are tension sensors and relatively insensitive to mechanical stimuli, unless the tendon strands on which they are sited are under tension **(FIGURE 2)**.

The vibration illusion can be demonstrated in both arms. In a position matching task, vibration of elbow flexors or extensors of the indicator arm produced errors in a direction opposite to that from vibrating the same muscles in the reference arm (412). This is to be expected in a task where, to achieve a match, the vibrated indicator must move in a direction that reduces the activity in its muscle spindles sufficiently to bring their responses closer to those in the nonvibrated reference arm. Vision of the indicator arm (or

its mirror image) can reduce the size of the vibration illusion (199) (see also Refs. 193, 218). Furthermore, the perceived speed of extension of the reference arm from vibration of its elbow flexors can be altered by flexion or extension movements of the indicator arm (199) (see also Refs. 82, 359). These experiments demonstrate that during tasks such as placement of the two hands close together, proprioceptive inputs from both arms are used. This is presumably part of a motor control strategy to allow use of the two hands as a single instrument in skilled tasks (199).

The vibration illusion can be manipulated by means of thixotropy. In animal experiments, deliberately introducing slack in muscle spindles by contraction of the muscle at a long length and then shortening it left all spindles insensitive to vibration applied longitudinally to the tendon (306). The effect of vibration on human position sense can be abolished if sufficient slack is introduced in the muscle (412). On the other hand, the speed of the movement illusion generated by vibration can be doubled by removing slack in the muscle with a conditioning contraction (160). These and other observations on thixotropy (e.g., Refs. 104, 417) point strongly to muscle spindles as the prime candidates for providing position and velocity information in proprioception.

C. The Senses of Position and Movement

Originally the senses of position and movement were considered a single sense: kinesthesis (18). Part of the reason for combining them is that both share inputs from the same receptor, the primary endings of muscle spindles. Second, muscle vibration elicits illusions of both movement and displaced position (159). Similar illusions can be produced with electrical stimulation of peripheral nerve, which probably excited spindle primary endings (135). An example is given in **FIGURE 5**. Primary endings respond both to the length change and rate of length change of the muscle (241). During stretches at increasing velocities, the response of the primary ending increases in direct proportion to the rate of length change. Movement sense is therefore signaled by the velocity component of the primary ending's response to the length change. As the muscle is stretched to longer lengths, the background rate of spindle discharge increases in direct proportion to the length change. Position sense can therefore be envisaged as signaled by the mean rate of background discharge in muscle spindles, including that generated by both primary and secondary endings (see also sect. II*B3*). Secondary endings are also likely to contribute to position sense (243). When the frequency of vibration was reduced from 100 to 20 Hz, the sensation of movement blended into one of position only. McCloskey (243) argued that the two senses were generated by separate lines of input and that position sense was not derived from an integration of the velocity signal (see also Ref. 360).

Other evidence supports the existence of two senses, both generated by muscle spindles. It is possible to manipulate the sense of position using thixotropy. The background rate of both primary and secondary endings can be increased by means of a conditioning contraction (165; see also Ref. 417). This led to a significant change in the perceived position of the limb, without any accompanying sensation of

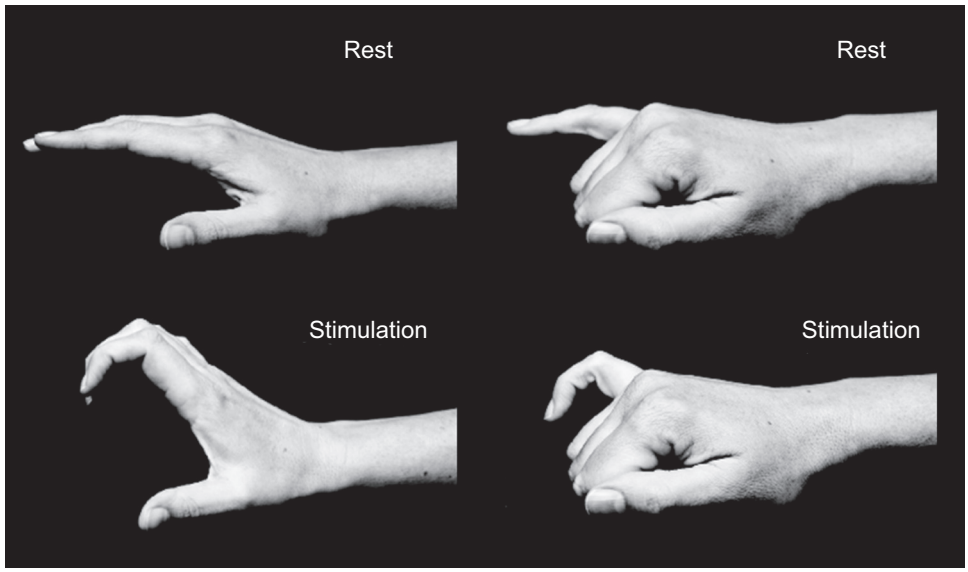


FIGURE 5. Photographs of illusory positions of the hand during trains of electrical stimulation of the ulnar nerve at the wrist using a stimulus strength below motor threshold. *Top panels*: rest positions before commencement of stimulation. *Bottom panels*: posture adopted during stimulation. *Left*: illusory positions adopted for all fingers, perceived flexion of the interphalangeal joints and extension at the metacarpophalangeal joints. *Right*: for the little finger, perceived flexion of the interphalangeal joints and extension at the metacarpophalangeal joint. For further details see text. [Photographs based on Gandevia (135).]

movement (165). In an experiment on the effect of muscle fatigue on position and movement sense (see sect. V), fatiguing exercise of elbow flexors produced errors in the perceived position of the exercised limb but without a change in passive movement sense (8). The result again suggested two senses, each responding differently to a potential disturbance.

In thinking about the two senses, it is easy to see how the spindle firing rate during a length change might be converted into a movement sensation. It is less clear how position sense is generated. Some spindles generate background activity at all muscle lengths, no matter how short the muscle; others fall silent at short lengths (167). Perhaps such differences become submerged within the population signal. How are the limits of the range of limb position established? Vibration and electrical stimulation of muscle spindles can produce sensations of position at anatomically impossible joint angles (85, 135, 218). This indicates that the brain can be misled to perceive an anatomically impossible position. Perhaps under normal circumstances it is the joint receptors, acting as limit detectors, that help to define the limits of limb movement (see sect. II*D*).

In experiments measuring limb position sense using a bilateral matching task, typically subjects are consistent in their matching performance, yet they can make substantial bias errors. Depending on how the reference arm has been conditioned, they often perceive its position as more extended or more flexed than it really is, and this error can persist in repeated trials on different days. So, for example, in a study of the effects of exercise on position sense, control errors after conditioning elbow flexors lay 2° or more in the direction of flexion (7). Such observations suggest that the calibration of absolute arm position is not very accurate, yet subjects are aware of the position of one arm relative to the other.

A comment on the processing of position and movement information is provided by studies of dorsal spinocerebellar tract (DSCT) cells in the anesthetized cat (29). Cells are described whose discharges are modulated by both position and movement of the foot. The two inputs summate nonlinearly, and the amplitude of the modulation depends on the position of the foot. In other words, a neuronal processing network is available that can simultaneously process position and movement information, making it unnecessary to postulate separate pathways. Furthermore, this conclusion is consistent with observations made on motor cortical neurones in monkeys (390).

D. Joint Receptors

Joint rotation will stretch the joint capsule on one side, as well as the overlying skin, while tissue on the other side is unloaded. Mechanoreceptors signaling tissue stress within the capsule are Ruffini-like endings, comparable to the cutaneous SA2 endings, while Paciniform corpuscles respond to local compression (for review, see Ref. 169).

In their study of joint receptor properties in the posterior articular nerve of the knee of the cat, Burgess and Clark (42) found ~70% of the receptors were slowly adapting. The vast majority of these responded only to marked flexion and marked extension of the joint, that is, they responded at both limits of the range of joint movement, making their position signal ambiguous. A true position sensor would change its discharge rate monotonically with joint angle in one direction only.

Within the rapidly adapting group of receptors, some were Pacinian corpuscle-like, responding briefly to joint movement in any direction. Other phasic receptors produced a rapidly adapting response at most joint angles but gave a sustained response to maximal extension of the joint if this was combined with a twisting force (42).

There are limited data on joint receptor properties in human subjects. Recordings were made from joint afferents supplying the metacarpophalangeal joint and the interphalangeal joints of the digits. These afferents responded to local pressure over the joint capsule (45) and generated a slowly adapting discharge at extreme angular displacements. They commonly discharged to more than one axis of movement and at both ends of an angular range. Only 1 of 18 joint afferents responded to passive joint movement across the physiological range. A limited number of joint receptors responding to joint flexion (but not extension) were found in the superficial radial nerve (99). Intraneural microstimulation of some joint afferents generated small movement sensations at the joint in response to trains of electrical stimuli (234). The perceived movements corresponded to the pattern of discharge observed when moving the passive joint in a similar way. Thus the brain can obtain some information about the movement of a joint from these kinds of receptors, although their signaling capacity was rather limited (234). There are no data for stimulation of single joint afferents at joints outside the hand.

Concerning the psychophysical evidence for a role for joint receptors in kinesthesia, the work of Gandevia and McCloskey (138, 143) showed that at the distal interphalangeal joint of the middle finger, in the absence of muscle afferent signals, subjects were poor at detecting small slowly applied angular displacements. When the experiment was done the other way around, with skin and joint input blocked but muscle afferent input intact, detection at low angular velocities was lower than with the full proprioceptive machinery intact. In other words, contributions from all sources were required for full proprioceptive acuity. When only skin and joint input were available, position sense deteriorated slightly if the joint capsule was infiltrated

with anesthetic, directly pointing to a role for joint receptors (116), although this result could not be reproduced by others (69). In similar experiments on the proximal interphalangeal joint, block of the digital nerves did not impair position sense (340). When the experiments on the hand were repeated over a wider range of joint angles, position errors occurred (117), particularly near the extremes of the range of joint movement. This finding led Ferrell and Smith (118) to conclude that joint receptors provided positional information principally at the extremes of the normal range of joint movements, perhaps acting as "limit detectors." In contrast, muscle spindles increased their discharge monotonically across the full angular range with some differences between synergists (43), but they did not behave like limit detectors. Hence, it is not surprising that illusions attributed to them generate perceptions of anatomically impossible joint angles (e.g., Refs. 85, 135, 159, 218).

To conclude, there is clear evidence in support of a role for joint receptors in signaling joint movement, but it appears that they are unable to signal movement direction or joint position within the normal range. This issue has recently been brought up again (131). The authors propose that as joints approach the limits of their movement range, joint receptor information may bias perception of joint angles. In considering proprioception at the finger joints, it should be kept in mind that for movements at these joints muscle afferent signals are coming both from short intrinsic muscles in the hand as well as from proximal muscles in the forearm that are connected to the fingers by long, compliant tendons. Under these potentially ambiguous circumstances, it may be that skin and joint input is more important than muscle afferent input. At more proximal joints it appears that muscle afferents provide the major proprioceptive signal (68).

E. Skin Receptors

Joint rotation causes skin on one side of the joint to be stretched and to be slackened or even folded on the other side. Such deformations will stimulate skin mechanoreceptors. There are four kinds of specialized mechanoreceptors in glabrous skin: rapidly adapting type I, the Meissner corpuscles; rapidly adapting type II, Pacinian corpuscles; slowly adapting type I, Merkel endings; and slowly adapting type II, Ruffini endings (e.g., Ref. 203). While all four receptor types are likely to contribute to movement sensations, slowly adapting type II, the skin stretch receptors, are potentially able to signal limb position (e.g., Refs. 64, 100, 101).

Illusions of finger joint movement are produced by strain of the adjacent skin, without any actual movement of the joint (78, 79, 103). In a recent study of the contribution of skin receptors to kinesthesia (80), skin input to position and movement sense was examined at the index finger, the elbow, and the knee. An example is shown for the illusions generated by muscle vibration and skin stretch at the elbow **(FIGURE 6)**. Skin receptors were activated by skin stretch using adhesive tape, and muscle receptors were activated by vibration. Graded skin stretch in a direction in line with muscle stretch applied during vibration significantly increased perceived movement sensation above that from skin stretch alone or vibration alone. This was not just a matter of skin input facilitating the muscle input because just skin stretch alone commonly produced illusory movements. Therefore, input from skin stretch is able to contribute to kinesthesia in its own right. The sensitivity of human skin stretch receptors when expressed as impulses per degree of joint motion is similar to that of muscle spindle afferents (101, 171).

Signals from skin receptors can also have an occluding action on kinesthetic sensations. Stimulating rapidly adapting receptors, presumably Pacinian type Is, with high-frequency vibration at very low amplitude interferes with movement detection (406, 408). Similarly, focal pain induced either in the skin around a joint or in the muscles which move it impairs movement detection at that joint (405). The neural basis for this is presumably convergence between cutaneous and muscle afferents at spinal cord and thalamic levels along the projection paths to the cortex.

A situation where the contribution to kinesthesia from skin receptors becomes indispensable is in the skin adjacent to the fingertips. The muscles that move the fingers lie in the forearm and hand and their tendons must cross three or more joints. Here signals from muscle spindles are potentially ambiguous (see also Refs. 347, 373). The presence of skin receptors adjacent to each finger joint allows them to provide joint-specific information (e.g., Refs. 79, 103). However, the skin input itself can be ambiguous. Slowly adapting type II afferents from hairy skin of the back of the hand show sustained responses to flexion of the finger joints at intermediate joint angles (102). However, most of these afferents responded to movements of more than one finger, and responses to flexion or extension of one finger depended on the posture adopted by another finger. Hence, it is only by considering the spatial array of particular inputs that the sizes and directions of imposed movements can be computed.

Electrical stimulation of single identified cutaneous afferents has provided further information about the contribution of different inputs from the hand, but with only limited insight into proprioceptive coding (234, 276, 387). Rapidly adapting afferents, when stimulated, evoke a sense of vibration or tapping, but there is no sense of movement. Stimulation of single afferents of slowly adapting type I receptors produces sensations of local indentation or pressure, while stimulation of slowly adapting type II receptors leads to no sensation at all. Furthermore, in a study which also assessed muscle afferents (234), stimulation of single spindle afferents produced no sensation. Thus, for the digits and probably all other joints, it is necessary to stimulate a population of stretch receptors to generate detectable sensations (see sect. IIIC).

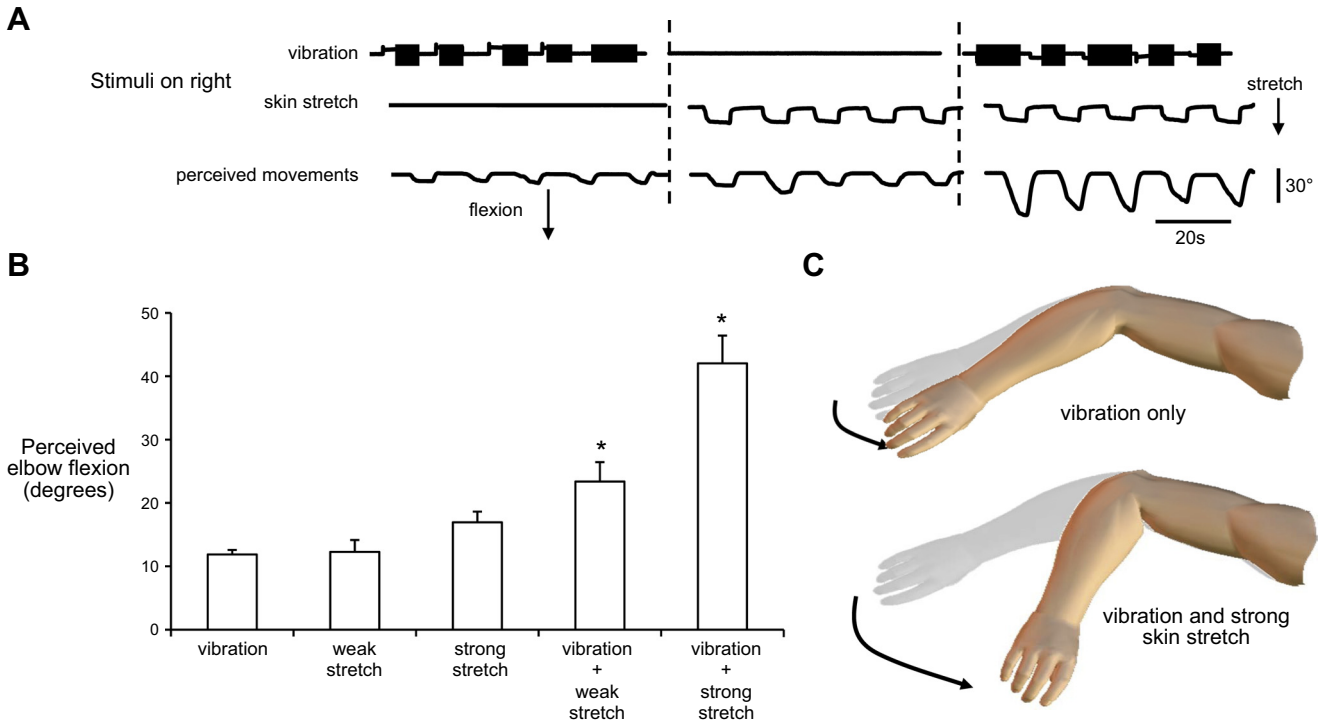


FIGURE 6. Illusory motion at the right elbow produced by muscle vibration, skin stretch, and combined vibration and stretch. *A*: stimuli delivered to the right arm, perceived as movements and indicated by the left arm. *B*: mean amplitude of perceived movements for all trials (vibration, $n = 15$ cycles; all others, $n = 10$ cycles). Asterisk indicates significant differences from vibration alone. Diagrams in *C* show the position of the right elbow during the experiment (gray silhouette) and the average perceived position when vibration was applied by itself (*top*) and simultaneously with strong skin stretch near the elbow (*bottom*). [From Collins et al. (80).]

In a population study of receptors in the skin over the ankle joint, responses were recorded to movements in different directions (2). The majority of movement sensitive afferents were from slowly adapting type II or rapidly adapting type II receptors. The response patterns of the skin afferents, when considered in terms of a population vector model, matched, in their directional sensitivity, those of muscle receptors in the underlying muscles, making both kinds of receptors suitable candidates for generating kinesthetic sensations. In conclusion, skin afferents play a significant role in kinesthesia, and they are likely to contribute to movement sensation at most joints. However, their contribution to position sense at the more proximal joints is likely to be less important than the input from muscle spindles. Perhaps a special case should be made for skin receptors in signaling facial expressions, since facial muscles are believed not to contain any muscle spindles (385).

