

Mechanisms of human proprioception

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Mechanisms of human proprioception

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Abstract

Proprioception includes sensations of the position of the limbs in space, the velocity they are moving, the force the muscles are applying and how hard the muscles are being driven. While we do not consciously attend to this information, it is critical for the control of movement and the loss of proprioceptive sensation causes devastating disability. This thesis reviews the history of research on proprioception and presents the work from four studies that investigated proprioception in healthy human subjects. The first study considered the sense of limb position and the interaction of signals from muscle spindles and motor commands. It investigated the combined effect of voluntary muscle contraction and the history of muscle contraction on position sense at the wrist. The results show a novel interaction that suggests the brain weights the sensory information available to it according to its reliability. The second study investigated the role of centrally-generated command signals in the sense of limb velocity. By inducing experimental phantom hands in human subjects this study showed that central command signals have a role in the sense of limb velocity. The next study investigated the influence of non-cutaneous proprioceptive signals on the sense of body ownership. It is well established that cutaneous signals influence body ownership, and the results from this study are the first to show conclusively that non-cutaneous proprioceptive signals also influence the sense of body ownership. The final study investigated the detail of a model proposed by others to explain why subjects overestimate external forces when matching them with voluntary forces. The results show that there are two separate effects in play, rather than one, as previously reported, and that the previously proposed model is insufficient to explain the overestimation of external forces. Furthermore, the overestimation is not preserved at high levels of force. In summary this thesis presents several novel findings on the mechanisms underlying proprioception in human beings and emphasises the need to explore how different proprioceptive signals are combined.

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Originality statement

'I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the award of any other degree or diploma at UNSW or any other educational institution, except where due acknowledgment is made in the thesis. Any contribution made to the research by others, with whom I have worked at UNSW or elsewhere, is explicitly acknowledged in the thesis. I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the project's design and conception or in style, presentation and linguistic expression is acknowledged.'

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Lee David Walsh

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Publications from this thesis

- <u>Walsh LD</u>, Smith JL, Gandevia SC & Taylor JL. (2009). The combined effect of muscle contraction history and motor commands on human position sense. *Exp Brain Res* 195, 603-610.
- <u>Walsh LD</u>, Gandevia SC & Taylor JL. (2010). Illusory movements of a phantom hand grade with the duration and magnitude of motor commands. J
 Physiol 588, 1269-1280.
- *Walsh LD*, Taylor JL & Gandevia SC. (Provisionally accepted). Overestimation of force during matching of eternally-generated forces. *J Physiol*.

These manuscripts are presented in Chapters 2, 3 and 5 as they were published or submitted with only minor revision for consistency within this thesis. Chapter 4 is presented as it was prepared for publication. In addition a brief summary article on the material in Chapter 3 was invited and accepted for publication:

Walsh LD, Gandevia SC & Taylor JL (2010). Phantom hands: a window into how we perceive limb position and movement. In press.

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Walsh LD, Gandevia SC & Taylor JL. (2010). Moving a phantom hand. *ANS-AuPS Sensorimotor Satellite Meeting*, Sydney Australia.

Walsh LD, Inui N, Taylor JL & Gandevia. (2011). Factors affecting body representation of the hand. *Experimental Psychology Society Meeting*, London England. Accepted.

Other publications during this candidature

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Chapter 1

Introduction

1.1 Human proprioception

The senses of limb position, limb movement, force and heaviness are all critical senses. These are the proprioceptive senses and we use these senses every time we make a voluntary movement and every time something in the environment acts against our body. Proprioception has been studied in one form or another for at least 150 years. Despite this, when asked to list the senses most people will not mention proprioception. Perhaps this is because, although proprioception is a conscious sense, we do not think about it like we do the other senses. We can focus on individual joint angles if necessary, but generally we are aware of the position of a limb as a whole, rather than being aware of the individual components. Cole and Paillard (1995) wrote "It is so deep within us and so integral to our independence and movement through the world that it has for the most part remained hidden from our personal and collective consciousness." Although it may be taken for granted that we know at all times where our limbs are as they move, it is not obvious how critical this sense is to us until we learn about a case where a person has lost their proprioception, and we realise how difficult it is without proprioception.

The sense of limb position tells the brain the position of the limbs in space and is distinctly different from the sense of movement, which is concerned with signalling the velocity of the limbs rather than static positions. The sense of force signals how much force the muscles are generating when they contract, as well as how much force is applied on the body by external events. The sense of heaviness (or effort) signals how hard the muscles are contracting, or how much effort is being used to perform a voluntary movement. This can be distinctly different from the sense of force because the muscles can fatigue, which will not affect how much effort is required to activate them, but does affect how much force is generated. The proprioceptive senses are derived from multiple sensory signals. Some signals are generated by peripheral receptors and transmitted to the brain, others are generated within the brain itself. Each proprioceptive sense relies on multiple sensory signals and some of these signals also contribute to multiple sensory signals.

the roles of some of these sensory inputs have been controversial over the history of proprioception. The following review covers the history of proprioception and outlines what is known and not known about human proprioception. Where an area is described broadly or there is a statement regarding *opinion at the time*, key reviews from that field and/or time have been cited. Otherwise citations have been focused on identifying the references that made an important discovery, changed the course of opinion or were controversial.

1.1.1 Information from the periphery

Peripheral sensory receptors play a big role in providing information that is used for proprioception and these receptors are located in the muscles, skin and the joints themselves. However the roles of these receptors are not necessarily straightforward and some of them have a controversial history. The following sections describe the structure and behaviours of each of the peripheral receptors involved in proprioception as well as the history of evidence that has led to the current opinion of their role in proprioception.

1.1.1.1 Muscle spindles

Since the discovery of the muscle spindle in the 1860s (Weismann, 1861; Kölliker, 1862; Kühne, 1863) it has been the focus of much scientific study, largely because of its complex structure, which made the function of these sensory end organs unclear and often controversial (for review see Matthews, 1972). Ruffini (1898) stated that "*apart from the organs of special sense (eye, ear, etc.) the body possesses no terminal organ that can compare with these in richness of nerve-fibres and nerve endings*" and almost a hundred years later Boyd (1980) made the similar remark that "*As a sensory receptor the muscle spindle parallels the eye in its physiological and anatomical complexity*." Now much is known about muscle spindles, including their structure, function and role in providing peripheral information for proprioception.

Muscle spindles are sensory end organs that are distributed throughout skeletal muscle with neck muscles and intrinsic hand muscles containing a higher density of spindles (Matthews, 1972). They lie between the skeletal muscle fibres and

most are connected in parallel with muscle fibres so that length changes of the surrounding muscle fibres are reflected in a length change of the muscle spindle (Cooper & Daniel, 1963; Boyd, 1980; Burke *et al.*, 1987). However about 10% of muscle spindles show behaviour consistent with them being located in-series with the muscle fibres (Burke *et al.*, 1987). Figure 1.1 displays the structure of a muscle spindle which consists of a fluid filled capsule containing a bundle of intrafusal muscle fibres.

Muscle spindles are generally less than 10mm long (Boyd, 1980) and, in human hand muscles, the length of the capsule varies from 1mm-5mm (Cooper & Daniel, 1963). Intrafusal fibres are categorised into two types 'nuclear bag' and nuclear chain' according to their structure (Boyd, 1962) and the nuclear bag fibres are further categorised into 'dynamic bag 1' and 'static bag 2' according to their behaviour during spindle stretch and their effect on their innervating afferent nerves (Boyd, 1980). The spindles are innervated by afferent nerve fibres which wrap around the central sections of the intrafusal fibres or form Ruffini type endings on the fibre. These nerve terminals are stretched if the section of intrafusal fibre on which they terminate is stretched. Thus muscle spindle afferents increase their discharge rates when the muscle spindle is lengthened. Two types of afferent nerve fibre terminate in muscle spindles, primary spindle afferents (Ia) and secondary afferents (II) and their differential innervation of the three categories of intrafusal fibre means that these afferents have different firing properties. Both types of afferent fire at higher rates when stretched to longer lengths. Both also fire at higher rates while being stretched than when held at a constant length, although this latter difference in firing rate is greater for primary afferents than it is for secondary afferents. This makes primary afferents more sensitive to the velocity of length changes, while the secondary afferents signal length (Edin & Vallbo, 1990).

When the extrafusal muscle fibres of the surrounding muscle contract and shorten the muscle spindles, the intrafusal fibres will be shortened as well. This would be expected to cause the intrafusal fibres to fall slack, taking tension off the spiral sensory endings and making the spindles insensitive to further length changes of



Figure 1.1: A diagram of the structure of the muscle spindle. The muscle spindle consists of several intrafusal fibres enclosed in a capsule (A). Sensory afferents enter the capsule and terminate on the central section of the intrafusal fibres. The γ -motoneurones enter the capsule to inervate the contracting section of the intrafusal fibres. Note that the location of the contractile sections of the intrafusal fibres means that when they contract the sensory nerve endings are stretched. **B** shows the different distribution of Group Ia (primary) afferents and Group II (secondary) afferents. Ia afferents terminate on dynamic and static bag fibres as well as the nuclear chain fibres. Group II afferents do not terminate on dynamic bag fibres. Afferent nerves may terminate by wrapping around the intrafusal fibre (as shown) or terminate in a Ruffini ending (not shown). The representation of nuclear bag fibres being fatter in the middle is diagrammatic. This does not occur in reality (Matthews, 1972). The figure is adapted from Pearson and Gordon (2000).

the surrounding muscle. However, this is overcome because the intrafusal fibres receive their own fusimotor supply through γ -motoneurones (Fig 1.1). These γ -motoneurones are generally assumed to be co-activated with the α -motoneurones of the surrounding extrafusal muscle (Granit, 1968; Hagbarth & Vallbo, 1968; Vallbo, 1974; Burke *et al.*, 1976a). This means that as the muscle shortens due to

the muscle contraction the intrafusal fibres also contract and shorten, thus maintaining an appropriate length to remain sensitive to further changes in muscle length. There is some evidence in cats (Eldred *et al.*, 1953; Granit *et al.*, 1955) and baboons (Koeze *et al.*, 1968) that γ -motoneurones can be independently activated, but it was thought that the γ motor system would be more important in postural muscles. This could be the reason that evidence of independent α and γ activation in humans, during voluntary contractions, is difficult to find (Gandevia & Burke, 1985; c.f. Ribot-Ciscar *et al.*, 2000).

When Sherrington (1900) described the 'muscular sense', muscle receptors, including muscle spindles, were assigned an important role in allowing us to perceive postural sway, passive movement, active movement and resistance to movement. Sherrington's views were widely accepted in the early 1900s (Pillsbury, 1901; Jackson & Paton, 1909; Winter, 1912) but at some point in early to mid 1900s fell out of favour and were rejected almost entirely during the 1950s and 1960s in favour of joint receptors being the main source of our senses of limb position and movement. Brindley and Merton (1960) had found no muscle receptors in the eye muscles and it was thought at the time that group Ia afferents did not project to the cortex. This later turned out to be because of the anaesthetics being used at the time (McIntyre et al., 1984). In addition an influential study by Mountcastle and Powell (1959) showed that, in the macaque monkey, neurones in the somatic sensory cortex with receptive fields in and around the joints responded to joint angle changes. Favour swung back to muscle spindles with the classic paper by Goodwin, McCloskey and Matthews (1972a) showing a clear role for muscle spindles in position and movement sense. They demonstrated that muscle vibration produced illusions of limb position and movement. Vibration powerfully excites muscle spindles (e.g. Brown et al., 1967; Burke et al., 1976b; Gregory et al., 1988; Cordo et al., 1993; Bergenheim et al., 2000). This was followed by evidence showing illusions of movement could be produced by pulling an exposed tendon (Matthews & Simmonds, 1974; McCloskey et al., 1983b; cf. Moberg, 1983). In addition, work by Grigg (1973) showed that after hip-joint replacement, assumed to remove all joint receptors,

joint position sense was unaffected and Burgess and Clark (1969) showed that joint receptors could not provide the information needed for joint position sense because they responded ambiguously with peaks in firing at both ends of the range of movement. In addition patients with transected dorsal columns did not loose joint kinaesthesia in their lower limbs (Wall & Noordenbos, 1977). The dorsal column carries the skin and joint afferents for the lower limbs, but not muscle afferents (Proske & Gandevia, 2009).

The current view is that muscle spindles are the primary source of afferent information for the sense of limb position and the sense of limb movement and velocity (Proske & Gandevia, 2009). Muscle spindle afferents signal limb position by providing information about the length and the velocity of length changes of skeletal muscles. If the brain knows the length of all the muscles around a joint it can determine the position of the joint and from there, the position of the limbs in space. Similarly, information about the rate of change of the length of muscles can be used to determine the velocity of limb movements. However muscle spindles are not perfect muscle length detectors. As shown in Figure 1.1 the contractile parts of the intrafusal muscle fibres are the ends of the muscle spindles with the sensory nerve endings in between. During isometric contraction (i.e. no change in the length of the muscle tendon unit) co-activation of the γ -motoneurones will cause the ends of the intrafusal fibres to contract. This fusimotor activation will stretch the centrally located afferent nerve terminals resulting in an increase in afferent firing rates without an increase in muscle length (Matthews, 1964; Vallbo et al., 1979). Such a situation means that muscle spindles provide potentially ambiguous information about muscle length and should result in a perception of movement and displacement of our limbs during isometric contractions. It has been suggested that the 'extra' firing of muscle spindle afferents caused by fusimotor activation is cancelled out by the brain using a 'corollary discharge' of the motor command to the active muscle (Goodwin et al., 1972a; Matthews, 1982; McCloskey et al., 1983b). Corollary discharge is a term coined by Sperry (1950) to describe a signal derived from the motor command that is sent to the muscles. Von Holst's (1954) 'efference copy'

is based on the same idea, which originated with von Helmholtz (1867). This concept is covered in more detail in section 1.1.2 of this Chapter. However there is no evidence that such a mechanism exists and the results of previous studies and the study presented in Chapter 2 of this thesis, show that we do perceive displacement of our limbs during isometric contraction, despite there being no actual movement (e.g. Smith *et al.*, 2009) or perception of movement.

In summary, muscle spindles provide afferent information from the periphery about muscle length and velocity of changes in muscle length via group Ia and II muscle afferents. This information is used in the senses of limb movement and limb position. However the presence of the fusimotor supply and the coactivation of its γ -motoneurones with the α -motoneurones of the surrounding muscle means that muscle spindles are not ideal length detectors, although they are better if the muscle is passive. Further information is needed, either to correct the signals of spindle afferents or to complement them.

1.1.1.1.1 Thixotropic properties of muscle

Thixotropic properties of striated muscle are important as they have a significant impact on muscle spindle firing rates. Thixotropy is a term used to describe materials which behave as solids on one side of a force threshold and behave as liquids on the other. Starch suspensions, such as corn flour and water or tomato sauce are examples of thixotropic materials. At low forces the material flows like a liquid but at high forces, for example shaking the tomato sauce bottle, it behaves as a solid and does not flow. Another example is non-drip paint, which behaves as a solid at very low forces, but flows if you apply a higher force with a brush. The first use of the word thixotropy was biological. Peterfi (1927) used it to describe the reduction in the viscosity of sea-urchin eggs when they were disturbed with a needle. The term has also been applied to striated muscle to describe its changing behaviour during movement (Lakie *et al.*, 1984).

Within skeletal muscle, thixotropy has been described as being present because of the formation of stable crossbridges (Proske *et al.*, 1993). During a muscle contraction crossbridges require Ca⁺ and ATP to go through their power stroke and then detach in preparation for the next stroke. When a muscle relaxes some

crossbridges spontaneously reattach, thus creating stable connections between the actin and myosin filaments. If the muscle is left undisturbed these stable connections remain for a long time. This means that passive stretch of the muscle will be resisted by some stiffness until sufficient force is applied to detach the stable crossbridges (Hill, 1968). If the muscle is passively shortened, the presence of the stable crossbridges will cause the muscle fibres to fall slack because the splinting effect of the bridges prevents fibres shortening during whole muscle shortening (Fig 1.2). If the muscle is then passively lengthened from this slack state, the initial length change of the fibres will be met with little resistance as the slack is taken up.

Thixotropy also affects the intrafusal fibres of muscle spindles. The impact of intrafusal thixotropy is that in a passive muscle the firing rate of a muscle spindle afferent is dependent on the contraction history of its intrafusal fibres. So, if a muscle contracts isometrically and is then allowed to relax at that length stable crossbridges form within the intrafusal fibres. When the muscle is shortened passively its intrafusal fibres will become slack and therefore the muscle spindle afferents drop their firing to a low rate, or fall silent, and become insensitive to further changes in muscle length (Morgan et al., 1984; Gregory et al., 1988; Wilson et al., 1995). In an active intrafusal fibre the cross bridges are cycling and so it could be thought that intrafusal thixotropy would not be an important influence in contracting muscles. However there is evidence, including from the study presented in Chapter 2, that thixotropy can have an impact on position sense during muscle contraction. This appears to be the case only at forces below 10% of a muscle's maximum voluntary contraction (Winter et al., 2005; Ansems et al., 2006). Presumably at these small force levels only some γ -motoneurones are firing and so the spindles which have not been fusimotor activated will still be vulnerable to thixotropic effects.

Thixotropic effects of striated muscle affect the study of proprioception and interpretation of results. If studies involve muscle spindle outputs, the effect of intrafusal thixotropy on muscle spindle firing rates must be considered. It is often necessary to control the contraction history of the test muscle so that the



Figure 1.2: The effect of thixotropy on passive muscle. The dotted arms show the position at which an isometric contraction was made. In A the elbow was extended after the contraction while biceps and triceps were relaxed. This action stretched biceps and shortened triceps, but because of the splinting caused by stable crossbridges the triceps falls slack. In this situation any passive lengthening or contraction of triceps will be taken up by the slack. A similar situation is depicted in **B**, the elbow has been passively flexed after an isometric contraction at a more extended position. This causing the biceps to fall slack. The intrafusal muscle fibres are affected by the same thixotropic property and spindles that fall slack will lower their firing rate and may go silent. Muscle spindles that are stretched (biceps in A and triceps in **B**) will increase their firing rates. For this reason conditioning contractions should be used to control the muscle contraction history so that the state of the muscle spindles is known. The situation depicted in A is known as flexion conditioning and **B** is known as extension conditioning.

thixotropic state of the spindles is known. Generally control of muscle contraction history is achieved though 'thixotropic muscle conditioning' (e.g. Gregory *et al.*, 1988; Wise *et al.*, 1996; Winter *et al.*, 2005; Ansems *et al.*, 2006), during which an isometric contraction is performed and the muscle is relaxed at the same length before each experimental trial (Fig. 1.2). This procedure is described and used in Chapter 2.

1.1.1.2 Tendon organs

Tendon organs are afferent end-organs (Barker, 1962), often called Golgi tendon organs after Camillo Golgi who first described them in 1880. They are much simpler in structure than muscles spindles and so, since their detailed description by Huber and DeWitt (1900), little has been done to update their morphology (Merrillees, 1962; Matthews, 1972; Zelená & Soukup, 1983). The structure of the tendon organ is shown in Fig 1.3. In man they are up to 1mm long and innervated by large diameter group Ib afferent nerve fibres (Matthews, 1972). Tendon organs are generally fewer in number than muscles spindles, with tendon organ to muscle spindle ratios ranging from 0.3 to 0.94 in the cat (Jami, 1992). Tendon organs are still quite numerous with counts of up to 86 in muscles. They are located mostly at the musculo-tendinous junction with a small number (8% in the cat (Barker, 1967)) being present in the tendon itself. A few may be present in the muscle belly (Proske, 1981). Some muscles of the cat, such as tenuissimus, contain no tendon organs (Proske, 1981). Tendon organs are in series with a small bundle of muscle fibres to which they directly connect and are in parallel to the surrounding muscle fibres (Fig 1.3). In man a tendon organ typically connects to 10 - 20 muscles fibres (Gandevia, 1996) with a few additional muscle fibres connecting to the outside of the tendon organ capsule (Bridgman, 1970).

Tendon organs have low sensitivity to passive muscle stretch but are very sensitive to contraction of the muscle (Houk & Henneman, 1967), specifically to contraction of the muscle fibres to which they are directly connected in series. Recordings in humans show that tendon organs modulate their firing rate closely with the force generated by the muscle (Vallbo, 1970; Burke *et al.*, 1976b) and this makes them ideal transducers of intramuscular force. A tendon organ can signal the contraction of a single motor unit within a muscle if it is connected in series with one of that motor unit's muscle fibres (Houk & Henneman, 1967), although they seem to ignore tension changes in other parts of the muscle (Gregory *et al.*, 1985; Proske & Gregory, 2002). This suggests that while tendon organs are excellent detectors of local muscle force they do not have the ability to signal the whole tension generated by a muscle. However, the muscle fibres connected to a single tendon organ would belong to different motor units (Burke



Figure 1.3: A diagram of the structure of the tendon organ. The tendon organ consists of a small bundle of encapsulated tendon strands. These tendon strands are longer than non-encapsulated strands and connect to single muscle fibres. Group Ib afferent nerves provide the sensory innervation and these nerves terminate in Golgi receptors on the encapsulated tendon strands. There may be encapsulated tendon strands which do not received Golgi endings. The figure is adapted from Zelená and Soukup (1983).

& Tsairis, 1973) and these motor units will have muscle fibres distributed throughout the muscle. Therefore a single tendon organ may sample the force from a large portion of the muscle (Proske & Gregory, 2002). It also seems that the group discharge of the population of tendon organs in a muscle signals the whole muscle tension (Gandevia, 1996, Fig. 4.4; Prochazka & Gorassini, 1998).

Evidence that tendon organs project to the cortex (McIntyre *et al.*, 1984, 1985) as well as suggestions from psychophysical experiments that there was a sense of muscle tension, distinct from the sense of effort and dependent on peripheral muscle receptors (McCloskey *et al.*, 1974; Roland & Ladegaard-Pedersen, 1977; Rymer & D'Almeida, 1980), helped build the case that tendon organs were proprioceptors. Tendon organs are now thought to be the primary receptor in the sense of muscle force. Their location and firing properties mean that they are excellent indicators of the force generated by muscle and their information is not corrupted by factors such as muscle weakness caused by muscle damage (Proske & Gregory, 2002; Gregory *et al.*, 2003) or fatigue. However on their own they cannot directly signal the force produced by a limb movement as the torque a

muscle applies to a joint depends upon the angle of attachment to the bone, which varies with joint angle. So while tendon organs provide robust information about intramuscular force, additional information about the position of the joint is required to provide an unambiguous sense of the forces produced by motor actions.

1.1.1.3 Skin receptors

Muscle spindles and tendon organs are both muscle receptors and their location within the skeletal muscles allows them to transduce information about the kinetics of the limbs. However whenever a joint is moved the skin around that joint will be stretched and thus receptors in the skin, normally thought of as being responsible for the sense of touch, can also provide information about joint movement and therefore contribute to proprioception. This was first noted by Adrian and Umrath (1929).

Afferents that innervate cutaneous mechanoreceptors in the skin are categorised into two types of slowly adapting afferents and two types of rapidly adapting afferents (for review see Johnson, 2001; Kaas, 2004). Rapidly adapting type I afferents (RA-I) terminate in Meissner corpuscles. These receptors are most dense in the glabrous skin of the hand, but are rare in the hairy skin. The RA-I afferents fire during the transient phase of skin indentation and are thought to be responsible for detecting transient stimuli such as taps to the skin. Pacinian corpuscles are classified as rapidly adapting type II afferents (RA-II) and are most sensitive to vibration, particularly of frequencies between 100-300Hz. Pacinian corpuscles are situated deep in the tissues and thus have large receptive fields but they are very sensitive to transient indentations within that field. Slowly adapting type I (SA-I) afferents terminate in Merkel disks, which have a small receptive field and are sensitive to light indentation of the skin. The SA-I afferent nerve fibres fire throughout an indentation up to many seconds. Slowly adapting type II (SA-II) afferents terminate in Ruffini endings, a little deeper in the skin than Merkel disks and thus have larger receptive fields. When the surrounding tissue is moved and is stretched the Ruffini endings are stretched and the SA-II afferents fire. These afferents are very sensitive to skin stretch. Less is known about the

hairy skin (Goodwin & Wheat, 2008), but it also has SA-I, SA-II, RA-I and RA-II afferents although the receptors can be different (Johnson, 2001). Some of the SA-I and RA-I afferents are concerned with the hair follicles and there are fewer or no Pacinian corpuscles. The hairy skin relies on deeper Pacinian corpuscles and is therefore less sensitive to vibration.

Hulliger *et al.* (1979) showed that all four types of skin afferent mentioned above respond to movements of nearby joints. The most responsive were the RA-II and SA-II afferents. Some of the SA-II afferents also changed their firing rates with static changes in joint angle. It had already been shown that SA-II afferents responded to skin stretch and had directional sensitivity (Knibestöl, 1975). In addition the SA-II afferents in the nail bed of the finger modulate their firing rate linearly with the angle of the adjacent distal interphalangeal joint. Both these results demonstrate that skin mechanoreceptors provide information that can be used in the proprioceptive senses of position and movement. That is SA-II afferents are capable of steady discharges with rates proportional to the degree of skin stretch around a joint. Thus they are capable of signalling joint angle, and therefore limb position. However the same receptors would be activated both by joint movements as well as by touch events, this means that some processing of the signal would be necessary to distinguish between the two.

A difficulty in determining the importance of skin receptors to proprioception was that experimental techniques could remove muscle afferents or skin *and* joint afferents from proprioception, but it was difficult to separate the skin and joint receptors from each other. However, this separation is easier in the knee (Clark *et al.*, 1979) and was exploited to investigate the contribution of skin and joint receptors to proprioception in humans. Clark *et al.* blocked the skin receptors and joint receptors independently or both together with local anaesthetic in the human knee. They concluded that cutaneous receptors did not contribute to static position sense at the knee but did report that when skin receptors were anaesthetised there was an increase in the standard deviation of their subjects' limb matching ability. This suggests that there was an effect from blocking the skin receptors. Clark *et al.* did concede that skin receptors may be involved in

movement sense in the hand as had been suggested previously (Gandevia & McCloskey, 1976). Further studies suggested that skin receptors contributed to limb position and movement sense (Gandevia *et al.*, 1983; Moberg, 1983) despite some opposition (Burgess *et al.*, 1982). However it was not clear at that time whether skin receptors provide a specific position and/or movement signal or whether they provide facilitatory inputs to signals from joint and muscle receptors (Gandevia & McCloskey, 1976; McCloskey, 1978; Matthews, 1982). It was later shown that a facilitatory role was not likely (Refshauge *et al.*, 2003). Edin and Johansson (1995) suggested that afferents from skin mechanoreceptors contribute to perception of movement by demonstrating movement illusions in the finger induced by stretching the skin around the joints. Collins and Prochazka (1996) showed similar illusions. Ten years later similar illusions were shown in the finger, elbow and knee, although the illusions were more common in the hand (Collins *et al.*, 2005).