III. WHAT DO PROPRIOCEPTORS SIGNAL?

A. Spindles as Length and Velocity Sensors

An important question is what aspects of a movement are signaled by spindles? The work carried out largely in the 1960s and 1970s established that the primary endings of spindles respond to ramp-and-hold stretches with a discharge rate that is proportional to the size of the stretch and to the rate of stretch. Secondary endings of spindles have a lower dynamic sensitivity, and their response is largely proportional to the size of the stretch. This led to the view that primary endings were muscle length and velocity sensors and secondary endings were length sensors (for a detailed account, see, e.g., Ref. 241).

These findings have led to the widely accepted view that spindles provide information about length changes in muscles, and this is represented as changes in joint angles. The question is then posed, Does the brain compile muscle movement and joint angular information from each muscle group to compute the sizes and directions of movements of the whole limb? When a vibrator is strapped to elbow flexors of one arm, vibration at 100 Hz produces an illusion of forearm movement into extension, as signaled by placement of the other arm. Vibration of elbow extensors produces movement illusions in the opposite direction, elbow flexion (159). So vibration of one muscle group is able to generate a muscle-specific sensation. It means that the brain has access to information specific to individual muscles. While that is so, it does not preclude the possibility that input from the whole limb is used to calculate movement related proprioceptive signals.

B. Movement Detection Thresholds

The dynamic sensitivity of muscle spindles and skin stretch receptors provides the basis for our ability to detect small movements of our limbs. A simple test of proprioception, widely used in the clinic, is to impose movements at a joint, usually a finger joint or big toe joint, and to ask the subject to declare when they feel the movement and to indicate its direction. It is an old observation that movement detection thresholds for proximal joints are lower than for more distal joints (157). This point has been reexamined more recently (178).

Measurements are imposed on the passive limb by a servomotor **(FIGURE 7)**. Threshold is usually measured as the movement amplitude required for generating 70% correct responses. Here subjects are asked to indicate both that a movement has occurred and its direction. Detection threshold at the forearm depended on the velocity of movement. At a speed of 1°/s threshold was ~0.2°, while at 0.1°/s it was eight times higher, at 1.6° (178). Lower thresholds can be achieved if the muscle is appropriately conditioned beforehand (300, 421). Thresholds at the finger joints were several times higher than at the elbow and shoulder joints. In thinking about their data, and assuming that muscle spindles were responsible for the threshold sensations, Hall and McCloskey (178) proposed that what mattered was not the angular range through which a joint was moved but the proportional length change the movement imposed on the muscles that operated at that joint. To check the point, measurements were made on muscle fascicles in human cadavers, and changes in fascicle length per degree of joint rotation were calculated. When these values were used to compare detection thresholds, differences in thresholds between the finger, elbow, and shoulder largely disappeared. A similar result was achieved for detection thresholds at joints in the leg (317, 319). This outcome was considered evidence in support of muscle spindles as the principal proprioceptor responsible for the detection of movements.

If muscle spindles signal changes in fascicle length, this raises a problem. Fascicle lengths are very different for muscles at different joints (285), yet muscle spindle lengths are about the same from one muscle to another (32). As fascicles in distal muscles are shorter than in more proximal muscles, it means that in distal muscles the spindles run the full length of the fascicle while in proximal muscles they span only a fraction of the fascicle length. However, as shown above, this difference in arrangement is not accompanied by any difference in movement detection threshold between proximal and distal muscles. How can a spindle, much shorter than the adjacent muscle fascicle, accurately signal length changes in the fascicle? To solve this problem, it is first necessary to assume that a muscle fascicle behaves

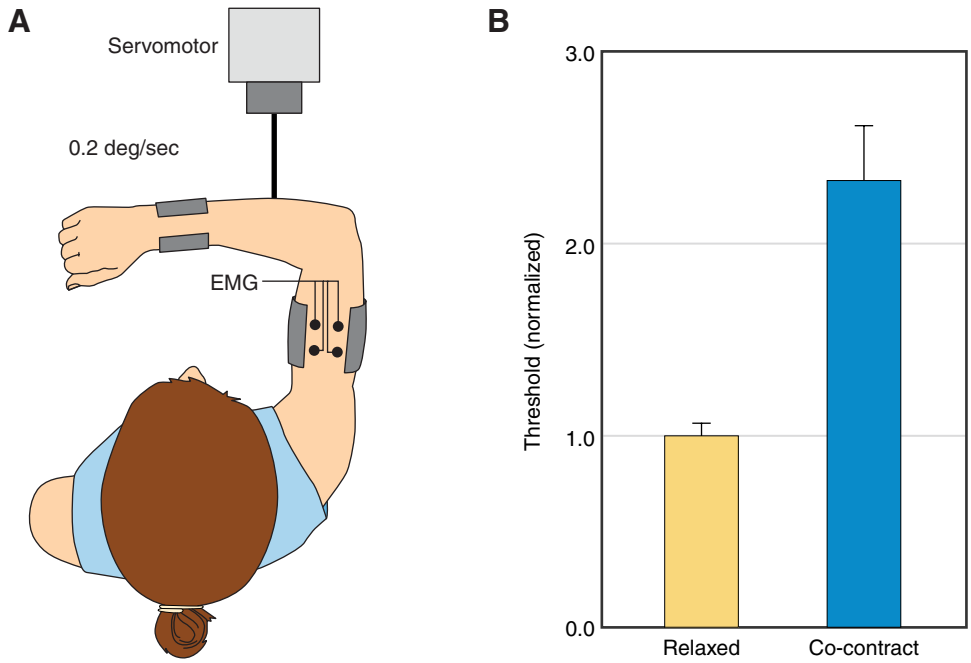


FIGURE 7. Measurement of movement detection thresholds. *A*: blindfolded subjects were required to indicate the direction of small movements (0.2°/s) applied to the right forearm with a servomotor. Detection thresholds were measured for elbow extension and flexion movements under relaxed and cocontraction conditions (15% MVC cocontraction of elbow flexors and extensors, monitored as EMG). *B*: average thresholds measured for 7 subjects. There were no differences between thresholds for flexion and extension movements, and values have been pooled. Thresholds have been normalized with respect to the average threshold measured for the relaxed condition. Thresholds measured during cocontractions of elbow muscles (blue bar) were significantly higher than when the arm was relaxed (orange bar). [Redrawn from Wise et al. (420).]

in a mechanically uniform manner, that is, an imposed stretch is distributed uniformly along all parts of the fascicle. If in proximal muscles the ends of the spindle make lateral attachments to the perimysium of the fascicle, the spindle will in effect signal length changes in only a part of the fascicle. With such an arrangement, the absolute length change a longer fascicle must undergo to produce the same spindle signal will have to be greater than for a shorter fascicle. Such a trend is evident in the relationship between fascicle length and the length change required to reach movement detection threshold (313).

Detection thresholds are higher for slow movements. If the movement is made slowly enough, it will go undetected, but the subject will eventually realize that the limb being moved is no longer where it was previously but be unaware of how it got to its new position (68). This is the sense of position, and its threshold is ~2.5° at the metacarpophalangeal joint (377). The much lower detection threshold for faster movements presumably reflects the dynamic sensitivity of spindle primary endings and skin stretch receptors.

Since in everyday life limb movements are invariably accompanied by muscle contraction, it raises the question of movement detection thresholds during a contraction. This has been measured at the elbow joint during flexion contractions (378) or isometric cocontractions (420). At the lower velocity end of the range of imposed movements, Taylor and McCloskey (378) have reported a 10-fold fall in detection threshold during contraction, compared with threshold measured with the passive arm. A similar result has been reported for finger movements when the input from joint and skin had been blocked (39, 143). In contrast, Wise et al. (420) obtained a fivefold increase in detection threshold at the elbow when subjects were generating a 15–20% of maximum cocontraction **(FIGURE 7)**. One possible explanation for this difference in results is the influence of thixotropy on threshold measurements in the passive limb (421). During a voluntary contraction there is coactivation of fusimotor neurons (see sect. II*B3*). So, does fusimotor coactivation increase or decrease the ability of spindles to detect movements? Experiments on animals have yielded the unexpected result that responses of primary endings of spindles to small movements are larger in the passive spindle than when the spindle's fusimotor supply was stimulated (422). After a conditioning contraction, responses of passive spindles to a stretch were larger than when the stretch was applied during static fusimotor stimulation, dynamic fusimotor stimulation, or their combination. Thus the passive spindle is more sensitive to movements than when its intrafusal fibers are contracting. This finding is at odds with the common view that proprioception is more accurate under active than passive conditions. This misconception has probably arisen due to thixotropic effects (see sect. II*B3*).

C. Signaling Properties of Spindle Ensembles

Does the brain access information from individual spindles or does it rely on the population response from the whole muscle? Here pertinent observations have been made using microneurography and stimulation of single afferents in human subjects. Stimulation of single muscle afferents innervating intrinsic hand muscles did not produce any sensations (234). However, electrical stimulation of a presumed population of muscle afferents did produce the expected position and movement illusions (135). Hence, for hand muscles, generation of a sensation required input from more than one muscle afferent. Since each spindle has its own location in the muscle and is therefore exposed to a unique set of mechanical conditions during muscle movements, it implied that these differences were combined and the signal arising from the muscle, relevant to proprioception, was the population response of its afferents.

An answer to the question of how direction of a movement may be signaled, while incorporating differences between individual neurons, has been proposed by Georgopoulos and colleagues (e.g., Refs. 151, 152). They recorded the discharges of movement-sensitive neurons in the motor cortex of conscious monkeys during arm reaching movements. Most neurons discharged maximally for movements in one preferred direction. However, the directional sensitivity of a particular cell was broadly tuned, with weaker responses for movements not in the preferred direction. Tuning curves of different cells overlapped. It was proposed that each cell made a vector contribution to the population response, with the size of the vector depending on the relation between the imposed movement and the cell's preferred direction of discharge. Vector contributions from individual cells summed to give the population vector which corresponded closely to the direction of the movement made by the monkey (345). This kind of proposition is relevant to how populations of spindles might signal limb movements (see sect. III*D*).

A further clue about the kinematic information provided by spindles and how it is processed centrally has come from recordings of second-order neurons in the central projection pathway for spindles (30). In anesthetized cats, the discharges of some DSCT cells were consistent with a limb-based rather than a joint-based reference frame. The authors demonstrated this by fixing a rigid splint between the thigh and shank of one leg, thereby reducing movement about the knee. In the splinted leg, about half of the DSCT neurons continued to signal the limb end-point representation, that is, position of the foot, as distinct from the specific limb geometry associated with the end-point. The findings suggested a wide convergence of muscle afferent input from the hindlimb to allow the DSCT circuitry to compute an estimate of foot position that was independent of overall limb geometry. This could be achieved by combining and

redistributing the relative weights of the inputs from the different limb segments.

In summary, we are now confronted by the realization that inputs are combined, not just of individual afferent responses from one muscle but of pooled responses from combinations of muscles acting at different joints. This concept is not restricted to muscle spindles, as it is likely to apply to other proprioceptive inputs as well (e.g., Refs. 2, 98, 101). Finally, recent observations of activity in cortical motoneurons during multijoint movements of the arm have shown that firing rates of individual neurons are modulated by the kinematics of multiple joints and that only a small pool of motoneurons is necessary for the generation of a wide range of movements (390). Such a conclusion adds support to the idea of limb-wide convergence of afferent information and its processing at spinal and cortical levels.

D. Generating Predicted Sensations With Vibration

The concepts of population coding and vector summation for motor cortical output (e.g., Refs. 151, 152) were used to model the generation of proprioceptive sensations (e.g., Refs. 4, 21, 332, 333, 381). Roll and colleagues used microneurography and muscle vibration to study the relevant features of a movement signaled by muscle spindles. The first point they made was that, based on the sensory percept reported by subjects, integration of afferent information from more than one muscle was possible. Vibration of agonist and antagonist muscles at similar frequencies and amplitudes produced little or no movement sensation (e.g., Refs. 153, 325). Similarly vibration of hand muscles at two different sites when carried out separately produced illusory hand movements in orthogonal directions. Simultaneous stimulation of the two sites produced a single percept in a direction with an oblique trajectory (330).

Population vector coding is based on the requirement that the directional sensitivities differ from one receptor to another in the muscle and that these properties overlap between receptors. Such requirements were met by muscle spindles studied in a group of ankle muscles (21). Example records are shown in **FIGURE 8**. **FIGURE 8*A*** shows microneurographic recordings of responses of an identified primary spindle ending of the extensor digitorum longus muscle during ankle movements in two dimensions, vertical and horizontal. Responses of the spindle are shown during movements in eight directions. Such responses, recorded for each of four different ankle muscles, were used to calculate the preferred sensory directions for the muscles **(FIGURE 8*B*)**. These corresponded well with the perceived directions of movements during vibration of individual muscles **(FIGURE 8*C*)**.

An estimate of the population responses of spindle afferents for each of a number of muscles involved in a movement was used to calculate the required patterns of vibration necessary to achieve such a response. Simultaneous vibration of various muscles, using the computed vibration patterns, allowed the generation of sensations in two (e.g., Ref. 331) and three dimensions (382). Subjects correctly reported illusory movement patterns including images of graphic symbols and complex three-dimensional figures.

To summarize, two important principles for proprioception emerge from this work. One is that it is not the activity of individual afferents but the combined response of the population of afferents that provides useful information about a movement. Second, proprioceptive signals generated during a movement by muscle afferents from a group of muscles are typically not interpreted in terms of muscle length or joint angle percepts, but in terms of the dynamic displacement of the limb's end-point. Similar conclusions have been reached by others using different techniques (e.g., Refs. 297, 370). Studies on the hindlimb of the cat indicate that the input from as few as 10 proprioceptive afferents can provide reasonably accurate information about the position of the limb (370). Issues that remain to be resolved are how muscle receptor responses combine to signal limb position as against limb movement, and how movement and position information is handled during active movements involving muscle contraction when the fusimotor system is engaged. Here an important issue is the process of central integration of afferent signals with signals of motor command or corollary discharge.

E. Motor Equivalence

It is a common experience that one's signature in a book is identifiably similar to the same signature written on a large blackboard. In terms of the direct motor output for the two tasks the requirements are very different, involving different muscles and forces. Yet the signatures closely resemble one another. This is referred to as the motor equivalence principle. It implies that actions are encoded within the CNS in terms that are more general than the commands to specific muscles. Details of motor implementation such as stroke speed and size are left unspecified until the effector is known (418). The principle of motor equivalence can be applied in proprioception to the signaled property for movements, that is, movement of the limb segment end-point (30).

Some psychophysical observations are consistent with such a view. In a two-arm position matching task, subjects were more accurate when they held their arms by their side, hands in front (160) and subjects aligned their arms by matching hand position rather than elbow angle. Subjects are better at matching arm orientation than elbow angle (368, 426). When subjects were asked to indicate the position of their unseen forearm, they were less accurate in determining elbow angle than when asked to locate fingertip position. This result was interpreted in terms of optimizing estimates of limb end-point position

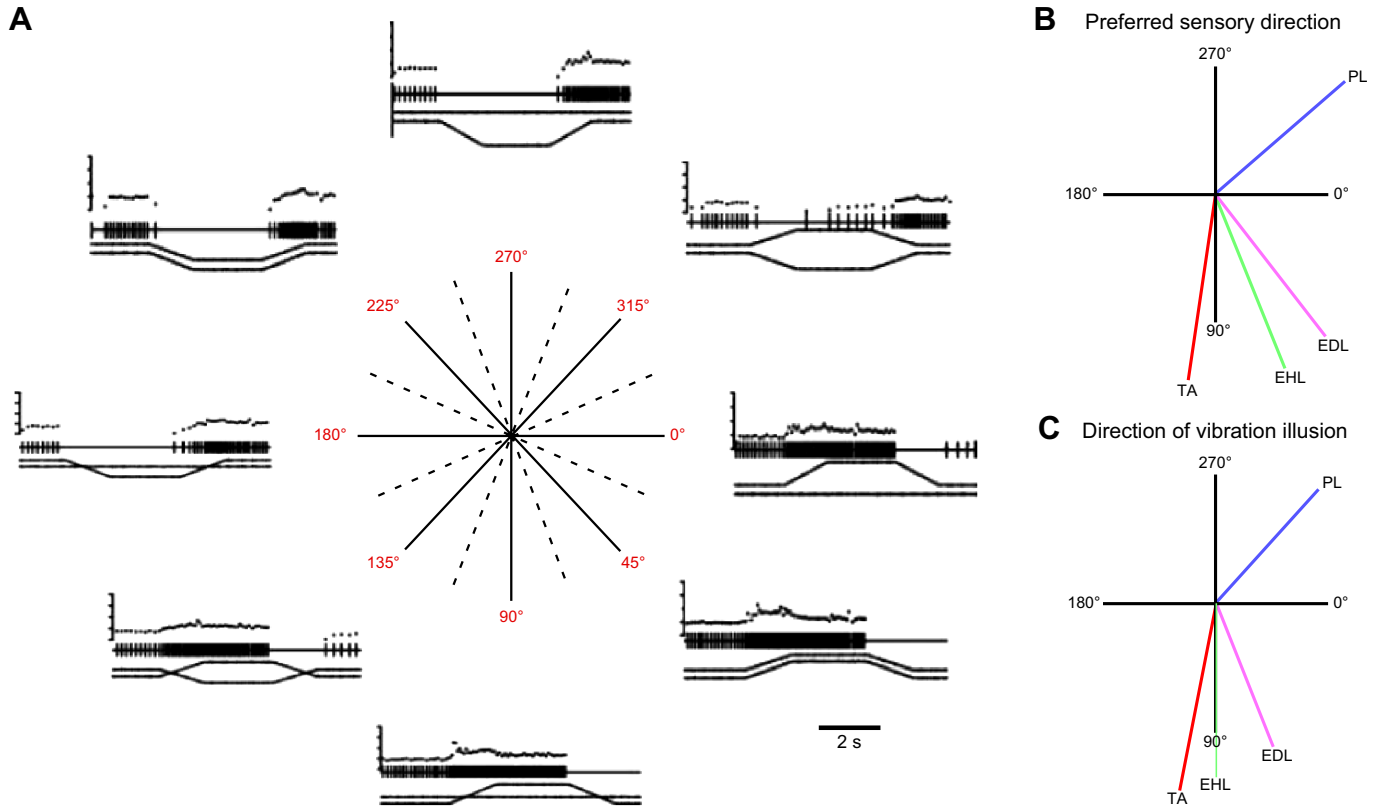


FIGURE 8. Coding of movement directions by human muscle spindles recorded by microneurography. *A*: responses of an extensor digitorum longus muscle spindle to ankle movement, shown for 8 of the 16 tested directions. The diagram in the middle indicates the directions: the solid lines, the directions for which responses have been shown, and the dashed lines, where the responses have not been shown. In the response record alongside each direction line, the top trace shows instantaneous frequency of spindle discharge, the middle trace the recorded impulse train, and the bottom two traces the X and Y coordinates (vertical and horizontal) of the movement. *B*: responses, like those in *A*, were used to determine the preferred sensory direction for each afferent and, using a population vector model, the mean preferred sensory direction for the population of afferents in the muscle was calculated. Different-colored lines indicate the mean preferred sensory directions for each of four muscles (PL, peroneus lateralis; EDL, extensor digitorum longus; EHL, extensor hallucis longus; TA, tibialis anterior). *C*: mean directions of vibration-evoked movement illusions in the four muscles, pooled from 10 subjects. Directions of the perceived illusions were indicated by subjects on a report sheet. They corresponded reasonably well with the calculated mean preferred sensory directions of the muscles. [Data modified from Bergenheim et al. (21), with kind permission from Springer Science and Business Media.]

(131). Similarly, observations on monkeys suggest that the desired end-point of a movement is one variable coded by the motor cortex (162, 293).

IV. THE BODY IN THE BRAIN: BODY SCHEMAS AND IMAGES

There are at least two reasons for including body schemas and images in a discussion of proprioception. First, while proprioceptors provide information about position and movement of the limb, they are unable to signal the length of limb segments and therefore the absolute location of the limb in space. So when we vibrate biceps brachii, it always leads to a sensation of elbow extension, but extension from where? There must be a reference point to which the vibration evoked proprioceptive information is referred. This requires knowledge of a body map. Second, there is the issue of body ownership. When we move an unseen limb, while proprioceptive feedback tells us about the movement, we need to be able to identify the moving limb as our own. So the body image tells us about the shape and location of different parts of our body and allows us to distinguish between what parts are our own and, in some circumstances, what parts are foreign. The subject of body images is a large one, and we have taken a somewhat narrow view, focusing on proprioceptors and their central actions. For more detail, the reader is directed to recent work (22, 89, 229).

A. The Deafferented Subject

The rare condition of deafferentation due to a large-fiber sensory neuropathy deserves particular attention because it

provides unique insight into aspects of movement control and the body image in the absence of proprioceptive feedback. These patients typically have sensory nerve fibers below 7 μm diameter and all motor nerves intact (e.g., Refs. 71, 75, 81). It is notable that reports of these large-fiber sensory neuropathies have involved adult subjects who have already acquired their full repertoire of movements. The subject loses proprioceptive and tactile inputs (from large-diameter afferents) from the neck down, while motor nerves (and small-diameter afferents) are left intact. On first experiencing the sensory loss, the prone subject is unable to move and feels as though they are disembodied, floating in air (72). This sensation receded as the subject taught themselves to move. Learning to move was a lengthy process, involving extensive retraining, and even then movements remained slow with some persistent ataxia. Recovery of a sense of embodiment in deafferented subjects suggests that in normal subjects the intention to move may be as important as afferent feedback in acquiring a sense of embodiment (72).

In the deafferented subject, control of movement is based on visual attention to the target and on cognitive effort (the will to move). The subject is required to focus on the act of the movement itself, such as making the arm move and the fingers flex to grasp the object. In the dark, the subject does not know where their limbs are and is unable to make controlled movements. The subject has to visualize external space and their own body to move one within the other. Here topokinetic movements, movements to target positions, are distinguished from morphokinetic movements used to shape the body part involved in the motor task, for example, shaping the hand to pick up an object (74). While the deafferented subject initially loses the ability to make gestures, they are able to recover them remarkably well. It has been suggested that in the deafferented subject some aspects of gestures remain normal, and this has led to the proposal that gesture is a linguistic phenomenon and not related to instrumental movements (74).

B. Representations of the Body

The concept of body images in the brain was introduced by Head and Holmes (182). They proposed the concept of body representations based on neurological patients with selective loss of particular sensations. These pioneering ideas have evolved over the years (for review, see Refs. 89, 133). One proposal is that there are two distinct body representations. The body image is a cognitive representation of the body that is based on stored knowledge and experience and is thought to underlie perceptual judgements. In addition, there is the body schema that is dependent on ongoing proprioceptive input, operates largely unconsciously, and is concerned with body movements (133, 279). Areas of cerebral cortex attributed to these functions are the parietal cortex for immediate guidance of action while conscious perception and memory may be associated with the insula (92).

In support of dual systems of body representation, Paillard (279) described two patients with specific neurological deficits. One subject had a stroke with damage to the parietal cortex on the left side. She was left with a complete cutaneous anesthesia in her right hand. Following touch of the anesthetic area by the experimenter, she was able to localize accurately the site of touch, yet she insisted that she had not felt anything. Such behavior was interpreted as an example of blind touch (by analogy with "blind sight," Refs. 409, 410). In other words, it was an example of being able to determine "where" without knowing "what." The second subject had a peripheral sensory neuropathy. She was able to detect pain and thermal stimuli applied to the hand but could not localize them to her own hand. Yet she could accurately locate the touched spot on a drawing of the hand. Here she appeared to resort to stored knowledge of the spatial configuration of the hand. Similar evidence for a dual system of body representation comes from cases reported by Anema et al. (9). They described two stroke patients, one who was able to accurately locate a touched spot on the hand, but poor at identifying where on a line drawing of the hand they had been touched. This was considered an example of a disturbance of the body image. The other patient exhibited the reverse behavior; they did not know where they had been touched, yet they could identify the spot on a line drawing of the hand. This was considered a disturbance of the body schema.

Patients with large-fiber sensory neuropathies typically have sensory nerve fibers below 7 μm diameter intact and all motor nerves intact (e.g., Refs. 71, 75, 81). In subjects with large-fiber sensory neuropathies, if itch was induced in the skin by local topical application of histamine, they could accurately indicate the site of the itch (22). This finding suggests that senses such as itch and pain, as well as warm and cold (73, 279), can, to a limited extent at least, act as de facto proprioceptors to guide movement. However, a small-fiber system, capable of only slow, sluggish responses, cannot replace the full proprioceptive feedback available to normal subjects. In experimentally deafferented subjects, the small-fiber system does seem to maintain the sense of limb ownership (282).

In the deafferented subject, partial motor control is achieved using a consciously maintained body image (134). Mental control of movements is limited to simple movements, is slower than normal, and the movements are relatively short, as otherwise they become too exhausting for the subject. Complex movements require a lot more energy to execute than simpler ones. By comparison, a normal subject can forget about their body in daily routines. It takes care of itself. In simplistic terms, this is because the body schema functions to control posture and movement unconsciously, without the intervention of a body image.

Difficulties in providing a precise definition for concepts such as body schema and body image have led to a variety of related but distinct proposals. Carruthers has proposed that all representations of the body are available to consciousness (60, 61). "On-line," newly constructed body representations, provided by inputs such as vision, touch, and proprioception, generate a perception of the body as it actually is at any moment in time, an image which is able to change from moment to moment. It is distinguished from an "off-line" representation constructed, in part, from current sensory inputs, in part, from stored memories and is available to consciousness both immediately and after retrieval of memories.

The idea of an off-line representation is useful as it helps to account for phenomena such as inclusion of hand-held tools in the body schema (58) and the development of phantom limbs after limb amputation (e.g., Refs. 154, 185, 252, 315). The failure to remove the amputated limb from the off-line representation leads to development of a phantom. A similar situation arises when a subject becomes unaware of paralysis of a limb following hemiplegia (anosognosia). Again, the paralyzed limb is not removed from the off-line image (125). One way to eliminate these phenomena at least temporarily is by use of mirror box therapy (125, 314).

An interesting comment on the sensory processing involved in the generation of a body image is provided by patients suffering from anorexia nervosa. They experience pronounced body image distortions in combination with the desire to maintain a low body weight. Anorexic patients, when looking into a mirror, do not see their actual body image, but an overweight one. In support of the idea that the integration of visual and proprioceptive information is abnormal in these patients, it was shown that anorexic individuals do not exhibit the normal size:weight illusion (63).

C. Phantom Limbs

A phantom limb can persist for months and years after amputation (252). Indeed, it even arises in some subjects with congenitally absent limbs (254). In response to motor commands, the phantom can be made to move in two ways. Component parts of the phantom may change position relative to one another. Here the sensation is thought to arise centrally. Second, when the body part bearing the stump of the limb is moved, the whole phantom may move with it while retaining its relative position to other body parts. Voluntary movements made in this way by a phantom limb are often accompanied by contraction of the appropriate muscles in the stump. If the remnant muscles are denervated, the ability to move the phantom is lost (185, 321, 374). However, observations with experimental phantom limbs (see below) suggest that movement sensations can also arise centrally.

Putting the observations together, the phenomenon of a phantom limb is largely of a static limb. The sensation does not appear to depend on peripheral input and can be generated by central neural activity, but which can be modified by peripheral sensory input. The phenomenon emphasizes the uniqueness of the sense of limb position. The sense of a moving phantom may be dependent on stump muscle activity, but it can also arise centrally (205, 256, 322).

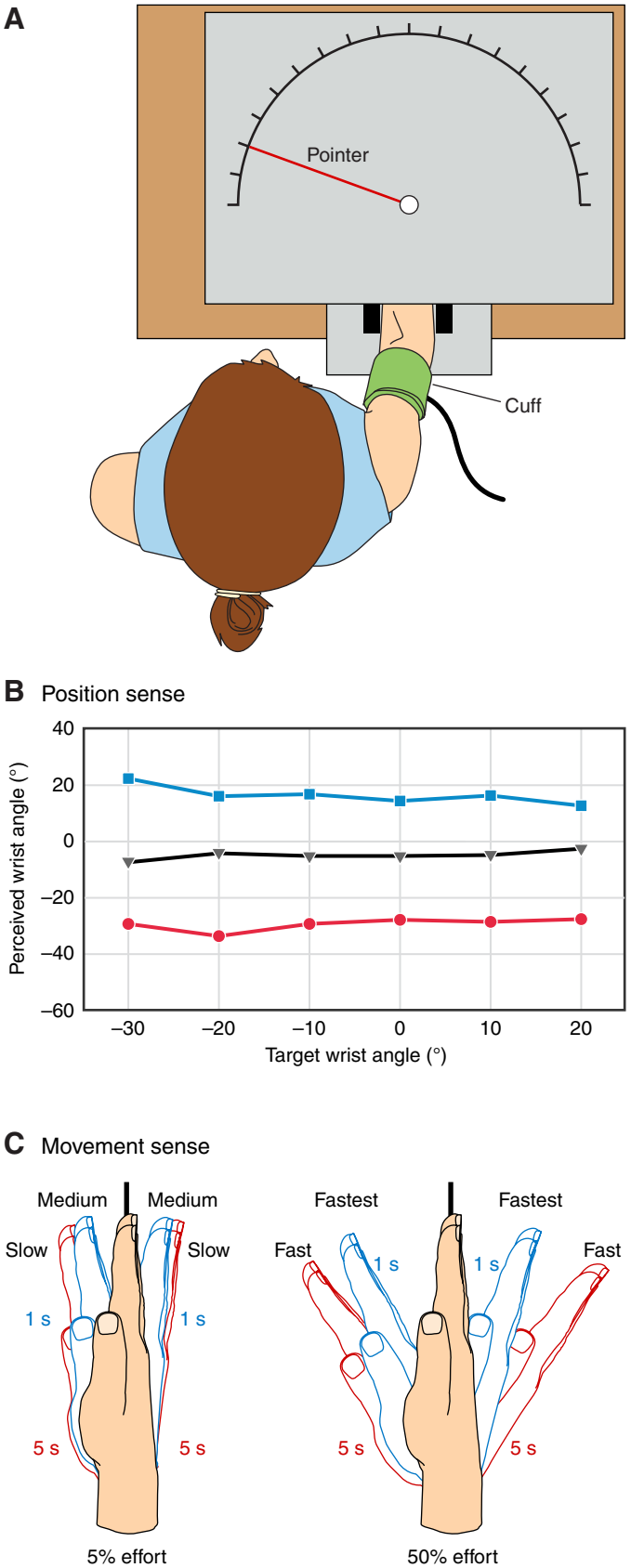
The more distal parts of a phantom limb such as the hands or feet, especially the digits, are more strongly perceived than proximal segments. This may relate to the denser peripheral innervation and, consequently, more extensive cortical representation of distal segments. Perception of the phantom limb changes with time, the more weakly perceived parts fading from awareness, often leading to a telescoping of the limb (e.g., Ref. 327). Such an effect presumably relates to a reorganization of the cerebral cortex where areas deprived of peripheral input are invaded by adjacent areas (e.g., Refs. 123, 294; for review, see Refs. 41, 207).

D. Experimental Phantom Limbs

The idea of producing an acute block of sensory and motor nerves to a limb to produce an experimental phantom was pioneered by Melzack and Bromage (253). With their eyes closed, prone subjects described the location of a phantom arm after an anesthetic nerve block at the brachial plexus. The phantom lay at the side of the body, above the lower abdomen or above the lower chest. During the block, orderly spontaneous changes in posture occurred between these three positions, positions which bore no direct relationship to the position of the arm at the time or before the onset of the block. The reported postures are reminiscent of postures of amputation phantoms (185).

Recent observations provide insight into how an on-line representation of the body might be constructed (198). An experimental phantom hand and forearm can be produced by means of an ischemic nerve block in the upper arm; the hand becomes both anesthetic and paralyzed (e.g., Refs. 148, 398). The method is depicted in **FIGURE 9*A***. To signal the position of the experimental hand, subjects manipulated an articulated model hand with their other hand. When the nerve block was established, subjects signaled the perceived position of the unseen hand every 3 min by adjustments of the model. As the block took effect, perceived posture of the hand gradually changed. If the fingers were held straight throughout the block, the perceived posture of the "dead" hand had the fingers flexed. When the fingers were held flexed during the block, the phantom adopted a more extended posture at the finger joints. The results are shown in **FIGURE 10**.

In the simplest interpretation of the observations, posture of the hand is signaled largely by afferents from the muscles



and skin stretched by that posture. Perhaps the key parameter is the difference in discharge rates between afferents in hand flexor and extensor muscles. When the hand is held extended, flexors are stretched and extensors shortened. As the nerve block takes effect, the discharge from the stretched flexors falls, and this is interpreted by the subject as the hand moving into a more flexed posture. When the starting position is a flexed hand, the declining discharge coming from stretched extensors leads to perception of a more extended posture. Such observations emphasize the lability of the body schema and its dependence on the moment-to-moment input of activity coming from the body periphery.

In relation to the question of movement sensations by a phantom limb, under the conditions of the above experiment, when subjects attempted to move their paralyzed, anesthetized hand, they perceived a distinct movement of the hand as well as displacement of its position (e.g., Refs. 148, 398). The velocity of the movements and total angular displacement of the hand graded with the level of effort while total displacement also graded with duration of effort. Increasing the effort 10-fold increased the size of the movement 2- to 3-fold and the perceived movement speed about 2-fold (398) (see **FIGURE 9*C***). There are interesting differences with movement sensations in the oculomotor system: here recent studies during full paralysis of the eye muscles have shown that in darkness commands to move

FIGURE 9. The experimental phantom hand: the effect of motor commands on perceived position and movement. *A*: method used to produce ischemic anesthesia and paralysis of the right forearm and hand using a pressure cuff on the upper arm. To test position sense, the wrist and hand can be placed in specific postures by the experimenter, and the subject uses their left hand to move the pointer to indicate its perceived position. *B*: when the hand had been anesthetized and paralyzed, the perceived position of the relaxed hand (▾), with the subject making flexion efforts (●), and with them making extension efforts (■) plotted against test angles from −30 to +20°. The neutral position of the phantom hand is perceived as slightly flexed (▾). Attempted flexion or extension movements at 30% maximum effort causes large perceived displacements in the direction of flexion for flexion efforts and in the direction of extension for extension efforts. [*B* from Gandevia et al. (148).] *C*: perceived motion of the phantom hand. The filled hands (thumb, index finger, and middle finger are shown) represent the actual position of the hand. Left figurine: subjects made effort of 5% maximum (for 1 or 5 s); right figurine: subjects made effort of 50% maximum (for 1 or 5 s). When subjects made voluntary efforts to move their paralyzed and anesthetized hand, the blue-outlined hands show the mean size of the phantom wrist movements reported during a voluntary effort that lasted 1 s. The red-outlined hand shows the mean size of the phantom movements reported during a 5 s voluntary effort. Subjects indicated that they perceived movements of their phantom that were bigger when they made stronger efforts (compare left and right figurine). Movements with the greatest speed over the duration of the efforts occurred for efforts at 50% maximum lasting 1 s (blue hand in right figurine). The speeds of the movements produced by the four voluntary efforts are ranked by the terms slow, medium, fast, and fastest. [*C* redrawn from data in Walsh et al. (398).]