Another consideration is whether input from skin receptors interferes with proprioception of the joints. Recently it has been shown that input from Pacinian corpuscles interferes with proprioception in the finger joints (Weerakkody *et al.*, 2007; Weerakkody *et al.*, 2009). This interference occurs centrally and manifests as an impairment of joint movement detection *during* a stimulus that selectively excites Pacinian corpuscles, for example a low-amplitude vibration of the the skin at 300 Hz. The input appears to interfere with the signals of skin afferents (Weerakkody *et al.*, 2009) adding further weight to the idea that some classes of skin receptors provide a specific signal about joint movement but also showing that the proprioceptive signals in the hand are able to interact.

We currently know that skin afferents provide information about joint movement and this information appears to be more important in distal joints like the hand than more proximal joints of the body. Muscle spindle accuracy is compromised when a muscle spans multiple joints (Sturnieks *et al.*, 2007), which is the case with the long flexors of the fingers. While the muscle spindles in this case may provide ambiguous information, the skin receptors are localised at the joint. In addition to information about joint movement, cutaneous receptors also provide information about force, or pressure, as the skin is compressed (Kaas, 2004) or sheared (McCloskey, 1974) as a force is applied to an object, or an object applies a force to the body. This role of skin receptors was established more quickly and with less controversy (McCloskey, 1978).

1.1.1.4 Joint receptors

The discussion of muscle spindles in section 1.1.1.1 of this Chapter showed that joint receptors competed with muscles spindles for the role of the primary receptor responsible for joint position sense and for this reason the role of joint receptors in proprioception has also been controversial over the last hundred years. Joint afferents terminate as both Golgi receptors and Ruffini receptors, with the Golgi organs being in the ligaments (Andrew, 1954; Skoglund, 1956) and the Ruffini endings in the joint capsule (Andrew, 1954; Boyd, 1954; Skoglund, 1956). Studies on joint receptors are difficult because the nerves only run a short distance before entering mixed nerves. In addition definite identification of joint receptors is difficult without exposing the joint capsule (Gandevia, 1996), which is not practical in humans. In the late 1800s Goldscheider (1889) attempted to anaesthetise joint receptors by passing trains of electrical stimuli through the finger joint. He concluded that joint receptors had a role in the detection of joint movement. However his method was later questioned when it was shown that the same deficits were produced with electrical stimulation of the hand or arm as well as by stimulating the elbow joint itself (Pillsbury, 1901; Winter, 1912).

In the 1950s when the role of muscle spindles in joint position and movement sense became controversial, the case against muscle receptors was strengthened when it was shown that deficits in kinaesthesia were evident in the toe (Browne *et al.*, 1954) and finger (Provins, 1958) after local anaesthesia of the joint. These deficits were confirmed (Chambers & Gilliatt, 1954; Goodwin *et al.*, 1972a; Goodwin *et al.*, 1972b; Moberg, 1972) but there was disagreement on whether there was anything left (e.g. muscle spindles) to provide kinaesthesia after the joint receptors were anaesthetised. A further problem was that this procedure usually anaesthetised the skin around the joint as well (Moberg, 1972; McCloskey, 1978) and, as discussed above, skin receptors located in the skin that

is stretched during a joint's movement will contribute to the proprioception of that joint. Specific injections of local anaesthetic into the joint showed little or no impairment of kinaesthesia (Siirilä & Laine, 1972; Christensen & Troest, 1975; Ferrell *et al.*, 1987). However this could be because complete anaesthesia of joint receptors had not been achieved.

It was in the 1970s that evidence against joint receptors being the primary source of kinaesthesia began to build up and this occurred in tandem with the stronger evidence for muscle spindles discussed above. Burgess and Clark (1969) showed that only ~5% of knee joint receptors in the cat responded to knee angle, and they suggested that some of these were actually muscle spindles. It has since been shown that spindle afferents share a nerve with joint afferents in the knees of the cat (McIntyre *et al.*, 1978). In monkeys less than 2% of knee joint afferents were found to fire monotonically with joint angle, and again these were suspected of being muscle spindles (Grigg & Greenspan, 1977). In contrast to these studies, Ferrell (1980) found that 18% of joint receptors discharged in the mid-range of the joint movement.

Studies in humans showed that after the total removal of the joint capsule patients still possessed joint position sense (Cross & McCloskey, 1973; Grigg *et al.*, 1973). Furthermore patients with a severed dorsal column still possess lower limb joint position sense (Wall & Noordenbos, 1977). Thus, joint receptors were not necessary for joint position sense. However this does not exclude them from having a supporting role. One microneurography study in humans showed that many joint receptors only respond to joint movements at the extremes of movements and that they often responded in both directions of movements (Burke *et al.*, 1988). Another study showed that while some joint afferents could encode movement throughout the range of the joint, their firing rates were affected by muscle activity (Edin, 1990). At the moment it is thought that joint receptors do have a supporting role in joint position sense and that they are important for signalling the extremes of joint movements. It is thought that the information they provide is too ambiguous to be a primary source. They may be more important in the distal joints (Ferrell *et al.*, 1987).

Peripheral receptors contribute to the senses of joint position, joint movement and muscle force. However no receptor is the exclusive contributor to these senses. All of the receptors discussed above have shortcomings that mean that under certain conditions the information provided by the receptor may be ambiguous. The conditions that lead to these ambiguous signals are not theoretical situations that rarely occur. They are common physiological conditions that occur in routine sensorimotor tasks. For example, the muscle spindle will increase its firing rate during an isometric contraction signalling an increase in muscle length, despite there being no change, and skin receptors will respond to skin stretch, whether it is due to joint movement, a shearing force or an unrelated non-proprioceptive stimulus. Having multiple sources of information available for each sense not only provides redundancy but overcomes the shortcomings of the individual receptors. It also means that proprioception cannot be fully understood by studying receptors in isolation, the interaction between the multiple sources of information must also be studied to learn how the proprioceptive senses are derived.

1.1.2 Information from central sources

The information received from receptors in the periphery is feedback of events that have already occurred. However observation is not the only way to gain information about an event. If the brain is responsible for causing an event it could simply monitor the actions it took to enact the event and rely on previous experience about the consequences of its actions. For example, during a voluntary movement the brain could know that the elbow moved into flexion because the muscle, joint and skin receptors signal such a movement, or it could know because it commanded the elbow to flex. The idea that we are consciously aware of the drive to our muscles is an old one. According to Bastian (1887) it originated in the 1500s, but the idea became more widely known and discussed in the late 1800s (e.g. von Helmholtz, 1867; Jackson & Paton, 1909; see also: Goodwin, 1976; McCloskey, 1978). The ideas have continued to evolve, along with the terminology up to the current day. The history is mixed in with the role

of muscle spindles and joint receptors and is often just as controversial. The early authors on this topic focussed on the proprioception of the eye and so the next part of the discussion will also focus on the eye and the extraocular muscles (for review see Donaldson, 2000). The discussion will then move on to cover the origin of some of the more modern terminology and the role of centrallygenerated signals in limb proprioception during the second half of the 20th century. This will include observations in phantom limbs and chronically deafferented subjects which were an important influence on the role of these signals during that period.

1.1.2.1 Sensation of innervation and the extraocular muscles

In the late 1800s the idea of a sensation of innervation became more widely known and discussed (McCloskey, 1978, 1981). Müller, Bain, Wundt and von Helmholtz were advocates, although von Helmholtz is credited with presenting the strongest case (Goodwin, 1976; McCloskey, 1981). This view was opposed by Ferrier (1876), James (1890) and Sherrington (1900) who favoured a peripheral origin for the awareness of muscle activation and movement. Von Helmholtz's (1867) description of the biomechanics of the eye was detailed. He commented that the eye, its contents and its accessory muscles and connective tissues formed a constant volume within the eye socket. He further stated that this situation, along with the attachments of the extraocular muscles made it impossible for the eye to be translated by voluntary activation of the extraocular muscles. Thus the only voluntary movements the extraocular muscles can make is to rotate the eyeball in the socket and this is done with several muscles acting with simple mechanical actions. These biomechanics are relatively simple when compared to the limbs where the voluntary movement of one joint requires not only activation of multiple muscle groups around the joint but postural activation to stabilise the rest of the body and compensate for the inertia of limbs translating through space. Von Helmholtz (1867) said that we are aware of the amount of "effort of will" used to activate a muscle for a particular task. He referred to this ability as a "feeling of innervation" where the innervation is the amount of drive the motoneurones provide to the muscle that is activated for the task. He stated that the direction of the eyes within the eye sockets was known simply from "the

effort of will involved in trying to alter the adjustment of the eyes." With the simple biomechanics he described, it would seem that Helmholtz's feeling of innervation could provide accurate information without the delays involved in afferent feedback from peripheral receptors. Furthermore it had been stated that there were no muscle spindles in the extraocular muscles (Jackson & Paton, 1909), although Buzzard (1908) did discover them and reported that they may have a different structure to normal. More recently it has been shown that in monkeys there is sensory input from the extraocular muscles to the sensorimotor cortex (Wang *et al.*, 2007). A similar projection has also been identified in humans (Balslev *et al.*, In press)

1.1.2.2 Corollary discharges and efference copies

It seems there was a strong polarity among the 19th century authors because they all seem to have favoured one extreme or the other. That is, proprioception was either entirely peripheral in origin or entirely central in origin. None of those authors proposed a hybrid system that incorporated both. However this interaction was suggested in the 1950s. Sperry (1950) suggested that a "corollary discharge" of the eye muscle excitation pattern may be sent to a visual centre to compensate for retinal displacement. He further suggested that corollary discharges accounted for the displacement illusions seen when the eyeball is passively moved and that they provided a neural basis for Helmholtz's sensation of the intensity of the effort of will. Von Holst (1954) proposed a detailed theory based on the subtraction of an "efference copy" from the reafference produced by a voluntary action. Von Holst referred to "the whole of the motor impulses" as the efference and peripheral impulses from "whatever stimuli in whatever receptor" as afference. Furthermore he separated the afference into two parts. The reafference is the component of the afference that is due directly to a voluntary action, for example if the elbow flexors are voluntarily flexed this produces a reafference indicating that the elbow has been flexed. Alternatively if the elbow were flexed by an external force with no voluntary input then a pure exafference would be generated. The exafference is the component of the afference that is due to events that are entirely outside of voluntary control. Von Holst's theory stated that when an efference was sent out to a muscle, it was copied and the action of

this efference copy was to cancel out the reafference coming back from the periphery with the remainder continuing on to higher centres to be perceived. Von Holst justified this theory with the results of his experiments on insects, observations of vertebrate behaviour and experiments on humans including reproducing the displacement illusions referred to by Sperry (1950) and von Helmholtz (1867). It should be noted that neither corollary discharges nor efference copies were said to be consciously perceived in their own right. The role of these signals on perception was as a preprocessor, correcting or modifying the peripherally derived afferent signal *before* it moved up to higher brain centres to be perceived. A similar idea was proposed by Goodwin, McCloskey and Matthews (1972a) to correct for the increased firing rates of muscle spindles due to fusimotor drive (see 1.1.1.1). The idea of a central command being used to correct for a reafference is not unique to proprioception. Bell (1982; 1989) showed this mechanism to be present in the electric sense of a species of electric fish. These fish have electro receptors which they use to detect other animals in the water. They also have an electric organ which is used with their electroreceptors for "active electrolocation." Discharging the electric organ will also activate the eletroreceptors and corrupt any sensory input. Bell showed that this fish uses a corrollary discharge, or efference copy, mechanism to correct for the reafference caused by discharging its electric organ. Neural networks that carry corollary discharges related to various task have been identified in several species (for review see Poulet & Hedwig, 2007; Crapse & Sommer, 2008) including the oculomotor system of non-human primates (Wurtz & Sommer, 2004).

The history presented so far shows that the early work on the proprioceptive role of centrally generated signals emphasised the motor control of the eye. It is not clear why this is the case, but perhaps it is because knowing the position of the eyes in the skull is related to how an animal relates to itself and the external environment (Donaldson, 2000). The relatively simple biomechanics described by von Helmholtz (1867) would make a proprioceptive system based on central command signals accurate. In addition, the system would be faster than one

dependent on afferent feedback and perhaps be better at keeping the visual world stable on the retina. However there is now strong evidence that extraocular muscle receptors contribute eye kinaesthesia and so it is currently thought that both ocular proprioceptors and centrally-generated signals contribute to proprioception of the eyeball (Donaldson, 2000).

1.1.2.3 Phantom limbs

The role of corollary discharges in proprioception remained controversial into the 1970s where evidence involving phantom limbs began to be involved. Many amputees continue to experience a perception of their limb after it has been removed. This sensation is referred to as a phantom. It was reported that some amputees could make movements of their phantoms with voluntary efforts (Henderson & Smyth, 1948; McCloskey, 1978). Clearly when a limb has been removed the brain can no longer receive any afferent information from the missing body parts and reports that an amputee can move their phantom voluntarily would appear to be strong evidence for a role of centrally-generated signals in the senses of limb position and movement. Despite this, corollary discharges were not thought to contribute to the senses of limb position and movement (Goodwin et al., 1972a; McCloskey & Torda, 1975; Gandevia & McCloskey, 1977b). It needs to be noted that this use of the term corollary discharge by authors in the 1970s refers to a signal that reaches consciousness and provides direct information about limb position and movement, in contrast to Sperry's (1950) definition. For the remainder of this thesis I will refer to these conscious corollary discharges as motor command signals or central command signals.