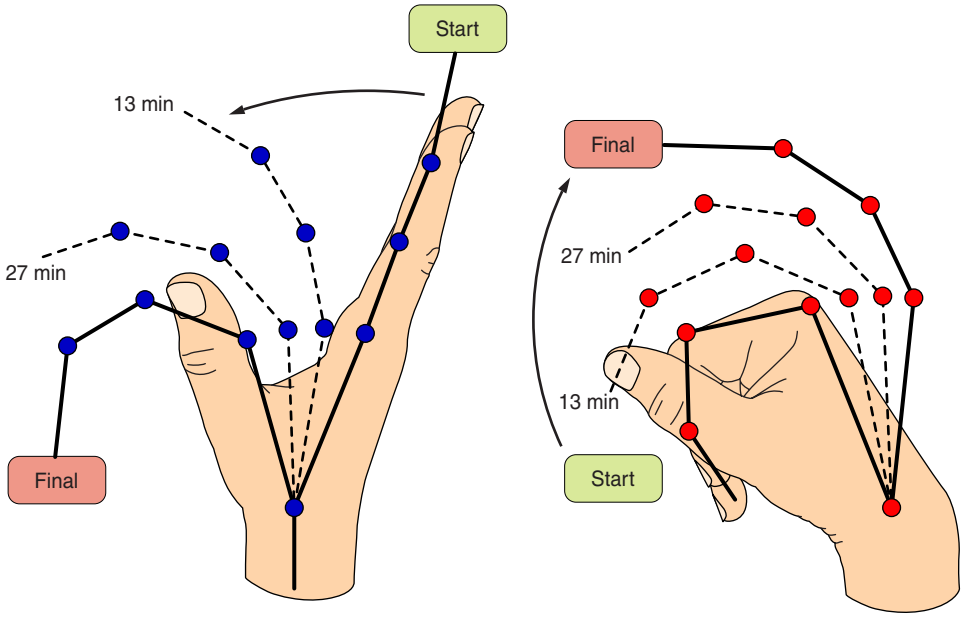


FIGURE 10. Perceived changes in posture of the relaxed hand during paralysis and anesthesia. When the starting position was an extended hand (Start, *left*, blue), as the nerve block took effect, the perceived posture became progressively more flexed over the 40 min the block was in place (Final). When the starting position was a flexed hand (Start, *right*, red), the perceived posture became progressively more extended. [Redrawn from Inui et al. (198).]

the eye are accompanied by a rapid shift of the visual world (413). In contrast, the illusory movements with paralyzed limb muscles are slow, as if the hand is moving through treacle (148, 398).

E. Local Anesthesia

In the above experiments, as the nerve block began to take effect, subjects reported an increase in the perceived size of their hand (198). It is a common experience that dental anesthesia leads to perceived increases in size of the lips, tongue, and parts of the face (384). Similarly, anesthesia of the thumb increases its size by 60–70% (147), and a brachial plexus block produces illusory swelling of the arm (281). These phenomena, while relevant to the broader subject of body image, probably relate to acute changes within cortical areas responsible for their representation. Interaction between excitatory and inhibitory influences at cortical and subcortical sites produce an expansion of cortical areas representing the body part and that expansion is presumably responsible for the perceived increase in size (54–56). It suggests that the cortical representation of each body part has an inhibitory surround maintained by small-fiber input which, if removed, leads to an expansion of the representation. Illusory increases in size may not appear to be so dramatic when a large part of the body is anesthetized or removed (227, 258). While these immediate distortions of body size with local anesthesia have been linked to loss of input from small-diameter afferents (e.g., Refs. 54, 281, 282), recent work using ischemic anesthesia indicates that the loss of large-diameter afferents also plays a role (198).

F. The Body Form

It has been known for some time that the consciously perceived body image is distorted. When normal subjects are asked to point with their left index finger to different parts of the hidden right arm, the resting arm is systematically perceived to lie closer to the midline as well as closer to the body than its true position. Errors increased the longer the arm remained hidden. The observed postures resembled those seen with phantom limbs (e.g., Ref. 173). More detailed, information about what we perceive to be the size and shape of our body has recently been provided (229). The authors make the point that although information about body posture is specified by ongoing afferent input, no sensory signals are available to detail body size and shape. The incoming positional information must be referred to a stored model of the body's metric properties. To reveal aspects of the model, maps of the mental representation of the unseen hand were drawn. The size of a finger was determined from landmark locations, the finger tip and knuckles, indicated by the subject. They revealed a distorted map with the fingers shorter than their actual size and the hand broader than it really was. These distortions resembled cortical somatosensory representations of the hand as drawn in the sensory homunculus (290). In contrast to these distortions, explicit judgements of hand shape assessed in a template-matching task revealed that the mental image of the hand lay close to reality, and it did not reveal the distortions measured by pointing. It was concluded that in addition to the body schema and body image, a new representation had to be included, which was called the "body

form." In answer to the question, how was the distorted body form reconciled with the body schema/image, one suggestion was that the motor system simply avoided explicit representation of initial limb position by coding the desired end-point of a movement (162, 293), although such end-point coding has some limitations (65). As the motor system typically relies on vision as well as proprioception, correction of the distorted body form may occur from motor learning using these additional inputs.

G. Development

There is some information on developmental aspects of a body image/schema. Soon after birth humans show a strong innate tendency to mimic sounds and motor acts, copying orofacial movements performed by adults before them (251). Such behavior supports the existence of mirror neurons (for review, see Ref. 180), with imitation providing the basis for an understanding of the relationship between oneself and others. This is postulated to lead to the sense of self as an agent and as the target of social interaction. Babies a few weeks old vocalize in response to language and attend to their mother's orofacial area, much more than her body, as a source of emotional support. They see movements and then copy them. Visual recognition of spatial configurations of the body below the face matures after one year of age, followed by the ability to recognize and name body parts, as well as acquisition of language skills (364). About this time the child begins to recognize his or her own face and body in a mirror, an ability considered an objective index of emerging self-consciousness (211).

A broader question concerns the role of proprioception in development of motor skills in children. There must be regular recalibration of the body schema in response to growth of the body. Pioneering observations by Laszlo and Bairstow (223) have led to the view that the ability of children to use proprioceptive feedback has matured by the age of 7 years. Other reports suggest that there is ongoing learning of movement control which continues through adolescence (156), and into adulthood (183). So, development of proprioceptively controlled movements continues beyond the period required for acquisition of motor skills, thought to be complete by the age of 10 years (348).

H. Body Ownership

Proprioception, by definition, is associated with actions occurring to the self. This begs the question, how does the brain know what is part of the body and what is not? Exteroceptive sensations such as vision and hearing cannot distinguish between foreign body parts and our own. Belief in what we think belongs to our body can be surprisingly easily manipulated by experiment. This has been revealed by many recent studies in which subjects become convinced that an artificial limb is their own, using what is known as the "rubber hand" illusion (e.g., Ref. 31). In extensions of this illusion, a subject can, for example, have multiple limbs (106, 274) or even appear to be located outside their own body (105, 291). In the rubber hand illusion, the subject's unseen hand is stroked at the same time as a rubber hand lying near it. Within seconds, subjects become convinced that the rubber hand is their own to the extent that it is used in motor planning (e.g., Refs. 31, 208) and they respond defensively when the artificial hand is threatened (e.g., Refs. 14, 110).

Adoption of "ownership" of the artificial limb does not require vision and can be equally effectively achieved in a blindfolded subject if the experimenter guides the subject's left hand to touch the rubber hand while at the same time touching the subject's own right arm (107). Cutaneous stimulation by brushing the skin has been the method used to induce the illusion. Recent studies have shown that ownership illusions can be evoked by both passive and active movements (97) even of just one finger (400). The illusion is just as strong after local anesthesia of cutaneous and joint afferents from the finger and thus the input provided by muscle spindle afferents with vision of a false finger is sufficient to generate sensations of hand ownership (400). Importantly, in unpublished work (Walsh, Heroux, Butler, and Gandevia), this role of muscle spindles has been established even when there is no vision of the hand (using a complimentary approach to Ehrsson et al., Ref. 107).

I. Brain Areas Associated With the Body Image

Neuroimaging studies have revealed regions that are activated by different aspects of proprioception and its interaction with the body representation. These include multisensory regions in the parietal cortex (e.g., Refs. 26, 83, 107, 109, 126, 176, 226, 289), as well as parts of more distributed networks including the frontal cortex and insula (e.g., Refs. 346, 383). There are brain areas selectively responsive to viewing human bodies, except the face, while others are preferentially responsive to viewing the face. The extrastriate body area is concerned with individual body parts like the fingers and recognizing that they belong to oneself (e.g., Refs. 96, 190, 269). Adjacent to it is the fusiform body area which also shows a selective responsiveness to viewing the body, but it seems to be more concerned with movement of large parts of the body like the torso. The fusiform body area overlaps in part with the face selective area in the middle of the fusiform gyrus. A second face area is the occipital area (150, 288). Even the primary somatosensory cortex, which is traditionally viewed as a map of the physical body, participates in illusory proprioceptive distortions of the limb (343, 344).

Left parietal lesions are implicated in an alteration of body awareness in which patients are unable to point to parts of their own body on verbal instruction, in spite of being able to respond to verbal commands to move that part towards an external object (e.g., "touch the pedal of that bicycle"). These patients have lost the sense of relations between body parts, knowing for example, that the mouth is between the nose and the eyes (114).

To conclude, there are a number of distinct brain areas responsible for recognition of body and face, arguing for more than just two "bodies in the brain." The posterior parietal cortex, anterior insula, and extrastriate body area are important areas. They are present in both hemispheres, but most studies have provided evidence for a right-sided dominance in many aspects of body awareness (22), and this may involve parts of the primary somatosensory cortex (271).

V. THE SENSES OF EFFORT, FORCE, AND HEAVINESS

When we carry out a motor task we are aware of the muscle contraction accompanying the action, how much effort is required and, if it is an object to be moved, we have a sense of its heaviness. The senses of effort, force, and heaviness are traditionally believed to be generated, at least in part, by signals of central origin associated with motor commands. Peripheral sensory receptors are also available to contribute to the sensation, including tendon organs, muscle spindles, and pressure-sensitive skin receptors.

As proprioceptive sensations, the senses of effort, force, and heaviness are distinct in that they are always associated with motor commands, while kinesthetic sensations can arise in a passive limb. It implies that for the senses of force and heaviness the peripheral input is always reafferent in origin. Another issue to consider is the meanings of the terms. What do we mean by a sense of effort as distinct from a sense of tension?

A. The Sense of Effort

As mentioned in section I, the prevailing view during much of the 19th century was that our muscle senses arose entirely centrally, and this included the sense of effort experienced during execution of a motor task. However, during the middle of last century, two influential reports argued for a combined central-peripheral mechanism for proprioception. The impact of these ideas is still evident today. In a study of eye movements in fish, Sperry (369) introduced the term *corollary discharge meaning*, "a corollary discharge of motor patterns into the sensorium may play an important adjuster role. . . . along with non-retinal and postural influences from the periphery". So here was the suggestion of a central sensory area acted upon by both motor command signals as well as signals originating in the periphery. In the same year, 1950, von Holst and Mittelstaedt (393) put forward a similar proposition based on experiments in insects. They introduced one additional important concept that continues to be influential. They distinguished between afferent signals generated by the animal's own actions and signals generated by external sources as the animal moved about in its environment. The term *exafference* was used for afferent signals generated by stimuli of an external origin and the term *reafference* was used for afferent activity arising from the body's own actions. The reafference was calculated using an efference copy of the motor command. It remains a matter of conjecture whether the efference copy is an accurate copy of the motor outflow, or a computation, based on past experience, of the expected afferent signal for a given motor outflow (95). The total afferent signal generated during a motor act is made up of two components: the predicted reafferent signal, determined by the motor command, and afferent activity generated independently of the motor command, as a result of external influences. While the corollary discharge hypothesis was put forward to deal with the problem of visual stability during eye movements, the efference copy hypothesis has implications for all movements (194). These ideas have recently been formalized in a model for motor control (19, 423). Some aspects of such a model are considered in **FIGURE 11**.

The underlying idea is that not all of the signals generated by a movement reach consciousness, and we perceive only the exafferent component. So, for example, the sensation when we are tickled by someone else differs in quality and is much more intense than when we attempt to tickle ourselves (23, 24). Part of the mystery of the proprioceptive senses is that much of the afferent information generated by self-initiated movements does not reach consciousness. As a consequence, the detection and perceived intensity of afferent signals are diminished during movement (for references, see Refs. 260, 414). Such suppression can occur along somatosensory pathways (e.g., Ref. 67) as well as from the actions of the motor command signals themselves (415).

If a compression force, generated externally by a motor, is applied to the hand and the subject is then asked to reproduce the felt force using their other hand, they invariably apply a greater force than was applied externally (353, 354, 394). This is illustrated in **FIGURE 12*A***. The overestimation is presumably due to the partial suppression of the afferent activity associated with self-stimulation. In everyday activities, such sensory suppression would allow us to focus attention on external stimuli and be less distracted by the sensations arising from our own movements. A model has been proposed for this attenuation of self-generated movements (19). A recent reexamination of the phenomenon showed that the overestimation of forces applied externally to the index finger of one hand when they were reproduced by self-generated force only occurs for low applied force levels but not higher forces (402). The overestimation per-

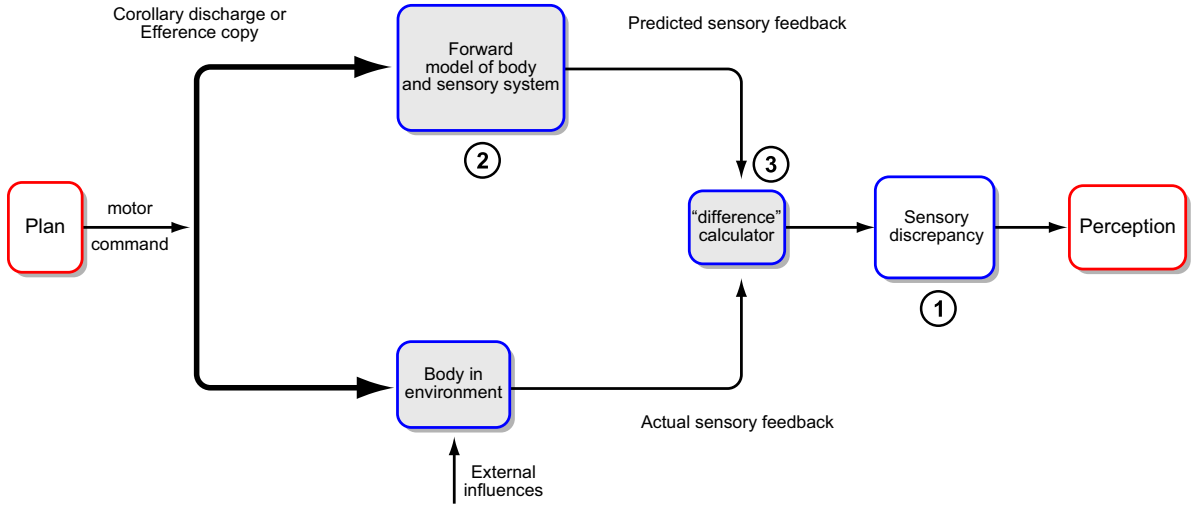


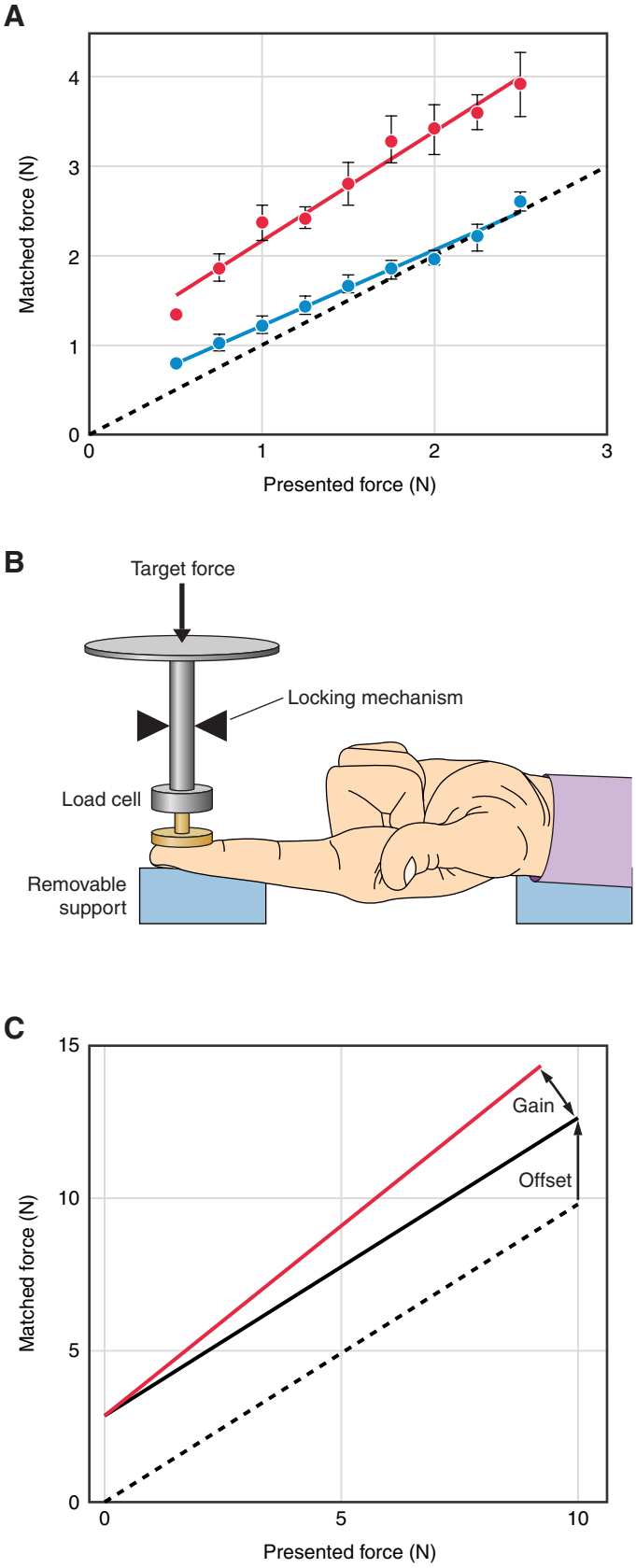
FIGURE 11. Model for a central comparison between sensory and motor signals, based on the proposal of Bays and Wolpert (19). The process begins with the intention to move (Plan), leading to generation of a motor command and its efference copy/corollary discharge. The Forward model uses the efference copy to calculate the expected outcome, and this is compared with the input (Body in Environment) by means of a difference calculator to quantify the sensory discrepancy that determines what is actually perceived (Perception). Three points for consideration are as follows: *1*) if the predicted and actual sensory feedback match, the anomalous situation arises where there is no perception at all; *2*) the forward model needs to be regularly updated over both short and long time scales; and *3*) the "difference calculator" is more complicated than depicted here because, at least for force sensation, its output is not determined by a simple subtraction process (for details, see Ref. 402).

sisted when digital nerve anesthesia was used to block cutaneous and joint sensation, leaving only combined inputs from muscle and central command sources available to signal the force. In addition, these new data revealed two components to the overestimation at low forces: an offset as well as an increase in the gradient between the matching and target forces. The latter was present only when the finger was actively held in position. That is, as the target force was increased, the discrepancy between target and matching forces increased. This is shown in **FIGURE 12*C***.

The operation of forward models should not be seen as static events, operating in isolation. So, for example, in learned motor tasks (overlearning), we carry out the action without thinking about it, unaware of its predictability. This is an example where the predicted and observed afferences match, and there is no accompanying sensation. This is very different from an attention demanding task which, incidentally, can be carried out simultaneously with the overlearned task (130). So, in our everyday behaviors, we should imagine constantly shifting strategies, from the operation of internally generated actions to actions dominated by feedback from the periphery. The example of overlearning also implies that there is a learning stage to the task where proprioceptive feedback is used to fine-tune its execution (130).

B. Paralysis and Fatigue

It has been known for a long time from the clinical literature that partial paralysis comes with abnormal sensations of increased heaviness (e.g., Ref. 192). So, if there is a discrepancy between the reafference generated by a movement and the efference copy derived from the command signal, that the subject is typically unaware of, sensory illusions may occur. Patients with partial paralysis from an upper motoneuron lesion feel weights to be heavier on the affected side (144). When paralysis is induced experimentally by infusing a neuromuscular blocker, the effort required to lift a weight and its perceived heaviness was increased, compared with the unparalyzed condition (e.g., Refs. 141, 144). The authors made the additional observation that during a lifting task using thumb flexors, if skin and joint input from the thumb was removed by anesthetic block, the perceived heaviness increased further (see also Ref. 145). This was interpreted as the removal of a reflex facilitation generated by the cutaneous input, leading to an increase in central command and therefore perceived heaviness. Such a result fits with abolition of the long-latency stretch reflex in the lifting muscles by thumb anesthesia (238). The digital anesthesia will also have removed the cutaneous contribution to a peripheral force signal. Perceived heaviness can be manipulated by altering reflex excitability of hand motoneurons (12). Inhibition of the motoneuron pool led to an increase and facilitation led to a decrease in perceived heaviness of weights. Presumably, the contribution from a central command signal is adjusted based on the level of other excitatory or inhibitory drives reaching the motoneurons being used in the task. In other words, what we feel is automatically adjusted according to any reflex contribution of which we remain unaware. Given that the strength of



cutaneous and muscle reflex effects on the human fusimotor system is low even during contractions (e.g., Refs. 11, 146, 149), it is unlikely that the changes in perceived heaviness that are evoked by reflex inputs (at least from skin and joint receptors) can be explained by a change in muscle spindle signals.

A method commonly used to disturb the sense of effort is through fatigue from exercise (e.g., Refs. 62, 142, 206, 245, 404). A contralateral force-matching task is used, in which the isometric forces generated in one arm are matched by the corresponding muscle group of the other arm **(FIGURE 13)**. Under control conditions subjects are quite accurate at matching forces, producing matching errors of 5% maximum voluntary contraction (MVC) or less between the two sides. However, when one arm is exercised to fatigue, the level of force generated in the fatigued muscle is usually overestimated. The overestimation was considered to arise from efferent signals of similar magnitudes being sent to the muscles of the two arms, the unfatigued muscle responding with a higher force for a given level of activation. Similar conclusions have been arrived at by others (142, 245). In the first of these studies, weights supported by fatigued muscles felt heavier than when supported before fatigue. In discussing the origin of the sense of effort, McCloskey et al. (245) declared, "Whether this sense of effort should be regarded as simply a centrifugal mechanism or as involving some inherent comparison of outflow with afferent inflow remains an open question."

In support of an "effort" hypothesis, Cafarelli and Bigland-Ritchie (51) carried out a force-matching task with muscles

FIGURE 12. Comparison of perceived forces generated by self stimulation compared with stimulation by an external source. *A*: subjects were instructed to reproduce a target force, applied to the left index finger by a torque motor, either directly by voluntary pressing with the right index finger (red) or indirectly by controlling the output of a torque motor with a remote joystick (blue). Average matching force (±SE) is shown as a function of target force. Dashed line represents perfect performance. [Redrawn from Bays and Wolpert (19).] *B*: the subject's forearm rested on a table. When the subject's index finger was required to be passive, it rested on a support, but when subjects were required to actively hold the index finger in position, the support was removed. The shaft of the load cell could be locked in place or free to move up and down. The subject was asked to generate a matching force either by pushing down on the top of the platform with the other hand while the shaft was free to move or by pushing up isometrically against the load cell with their index finger while the shaft was locked. [From Walsh et al. (402).] *C*: diagrammatic representation of results obtained for forces below 10 N. Subjects overestimate an externally generated target force to a passive finger by 2–3 N (offset) when matching it with a voluntary contraction (e.g., flex the test finger or push down with the other hand). This occurs at low forces and even when cutaneous and joint inputs were blocked in the test finger. A central factor increases the gradient (gain) of the relationship between matching and target forces by ~20 if the target force is received on an active finger. [Data from Walsh et al. (402).]

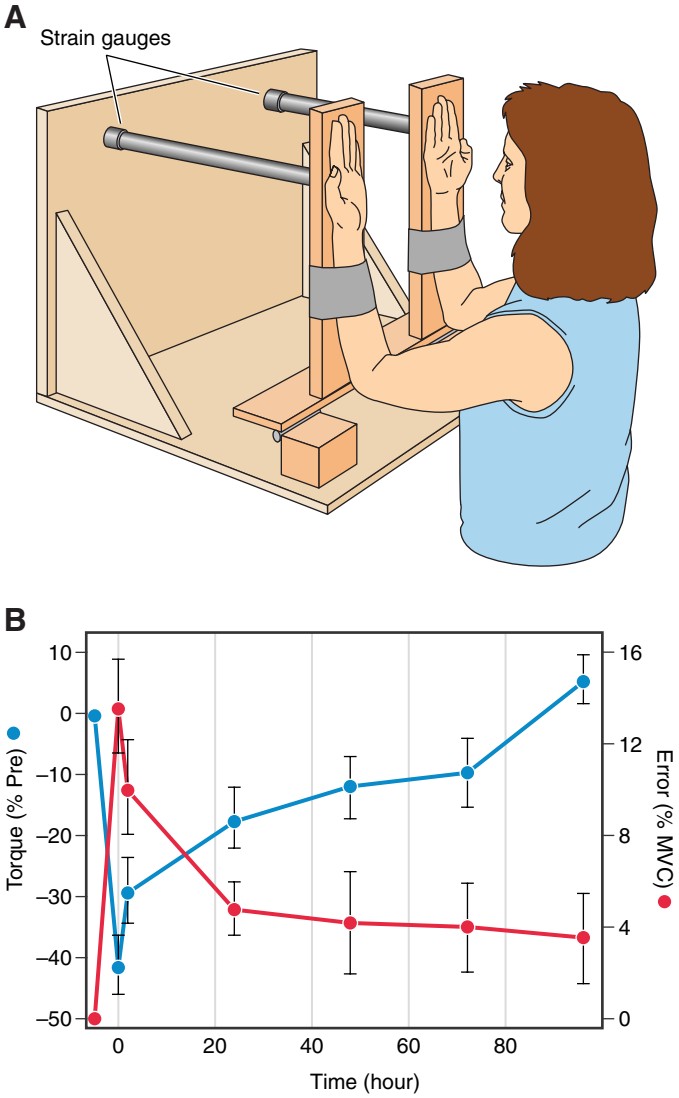


FIGURE 13. Isometric force matching before and after fatigue. *A*: the subject is seated with their forearms in the vertical position, strapped to paddles locked at 90°. The torque generated by elbow flexor muscles is recorded by strain gauges, and the output of the reference arm is displayed on a computer screen visible to the subject. The subject is required to match its torque level with their other arm (output not visible). *B*: the control error (red, right hand ordinate) is close to zero. Then the subject was required to carry out a series of fatiguing eccentric contractions that led to a 40% drop in MVC torque (blue, left hand ordinate). The fall in torque led to an overestimation of 14% by the unexercised arm of the torque generated by the fatigued reference arm. Over the subsequent 100 h, the matching errors gradually fell to a residual 4% while torque recovered to control levels. [Redrawn from Weerakkody et al. (404), with kind permission from Springer Science and Business Media.]

of different strengths. In thumb adductors and elbow muscles, using the muscle's length-tension relation to alter the level of force produced, it was concluded that matches were being made on the basis of equal sensations from the muscles being compared, not their forces. A similar conclusion was reached in a related experiment on elbow flexors. When the reference arm was held at angles representing the ascending or descending limb of its elbow flexor torque-angle relation, the matching torque generated by the indicator, held at its optimum length, was always larger (404).

Another potential source of errors in a force-matching task comes from activation of the small myelinated group III and unmyelinated group IV afferents in skeletal muscle. It is known that these afferents become active during a muscle contraction (209). Muscle afferents mediating pain, presumably involving both group III and IV (255), can be stimulated by injecting hypertonic (5%) saline into a muscle (161). In a two-arm force-matching task, when biceps of one arm was made sore by injecting hypertonic saline, the force in that arm was overestimated. That is, the subject thought the painful arm was generating more force than it actually did (407). This kind of mechanism is likely to account for the force-matching errors observed after eccentric exercise (312). Eccentric exercise is known to produce muscle damage and soreness (309). It remains uncertain how such an effect is mediated. Perhaps it is the result of influences on central sensory rather than motor pathways (213).

C. Two Senses

In an experiment in which they used muscle vibration, McCloskey et al. (245) claimed that if appropriately instructed, subjects had the ability to select between a sense of effort arising centrally and a sense of muscle tension, presumably deriving from intramuscular receptors. The same conclusion was reached by Roland and Ladegaard-Pedersen (329). Subjects compressed springs of different stiffness with one hand and matched the extent of compression and the force required with the other hand. During partial paralysis, the observed errors were below the expected levels if there had been a proportional relationship between the exerted effort and the generated force. When subjects were instructed not to match forces but efforts, this led to the expected increases in errors during neuromuscular blockade.

Put together, these various observations suggest that we may have two senses, a sense of effort and a sense of muscle tension. The sense of tension can only be revealed if the subject is appropriately instructed. This is a difficulty for studies in proprioception as it raises the problem of how to instruct subjects to perform a task. In experiments concerned with the effects of fatigue on force sense, subjects were specifically instructed to match the force generated in the reference arm, not the effort. Nevertheless, fatigue-related matching errors were observed that were interpreted as the subject relying predominantly on a sense of effort (407). Comparable observations had been made earlier (62, 206; see also Ref. 214). Such observations left open the question of the contribution from peripheral receptors to the sense of force.

D. Muscle Vibration

Another way to manipulate muscle force sense is to use muscle vibration during the matching trials. However, the effects of vibration are not straightforward to interpret. In a passive muscle, vibration will stimulate predominantly primary endings of muscle spindles. The Ia input facilitates spinal motoneurons and may produce a tonic vibration reflex (TVR) in the vibrated muscle (175). Once the muscle begins to contract, the contribution of tendon organs to the afferent activity will start to increase (113), adding segmental inhibitory reflex effects while generating force sensations centrally. After a period of vibration, muscle receptors are likely to become desensitized, and there may be reduced motoneuron excitability from postactivation depression (196, 425). Because of these multiple influences, psychophysical results from vibration experiments must be interpreted with caution. Not surprisingly, they have produced contradictory findings.

McCloskey et al. (245) reported that in 9 of 15 subjects carrying out a force matching task, vibration of biceps of one arm led subjects to match the reference force in the vibrated arm with smaller forces in their other arm. In experiments on force matching in quadriceps, the opposite result was obtained (52). When a vibrated muscle's force was matched with a nonvibrated muscle, subjects systematically chose higher forces with the nonvibrated muscle. To explain their result, the authors proposed that force generated in the TVR was sentient and the extra central input from it led the nonvibrated muscle to match with a larger force. Alternatively, vibration of the contracting muscle acted as a powerful stimulus for tendon organs, and the additional tendon organ input was interpreted as a higher level of muscle force. This is an interesting interpretation in view of the more recent observations by Luu et al. (233) who interpreted their observations on the senses of force and heaviness after prolonged muscle vibration as the result of a vibration-evoked desensitisation of muscle receptors. The findings of Cafarelli and Kostka were extended by Cafarelli and Layton-Wood (53) who showed that the increase in perceived force produced by vibrating a muscle gradually faded if the muscle was subjected to fatiguing exercise. One interpretation is that muscle receptors have become desensitized by the fatigue process so that their response to vibration diminishes.

E. The Sense of Force and the Tendon Organ

The most eligible candidate for a tension receptor is the tendon organ (for a review, see Refs. 136, 201, 302). Tendon organs, located at the ends of muscle fibers, are ideally sited to monitor muscle tension **(FIGURE 2)**. Like muscle spindles, tendon organs are stretch receptors. However, they are principally contraction receptors. A tendon organ will respond powerfully to contractions of motor units that contribute muscle fibers that insert into the receptor capsule. It will largely ignore contraction of fibers outside the capsule. Most of the muscle fibers inserting into the capsule of a tendon organ come from different motor units, so one tendon organ can be excited by 10–20 motor units. Calculations indicate that every motor unit in a muscle is linked to at least one tendon organ (302). Most tendon organs signal tension in a select group of motor units and can be considered to be regional tension sensors. They are therefore able to monitor submaximal contractions involving the motor units to which they are linked. Populations of tendon organs can signal whole muscle force (e.g., Refs. 84, 136).

Group I afferents, including those of tendon organs, project to the cerebral cortex (248), with projection to the cortex being a prerequisite for conscious perception of the receptor's activity. If impulses from tendon organs evoke conscious sensations, it raises the possibility that they are directly involved in the sense of tension. Here a consideration is that some central processing is necessary to convert signals of intramuscular tension into the required torque levels for moving a limb about a joint (140).

In an attempt to link tendon organ activity to proprioceptive sensations, Thompson et al. (380) asked subjects to reproduce a learned low force (4% MVC). After subjects could reproduce the reference force reliably, they repeated the task immediately after the muscle had undergone a MVC. The force reproduced after the MVC was twice as large as after a rest period. It was suggested that desensitization of tendon organ discharges during the MVC led subjects to overestimate the level of force. This suggestion was supported by observations in animal experiments that showed responses of tendon organs to a low-force contraction were much smaller when this was preceded by a maximal contraction. The time course of this desensitization of tendon organ responses matched the decline in matching errors observed in the human experiments.

F. Force-Movement Illusions

Perceived limb position is influenced by the forces required to move the limb to that location (for review, see Ref. 205). In a position matching task limbs can be accurately aligned when they remain passive or are supporting a static load (13, 340). However, when the loaded arm is moved, errors emerge (13). If a subject is required to generate an isometric force against the device imposing a flexion movement, the limb is perceived to be more flexed than it really is (340). A similar result was obtained when positions were matched with one arm undergoing elastic loading (403). The magnitude of the errors increases with greater applied force. Similar conclusions were arrived at in experiments involving compression of springs of different stiffnesses (329).

There is the old observation that when voluntary movement of an arm is unexpectedly blocked by an obstacle, the dis-

tance the subject thinks the arm had moved through, as indicated by the other arm, is consistently overestimated (191). The size of the illusion was influenced by the impact force and by the time after movement onset at which the impact was encountered; the later the impact point, the smaller the illusion.

Finally, blindfolded subjects were asked to match the positions of their forearms in the horizontal plane, under conditions where there were no direct effects of gravity. When one arm was loaded and the subject moved the loaded arm to the test angle, matching errors were seen that were not present when subjects simply supported a static load at the test angle (13).

All the experiments in this section have the common elements of position errors from the combined effects of load and movement. Modern theory proposes that during a movement, predictions about future states of the limb based on efference copy combine with sensory feedback signals, delayed by their conduction and processing times, to provide an estimate of the current state of the limb, allowing for a continuous updating of the estimate during the movement (see, for example, Ref. 423). If an arm movement is stopped shortly after its onset, the subject's estimate of hand position is dominated by the efference copy based predictive model, and the subject perceives the hand to be further from its starting position than is actually the case. During passive movements, in the absence of any efference copy, because of transmission delays in the afferent input, such an overestimate should convert to an underestimate. In a recent study that tested this prediction (172), with passive movements subjects still overestimated hand position, with errors that were as large as or larger than with active movements. The preferred explanation put forward by the authors was that the kinesthetic system used a Bayesian inference process in which afferent input and efference copy were both used continuously during the movement to determine the current position. This included an estimate of the expected state of the arm, based on past experience. The greater the uncertainty associated with the afferent input, the more the system relied on past experience estimates.

G. Emerging Ideas

When a muscle is weakened by fatigue or paralysis, a given level of force generated by the weakened muscle is accompanied by a less than proportional increase in the perceived effort. This has been noted by many investigators for both perceived heaviness and force (141, 242, 407; see also Ref. 328). More recently, Luu et al. (233), in a reexamination of the problem, began by pointing out that during fatigue or paralysis, the increase in perceived heaviness of objects, or perceived level of force generated, was less than expected, had a central command signal been entirely responsible for the sensations. If a peripheral force sensor had contributed, such sensations of increased heaviness or increased force should not have occurred, since force would have been accurately reported. It appears that the real situation lies somewhere between these two extremes, that is, force and heaviness sensations are generated by signals of both central and peripheral origin.

A new proposal put forward by Luu et al. (233) was that muscle spindles contributed to force sensations. In a heaviness matching task after deep paralysis of one arm, lifted objects felt lighter rather than heavier compared with the control arm. They proposed that this was due to a weakened spindle signal as a result of an intrafusal motor terminal blockade. It is known that when a muscle is deeply paralyzed, sufficient to block motor terminals on both extrafusal and intrafusal fibers, during the recovery period the extrafusal fibers unblock first, with recovery of intrafusal terminals being delayed (365, 427). During recovery, in the face of rapidly rising muscle force, the persisting intrafusal paralysis weakens the coactivation of spindles, and the lower level of afferent discharge leads to a reduction in the sense of force. In any case, the observations provided by this experiment were the opposite of what would have been expected if a signal of purely central origin had been responsible. An explanation based on a spindle signal can also account for the increase in perceived heaviness at the onset of paralysis. Extrafusal terminals block first, leaving intrafusal terminals functioning to evoke a strong spindle signal during a voluntary contraction, as the spindle signal is not suppressed by any unloading effects from extrafusal contraction. As a result of the increase in spindle signal, perceived heaviness increases.

In a weight-matching experiment on thumb flexor muscles fatigued with a sustained MVC, after fatigue of the reference muscle it was matched by a lighter load than before fatigue (233). This was again contrary to what would have been expected if a central command signal had been responsible for the sense of force. The load should have felt heavier! A similar reduction in perceived heaviness was not seen if instead of using an MVC to fatigue the muscle, a smaller contraction of 40% MVC was used. However, for the exercise at 40% MVC, if the muscle was vibrated during the fatigue process, the reference load was again matched afterwards by a lighter load. Here the interpretation was that the recruitment of muscle spindles and tendon organs by the vibration led to their desensitization. As a consequence, during test matching, the afferent component of the force signal decreased, leading to perception of a lighter load.