Phantom limb movement can also be examined in healthy subjects. A phantom limb can be induced acutely in a subject using an ischaemic block (Walsh *et al.*, 2009). This is done by inflating a sphygmomanometer or anaesthetist's cuff to above arterial pressure around the upper arm. Over about 40 minutes the arm below the cuff becomes paralysed and anaesthetised but the subject continues to perceive it, that is they develop a phantom hand, wrist and forearm. It was shown recently that after a complete ischaemic block subjects perceived their phantom

wrist to become displaced if they made voluntary efforts (Gandevia *et al.*, 2006). Thus central command signals have a role in the sense of limb position. Similar illusions occurred when the arm was paralysed but the afferents were intact (Smith *et al.*, 2009). Along with the evidence from experimental phantoms, if the elbow flexors are weakened by fatigue or eccentric muscle damage, subjects make large errors of up to 15° when matching the angle of the exercised elbow to the unexercised elbow (Walsh *et al.*, 2004; Allen & Proske, 2006; Walsh *et al.*, 2006). These errors are consistent with, and were attributed to, subjects using cues from central command signals (or effort cues) to match the position of their elbows.

Currently a role for central command signals in the sense of limb position has been established. However the role of central command signals in the sense of limb movement has received little attention. There was an anecdotal report of a perception of *movement* in the recent experimental phantom study by Gandevia et al. (2006). In contrast to this, Melzack and Bromage (1973) reported that movements of experimental phantoms only occur if the block is incomplete and electromyographic activity continues. However Melzack and Bromage did not report how much effort their subjects made. They did say that it is difficult to attempt to move paralysed muscles and others have reported that it is difficult to maintain an effort to paralysed muscles (Stevens, 1978; Gandevia et al., 1993). Amputees that report phantom movements also have twitching in the stump muscles (Henderson & Smyth, 1948) which has been suggested to be differentially activated for different phantom movements (Reilly et al., 2006). In contrast perception of phantom movements can be elicited with transcranial magnetic stimulation (TMS) applied over the hand area of the motor cortex and these movements do not depend upon specific muscle activity (Mercier et al., 2006). Movements from TMS are only muscle twitches and can be difficult to localise even in intact subjects. Chapter 3 presents a study which investigates the role of central command signals in the sense of movement.

1.1.2.4 The sense of heaviness

So far the discussion about the proprioceptive role of centrally-generated signals has focussed on the sense of limb position and movement. The senses of

heaviness and effort also need consideration and the role of central command signals in these senses has been less controversial. The terms 'sense of heaviness' and 'sense of effort' are sometimes used interchangeably, but there is a slight difference. Judging effort only requires you to know the motor output to the muscles, but to judge heaviness requires you to know if you succeeded in lifting or moving the load. For example, you can pull up under a car and know how much effort you are applying, but you cannot judge its heaviness, unless you successfully lift it.

As a muscle is used continually it is weakened by muscle fatigue and this often results in a perception of the load getting heavier. A common experience is carrying a heavy suitcase. As the muscles holding the suitcase get fatigued the suitcase feels as if it is getting heavier and heavier, despite its weight not changing. If you switch the suitcase to the other arm it feels 'light' again, until those muscles begin to fatigue. This effect has been measured objectively by having subjects match weights that are lifted with a fatigued muscle versus an unfatigued muscle on the contralateral side (e.g. McCloskey et al., 1974). This perception of increased heaviness with increasing muscle fatigue is difficult to explain with afferent mechanisms as it is likely that skin, joint and tendon receptors would continue to accurately signal the tensions and pressures involved in bearing the load. The one peripheral receptor that might possibly signal this sensation of increasing heaviness is the muscle spindle (Luu, B and Fitzpatrick, R, unpublished observations). As the muscle fatigues, the centrally generated motor command must increase to maintain the same tension with a weakened muscle. As the drive to the α -motoneurones increases it could be expected that the drive to γ -motoneurones would increase as well. This increase in fusimotor drive will increase the firing rates of the muscle spindles and could form the basis of a sensation of heaviness. However experiments with vibration (Hagbarth & Eklund, 1966; McCloskey et al., 1974), which excites muscles spindle endings (see 1.1.1.1), showed that subjects perceived a smaller tension, not larger, when the muscle was vibrated. This suggests that spindles are not the source of the sense of heaviness.

While the sense of heaviness is difficult to explain with afferent mechanisms, it is relatively simple with von Helmholtz's sense of innervation. The motor commands sent to a muscle will increase with the sense of heaviness, or effort, that is perceived. It was noted by Wundt (1863) that when a patient's leg is half paralysed it takes great effort to move it and the patient is aware of this high level of effort. Other studies showed that when a muscle on one side is weakened by fatigue (Gandevia & McCloskey, 1977b) or a neuromuscular blocker (Gandevia & McCloskey, 1977a, b), subjects judge weights and isometric contractions to be heavier and greater, respectively, than is normal. Patients suffering from motor strokes that result in weakness, but not paralysis, and with no apparent sensory loss perceive an increase in heaviness of their movements (Gandevia & McCloskey, 1977b). This is consistent with using a motor command signal to judge effort and heaviness. Furthermore when patients suffer motor strokes resulting in complete paralysis the sense of heaviness can be absent (Mach, 1959; Gandevia, 1982). It is suggested that this indicates a central source of the sense of heaviness because when paralysis is caused by a peripheral nerve block (Goodwin et al., 1972a; Melzack & Bromage, 1973) or neuromuscular block (McCloskey & Torda, 1975) the sense of increased heaviness and effort remains. Ferrier (1876) objected to the idea of a centrally derived sense of heaviness and proposed that the sense of heaviness could be perceived from other muscles which are activated during an effort. The example he used was the respiratory muscles which are activated in a graded way during voluntary efforts of limb muscles. However with complete paralysis that includes the respiratory muscles, attempted voluntary movements are still accompanied by a sense of effort (Gandevia et al., 1993)

It is important to realise that in order to judge the heaviness of an object the brain needs to know that the object was successfully lifted. Without this information the brain cannot know how to interpret the amount of effort that is perceived in attempting to lift or move a load. This information could come from vision but weight matching experiments are frequently done in the absence of vision and subjects can still perform the task. It would seem that some afferent information about whether or not a load is lifted is required to contribute to a sense of
heaviness. Gandevia and McCloskey (1978) showed that only a very crude afferent signal that indicates that the load has moved is required. They showed that muscle receptors can provide this signal, but it is also probable that a crude indication of movement could also be provided by skin and/or joint afferents as well.

The sense of force is separate from the sense of heaviness. While the sense of heaviness is a sense of how much effort is being exerted to activate muscles, the sense of force is a sense of how much force is actually output from the muscles and is independent of muscle fatigue. As discussed above, the sense of force is thought to be primarily provided by tendon organs, but a central signal could also contribute. In an unfatigued muscle the amount of effort exerted will be proportional to the force that the muscle generates and this calibration could be stored by the brain. It has not been shown that central effort signals are always used to judge force, but it has been shown that when asked to match forces subjects match an effort cue rather than a force cue (Jones, 1983; Weerakkody *et al.*, 2003). In contrast when the sense of effort has been disrupted by neuromuscular block, subjects are able to accurately match force (Roland & Ladegaard-Pedersen, 1977).

1.1.2.5 Deafferented man

It might seem that the best way to look at the role of centrally-generated command signals in proprioception would be to study subjects who have been deafferented. Experimental phantoms are a way to do this (see above), but the methods for inducing them typically block the motor system as well. Thus the study of deafferentation on an intact motor system is not possible with phantoms. There is also no easy method for acutely blocking large diameter afferents selectively. Surgical deafferentation has been studied in monkeys (e.g. Taub & Berman, 1968; for review Bossom, 1974) and shows that movement control can be recovered in deafferented animals, although they will favour an intact limb over a deafferented limb and movements with the deafferented limb are not 'normal.' In humans, we can study the rare cases in which patients have lost the function of their large-diameter afferents without their motor system being affected. One of these cases

is IW in the United Kingdom. IW suffered an infection and lost the function of his large diameter afferent nerve fibres. The effect of this was that he lost his sense of touch and afferent proprioceptive pathways (Cole, 1991; Cole & Paillard, 1995). Initially he was unable to control the movement of his limbs. Cole writes that although IW was able to make some movements, "he had no ability to control the speed or direction of the movement. Any movement happened in a totally unexpected way. It was pointless to try." Cole also wrote that IW's limbs moved on their own when not watched by IW. Despite this inability to make controlled movements of his limbs, IW was able to learn through determination and trial and error, how to make controlled limb movements. Eventually he was able to live and work in the community as well as drive a car. IW became heavily dependent on vision to keep himself standing, presumably because lacking any information from muscle, skin and joint receptors, he had no other way of knowing if his legs were straight and he was upright. Cole writes that in the dark IW would fall down into a heap. Was IW able to recover the ability to make controlled movements entirely from vision and cues from his intact small-diameter afferent nerves, or did central motor command signals make a contribution?

IW and another deafferented subject, GL, are both able to judge weight with visual feedback (Fleury *et al.*, 1995; Miall *et al.*, 2000). However, once vision is removed, their ability to judge the heaviness of an object is impaired. Fleury *et al.* proposed that the deafferented subject (GL) was using visual information, such as the velocity of the movement. The idea was that GL would apply a constant force, or effort, and judge the weight from the speed of the resulting movement, which requires vision and the ability to make a *constant* effort. Fleury *et al.* supported this by showing that other subjects could judge weights by watching GL judge the same weight. This explanation is feasible but an alternative would be that GL was using a central sense of effort to judge heaviness and in the absence of afferent information, requires a visual cue to know when the weight is lifted. The study by Miall *et al.* (2000) involving IW was not a weight-matching study, but asked subjects to judge if a weight was getting heavier or lighter, when it could be getting heavier, lighter, or not changing. They noted that IW's weight

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judging behaviour in the absence of visual feedback was consistent with a lack of information about whether the load moved in response to his applied forces. Miall *et al.* also showed that without visual feedback IW would judge all weights as getting heavier. This is consistent with the muscle fatiguing and requiring an increase in effort, but it is unclear how IW would know that his muscles are fatiguing and the weight lowering without visual feedback. He may know this from experience. Miall *et al.* suggest that IW makes use of other cues that may come from his still intact group III afferents. They suggest that IW may get some crude indication of muscle tension from these remaining small-diameter afferents. Where the sense of heaviness is concerned the behaviour of two deafferented subjects is consistent with the sense of heaviness using a central sense of effort or motor command coupled with a simple indication that the weight has been lifted.

When it comes to judging movements without visual feedback, it seems that both IW and GL are able to control the amplitude of wrist pronation/supination movements, but not their starting or end position (Nougier *et al.*, 1996). Furthermore when their movements were prevented by a magnetic brake the deafferented subjects behaved as if they were unaware of this and reported that they did not know the brake had interfered. They could not judge passive wrist pronation/supination movements. Despite a lack of afferent proprioceptive information IW and GL were able to control the amplitude of their voluntary movements. Perhaps centrally derived signals can provide information to the sense of limb movement. If properly calibrated through vision or afferent signals in intact subjects, the strength and duration of a voluntary effort could accurately indicate the amplitude of a movement, provided that perturbations from the environment were signalled through a peripheral source, such as afferent signals or vision. Chapter 3 investigates the role of central motor command signals in the sense of limb movement.

In summary, central motor command signals are currently thought to be principal in the sense of heaviness, and effort is used as a cue by subjects when matching forces. Recent studies have shown that motor command signals can contribute to the sense of limb position but how these central signals interact with afferent signals to generate this sense is still not understood (see Chapter 2), nor is the role of motor command signals in the sense of limb movement (see Chapter 3).

1.1.3 One sense or four?

As mentioned in the opening section proprioception is generally broken down into four 'sub-senses', the sense of limb position, the sense of limb movement, the sense of force and the sense of heaviness and effort. I have referred to these four separate senses above when discussing the various receptors and how signals from them contribute to proprioception. However these four senses are not truly separable and cannot normally be used in isolation. Every movement, voluntarily controlled or externally imposed, will involve all the proprioceptive receptors and signals, and all four 'sub-senses'. When a receptor is assigned to one of the four sub-senses it means that the receptor in question is thought to be good at detecting that type of information. It does not mean that receptor cannot contribute to the other sub-senses. Proprioception is complex and relies on multiple sources of information. Division into four senses makes it easier to study, but it must not be forgotten that proprioception is really one sensory system with multiple inputs.

1.2 Body schema and ownership

The above sections have discussed how sensory signals contribute to the proprioceptive senses. The proprioceptive senses all reach consciousness, but human beings are not specifically aware of the angle of every joint, velocity of every movement and force of every muscle contraction all the time. Instead, we tend to merge this information and be aware of the position of the body as a whole, this occurs through a representation of the body. The idea that an image of the body is required to control movements has been around at least since James (1890). Head and Holmes (1911) introduced the 'postural schema' and described it as a "*plastic schema*" that is updated by every new movement and posture. The postural schema is now often referred to as the "*body schema*" (e.g. Longo *et al.*, 2010) and the terms will be used interchangeably here. One important reason to

maintain a body schema is that to control movement the brain needs to know not only about the position and movements of the joints, but also the length of the body segments. There is no sensory receptor that signals the length of the body segments and so this information is provided by the body schema (Head & Holmes, 1911; Cole & Paillard, 1995). Although this information does not appear to be completely veridical (Longo & Haggard, 2010).

The body schema cannot be static as the body is constantly changing size and shape as well as moving through space. Changes in the length, size and mass of the body segments are relatively slow. Even in adolescent boys the peak change in total height is about 80 to 100 mm per annum (Tanner, 1962; Visser et al., 1998). There is some evidence that motor skills are adversely affected during rapid changes in height (Visser et al., 1998; Hirtz & Starsota, 2002; Dominici et al., 2009) and it has been suggested that this may be due to the body schema lagging behind the true body parameters (Longo et al., 2010). However changes of 100 mm per annum are trivial when compared to the rapid changes in joint position that accompany every movement. Movements of the joints commonly involved changes in joint angle of tens of degrees in a fraction of a second resulting in distal body parts translating at speeds in the order of m s⁻¹. To be accurate at all times and therefore be useful for controlling movement the body image must be updated rapidly and continuously by multiple sensory inputs. The body schema is thought to be generated in the parietal cortex from somatosensory, visual and vestibular inputs (Freund, 2003; Blanke & Arzy, 2005; Pellijeff et al., 2006; Corradi-Dell'Acqua et al., 2009). Information from muscle, joint and skin receptors as well as central motor command signals will be crucial to provide information about the position and movements of the joint and limbs. Vibration illusions (e.g. Goodwin et al., 1972a) and illusions caused by skin stretch (e.g. Collins et al., 2005) demonstrate these signals influence the body schema. A stored body schema provides a framework for perception of phantom limbs and at the same time phantom limb sensations provide some insight into the body schema. Centrally-generated motor command signals must influence the body schema because voluntary efforts can move both experimental phantoms

(Gandevia *et al.*, 2006; see also Chapter 3) and the phantoms of amputees (Henderson & Smyth, 1948). Information from the body schema could also be combined with central motor commands to correct sensory errors (Wolpert *et al.*, 1995).

We know what belongs to our body and what does not, and we know this without needing to interrogate the thing in question. In addition to the body schema the brain develops a map of what belongs to it and what does not, that is the brain has a sense of ownership over its own body. Presumably this map is built up from sensory information, but not all of the senses are suitable for this task. For example, vision can provide information on the body, but it can provide the same information on external bodies and has no way of differentiating between *self* and *other*. In contrast any event perceived by the sense of touch must, by definition, be occurring against the brain's body. This property would seem to make the sense of touch ideal for identifying which things belong to the brain. Similarly the proprioceptive senses only detect events occurring on the body and would also seem ideal for this role.

The sense of body ownership seems robust but it is easily manipulated. An example of this is the application of careful visuotactile stimuli. When a false arm is placed in front of a subject and their arm is hidden from view, simultaneous brushing of both the subject's hidden hand and the visible false hand will lead to the subject feeling the brushing not on their hand, but on the false hand (Botvinick & Cohen, 1998). This illusion of body ownership is often referred to as the 'rubber hand illusion' and demonstrates the influence of tactile stimuli on the sense of body ownership. The brain interprets the synchrony of the brushing sensation on the hand and the vision of the brush touching the false hand as meaning the false hand belongs to it. This illusion is strong enough to cause a physiological response if the false hand is threatened while the illusion is established (Ehrsson *et al.*, 2007). The real hand that has been supplanted by the false hand undergoes physiological changes, including cooling (Moseley *et al.*, 2008), which suggests that the brain may be neglecting the real hand in favour of the rubber hand. The rubber hand illusion provides strong evidence that tactile

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signals play a critical role in the sense of body ownership and a similar illusion can be induced for the whole body, creating an an out-of-body illusion (Lenggenhager *et al.*, 2007). However it is not known if non-tactile proprioceptive signals have a similar influence on body ownership. This is investigated in Chapter 4.

1.3 Concluding remarks

The review presented in this Chapter shows that proprioception has been studied for more than century and while much is known about the proprioceptive senses, much is poorly understood. Each of the proprioceptive senses can arise from multiple sources, including muscle, skin and joint receptors as well as information about centrally-generated motor commands. Little is known about how the peripheral signals interact with each other and the centrally-generated signals within the brain. Models have been proposed which rely upon interactions between signals. A popular theme is the use of a version of a motor command signal to correct for reafference. Examples of this are von Holst's (1954) efference copy model, or a more recent force attenuation model that was proposed to explain why subjects overestimate externally-generated forces when matching them with a voluntary force (Shergill *et al.*, 2003; Bays & Wolpert, 2007). This force attenuation model, shown in Figure 1.4, was suggested seven years ago, but has not yet been investigated in detail.

The discovery that centrally-generated signals related to motor commands contribute directly to limb position sense is recent and it is still unknown if they contribute to the sense of movement, which while closely related to the sense of position is a different sense. Some recent work showed that fatigue has no effect on the ability to track velocities (Allen & Proske, 2006), but the methods were not well suited to investigating a role of motor command signals. Another point relating to motor command is that these signals cannot provide enough information on their own about limb position and movement. Motor commands can only signal the commencement of a movement and its intended duration, the direction of the movement (by knowing which muscles are driven to contract) and



Figure 1.4: A model using an efference copy to attenuate reafferent force. This model was first proposed by Shergill et al. (2003) to explain why subjects match an external force with a larger voluntary force. The model proposes that an efference copy is used in conjunction with a forward model of the afferent sensory system to predict the afferent signals that will be caused by the motor command (i.e. the reafference). The predicted sensory feedback is used to attenuate the reafferent component of the actual sensory feedback, which is a combination of reafference and exafference. The proposition is that attenuation of the reafferent component of the feedback sensitises us to the exafferent component (i.e. external influences), on which we have no other information. This model uses a concept similar to von Holst's (1954) efference copy model. Note that this figure suggests that all of the reafference is subtracted out, leaving only the the external influences to be perceived. This is unlikely as a total subtraction makes this system incapable of detecting self generated forces. The figure is reproduced from Bays and Wolpert (2007).

the intended level of activation in the contracting muscles. To provide information about limb position and movements these signals must be combined with a calibrated model or representation of how the body reacts to the brain's motor commands. The interaction of proprioceptive signals with body representations (e.g. the body schema or the sense of body ownership) is not well understood. The positions and movements of our limbs and body are not perceived as a series of joint angles and movements, they are perceived as an integrated image of where our body is in space and how it is currently moving. Thus proprioception feeds into these representations, particularly the postural image, or body schema. The role of central signals and representations in proprioception still requires further investigation.

The following Chapters present four experimental studies which investigate important areas of proprioception identified above. Chapter 2 investigates the interaction between peripheral and central signals in limb position sense. Chapter 3 investigates if there is a role for central motor command signals in the sense of limb movement. Chapter 4 looks at the contribution of proprioceptive signals to the sense of body ownership. Finally Chapter 5 investigates the detail of a model that was proposed to explain why subjects overestimate externallygenerated forces when matching them with voluntary forces. Chapter 2

The combined effect of muscle contraction history and motor commands on human position sense

2.1 Abstract

Along with afferent information, centrally-generated motor command signals may play a role in joint position sense. Isometric muscle contractions can produce a perception of joint displacement in the same direction as the joint would move if unrestrained. Contradictory findings of perceived joint displacement in the opposite direction have been reported. As this only occurs if muscle spindle discharge in the contracting muscle is initially low, it may reflect increased muscle spindle firing from fusimotor activation, rather than central motor command signals. Methodological differences including the muscle contraction task and use of muscle conditioning could underlie the opposing findings. Hence, we tested perceived joint position during two contraction tasks ('hold force' and 'hold position') at the same joint (wrist) and controlled muscle spindle discharge with thixotropic muscle conditioning. We expected that prior conditioning of the contracting muscle would eliminate any effect of increased fusimotor activation, but not of central motor commands. Muscle conditioning altered perceived wrist position as expected. Further, during muscle contractions, subjects reported wrist positions displaced $\sim 12^{\circ}$ in the direction of contraction, despite no change in wrist position. This was similar for 'hold force' and 'hold position' tasks and occurred despite prior conditioning of the agonist muscle. However, conditioning of the antagonist muscle did reduce the effect of voluntary contraction on position sense. The errors in position sense cannot be explained by fusimotor activation. We propose that central signals combine with afferent signals to determine limb position and that multiple sources of information are weighted according to their reliability.

2.2 Introduction

The sense of limb position is vital to our ability to accurately control the movement of our limbs in space. The traditional view is that the sense of limb position is derived from afferent information in which muscle spindle endings are attributed the major role (McCloskey, 1978; Gandevia, 1996; Proske, 2006) with skin stretch receptors and slowly adapting joint receptors providing supplementary information (e.g. Ferrell *et al.*, 1987; Collins *et al.*, 2005; cf. Weerakkody *et al.*, 2007). Evidence for muscle spindles as limb position sensors includes the presence of position and movement illusions induced by muscle vibration (e.g. Goodwin *et al.*, 1972a; Roll & Vedel, 1982), which is known to be a strong stimulus for muscle spindles (e.g. Brown *et al.*, 1967; Burke *et al.*, 1976b; Gregory *et al.*, 1988; Cordo *et al.*, 1993; Bergenheim *et al.*, 2000).

Two groups of recent studies have shown that voluntary contractions affect position sense. Gandevia et al. (2006) reported that when the arm was paralysed and anaesthetised by ischaemia a steady effort about the wrist created the perception of displacement in the direction of the attempted contraction. That is, when subjects pushed into flexion they perceived their paralysed wrist to be more flexed than during rest, and this effect was large ($\sim 15^{\circ}$). The same effect occurs with isometric contraction of the wrist muscles with the motor and afferent pathways intact, although this effect is smaller in magnitude (Smith et al., 2009). These results suggest a role for motor command signals in the perception of limb position. In contrast, Ansems et al. (2006) exploited the thixotropic properties of muscle (Proske et al., 1993) to set an initially high spindle firing rate in either the elbow flexor or extensor muscles. They reported that perception of joint position is only affected by muscle contraction if the muscle spindles in the agonist muscle have low firing rates before the contraction. Moreover, when judgements of limb position were altered, perceived displacement was in the *opposite* direction to the contraction, so that when subjects contracted the elbow flexors they perceived the elbow to be more extended (see also Walsh et al., 2004; Allen & Proske, 2006; Walsh et al., 2006). Ansems and collegues' results are consistent with the effect of the muscle contraction on position sense being due to an increase in muscle

spindle firing rates produced by coactivation of fusimotor drive with descending drive to the alpha motoneurones.

Thus, two sets of studies show that muscle contraction has an effect on limb position sense. However, one set supports the role of central motor command signals in position sense during muscle contraction, while the other set suggests an effect due to changes in muscle spindle firing caused by the fusimotor activation that accompanies muscle contractions. We postulated that these different findings were due to the different loading tasks used. One task was a 'hold force' task in which subjects pushed isometrically against a fixed object and were given force feedback to maintain the level of contraction (Gandevia et al., 2006; Smith et al., 2009). The other was a 'hold position' task in which subjects were instructed to maintain the position of their arm and the contraction level was controlled because they supported a weight (Ansems et al., 2006). Altered reflex responses and motor unit firing suggest that muscle spindle inputs contribute to motor output more during hold position than hold force tasks (Akazawa et al., 1983; Maluf et al., 2007; Baudry et al., 2009). As H-reflexes and long-latency stretch reflexes are altered in these tasks, muscle spindle input is likely to be processed differently at both the spinal and cortical levels (e.g. Doemges & Rack, 1992; Maluf et al., 2007). However, it is not known whether the altered motor actions of muscle spindles are associated with changes in the perception of limb position. In addition, if motor cortical neurones or motoneurones are more facilitated by muscle spindle input, then less voluntary descending drive should be required to produce the same motor output. We hypothesised that, in the hold position task, the balance between the higher spindle discharge caused by fusimotor activation and voluntary motor output was altered compared to the hold force task so that the spindle discharge was perceived as signalling that the contracting muscle was lengthened. We set out to test this hypothesis by having subjects do both a hold force and hold position task at the same joint in the same experiment under controlled conditions.

Due to the thixotropic properties of intrafusal muscle fibres the contraction history of the muscle can alter the effect of subsequent contraction on perceived limb

position (Ansems *et al.*, 2006). Therefore, in the current study, we used prior conditioning contractions to control the contraction history of the muscle. This allowed us to set the firing rates of the muscle spindles in either the wrist flexor or wrist extensor muscles to a high firing rate, which meant we would then be able to predict changes in muscle spindle firing with muscle contraction. The study was designed to test whether voluntary contraction about the same joint in the same experiment resulted in different effects on perceived limb position in hold position and hold force tasks. We expected that prior contraction of the muscle at a short length would eliminate any effect that increased muscle spindle firing induced by fusimotor co-activation had on position sense. Effects due to a central motor command signal would be unchanged.

2.3 Methods

Eight subjects (5 male) aged 23-37 participated in this experiment. All subjects gave informed consent and the experimental procedures were carried out in accordance with the Declaration of Helsinki and with the approval of the University of New South Wales Human Research Ethics Committee. Subjects were unaware of the experimental hypotheses.