In a further experiment, weight matching was carried out in two subjects who had a large-fiber sensory neuropathy (76, 371). In these subjects who lacked input from muscle spindles and tendon organs in limb muscles, there was no opportunity for a peripheral contribution to the sense of heavi-

ness. While before fatigue both subjects were reasonably accurate in weight matching, when thumb flexors of one hand were fatigued to 50% of their control force, the reference load was reported to double in weight, as expected if the sense of heaviness was generated by a proportional signal of purely central origin.

These observations (233) throw new light on the senses of force and heaviness and point to further experiments. It is proposed that in normal subjects a reafference is generated in peripheral receptors in response to a motor command during weight matching. The signal includes input from skin receptors, muscle spindles, and tendon organs. When the sense of force is disturbed by fatigue or weakness, this can be accounted for by an altered peripheral signal. The new results suggest that signals of purely central origin are available but do not play a dominant role in normal subjects. It remains uncertain what the exact mix is of signals of peripheral and central origin for the sense of force. The sense of heaviness is closely related but includes a component of movement that will alter the responses of muscle spindles and tendon organs. We typically move our hands up and down during the estimation of the heaviness of objects. Subjects are less accurate if such movements are not allowed (245). However, only small movements are needed to achieve accurate judgements (142).

In a force-matching task during fatigue, can a spindle signal account for the amount by which the unexercised muscle overestimates the level of force in the fatigued muscle? It has been calculated (416) that a 10-fold increase in force in ankle dorsiflexor muscles produced only a 2- to 3-fold increase in spindle firing. Such a nonlinear relationship between spindle firing and tension could explain why the loss of force in the fatigued muscle is not fully expressed in the overestimate indicated by the unexercised muscle.

There is one further recent development. It has been possible to study some proprioceptive effects of the sense of effort in isolation by using an experimental phantom of the hand. The sense of position at the wrist was studied before and after a total nerve block at the upper arm using a pressure cuff. In the anesthetized and paralyzed arm, attempted flexion and extension movements at 30% of maximum effort produced perceived displacements of the phantom hand by 20° in the direction of the attempted movement (148) **(FIGURE 9*B*)**. Smaller displacements were perceived when the arm was paralyzed but not anesthetized, presumably because the available afferent signals influenced the final perception (367).

The sense of movement was studied while subjects attempted to move their paralyzed, anesthetized hand (398). Contrary to earlier observations (246), sustained efforts produced illusory movements. The position change accompanying an effort increased monotonically with both the duration and size of the effort. Perceived movement velocity only increased with effort, not its duration: a 10-fold increase in effort producing a doubling in speed (398). It is concluded that a sense of effort, arising centrally in association with motor commands, is able to contribute to a number of proprioceptive sensations including the sense of limb position and the sense of limb movement. Similarly, motor command signals may contribute to the senses of force and heaviness. We will have to wait for future experiments to reveal the precise mix of signals of different sources that are responsible for these sensations.

There is one further role of the sense of effort which is almost outside the scope of this review. In looking at a hill, subjects consistently overestimate its steepness. Judgement of the slope is influenced by the subject's level of fatigue and whether or not they are wearing a heavy backpack (298). Similarly, perceptions of distance are influenced by the subject carrying a load or after visuomotor adaptation that reduces optic flow during walking (299; see also Ref. 90). The proposal is that the perceived distance increases as the effort required to walk it increases. These observations suggest that the sense of effort has wider perceptual consequences than just signaling muscle fatigue and the information can contribute to signal our current physiological potential to perform intended actions.

VI. PROPRIOCEPTION AND EXERCISE

A. Introduction

In recent years there has been increased interest in the physiology of exercise. One reason is that exercise has become a part of many people's lives as they strive to maintain fitness in the face of largely sedentary life-styles. This is in the face of the global obesity epidemic (the majority of the United States population is overweight) with everyone focusing attention on strategies to reduce adiposity and improve health (e.g., Refs. 34, 189, 350). Questions arise about the effectiveness of different kinds of exercise and the risks of exercise-related injury. Finally, television has led to a rise in popularity of spectator sports. The elite athletes who participate in such sports are constantly in search of exercise strategies that will give them a competitive edge. All of this has meant that today there is growing interest in exercise physiology.

B. Exercise Disturbs Proprioception

It is common to feel awkward and clumsy after intense exercise. It is not just muscle weakness from fatigue; we are less sure about placement of our fatigued limbs if we are not looking at them. This has led to the realization that exercise can disturb proprioception, probably as a result of the accompanying fatigue. Muscle fatigue is not just a matter of

peripheral mechanisms accompanying depletion of muscle energy supplies, but includes activation processes at spinal and cortical levels (for review, see Ref. 137).

It has long been known that limb position sense can be disturbed by exercise (e.g., Refs. 35, 323, 342, 361). To explore underlying mechanisms, it is first necessary to distinguish between different kinds of exercise. There are three types of muscle contractions: concentric, isometric, and eccentric. In concentric exercise, the contracting muscle shortens, typically while under load. In isometric exercise, the load is too heavy to allow any shortening and the muscle contracts at constant muscle length. In eccentric exercise the load is sufficient to forcibly lengthen the contracting muscle. All three kinds of exercise, if carried out sufficiently intensively, cause muscle fatigue and disturb proprioception. The loss of force from concentric exercise is largely due to depletion of metabolic factors and is therefore short-lasting, with recovery complete within 2 h (366). Eccentric exercise is distinguishable from other forms of exercise because it is accompanied, not only by metabolic fatigue, but a component of the loss in force is due to muscle damage. Force recovery after eccentric exercise is only partial, and a significant deficit persists for up to a week, the time taken to repair the damage. Accompanying the muscle damage is delayed-onset muscle soreness (DOMS) that also persists for about a week (for review, see Ref. 309). The damage from eccentric exercise raises the possibility that it may damage muscle proprioceptors and that this was responsible for the disturbance to proprioception. The soreness, too, can alter proprioception (407), an effect presumably mediated by group III and IV muscle afferents (e.g., Ref. 255).

Position sense, movement sense, and force sense have all been studied before and after exercise. For position sense an important consideration is the method of measurement. Commonly a two-limb matching task is used **(FIGURE 14)**. Other methods include displacing a limb and asking the subject to indicate its position with a pointer or asking the subject to reproduce a previously remembered position. With the two-arm or two-leg matching task, both limbs contribute to matching accuracy (199, 412). As we use our limbs in combination in everyday activities there is some logic in measuring position sense in this way. However, it makes the interpretation of results more difficult. For single limb tasks, where the subject is asked to indicate a remembered position, it introduces the extra variable of memory. Measuring position sense in one limb with a pointer avoids the problem of influences from the other limb but subjects are less accurate. For all experiments aimed at measuring position sense after exercise, an important consideration is the way the test muscles are conditioned at the start of the experiments, particularly if any measurements are made on the relaxed limb (see sect. II*B3*).

C. Concentric and Isometric Exercise

Skinner et al. (361) reported a decrease in the ability of subjects to reproduce the position of the knee after flexion and extension movements. They attributed this decrease to changes in muscle receptors (see also Ref. 66). The subject of proprioception at the knee and clinical aspects have been reviewed (e.g., Ref. 187; see also Ref. 224). In an experiment on elbow flexors, fatigue of one arm using maximum voluntary contractions led to position matching errors (352). However, the errors were not consistent between subjects, and there were no "reciprocal" changes when the fatigued arm was the indicator arm, compared with when it was the reference. It was concluded that central as well as peripheral influences were responsible for the exercise effects. In related experiments, Walsh et al. (399) found that both concentric and eccentric exercise of elbow flexors produced position errors, although here, too, the effects were not reciprocal. To examine the issue of reciprocity, Allen and Proske (8) showed that if the errors after concentric exercise were large enough, reciprocal effects could be demonstrated reliably. However, while concentric exercise altered position sense, it did not appear to impair the ability to track the movement of a passively displaced arm. So concentric exercise disturbs position sense but leaves movement sense unaffected. In that context, it has been claimed that movement detection thresholds at the shoulder joint are significantly raised by fatigue from exercise (59), while the acuity of movement sense is reduced (287). Finally, it has been claimed that concentric exercise disturbed position sense to a greater degree than isometric or eccentric exercise (124).

D. Eccentric Exercise and Damage to Muscle Receptors

The first study to use eccentric exercise to examine its effects on position and force sense was by Saxton et al. (342). Both joint position sense and force sense were impaired after the exercise. To account for their observations, the authors considered the possibility of disturbance to muscle proprioceptors by the exercise. In a related experiment, Brockett et al. (35) similarly suggested that eccentric exercise damaged muscle receptors. This was against a background of evidence indicating that eccentric exercise damaged muscle fibers. These proposals prompted animal experiments in which responses of tendon organs (163) and muscle spindles (166) were tested before and after a series of eccentric contractions. After exercise which reduced muscle force to 50% of its control value, responses of both receptor types to length and tension changes remained essentially unaltered. This is shown in **FIGURE 15**. There was no evidence that the intrafusal fibers of muscle spindles were susceptible to the damaging effects of eccentric contractions, unlike their extrafusal neighbors. Presumably the compliant ends of spindle attachments to the adjacent endomysium protected them from damage.

These considerations led to the conclusion that answers to the question of the source of the disturbance to proprioceptor-

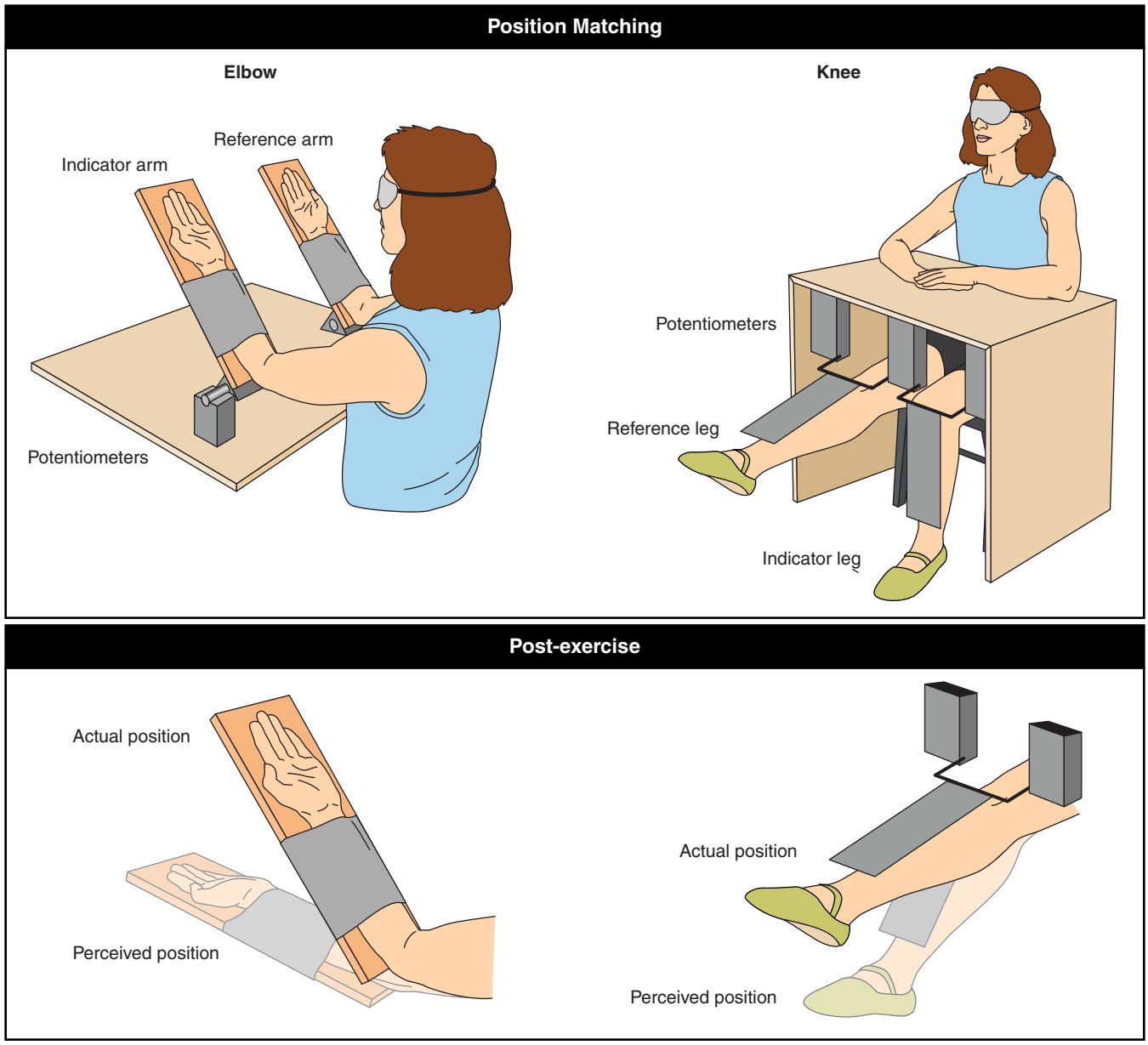


FIGURE 14. Position matching at the elbow and knee before and after fatiguing exercise. *Top left*: position matching at the elbow. Blindfolded subjects sat at a table with their forearms strapped to lightweight paddles. The hinges of the paddles were aligned with the elbow joint and had potentiometers attached to them, providing a voltage signal proportional to elbow angle. *Top right*: position matching at the knee. Subjects were seated in a chair mounted on a steel frame. The height of the chair was adjusted so that the medial and lateral epicondyles of the knee were in line with the pivot point of the position matching apparatus. This consisted of a pair of paddles lying on the shin with potentiometers at their hinge points giving voltage outputs proportional to knee angle. *Bottom panels*: perceived positions of the elbow (*left*) and knee (*right*) after a series of fatiguing concentric contractions that led to a 30% fall in torque in elbow flexors and knee extensors, respectively. The exercised arm felt more extended than it really was, the exercised knee more flexed. [Redrawn in part from Allen et al. (7).]

tion by exercise had to be sought outside the muscle. However, one report was not consistent with that conclusion (320). Measurements were made of the vibration illusion (159) in ankle extensor muscles before and after a series of stretch-shortening cycles. Two days after the exercise, vibration of the exercised muscle led to a reduced vibration illusion for the frequencies of 80–100 Hz, but an increased illusion at 40 Hz. It was suggested that the delayed recovery from the exercise was associated with a decreased dynamic sensitivity of spindle primary endings.

E. Exercise and the Sense of Effort

The question of whether the sense of effort could contribute to position sense was tested using both concentric and ec-

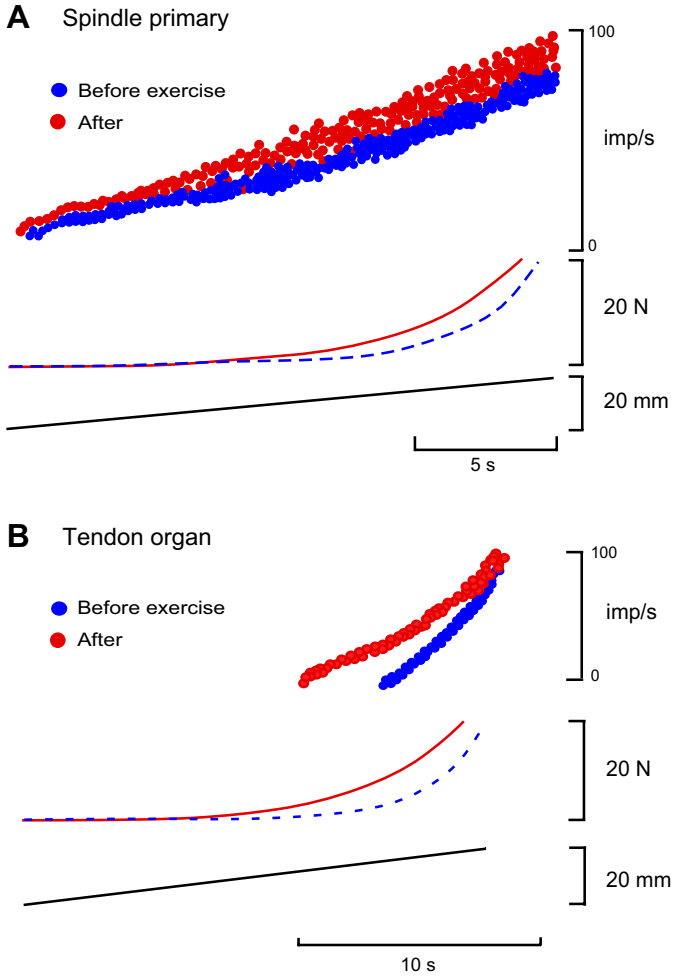


FIGURE 15. Responses of muscle spindles and tendon organs before and after a series of eccentric contractions. *A*: response of a single spindle primary ending to a slow stretch of the soleus muscle of the anesthetized cat. Responses are shown as instantaneous rates. Response in blue is before exercise, and responses in red are after exercise. The trace at the bottom (black) represents muscle length, and the two traces above represent muscle passive tension before exercise (dashed blue line) and after exercise (continuous red line). The eccentric contractions led to a rise in whole muscle passive tension. [Redrawn from Gregory et al. (166), with kind permission from Springer Science and Business Media.] *B*: responses of a single tendon organ of the soleus muscle of the anesthetized cat to a slow stretch before and after exercise. Traces are as in *A*. The tendon organ remains a true tension sensor, responding to the rise in passive tension from the eccentric contractions. [Redrawn from Gregory et al. (163).]

centric exercise (5, 397, 399). After eccentric exercise of elbow muscles, subjects matched the position of the exercised arm by placement of the unexercised arm in a more extended position (399). The size of the errors correlated with the drop in force. A similar pattern was seen after concentric exercise. It was proposed that to hold the fatigued arm at the test angle against gravity required more effort, and this was interpreted as the arm having adopted a more horizontal position than was actually the case. This view was supported by observations in subsequent experiments (397) in which, in one condition, arm position matching was done using a counterweight to balance the weight of the arm. No effort was required to hold the arm at the test angle. In a second experiment, position matching was done in the horizontal plane to remove the effect of gravity. After eccentric exercise, position matching errors increased significantly for unsupported matching, but not for counterweighted matching or matching in the horizontal plane.