Subjects had their right forearm strapped down and their hand fixed in a manipulandum with the fingers extended and the dorsal surface of the hand aligned with the vertical plane. This manipulandum was connected to a rotating platform via a load cell (XTran 250N, Applied Measurements, Australia) and this arrangement restricted movement of the wrist to flexion and extension only (Fig 2.1). The signal from the load cell was amplified and low-pass filtered with a 1kHz cut-off. The manipulandum was marked with graduations in degrees so that wrist angle could be accurately set, and reproduced, by the experimenter. An angle of 0° was defined as when the hand and fingers were colinear with the forearm, with angles into flexion defined as negative and into extension as positive. A pointer placed above the wrist and with its axis colinear with the flexion-extension axis of the wrist, allowed subjects to signal the perceived angle of the wrist using their left hand. The scale was graduated in degrees and could

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Figure 2.1: A diagram of the experimental setup. Left panel shows the subject's right hand held in the manipulandum on the rotating platform. The right panel shows how the subject's arm was covered with the dial used to indicate wrist angle. The axis of the dial was colinear with the axis of the wrist and rotating platform. The wrist flexors or extensors were conditioned with a muscle contraction then the wrist was moved to the test angle and loaded into flexion or extension. Subjects either supported a weight (hold position) or made an isometric contraction (hold force) with the platform clamped into position. At the same time, they made a judgement of their wrist angle and indicated it with the pointer using their left hand.

only be seen by the experimenter. The subject's arm was covered below the elbow to block the subject's vision. Prior to experimental trials, the subjects performed maximal voluntary contractions (MVCs) into flexion and extension with the wrist clamped at 0 °. Subjects then performed a series of trials in which they signalled the angle of their wrist under one of the three conditions detailed below. EMG was monitored using surface electrodes over the flexor and extensor carpi radialis muscles (band filtered at 16-1000 Hz; CED 1902 amplifiers) in order to ensure that the muscle conditioning was applied. It was important in these experiments that we knew that subjects were contracting the correct muscles and following instructions to stay relaxed. EMG, torque at the wrist and wrist

angle were sampled at 100Hz and recorded using a CED 1401 data acquisition system (Cambridge Electronic Design, Cambridge, England).

Conditioning contractions of either the wrist flexor or wrist extensor muscles were used at the start of each trial. We did this to manipulate the ongoing firing rate of muscle spindle endings (Proske *et al.*, 1993). For flexion conditioning the wrist was fixed into 20° of flexion, the subject then performed a contraction that was 4 s long with the wrist flexors, at 30% of the force measured during their MVC. Visual feedback of the force was provided on an oscilloscope. Extension conditioning was done in the same way, with the wrist fixed at 20° of extension. One of these muscle conditioning procedures was used before every trial throughout the experiment.

After each conditioning contraction, the experimenter moved the wrist into a test position while wrist extensor and wrist flexor EMG were monitored to ensure that these muscle groups were relaxed. Occasional trials had to be repeated due to poor relaxation, typically only 2-3 per subject. Based on pilot studies, the following three experimental conditions were combined and studied in one testing session.

2.3.1 Condition one: Position signalled at rest

The purpose of this condition was to confirm that the muscle conditioning was working as expected and to provide a baseline for the comparison of the loaded conditions. After muscle conditioning, the manipulandum was moved and then clamped at either 10 ° wrist flexion or 10 ° wrist extension (0 ° is a straight wrist) (Fig 2.2A). While the right arm remained relaxed, subjects used the pointer to indicate their perceived wrist angle. The instruction was "show me where your wrist is." This task was performed three times at both 10 ° wrist flexion and 10 ° wrist extension, after both types of muscle conditioning. This gave a total of 12 trials for this condition.

2.3.2 Condition two: Position signalled during a 'hold force' contraction

After the same muscle conditioning as above, the wrist was moved passively and clamped into either 10 ° flexion or 10 ° extension. Using visual feedback of force, subjects were required to produce either a wrist flexion force or a wrist extension force using isometric contractions of 30% MVC for the relevant muscle group. While maintaining this contraction, the subject indicated the perceived wrist angle using the pointer (Fig 2.2B). Subjects usually took 2-3 s to stabilise the contraction before they signalled wrist position. If subjects took more than 5 s the trial was aborted and restarted. The condition involved a total of 24 trials. Three trials were performed at both test angles after both muscle conditioning types, and during both wrist flexion and wrist extension (4 different tasks at two test angles). With this hold force task, we expected to confirm that perceived wrist position was displaced in the direction of effort (Smith *et al.*, 2009) and that this was not affected by manipulation of muscle spindle firing rates with muscle conditioning.

2.3.3 Condition three: Position signalled during a 'hold position' contraction

After muscle conditioning, the wrist was moved into the test position (10 ° wrist flexion or wrist extension) but was not clamped (Fig 2.2C). Instead, the subject was given visual feedback of wrist angle on an oscilloscope and was instructed to maintain their wrist angle. The wrist was then loaded in the direction of wrist flexion or wrist extension by applying a weight. The weight was chosen to produce a force equal to that in the isometric task (30% MVC). Subjects were required to maintain an isotonic contraction and, at the same time, indicate perceived wrist angle with the pointer. Again the instruction was "show me where your wrist is." As for condition two, subjects performed three trials at each of the eight different task combinations resulting in another 24 trials. Visual feedback of wrist angle was only available once the weight was applied to the wrist and provided no information on absolute wrist angle. This was achieved by applying a DC offset to the feedback signal so that it always had the same baseline when the



Figure 2.2: Stylised examples of trials for the three experimental conditions. The two boxes mark the conditioning phase (left in each panel) and the judgement phase (right in each panel). The arrows indicate the direction of wrist flexion. **A**: An example of a 'rest' trial. The wrist extensor muscle was conditioned but there was no contraction while wrist angle was judged. **B**: An example of a hold force trial. In this task the subject contracted during the judgement of wrist angle, but wrist position was fixed by clamping the manipulandum. This panel is an example of a trial when the same muscle was conditioned and loaded (i.e. agonist conditioning). **C**: In the hold position task the subject also contracted during the judgement phase. Here both the position and force were unsteady, as the subject had to control the load and hold it in position. This is an example of a trial in which the muscles that were conditioning).

subject saw it. Trials in which subjects did not maintain wrist angle accurately were aborted and repeated. With this hold position task, we expected that, as previously shown at the elbow, perceived wrist position would be displaced in the direction opposite to the effort and that this would be abolished by prior conditioning of the contracting muscle. The combined trials for each of the three conditions (total of 60) were presented in a random order. They were presented in blocks of 20 with 5 minute rests between blocks to avoid loss of attention or muscle fatigue. At no time was the subject removed from the apparatus or allowed to see their arm.

2.3.4 Data and statistical analysis

The errors made by subjects were calculated as the difference between their actual wrist angle and the angle they indicated with the pointer. Data from the two test angles were pooled after a paired t-test showed that there was not a significant difference between these two groups of data. Within each type of muscle conditioning the mean position error during the rest task was subtracted from the mean position error for each loading task. This is the subtraction of a large number from a small one, and so has the visual effect of reversing the direction of the muscle conditioning effect in Fig. 2.4. This reversal indicates the reduced effect of the prior conditioning during muscle contraction. The statistical analysis for the hold force and hold position data consisted of three-way repeated measures ANOVAs testing the factors of task (hold force/hold position), direction of loading (flexor muscles/extensor muscles) and type of muscle conditioning (flexion conditioning/extension conditioning) as well as all of the interactions. Analysis of the rest condition was carried out with a paired t-test. The EMG was compared across tasks (hold force/hold position) with a t-test and there was no significant difference. For all tests the threshold for statistical significance was set at p<0.05 and all data are presented as the mean \pm SEM.

2.4 Results

The perceived position of the wrist was compared under three conditions: during muscle relaxation, in a 'hold force' contraction and 'hold position' contraction. The subjects were able to maintain the target force during the hold force task and did so to within 20% of the target force (\pm 6% MVC). During the hold position task, subjects were typically good at maintaining wrist angle given visual feedback. They were able to do this within ~1 °.

After conditioning of wrist extensor muscles with a voluntary contraction at short length, subjects at rest perceived the wrist to be more flexed than it actually was. With conditioning of the wrist flexor muscles, there was a trend towards perception of a more extended wrist angle. Pooled data for 8 subjects is shown in Figure 2.3. Perceived wrist angle was significantly different after extension and flexion conditioning (13.3 ° ± 1.5 ° into flexion and 1.8 ° ± 1.5 ° into extension respectively, t₇=10.00, p<0.0005). This difference is consistent with a contribution from the muscle spindles in the conditioned muscle to the perception of joint position. During the hold force trials, the difference between extension and flexion muscle conditioning was on average 5.9 ° ± 6.5 ° (F_{1,7} = 27.95, p<0.005), which was smaller than during rest (15.1 ° ± 3.0 °).

Figure 2.4 displays pooled data for both tasks (hold force and hold position). Each data point is the mean position error for that type of muscle conditioning and loading task, minus the mean error for that type of muscle conditioning during rest. Thus Figure 2.4 displays the component of the position error that is associated with the muscle contraction. These results show an effect of the direction of the load ($F_{1,7}$ = 6.24, p<0.05), such that when subjects contracted the wrist flexors and judged position they perceived the wrist to be more flexed than when they contracted the wrist extensors. This difference between a contraction of the wrist flexors and a contraction of the wrist extensor muscles was ~12°. There was no difference in the size and duration of this effect between hold force and hold position contractions.

In Figure 2.5, instead of grouping trials depending upon whether the flexors or extensors were conditioned, data are grouped depending on whether the conditioned muscle was the agonist or antagonist compared to the muscle used in the hold force and hold position tasks. Figure 2.5 shows that when the agonist muscle was conditioned, subjects perceived a change of the position of the wrist in the direction of the muscle contraction. There was no difference in this effect between flexion or extension conditioning. However, when the antagonist muscle was conditioned there was little or no change in perceived wrist angle associated with muscle contraction. The difference in perceived wrist angle between prior



Figure 2.3: Errors in indication of wrist angle during rest and during hold force contraction after muscle conditioning. The means (\pm SEM) of 8 subjects for indicated wrist position after muscle conditioning during rest and during hold force contractions. Either the subject's wrist flexor muscles (closed circles) or wrist extensor muscles (open circles) were conditioned with a prior contraction. The wrist was then moved to the test position and wrist position was signalled with a pointer, either at rest, or during a hold force contraction into flexion or extension. The effect of the muscle conditioning was consistent with increased firing rates in the conditioned muscles. The effect of the muscle conditioning was less during a contraction than during rest. * indicates a statistically significant difference (p<0.05) and the arrow indicates the direction of the errors.



Figure 2.4: Errors in indication of wrist angle for the group of subjects. Means (± SEM) of 8 subjects for the two loading conditions shown as differences from the resting conditions. Trials with extension conditioning are shown as the difference from rest trials with extension conditioning. Trials with flexion conditioning are shown as the difference from the rest trials with flexion conditioning. The hold force task required subjects to indicate wrist angle while they pushed into flexion or extension (left) against an immoveable surface and the hold position task required subjects to indicate wrist angle during contraction into flexion or extension (right) to support a weight. When subjects made either hold force or hold position contractions into flexion, they perceived their wrist to be more flexed than when they made extension contractions. Open circles indicate data obtained when the wrist extensor muscles were conditioned with a brief contraction at a short muscle length before the trial and closed circles indicate data when the wrist flexor muscles were conditioned with a brief contraction at short length. * indicates a statistically significant difference (p<0.05) and the arrow indicates the direction of the errors.





Figure 2.5: Error in indication of wrist angle for the group of subjects when the data are separated into trials in which there was conditioning of the agonist or antagonist muscles. The mean (\pm SEM) of 8 subjects for the two loading conditions of hold force (left) and hold position (right). Errors have been plotted in reference to the agonist or antagonist direction for both the direction of the errors and the muscle conditioning. Open circles indicate data obtained when the antagonist muscles were conditioned with a brief contraction at short muscle length before each trial and the closed circles indicate data obtained when the agonist muscle was conditioned at short length. * indicates a significant difference (p<0.05) between agonist and antagonist conditioning.

conditioning of the muscle contracting in the task (agonist) or the antagonist muscle was ~9 °, which was significant ($F_{1,7} = 27.95$, p<0.005).

2.5 Discussion

When subjects performed a contraction with the wrist muscles they perceived the angle of the wrist to be displaced in the same direction as the contraction although the actual wrist angle did not change. Voluntary flexor or extensor contractions were made prior to trials to control the contraction history of the muscle. Thixotropic muscle conditioning manipulates muscle spindle firing rates (e.g. Morgan *et al.*, 1984; Wilson *et al.*, 1995) and also produced illusions of altered wrist position.

We hypothesised that for the 'hold position' task higher spindle discharge rates with contraction would be perceived as signalling that the contracting muscle was lengthened. This is not what occurred. We did not find any differences in subjects' perception of wrist position between the two loading tasks 'hold force' and 'hold position' (Fig. 2.4). However, there was a novel interaction of the muscle conditioning and the muscle contraction (Fig. 2.5), but not in the way we expected. If the interaction were due to the effects of fusimotor drive on spindle firing then we would expect that the muscle contraction would have no effect on perceived wrist position when the agonist muscle was conditioned, as found by Ansems et al. (2006). However, the interaction we observed was that conditioning the *antagonist* muscles reduced or removed the effect of the muscle, muscle contraction resulted in perceived displacement of the wrist in the same direction as the contraction.

One interpretation of our results, which could be suggested by the data in Fig. 2.3, is that contraction of the muscle to perform the task removes any effect of the thixotropic conditioning of the muscle when the intrafusal muscle fibres are activated by fusimotor drive. This would imply that an accurate perception of wrist position is signalled by muscle spindles in the contracting muscle and that

some central process subtracts the increases in spindle firing rates resulting from fusimotor drive. However if cancellation of thixotropic conditioning was the sole mechanism for perceived wrist displacement associated with muscle contraction, then we would see no effect when an 'unconditioned muscle' was contracted. Although it is not possible to test a muscle with no contraction history (i.e. unconditioned), it is possible to produce neutral conditions where wrist position is perceived as midway between those produced by wrist flexor or wrist extensor conditioning. In Smith et al. (2009;) prior to each test "the wrist was rapidly moved backwards and forwards over a range of angles from 30 to 90°" to minimise the effect of thixotropy on position sense. After this neutral muscle conditioning, both wrist flexor muscle spindles and wrist extensor muscle spindles are in a state of low firing. In this state an effect of muscle contraction cannot be due to the removal of thixotropic conditioning that leaves muscle spindles with a high rate of firing. Smith et al. found an effect of muscle contraction after neutral muscle conditioning. In addition, that effect resulted in perceived displacement of the wrist in the direction of contraction. This is the opposite direction to that expected if the change was due to the take up of the slack present in the muscle spindles because of neutral conditioning, but it is consistent with motor command signals influencing position sense. Therefore, muscle contraction influences perceived limb position independently of changes in muscle spindle firing produced by fusimotor drive.

Some proprioceptive judgements require a combination of afferent and efferent signals (Gandevia & McCloskey, 1978). Another possible explanation for the differential effect on perceived wrist position of antagonist or agonist conditioning combined with contraction is that the brain is weighting the signals available to it. In order to determine the position of a joint the brain has access to muscle spindles on both (or more) sides of the joint, motor commands from any muscles that are contracting, as well as information from skin and joint receptors. None of these signals is a perfect indicator of position and all can be affected by outside sources of noise. In some conditions, multisensory cues are weighted according to their reliability so that the integrated perception is statistically optimal (e.g.

Ernst & Banks, 2002; Alais & Burr, 2004; Helbig & Ernst, 2007). Here, the brain may give less weight to signals that it knows are contaminated, for example muscle spindles in a contracting muscle, when it combines all of the sensory information available into a perception of limb position.

In summary this study has shown that despite any mechanistic difference in motor control behaviour between hold force and hold position loading tasks (e.g. Mottram et al., 2005; Rudroff et al., 2005; Maluf et al., 2007), when subjects indicated their joint angles the perception was the same for both types of task. Our hypothesis that the different loading tasks would cause different effects of muscle contraction on perceived limb position was disproved and the reason for discrepancies between the findings of previous studies remains unclear. One possible reason is the different methods used to indicate joint angle (a bilateral match e.g. Ansems et al., 2006; an indication with a pointer Gandevia et al., 2006; Smith *et al.*, 2009). The sense of limb position is complex, with many sources of information interacting to produce perception. An interaction between the perception of the position of both arms and with the internal body image could result in the suppression or removal of the influence of motor commands when a matching task is performed, as opposed to the indicating task we have performed here. The question needs further investigation. In addition to the demonstration that perception of arm position does not depend on the type of loading, we have also shown a novel interaction between thixotropic muscle conditioning and muscle contraction during perception of limb position. We interpret our findings as consistent with a role of motor command signals in position sense and with the brain weighting the multiple sources of information available to it to create a perception.

Chapter 3

Illusory movements of a phantom hand grade with the duration and magnitude of motor commands

3.1 Abstract

The senses of limb movement and position are critical for accurate control of movement. Recent studies show that central signals of motor command contribute to the sense of limb position but it is not clear whether such signals influence the distinctly different sense of limb movement. Nine subjects participated in two experiments in which we inflated a cuff around their upper arm to produce an ischaemic block, paralysing and anaesthetising the forearm, wrist and hand. This produces an experimental phantom wrist and hand. With their arm hidden from view subjects were asked to make voluntary efforts with their blocked wrist. In the first experiment efforts were 20% and 40% of maximum and were 2 s and 4 s in duration. The second experiment used 1 s and 5 s efforts of 5% and 50% of maximum. Subjects signalled perceived movements of their phantom wrist using a pointer. All subjects reported clear perceptions of movement of their phantom hand for all levels and durations of effort. On average, subjects perceived their phantom wrist to move between 16.4 $^{\circ} \pm 3.3 ^{\circ}$ (mean \pm 95% CI) and 30.2 ° \pm 5.4 ° in the first experiment and between 10.3 ° \pm 3.5 ° and 38.6 ° \pm 6.7 ° in the second. The velocity of the movements and total displacement of the phantom graded with the level of effort, and the total displacement also graded with duration. Hence, we have shown that motor command signals have a novel proprioceptive role in the perception of movement of human joints.

3.2 Introduction

How efferent command signals contribute to the proprioceptive senses has long been controversial. Much of the focus has been on whether or not these command signals can create '*sensations of movement*'. Von Helmholtz (1867) proposed that to perceive the position of an object in our visual world it was necessary to know where the image formed on the retina and the position of the eyeball. Eyeball position could be signalled by ocular proprioceptors or by knowledge of the motor commands that moved the eye, termed a '*sensation of innervation*'. Later this sensation of innervation was termed a '*corollary discharge*' (Sperry, 1950) or '*efference copy*' (von Holst, 1954). Both terms refer to a signal derived from the motor command sent to the muscles. Such a system would minimise the reliance on delayed feedback from the periphery. The simple biomechanics of the eyeball are such that information from corollary discharges could be quite accurate. The current consensus is that the input from both ocular proprioceptors and centrallygenerated sources signal eyeball position (Donaldson, 2000).

Despite anecdotal reports from amputees that their phantom limbs moved with voluntary efforts (see Henderson & Smyth, 1948; McCloskey, 1978), it was thought that corollary discharges were not involved in sensations of limb movement (e.g. Goodwin *et al.*, 1972a; McCloskey & Torda, 1975; Gandevia & McCloskey, 1977b). No movement or change in position was perceived when voluntary efforts were made to move paralysed limbs (for review see Matthews, 1982; McCloskey *et al.*, 1983b; Gandevia, 1987). The only role given to corollary discharges in the sense of limb position and movement was a central subtraction whereby the corollary discharge corrected for muscle spindle input provided by fusimotor co-activation during a voluntary contraction (Goodwin *et al.*, 1972a; McCloskey *et al.*, 1983b). However, recent studies have found that motor command signals are involved in the sense of limb position. By 'motor command' we mean a centrally generated signal that is monotonically related to motoneuronal output to the muscle. This signal may be related to drive reaching

the motor cortex or it may arise in parallel to it. Voluntary efforts resulted in illusory changes in the position of a phantom hand which was created experimentally by ischaemic anaesthesia and paralysis of the arm (Gandevia *et al.*, 2006). Similar illusions occurred when afferents were intact but the arm was paralysed, as well as when the arm was fully intact (Smith *et al.*, 2009; Chapter 2). In addition, other studies have shown an effect of fatigue on position sense that has been attributed to an influence of central command signals (Walsh *et al.*, 2004; Allen & Proske, 2006; Walsh *et al.*, 2006). Little has been done to look at the effect of central commands on the sense of limb movement.

In a recent study in which phantom hands were produced by ischaemia, some subjects gave a verbal report of movement (Gandevia et al., 2006). By contrast Melzack and Bromage (1973) showed that experimental phantoms 'move' only if the block was incomplete and electromyographic activity persisted. However, they gave no indication of the level of effort produced by the subjects and thus the efforts may have been below the threshold to generate movement. They reported that it was difficult to attempt to move paralysed limbs, and others have shown that it is difficult to sustain an effort to paralysed muscles (Stevens, 1978; Gandevia et al., 1993). From our studies that have assessed motor performance in the presence of deafferentation and paralysis (e.g. Hobbs & Gandevia, 1985; Gandevia et al., 1990; Gandevia et al., 2006; Smith et al., 2009), we have found that subjects may need encouragement to perform tasks that are physically impossible. In amputees who reported voluntary movements of phantoms, the movements were accompanied by twitching of muscles in the stump (Henderson & Smyth, 1948). It has been suggested that the muscles in the stump are differentially active for different phantom movements (Reilly et al., 2006) and that perception of movements depends on this activity through remapping of the hand representation onto remaining muscles. In contrast, transcranial magnetic stimulation over the hand area of the motor cortex in amputees can elicit phantom movements which do not depend on specific activation of stump muscles (Mercier et al., 2006). However, these movements are twitches, which can be hard to localise even in intact subjects, and it is difficult to know how specific the

stimulus is for the motor hand area, especially if there has been cortical reorganisation,

Here we aimed to determine if subjects could perceive continuous movements of a paralysed and anaesthetised wrist when they made voluntary efforts. The alternative is that they perceive an instantaneous change in position without any movement. The aim was to quantify any illusory movements that were experienced and to determine if there was a dependence of the size and velocity of these movements on the direction, magnitude and duration of effort. An important control was to check that subjects could accurately indicate unexpected movements of their real hand in the absence of visual feedback. It was also important to establish that subjects could produce at least two different efforts without this feedback. Our hypothesis was that subjects would perceive the velocity of their phantom wrist during voluntary efforts and that these movements would move the joint further and faster for larger efforts and further for longer efforts.

3.3 Methods

Nine healthy subjects (4 male) aged 23-51 participated in the study. Eight participated in the first experiment and five of those plus the ninth participated in the second experiment. All subjects gave informed consent and the experimental procedures were carried out in accordance with the Declaration of Helsinki. The University of New South Wales Human Research Ethics Committee approved the study. All subjects were informed about the experimental procedures but were kept unaware of the experimental hypothesis. They were informed that their right arm would be paralysed and anaesthetised and that they would be asked to make voluntary efforts and then signal any movement with their left hand using a pointer.

3.3.1 Experimental setup

Subjects had their right hand strapped into a manipulandum mounted on a table that held the hand in a semi-pronated position with the fingers extended (Fig. 3.1).



Figure 3.1: **The experimental setup**. Subjects sat with the forearm strapped to the table and hand clamped in a manipulandum that allowed movement around the axis of the wrist joint into both flexion and extension. The rotating platform could be locked into position for isometric trials otherwise it was free to move against a viscous load, which was applied by a motorcycle steering damper. The forearm was hidden from subjects for the whole experiment. A pointer with an axis colinear with the axis of the wrist joint was moved by the subject's left hand to indicate the position and movement of the right wrist joint throughout the experiment. The cuff was placed around the upper arm.

The manipulandum restricted movement of the wrist, allowing only wrist flexion and extension. The manipulandum was fitted with a load cell (250N XTran, Applied Measurement, Australia) to measure forces generated by the wrist. Electromyographic activity (EMG) was measured from over the flexor and extensor carpi radialis muscles using Ag-AgCl surface electrodes (band-pass filtered 16-1000Hz, CED 1902 amplifier). The purposes for measuring EMG were to ensure subject compliance during the control experiment and to ensure EMG was absent during the block. The subject's arm was covered below the elbow. A pointer, the axis of which was colinear with the axis of the wrist, sat above the wrist and could be moved by the subject's left hand to indicate position and movement about the right wrist. Potentiometers mounted in the wrist manipulandum and the pointer were calibrated to measure actual wrist angle and pointer angle (i.e. perceived wrist angle) respectively. The manipulandum could be locked so that subjects could perform isometric contractions with the wrist. When unlocked, the manipulandum acted against an adjustable motorcycle steering damper, which applied a viscous load to the wrist. The damper had seven discrete settings allowing us to choose viscosities for each subject based on their strength. The reason for using this type of load was that we had an anecdotal report from a previous study that perceived movements of a phantom wrist had the quality "as if moving through treacle" (Gandevia *et al.*, 2006, page 707). Using this load also allowed us to change the resistance so that the subjects could not predict the movement that would occur for a particular effort. The force, angle and EMG data were all sampled through a CED Power1401 data acquisition system (Cambridge Electronic Design, Cambridge, UK) and stored on a computer for analysis. The sampling rates were 3000 Hz for EMG, and 100 Hz for force and angle.

3.3.2 Experiment one

Subjects (n = 8) initially performed maximal voluntary contractions (MVCs) of the wrist flexor and wrist extensor muscles to determine maximal flexion and extension forces which were used to set submaximal target forces. Subjects were then trained to perform efforts of 20% and 40% of maximum for two or four seconds. At first, visual feedback of force was provided on an oscilloscope, and then it was removed and verbal feedback was given by the experimenter. Once subjects could repeatably make 20% and 40% efforts with their wrist flexors and wrist extensors without feedback, they performed a series of control trials designed to test their ability to indicate the position and velocity of their wrist during these efforts. There were trials in which subjects missed the target force by a large margin and these trials were discarded and repeated. This only occurred in about one in ten trials.