Despite these apparently unambiguous results, some uncertainty remained about the possible contribution from the sense of effort to position sense, because of uncertainties over the state of conditioning of muscles at the start of each trial. The point was addressed in knee extensor muscles, with care being taken to ensure that for each measurement the muscle was in a defined state (155). Significant position errors were produced by both eccentric and concentric exercise, but they were in the opposite direction to that predicted if gravity had played a role. That is, the position of the exercised leg was matched by the unexercised leg adopting a more flexed posture at the knee, not a more extended posture. In contrast, for exercise of elbow flexors, the errors were in the direction of arm extension (5) (see **FIGURE 14**).

The result with knee extensor muscles (155) has been confirmed (283). In a repositioning task of a remembered position after eccentric exercise, subjects placed their exercised leg in a more extended position, representing a shorter knee extensor muscle. The result suggested that subjects believed their exercised muscle was longer than it really was, so they placed it in a position that shortened the muscle. Finally, another recent study on the same muscle group found errors in the same direction, but these were significant only in non-weight bearing tasks (392).

F. Mechanism of Exercise Effects on Position Sense

A possible explanation for the above observations was that fatigue of a muscle had increased the discharge rate of its muscle spindles and that led to a shift in perceived limb position representing a more stretched muscle. To obtain further information about the distribution of the errors, rather than exercising elbow flexors, elbow extensors were exercised (7). The unexpected result was that, as for elbow flexors, the arm still felt more extended than it had before the exercise. A similar result was obtained at the knee. Exercise of knee flexors led the leg to be perceived as more flexed than its actual position, the same result as after exercise of knee extensors. Any direct involvement of muscle receptors in the observed position errors was ruled out by this result because, if the errors had been generated within the muscles, they should have been in opposite directions for exercise of antagonist muscles. Finally, exercise of finger flexors did not lead to any position errors at the elbow, and

thus the exercise effect was joint specific and did not spread across several joints (7).

Additional control experiments have recently been carried out (Leung, Allen, and Proske, unpublished observations). If, instead of exercising elbow flexors, the passive elbow was moved through the same angle range, over the same period of time as during the exercise, but without any active contractions, there were no effects on position sense. So it was not the repeated movements that were responsible. Alternatively, if elbow muscles were exercised isometrically, without any accompanying overt movement at the elbow joint, provided the test muscle was sufficiently fatigued, it led to position errors. There was one final consideration: Was the fatigue effect a consequence of the reduced force generating capacity of the muscle, or was it the result of the accumulation of metabolites that accompanies fatigue from exercise? The influence of metabolites could arise peripherally, presumably mediated by small-fiber afferents or, alternatively, it could exert effects within the brain (e.g., Ref. 275).

Concentric exercise produces both a fall in force and the accumulation of metabolites. Typically fatigue from concentric exercise is fully reversed within 2 h after the exercise (366). When measurements of force are made immediately after eccentric exercise, there will be a component of the force loss due to metabolic factors. However, a second component will be present from damage to muscle fibers, and this takes days to resolve. In most previous experiments testing the effects of eccentric exercise on position sense, the exercise was not made severe enough for a significant force drop to persist at 24 h post exercise. In a new study, subjects' elbow flexors were eccentrically exercised, the exercise being made sufficiently severe (50–60% fall in force immediately after exercise) to ensure that a significant force drop persisted at 24 h (25–35%) (Tsay, Allen, Leung, and Proske, *Exp Brain Res*. In press). After 24 h, significant position errors accompanied the fall in force. In other words, at a time long after the exercise was completed, the effects on position sense were still present. This made it unlikely that local effects of metabolites were responsible. One possibility was that the fall in muscle force had altered the body schema. This change in the representation would persist for as long as there were any sensory cues indicating that recovery from fatigue was not complete.

After exercise of elbow muscles, the forearm is perceived as more extended, and after exercise of knee muscles, the lower leg is perceived as more flexed **(FIGURE 14)**. The directions of these errors can be incorporated in the hypothesis by suggesting that the changes in the central map are given by the direction in which gravity is exerting its effect on the limbs. It is as though the brain is compensating for the weaker limb muscles by shifting the position of the map into a more nearly gravity-neutral posture. For the arm it is in a direction towards a posture where the arm is hanging by the side of the body, and for the leg, it is in a direction where the lower leg is hanging vertically.

How can a change in the motor command:force relation provoked by fatigue alter a central map? The work on phantom limbs (314) suggests that motor commands, in the absence of any afferent feedback from the arm, can lead to sensation of a distorted, contracted phantom arm with phantom limb pain. This pain can be relieved with mirror box therapy. The mirror provides the missing afferent feedback (vision of the intact arm) convincing the subject that their phantom arm can be relaxed and straightened. So, motor commands can alter the body map, at least for the phenomenon of phantom limbs. For the effects of exercise there is, of course, no loss of afferent feedback. So in that sense, it is unique.

Why place such importance on the disturbance to position sense after exercise? Interest is driven by the possibility of fatigue-related proprioceptive errors leading to injury. The marathon runner who staggers into the stadium at the end of the run is unsteady on his feet not just because his leg muscles are fatigued but because he is unsure of where his legs are. The finding that exercise of knee muscles leads to perception of a more flexed knee (155) may mean that tiring runners will overextend their knee, raising the possibility of strain injuries in knee flexors (277). In the elderly (see sect. VII), the progression of muscle frailty due to sarcopenia implies reduced proprioceptive control (50) so that any disturbance to proprioception in leg muscles from unaccustomed exercise may increase the risk of falls. Given the adaptability of skeletal muscle, selected training programs may help to reduce the disturbance to proprioception from unaccustomed exercise and thus reduce the risk of injury.

G. Exercise and Force Sense

The effect of eccentric exercise on force sense has been studied by a number of groups (35, 62, 342, 404). The main finding is that in a bilateral force matching task in elbow flexors, if subjects are instructed "to make both arms feel the same," after the exercise they will overestimate the force in the exercised arm (see sect. V, **FIGURE 13**). Errors attributable to the drop in force after exercise can be taken into account by expressing them, not in terms of the preexercise MVC, but the postexercise MVC. For example, a mismatch of 14% expressed in terms of the preexercise MVC reduces to 4% when fatigue is taken into account (404). This remnant difference was attributed to a change in muscle EMG (404). It is known that after eccentric exercise the EMG for a given level of force increases (62, 351, 404). Thus a larger neural drive was required to achieve a given level of force. In addition, Carson et al. (62) observed a larger MEP in response to magnetic brain stimulation of motor cortex after eccentric exercise. That led to the suggestion that after eccentric exercise there was an increase in gain of the effort:

motor command relation such that a given level of effort resulted in greater excitability of motor cortex and greater muscle activation. In that context, it has been shown that single stimuli to the motor cortex are not associated with any sensations of effort (e.g., Refs. 112, 139), but this may simply reflect the unphysiological nature of the electromagnetic stimulation. A similar observation was made on a deafferented subject, and here the possibility was considered that the transcranial magnetic stimulus might itself have inhibited any sensation (76).

Another factor to consider after eccentric exercise is DOMS which begins ~24 h after the exercise. Does the muscle pain from eccentric exercise produce force matching errors? The pain is mediated by group III and IV afferents (see sects. V*B* and VIC). Noxious muscle input generated by injection of hypertonic saline into muscle reduced excitability at the level of the motor cortex (225, 239). Therefore, in the presence of pain, it should require a larger effort to generate a given level of force. As a consequence, in an isometric force matching task, the sore muscle would generate less force (e.g., Ref. 307). The question of the roles of peripheral and central factors, as well as pain in producing the force loss after eccentric exercise, was addressed by Prasartwuth and colleagues (295, 296). They concluded that eccentric exercise produced a length-dependent impairment of voluntary activation of the muscle, and this contributed to the loss in maximal voluntary force. However, soreness did not contribute to the early force loss (407). Note that because of the recent evidence for a peripheral contribution to force sensation (233), studies of changes in perceived force with pain and fatigue may need to be reevaluated.

VII. PROPRIOCEPTION IN THE ELDERLY

A. Introduction

"Even a long human life adds up to only 650,000 hours. And when that modest milestone flashes into view. . . for reasons unknown, your atoms will close you down, then silently disassemble and go off to be other things. And that's it for you." (40). With the effectiveness of modern medicine, most human populations are ageing, and age-related problems are becoming a progressively larger proportion of national health budgets. One of the most important problems for the elderly is injury from falls (e.g., Refs. 15, 358, 372). At least one-third of people aged 65 years or older fall one or more times a year, with a significant proportion requiring hospitalization. Proprioception is a critical factor in stable standing (120, 230, 232), and both deteriorate with age (e.g., Refs. 50, 231, 232; see also Ref. 324). As people age they become more frail. One expression of frailty is muscle weakness from sarcopenia (for a review of sarcopenia, see Ref. 272). There is a correlation between muscle strength and proprioceptive acuity in the stability of standing (50), with acuity diminishing at high levels of muscle force. Thus an important reason for the increase in falls in the elderly is a deterioration in proprioception, and this has important clinical and public health implications (see also sect. VI).

B. Sarcopenia

The term *sarcopenia* (337) refers to the loss of muscle mass associated with ageing, but is usually meant to include the age-related loss of muscle strength or performance. The decline is greater in the lower limbs. Sarcopenia is associated with a loss of motor units (38, 389). There may be a greater loss of units in lower limb muscles given that there is evidence that distal limb muscles show a bigger decrease in units than proximal muscles (132). The loss of motor units decreases muscle cross-sectional area. Loss of contractile tissue is accompanied by infiltration by fat and connective tissue. These changes reduce muscle power that can be reduced by as much as 60% in elderly subjects (379).

Throughout life, skeletal muscle undergoes a continuous cycle of denervation and reinnervation, but in old age it seems the process of reinnervation cannot keep pace with that of denervation, leading to a loss of motor units. This appears to be related to a decline of neurotropic factors concerned with motoneuron survival (174). In addition, there is evidence of apoptosis of skeletal myocytes (94). The evidence suggests that regular, intense physical activity can keep age-related loss of muscle mass at bay by leading to fiber hypertrophy, but it is unable to reverse the loss in fiber numbers as a result of neuropathic processes (272).

C. Muscle Spindles and Aging

As muscle spindles play a key role in kinesthesia, does sarcopenia affect muscle spindle responses? First, the changes with age in muscle architecture are likely to impact on responses of spindles. Changes in fibers lengths, pennation angles, and tendon compliance (273) are all likely to alter spindle responses to passive and active lengthening. Changes in tendon properties are likely to alter tendon organ responses and therefore change the relation between muscle tension and tendon organ discharge. The losses of muscle fibers and motoneurons that are a part of sarcopenia could include intrafusal fibers and fusimotor neurons. In aged human peripheral nerve (tibial), there is a significant fall in numbers of nerve fibers. This includes a bigger proportion of large-diameter fibers (375). Some of these could be sensory fibers. Therefore, the possibility exists that aged muscle contains denervated spindles. There is some evidence on this point.

Spindles dissected from aged muscles have fewer intrafusal fibers (376). Other structural abnormalities were consistent with the signs of denervation atrophy. In addition, spindles in aged rats may contain intrafusal fibers without any sen-

sory innervation altogether (91). Kim et al. (215) showed that in aged rats the number of the sensory endings in each spindle was about normal, but most primary endings had lost their typical annulospiral configuration. They were tapered and irregular in shape. Comparable abnormalities could not be detected for secondary endings. This leads to the question of the responsiveness of spindles in aged muscles.

Responses have been recorded from spindles in muscles of rats of different ages (215, 261). As expected, in muscles of young animals, the conduction velocity of presumed primary spindle endings was significantly higher, and they had larger diameter axons than the presumed secondary endings. In contrast, in aged animals, the conduction velocity and axon diameter spectra had shifted in the direction of slower speeds and smaller axons. There was no longer a clear difference between primary and secondary endings. Dynamic responses of spindle primary endings in aged animals were much lower than in young animals, including responses to the depolarizing drug succinylcholine. The responses of aged primary endings resembled those of secondary endings, probably as a result of loss of their annulospiral terminal structure.

These observations on muscle spindles have potentially important implications for proprioception. Given that primary endings of spindles contribute both to the sense of limb position and the sense of limb movement (see sect. II), the observations of Kim et al. (215) raise the possibility that elderly human subjects may have a reduced sense of movement as a result of a degraded dynamic sensitivity of spindle primary endings. There is some psychophysical evidence on this point. Human subjects were asked to discriminate between joint angles during movement of the ankle joint over the range, 15–30°/s. Normal elderly subjects produced larger errors than young adults. However, unexpectedly, vibration of ankle dorsiflexors led to larger errors in the elderly. It was concluded that there was no change with age in the responses of spindles to vibration (391). However, in a more recent report, dynamic position sense declined with age if ankle rotations were extended beyond 30°/s to 90°/s, to cover the full range of walking speeds over which subjects are likely to fall (235). Another, more recent, observation of the effects of calf and neck muscle vibration suggested that neck vibration produced a greater postural disturbance in the elderly (284). Here, however, there are potentially confounding influences from vibration affecting the vestibular system. To conclude, while evidence has been provided that muscle spindle structure and function change with age, supporting observations of functional outcomes remain limited.

D. Falls in the Elderly

Proprioception plays an important role in stable standing (121, 122). This was shown by measuring body sway in subjects whose bodies had been splinted, and they balanced an equivalent weight with their feet. Under these conditions, in normal subjects proprioception in leg muscles provided sufficient information to allow for a stable upright stance. Vision and the effect of the segmented body were important for maximal stability, while sensory input from the feet had a smaller effect (36, 197, 210). It was concluded that during simple standing vestibular input did not contribute to body sway.

In studies of sensorimotor functions and balance under normal standing conditions in groups of subjects of different ages, all of the sensory functions measured, particularly lower limb sensations, showed age-associated differences in their influence on standing stability, measured as body sway (230, 231; see also Ref. 411). When conditions were made more challenging by asking subjects to stand on foam, vision, strength of the quadriceps muscle group, and reaction times to a visual stimulus played significant roles. In addition, standing on foam with the eyes shut revealed a vestibular component. Up to the age of 65 years vision played a major role in stable standing, but as visual acuity declined, it became less important. In a cohort of elderly women, the incidence of multiple falls was associated with poor position sense at the knee, reduced cutaneous vibration sensitivity, impaired lower limb strength, slower reaction times, and low-contrast visual acuity (232; see also Ref. 236).

It is a common wisdom that exercise improves postural stability (e.g., Ref. 292), perhaps as a result of the increases in muscle strength. As we grow older and come more and more under the influence of sarcopenia, it raises the questions, What is the relationship, if any, between muscle strength and proprioception and can their decline with age be offset by exercise? The relationship between muscle strength and standing stability is not straightforward (50). Muscle weakness, measured as ankle dorsiflexor strength, by itself, does not reduce standing stability. However, there was reduced proprioception in the weaker subjects, as measured by the amount of body sway, when they were asked to stand with their eyes shut. This was the case despite there being no differences in sensory functions between the weak and strong groups, including a measure of knee position sense, although the position sense data need to be confirmed. In a group of older subjects (>70 yr), this relationship between muscle strength and proprioception was not apparent. In these subjects visual acuity and knee joint position sense had deteriorated significantly, and it was concluded that older subjects relied more on the cues provided by a range of sensory inputs and not just vision and proprioception to achieve stable standing. Nevertheless, in subjects of all ages, weaker leg muscles mean poorer proprioceptive control in the absence of vision. Why that might be so remains unclear, but it implies an important link between the contractile and sensory functions of muscles, a link which is likely to apply to all skeletal muscles. Perhaps, the

need to drive the motor system harder, because of weakness, compromises the signaling capacity of the proprioceptive system (see **FIGURE 16**).

To conclude, it is clear that proprioceptive inputs are an important determinant of stable standing. The evidence suggests that there is not only a loss of muscle strength with age, but this is accompanied by a deterioration of the signaling capacity by muscle receptors. That, in turn, implies a proprioception-related increase in the incidence of falls. The specific relationship between muscle strength and proprioception should be explored further as it may provide a basis for the claim that exercise improves standing stability. Interestingly, to achieve a reduction in the incidence of falls, it is not sufficient to improve muscle strength alone as exercises are required which actually challenge standing stability (357).

VIII. PROPRIOCEPTION IN THE CLINIC

A. Clinical Tests of Proprioception

Tests of proprioception are one important component of the standard neurological examination. Proprioception in the lower limbs is measured using movement detection thresholds at the big toe. Position sense in the upper limbs is determined by the patient's ability to maintain their arm in an extended position without undue positional drift. Finally, there is the well-known Romberg's sign, maintenance of an upright posture with the eyes closed.

The Romberg sign is probably the most commonly used diagnostic test for proprioceptive abnormalities. The test is attributed to M. H. Romberg, a German neurologist practicing in the mid-19th century (334). He presented the first detailed account of tabes dorsalis, a demyelinating syphilitic condition. Romberg described the loss of balance demonstrated by the erect patient when he closes his eyes while standing with his feet together. This behavior is to be distinguished from the condition in which the patient already sways with his eyes open, a symptom typical of cerebellar ataxia.

For the lower limb, a decision about whether there is any proprioceptive deficit is based on a comparison of the movement detection thresholds of the big toes. Unfortunately, detection thresholds at the big toe, when expressed in terms of proportional changes in fascicle length for the muscles acting at the big toe, are much poorer than for the ankle, knee, or hip joints (317). The reason for this is the anatomy of the foot and ankle, leading to poor mechanical coupling between the toe and the muscles that operate it (318). It is important to keep this in mind when comparing the patient's proprioceptive performance at different joints.

Another important consideration when making measurements of position and movement sense is to take into account any thixotropic effects that may be present in the muscle or its spindles (see sect. II*B3*). Particularly when making measurements of position sense in the relaxed limb, before the measurement is made, it is advisable to ask the subject to contract their muscles isometrically at the test position.

B. Parkinson's Disease

One common neurological condition in which there have been claims of disturbed proprioception is Parkinson's disease. Such a view is supported by the casual observation of a Parkinsonian patient while they are eating. Provided the person does not have too pronounced a tremor, these patients are able to eat liquid foods with a spoon, but they have difficulty in locating their mouth unless they concentrate on visually tracking the arm movement. Such behavior suggests not just disturbed proprioception but implies a derangement of spatial maps of the body.

The experimental evidence for a disturbance of proprioception in Parkinson's disease has not yet revealed a clear picture. It has been reported that illusions of movement and displacement of a limb evoked by muscle vibration are normal in Parkinson's disease (e.g., Refs. 265, 335). It implies that muscle receptor responses to the vibration are normal. That view has been backed up by microneurographic recordings of muscle spindle responses in patients with Parkinson's disease (48, 237). It leads to the conclusion that if proprioception is disturbed in Parkinson's disease, it is not due to malfunction of the peripheral sensory apparatus but results from problems with central processing of proprioceptive information.

In a forced-choice comparison of elbow angles by patients with Parkinson's disease they achieved fewer correct matches than normal subjects (428). In another test, patients' wrist extension movements were monitored during vibration of the flexor tendon. Vibration led to a smaller undershoot of the target than it did in healthy control subjects (326). It was concluded that in Parkinsonian patients there was an abnormality in the higher level integration of proprioceptive information. One possible source for such an abnormality was in the comparison between afferent feedback and the corollary discharge of the motor command (264). It has been suggested that there is a saturation of central sensory processing in Parkinson's disease (326), a view that is supported by animal observations. An animal model of Parkinson's disease can be produced by injection of methyl phenyl tetrahydropyridine (MPTP). In monkeys with symptoms of Parkinson's disease produced by MPTP, pallidal neurons had increased sensitivity and reduced selectivity in their responses to peripheral sensory inputs (119).

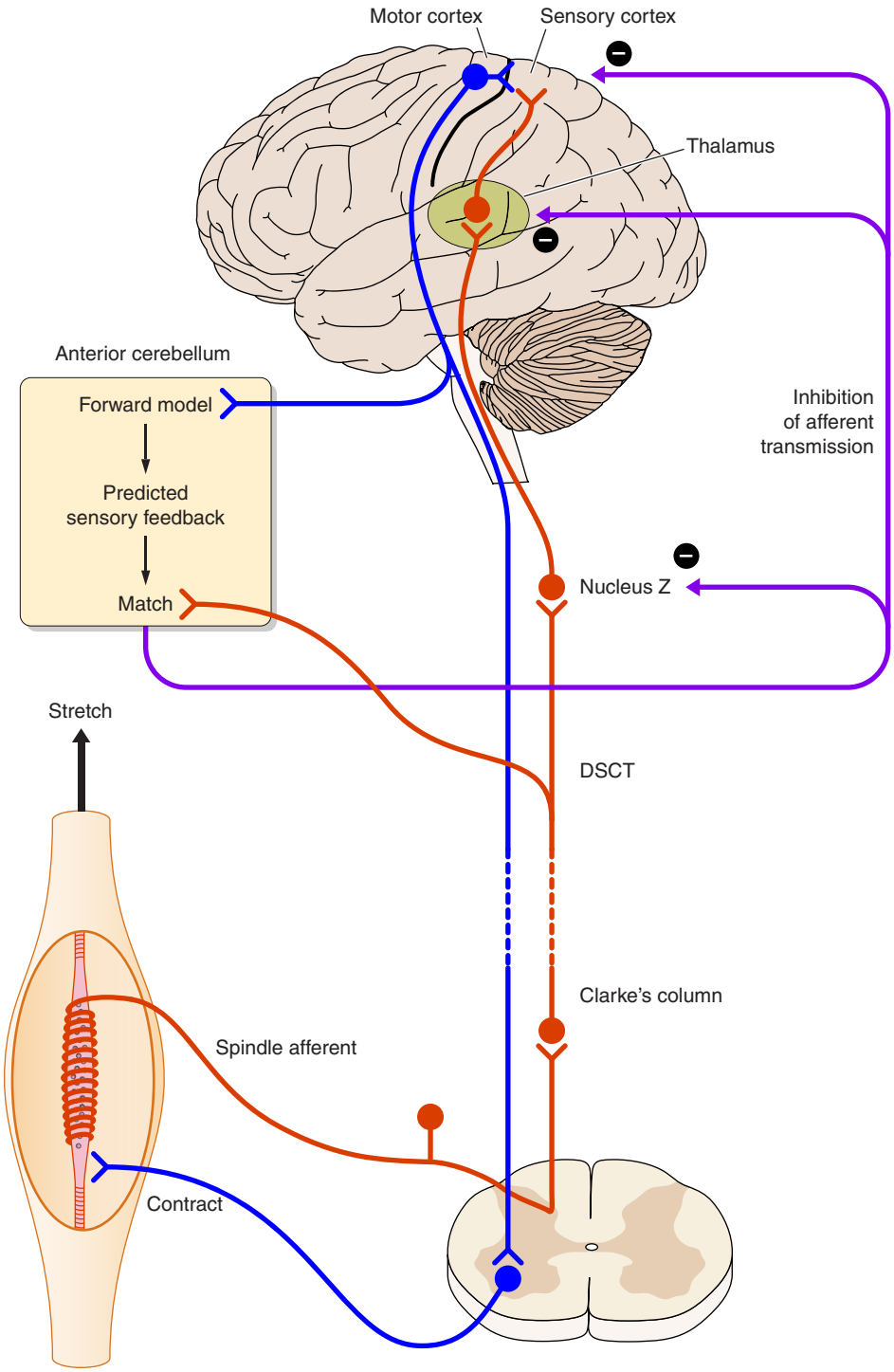


FIGURE 16. Possible mechanism (shown in diagrammatic form) for how the brain distinguishes between impulses coming from muscle spindles that are generated by muscle stretch (exafference) or by fusimotor activity (reafference). When the muscle is stretched, spindle impulses travel to sensory areas of the cerebral cortex via Clarke's column, the dorsal spinocerebellar tract (DSCT), Nucleus Z, and the thalamus (shown in red). Collaterals of DSCT cells project to the anterior cerebellum. When a motor command is generated, it leads to coactivation of skeletomotor and fusimotor neurons (shown in blue). A copy of the motor command is sent to the anterior cerebellum where a comparison takes place between the expected spindle response based on that command and the actual signal provided by the DSCT collaterals. The outcome of the match is used to inhibit reafferent activity, preventing it from reaching the cerebral cortex. Sites of inhibition could be at Nucleus Z, the thalamus, or the cortex itself. For further details, see text.

A feature of Parkinson's disease is bradykinesia. Patients with bilateral asymmetry in expression of the disease overestimate the trajectory of the more affected limb in a matching task using slow, active movements of the arms (264). One interpretation of this result is a lower-than-normal central modulation of the afferent input, perhaps the result of the previously postulated saturation mechanism.

C. Schizophrenia

As described in section IVC, we know that in a subject with a paralyzed, anesthetized arm attempts to move the hand at the wrist leads to illusory sensations of movement (148, 398). This observation shows unambiguously that central motor mechanisms are, by themselves, able to generate kinesthetic sensations in a normal subject. They are therefore available to contribute to proprioceptive sensations during load bearing as well as being potentially capable of generating phenomena such as the phantom limb. Subjects overestimate externally generated forces by 20% when they generate them themselves (353, 402) **(FIGURE 12)**. Similarly, attenuation of the muscle sense has been reported during active movements (77). Such suppression mechanisms may allow us to distinguish between self-generated and externally generated actions; that is, during active movements, the efference copy is used not only for predicting the reafference **(FIGURE 11)**, but it gives rise to a sense of body "ownership". Such a sense appears to be reduced in schizophrenics.

In Parkinson's disease the patient fails to transform a willed intention into action, leading to symptoms of bradykinesia, and this is alleviated by giving dopamine. Schizophrenics who complain that they are under alien control appear to have a reduced awareness of self-initiated motor acts that they have just carried out (127, 129). The failure to form a conscious percept for an intended action leads to the negative symptoms of schizophrenia (e.g., Ref. 128). Thus a breakdown of the awareness of generation of willed acts can have profound consequences.

D. Clinical Symptoms of Fatigue

The subject of fatigue is extensive and complex because it includes both central and peripheral components (for review, see Ref. 137). Fatigue is relevant to a review of proprioception because sensations of fatigue are typically accompanied by increases in the sense of effort. Throughout this review the term *effort* has been used to imply sensations generated by motor commands, in isolation, or in combination with inputs from the periphery. An abnormal sense of effort therefore has a place in clinical considerations of disturbed proprioception. The fatigue felt as a result of mental effort, mental calculations, etc. is not included here.

Many pathological conditions are accompanied by abnormal perceptions of effort and fatigue and are therefore relevant to a discussion of proprioception. These include corticospinal lesions, spinal cord injury, and multiple sclerosis (for a review, see Ref. 137). The influence of joint pathology, particularly when associated with arthritis, can reduce voluntary strength and proprioception (388), perhaps as a result of the action of the nociceptive input generated by joint movement (179). Twitch interpolation, when used with patients with chronic fatigue syndrome, fibromyalgia, and heightened effort syndromes has led to rather variable results (e.g., Refs. 212, 228, 259). So, the clinical picture for patients exhibiting symptoms of fatigue syndromes, with or without other accompanying pathologies, remains unclear, at least with respect to the role played by proprioception.

IX. CONCLUDING COMMENTS

A. To Summarize and Look to the Future

It is interesting to compare the material included in the present account with that covered in a similar review 35 years ago by McCloskey (244). That account not only provided an up-to-date picture of the state of knowledge at the time, but it included a comprehensive review of the historical background. While in the present review some historical material has been included, it is not as detailed or wide-ranging. Much of the background provided by McCloskey is relevant to the present review, and the reader is encouraged to consult it.

In looking back to the state of knowledge in 1978, it is astonishing to see the increase in breadth of coverage that has been necessary since then to include the many recent developments. An obvious example of an area that did not exist 35 years ago and where rapid progress is currently being made, is in the application of neuroimaging techniques and their application in different experimental contexts (e.g., Refs. 83, 177, 270, 289). As imaging techniques are further refined, and new methods are introduced, such as diffusion tensor imaging (202), more progress will be made in our understanding of the brain areas concerned with the processing of proprioceptive information and how proprioceptive inputs are combined with information coming from the other senses during normal movements.

Another important development is that derived from observations on motor cortical neurons (e.g., Refs. 151, 152). It has brought about the realization for the kinesthetic senses that the brain is not concerned with information about muscle length changes provided by individual afferents, but with the population of muscle afferent signals arising in groups of muscles. Furthermore, studies on second-order neurons point to the regulated property as being limb movement end-point (28) not the disposition of limb segments, one relative to another. Here it is interesting to reflect on the fact that there is already significant processing of the information at the first relay in the central projection pathway of

proprioceptive afferents. The population approach has been successfully applied to disturb limb muscles with vibration to generate perceptions of complex movements (331).

At the time that McCloskey wrote his review, the important concepts of efference copy, reafference, and exafference were already known. However, they had not yet been fully integrated into the thinking about proprioceptive mechanisms. The idea that afferent information generated as a result of motor commands is processed differently from activity generated by external stimuli has only recently begun to be exploited more directly (86, 87). Models have also been generated to account for the events underlying the generation of predicted information in association with motor commands for movements, the forward models, and how these might interact with activity arising in the periphery (19). Such models may have to operate differently depending on whether the regulated property is posture or movement (65). This is another area where it is likely that further important steps forward will be taken in the future. How is the outcome of a comparison processed and what are the sensory consequences?

One area of proprioception where entirely new proposals have been put forward concerns the senses of effort, force, and heaviness (233). Here the ideas of von Holst and Mittelstaedt (393) have been directly applied to the problem. The currently prevailing view is that the motor command is directly involved in the generation of sensations of effort, force, and heaviness. Luu et al. (233) have taken a broader view and proposed that the reafferent signal generated by the motor command plays a dominant role in generating the sensation. The peripheral input is proposed to include signals from muscle spindles that have traditionally been thought of as length and movement sensors, not force sensors. If future experiments support such a view, it will require a rethink of views about the role of muscle spindles and the fusimotor system. Most current theories of the role of the fusimotor system have focused on the reflex action of muscle spindles and how this can be supported by fusimotor activity. The prospect of fusimotor-mediated spindle discharges generating proprioceptive sensations represents a significant departure from current views of the role of spindles in motor control.

The emergence of proposals for a reafferent contribution to force and effort sensations comes at a time when it has become possible to study sensations arising entirely centrally (148, 398). These findings are supported by observations made on subjects with a large-fiber sensory neuropathy (233). So, presumably, we routinely have available the capacity to access sensations generated by signals arising from motor commands, but in everyday situations it remains uncertain what is the precise mix of signals contributing to the senses of position and movement during load bearing, the senses of force, effort, and heaviness. It is interesting that chronically deafferented subjects do not experience phantom limb phenomena and are able to imagine movements visually, without feeling them. Any central sense of motor command appears to fade without regular sensory recalibration.

Another important concept that has evolved rapidly is the idea of a body image and a body schema, central maps to which incoming proprioceptive information is referred for determination of starting points and endpoints during the generation of movements. The body schema is a labile map, constantly updated by the immediately previous afferent input (e.g., Refs. 108, 147, 198), yet remarkably stable, as shown by persistent phantoms after limb amputation. The other is a cognitive representation based on stored knowledge and used for perceptual judgements. Recent observations suggest an additional map incorporating the body's metric properties (229). Interestingly the map is distorted and crudely resembles the maps drawn years earlier by Penfield and colleagues using electrical stimulation. Yet subjects consciously perceive only the undistorted map. These findings emphasize that there must be multiple representations of body form, some accessible to consciousness, some unconscious. It will be interesting in the future to explore further the different body forms and their distortions produced experimentally. The phantom limb phenomenon emphasizes the potency of central processes in maintaining representations of body form. A question for the future concerns the integration of the different body parts into a perception of the body as a whole.

Other recently expanding areas include the study of proprioception after fatigue from exercise and the realization that some of the clumsiness in movements experienced following intense exercise may be proprioceptor-mediated. In our ageing society, an important topic where there is a growing need for further progress is in documenting the changes in proprioception with age. The evidence points, at least in part, to declining proprioception as responsible for the increased incidence in falls in the elderly, a major public health issue. Finally, the knowledge obtained from experiments on proprioception has provided new insights into pathological aspects and allowed more objective assessments in the clinic. There are likely to be further important advances in the clinical arena.

B. Some Speculations

As proprioceptive sensations, the senses of effort, force, and heaviness are distinct in that they are always associated with sensory input reafferent in origin, being generated exclusively by motor commands. The same is not true of the senses of limb position and movement. Here, as Sherrington noted (355), kinesthetic sensations can arise in the passive limb, in the absence of any motor commands, that is, the

sensory information can be exclusively exafferent in origin. Yet we can also accurately perceive the position and movement of our limbs when these are accompanied by voluntary muscle contractions, for example, moving our arm when it is supporting a load. So position and movement signals can provide accurate kinesthetic information, regardless of whether they are of exafferent or reafferent origin. It raises the question, How does the brain extract the relevant kinesthetic information from a reafferent signal? Differences in the central processing of self-generated and externally generated afferent activity have been discussed previously in relation to the proprioceptive system (242), vestibular system (87), the tactile system (25), and the electrosensory system in fish (262, 263).

Recordings in alert, behaving monkeys have shown that vestibular afferents respond equally well to passive and self-generated head movements. However, the vestibular nuclei included cells, the vestibular-only cells that were less sensitive to active, compared with passive movements. It was proposed by Cullen et al. (87) that during active head movements an efference copy is processed by an internal model which computes the sensory consequences of the motor command. Neck proprioceptive inputs are compared with this estimate of reafference in a matching center, probably located in the cerebellum. If there is a match, a cancellation signal is sent to the vestibular-only cells, thereby diminishing their activation by reafferent inputs.

How this works for the proprioceptive system remains uncertain, but there are a few clues. It was observed by McCloskey (243) and subsequently confirmed (13) that the illusion of limb movement and displacement evoked by muscle vibration is at its most vivid in a passive or slightly contracted muscle. If the illusion is measured during graded voluntary contractions, it becomes progressively weaker until a point is reached, at ~25% MVC, where it disappears altogether (13). This result is unlikely to be due simply to the changing mechanical conditions in the muscle from the extrafusal contraction (37), since the vibration was applied to the muscle belly, not the tendon. It suggests that if the muscle contraction is sufficiently strong, the exafferent activity, represented by the vibration response of spindles, is no longer able to access consciousness.

Combining the vibration observations with the proposals of Cullen et al. (87) and incorporating them into the known central projection pathways for muscle afferents allows speculation about a possible mechanism for distinguishing between exafferent and reafferent muscle inputs during limb movements **(FIGURE 16)**. Animal studies indicate that spindle afferents from the hindlimb of the cat have their first synapse in the lumbar spinal cord, in Clarke's column. The second-order neurons comprise the DSCT which projects to the anterior cerebellum with collaterals terminating in Nucleus Z in the brain stem. Nucleus Z cells project to the thalamus and cerebral cortex (249). The forelimb projection is not quite the same but conforms to a similar pattern (see Ref. 248). While this level of detail is not available for human subjects, the general pattern is likely to be similar.

FIGURE 16 shows these arrangements and some hypothesized signal processing. If a muscle is stretched passively, spindle exafferent signals are generated and project to the cortex to generate a sensation of movement corresponding to elongation of the muscle. If, on the other hand, spindle activity is generated as a result of muscle contraction, including, in part, through the fusimotor system, this represents a reafferent signal. A copy of the motor command, the efference copy, is sent to the anterior cerebellum, a region thought to be concerned with differentiation between movements, depending on their sensory consequences (25). Here the efference copy accesses an internal model (e.g., Ref. 424), which has been generated, based on past experience, to calculate the anticipated afferent signal for the given motor command. The anticipated signal is compared with the afferent signal coming from the muscle and projecting there via the DSCT. Depending on the precision of the match, an inhibitory signal is generated which suppresses the reafferent component of the signal, allowing passage to the cortex of only the exafferent component. The inhibitory interaction could occur anywhere along the pathway **(FIGURE 16)**. There is evidence that for suppression of cutaneous reafferent signals spinal presynaptic inhibitory mechanisms are available (e.g., Ref. 349). Similar inhibitory interactions, perhaps acting at brain stem, thalamus, or cortical levels, would enable suppression of signals generated by self-generated activity while leaving unaffected activity generated by external sources like, for example, by muscle length changes. Such a mechanism would resolve the problem of how the brain deals with signals from the same receptor, but generated in two very different ways, only one of which has access to consciousness.

One final point about the proposed arrangement is that it must be able to accommodate the ability to perceive sensations of motor commands in the absence of peripheral feedback, as a result of an acute experimental deafferentation or in chronically deafferented subjects. Therefore, an additional direct projection from motor cortex to sensory areas has been postulated.

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