3.3.2.1 Efforts with the arm intact.

In each trial, subjects performed the same effort twice. The first time, the manipulandum was locked in position so that the effort resulted in an isometric contraction. The second time, the manipulandum was unlocked so that the subject pushed against an unknown viscous load. Here it was possible for the subject's wrist to move during the effort but the distance and velocity of any movement

depended upon the voluntary force exerted. To provide a variety of unpredictable movements required efforts at two intensities (20% and 40% of maximum), two durations (2 s and 4 s) and two viscous loads (big and small). We used four conditions. The first condition comprised a 20% effort for 2 seconds against the big load. The second was a 20% effort for 2 s against the small load. The third was a 40% effort for 2 s against the big load and the fourth was a 20% effort for 4 s against the big load. Subjects performed each condition four times, in both directions of wrist flexion and extension (total of 32 trials) and the order of trials was randomised.

Subjects were not told which viscous load they would be pushing against or the duration of the effort, but they were told to maintain the effort until the experimenter said "relax." The order of events was as follows. The subject was told the level and direction of effort (e.g. "get ready to make a 40% effort into flexion"). Then the subject was asked to push and the experimenter counted them though the effort before telling the subject to relax (e.g. for a trial that was 4 s long, "Push, 2, 3, 4, relax"). Next, the subject was instructed "show me where your wrist is". The subject then used the pointer to indicate the current position of their wrist. The manipulandum was then unlocked and the subject was instructed to make the same effort with the same instruction as previously (when wrist movements could occur). After the subject relaxed, the experimenter sometimes moved the manipulandum in the direction opposite to the subject's active movement, so that the subject experienced a combination of active and passive movements. The subject was then instructed, "show me what your wrist did". The subject then moved the pointer through the perceived path taken by their right hand during the just completed effort. Instructions to the subjects emphasised that all parts of each movement should be tracked, including any pauses in movement, so that the record of the pointer signal should duplicate that of the wrist in both time and displacement. The left panel of Fig. 3.2 shows an example of one of these trials and the data derived from it.

3.3.2.2 Efforts with the arm blocked.

After subjects had completed the control trials, an ischaemic block of the right forearm and hand was performed. A two-chamber cuff placed around the upper arm was inflated to 250 mmHg and subjects remained relaxed until light touch sensation was abolished below the elbow. This typically took 35 - 40 minutes. At this time, the forearm and hand were paralysed and anaesthetised (Gandevia *et al.*, 2006). However, all subjects continued to have a perception of wrist and hand position although this did not necessarily correspond to the actual position of their wrist and hand. That is, subjects developed a 'phantom' of their forearm and hand (Walsh *et al.*, 2009).

Once the block was complete, the subjects were instructed to perform efforts that were 20% or 40% of maximum into flexion or extension at the wrist for durations of two or four seconds. Each trial was repeated three times (total 24) and the order was randomised. Again, subjects were not told in advance the duration of each effort. Before each effort subjects were told to "show me where your wrist is" and they did so with the pointer. Next the experimenter told them the size and direction of the effort to make. After they made the effort with the experimenter counting them through it and relaxed on instruction, the subjects were told to "show me what your wrist did." As in the control trials, they moved the pointer to track the path of any perceived movement of their phantom that was associated with the preceding effort. An example of the data from these trials is shown in the right panel of Fig. 3.2.

After the experiment the cuff was deflated and subjects recovered from the block within 5 - 10 minutes. Subjects were then asked about any additional perceptions that they could not indicate with the pointer during the experiment. In addition, a structured interview was conducted to gain additional information about each subject's perception of any wrist movements during the block. The experimenter transcribed the responses.


Figure 3.2: Typical trials from one subject during the 'intact' and 'blocked' states. A shows one trial during the control experiment when the arm was intact. The downward arrow indicates when the subject was told "show me where your wrist is" at which point the subject moved the pointer from its starting position to where they perceived their wrist. The upwards arrow indicates when the subject was told "show me what your wrist did." The upper row of boxes below the indicator trace mark when the wrist was locked, so that when the subject made the effort their wrist was either

'isometric', or 'free to move'. The lower row of boxes shows when the subject made a voluntary 'effort'. The subject was told a level and direction of effort. For example "get ready to make a 20% effort into flexion." The box labelled 'EM' indicates experimenter movement, when the experimenter moved the wrist back towards the starting position. After the experimenter-imposed movement, the subject was told "show me what your wrist did." The horizontal dashed lines in the top of panel **A** indicate where the change in position was measured and the dotted line indicates where the average velocity was measured. **B** is a trial from the same subject during the block. For these trials the subject was first instructed "show me where your wrist is" (at the downward arrow) and moved the pointer from its starting position at either full extension (shown here) or full flexion to their perceived wrist position. Then they were told the level of effort and the direction of effort to make and after the effort was complete the subject was told to "show me what your wrist did" (at the upward arrow).

3.3.3 Experiment two

In experiment one, subjects perceived wrist movements when they made voluntary efforts during an ischaemic block, but the differences between conditions were small (see Results). Therefore, the experiment was repeated with greater differences between levels of effort (5% and 50%) and durations of effort (1 s and 5 s). As in experiment one, subjects (n = 7) initially made maximal voluntary flexion and extension contractions about the right wrist and were then trained to make 5% and 50% maximal flexion and extension efforts without feedback. One subject, who did not participate in experiment one, completed a series of control trials with the arm intact to demonstrate an ability to reproduce unexpected wrist movements using the pointer. All subjects then underwent an ischaemic block of the right forearm and hand. When light touch was lost below the elbow, six of the seven subjects reported a phantom wrist and hand. One subject reported phantom fingers but no wrist and was excluded from the study. With the forearm and hand paralysed and anaesthetised, subjects (n = 6)performed trials as described in experiment one above. Subjects tracked perceived wrist movement after making 5% or 50% efforts into flexion or extension at the wrist for durations of 1 s or 5 s.

3.3.4 Data and statistical analysis

Data processing was done using Spike 2 ver. 6 (Cambridge Electronic Design, Cambridge, UK) and Igor Pro ver. 6 (Wavemetrics, Lake Oswego, OR, USA). Statistical testing was done using SPSS ver. 17 (SPSS Inc., Chicago, IL, USA). Wrist angle was measured immediately prior to each effort and at peak displacement. Pointer angle was measured immediately prior to being moved and at peak displacement. Changes in angle were calculated for both the wrist and the pointer. Average velocity was taken as the average slope of the position trace between the start and end angle for both the wrist and the pointer. Peak velocity was also measured, but the results were qualitatively similar to those for the average velocity and are not mentioned further. Data are presented as a mean \pm 95% confidence interval, except data about the timing of movements, which are presented as a range with a median. The data from the control experiment (Fig. 3.3) were analysed with regression analyses between perceived wrist position and the actual wrist position, and perceived velocity and actual velocity. The changes in angle and velocities were tested using a repeated measures general linear model with the factors of direction (flexion vs. extension), level of effort (20% vs. 40% or 5% vs. 50%) and duration (2 s vs. 4 s or 1 s vs. 5 s). Threshold for significance for all statistical tests was set as p < 0.05.

3.4 Results

We measured subjects' ability to indicate, with a pointer, position and movement about the wrist joint during efforts against viscous loads. Subjects then used the same pointer to indicate any perceived movement of the wrist during efforts made while the forearm and hand were anaesthetised and paralysed by an ischaemic block. After the initial training period, subjects were able to reproduce target efforts repeatably without feedback. Efforts varied about the target by $5.3\% \pm 0.5\%$ (mean $\pm 95\%$ CI) of their maximum.



Figure 3.3: Subjects' performance during the matching of wrist position and velocity in the control study before the arm was paralysed and anaesthetised. A shows the change in position that subjects indicated with the pointer versus the actual change in the wrist position. **B** shows the wrist velocity that subjects indicated versus the actual wrist velocity. The solid lines are the lines of best fit and the dashed lines show their 95% confidence intervals. The dotted lines are the lines of identity and positive angles indicate a displacement or velocity into extension of the wrist. Subjects overestimated changes in the position and the velocity of their wrist movements, but their judgments have a strong linear correlation to the true movements of their wrist (p < 0.001).

3.4.1 Experiment one

3.4.1.1 Efforts with the arm intact.

The purpose of this condition was to ensure that subjects could indicate unexpected movements of their wrist. With the arm intact, subjects tended to overestimate both the change in position and the velocity of any wrist movements (Fig. 3.3). However, there were significant linear relationships between movements of the pointer and actual wrist movements (p<0.001). These correlations were strong with R^2 values of 0.83 and 0.88 for changes in position and velocity respectively. Thus, subjects were able to signal different magnitudes and velocities of unexpected movements of the wrist joint shortly after the event using a pointer.

3.4.1.2 Efforts with the arm blocked.

With the arm blocked (i.e. paralysed and anaesthetised), subjects made efforts of 20% or 40% maximum for 2 s or 4 s. On average, subjects perceived their wrist to move between 16.4 ° \pm 3.3 ° and 30.2 ° \pm 5.4 ° with all combinations of level and duration of effort. However, movement was not always perceived to continue for the entire duration of the effort. In many trials the initial movement of the phantom was fast at the start of the effort with the phantom then pausing at the final position until the subject ceased making an effort (Fig. 3.4). The duration of the perceived movement varied from 0.6 s to 2.4 s (median 1.4 s) for efforts that were 2 s in duration and 0.4 s to 3.9 s (median 2.3 s) for efforts of 4 s duration. The duration of the pauses at the final position was 0 s to 1.6 s (median 0.47 s) and 0 s to 3.3 s (median 0.6 s) for 2 s and 4 s efforts, respectively. Larger displacements of the wrist were reported for 40% efforts compared to 20% efforts $(F_{1,7} = 13.0, p < 0.01)$ as well as for efforts of 4 s duration compared to efforts of 2 s duration ($F_{1,7} = 8.95$, p < 0.05; Fig. 3.5). However, these differences in displacement were small (2 ° to 9 °). Perceived velocities of wrist movement were between 10.9 °·s⁻¹ \pm 2.2 °·s⁻¹ and 16.9 °·s⁻¹ \pm 4.1 °·s⁻¹ in the different conditions. There were no significant effects of level or duration of effort on the perceived velocity. After the efforts were stopped, subjects signalled that their hand returned, on average, to within $\sim 0.1^{\circ}$ of their pre-effort position. While this



Figure 3.4: **Examples of perceived movements during 4 second efforts.** Traces of perceived wrist position from two subjects when they moved the pointer to signal perceived movement during a preceding 4-s effort. The thick line is a trial in which the subject's phantom wrist moved throughout the effort. The dashed line shows a trial in which the subject perceived a quicker movement at the start of the effort followed by a slower movement and a pause at the final position for the remainder of the effort. In this example the mean velocity (10 °s⁻¹) does not match the velocity calculated (3 °s⁻¹) from the final displacement (14 °) and the duration of the effort (5 s). In each trial, the return of the phantom towards its original position occurred with the end of effort and has been truncated for the illustration.

number was significantly different from zero, it is too small to be physiologically relevant.

3.4.2 Experiment two

Subjects made efforts of 5% or 50% maximum for 1 s or 5 s with the arm blocked. As in the first experiment, subjects perceived movements of their phantom wrist but sometimes the movement did not last the entire duration of the effort. For 1 s efforts the duration of the movement was 0.7 s - 0.8 s (median 0.7 s) and the pause at the final wrist position was 0 s to 1.4 s (median 0.6 s). The duration of the



Figure 3.5: Perceived change in phantom wrist position and wrist velocity during 20% and 40% efforts for individual subjects and the group. A shows the changes in wrist position perceived during efforts of 20% and 40% of maximum and with durations of 2 and 4 seconds. B shows the velocity of the perceived movements. The thick lines and circles indicate the group mean \pm 95% CI (8 subjects) and the thin lines represent the mean data from each subject. Data for efforts into wrist extension (solid lines, filled circles) and flexion (dashed lines, open circles) are shown. On average, subjects reported velocities of greater than zero for all efforts. * indicate significant differences in the change in wrist position perceived during a 20% effort versus a 40% effort, and between a 2 s effort and 4 s effort (p < 0.05).

movement for 5 s efforts varied from 0.1 s to 4.4 s (median 1.3 s) and the pause at the final position varied from 0 s to 4.1 s (median 1.0 s). This range is large because one subject indicated very rapid movements and reported that their phantom changed position instantaneously. On average, subjects perceived the wrist to move between 10.3 ° ± 3.5 ° and 38.6 ° ± 6.7 ° with all combinations of level and duration of effort (Fig. 3.6). There was an effect of both level of effort ($F_{1,5} = 50.9$, p < 0.005) and duration ($F_{1,5} = 10.4$, p < 0.05) on the perceived change of wrist angle and these effects are larger (15 ° to 30 °) than in experiment one (2 ° to 9 °). The longer duration (5 s) and the larger effort (50% maximum) produced the larger perceived movements. The velocity of perceived movements was 13.0 °·s⁻¹ ± 3.6 °·s⁻¹ to 37.0 °·s⁻¹ ± 7.9 °·s⁻¹ with a significant effect of the level



Perceived change in phantom wrist position and wrist Figure 3.6: velocity during 5% and 50% efforts for individual subjects and the group. A shows the changes in wrist position perceived during efforts of 5% and 50% of maximum and with durations of 1 and 5 seconds. B shows the velocity of the perceived movements. The thick lines and circles indicate the group mean ± 95% CI (6 subjects) and the thin lines represent the mean data from each subject. Data for efforts into wrist extension (solid lines, filled circles) and flexion (dashed lines, open circles) are shown. The mean data show that on average movements were perceived by subjects during all conditions except the 1 s long 5% efforts (the CI for the mean velocity includes zero). * indicates significant differences in the change in perceived wrist position during a 5% effort versus a 50% effort within durations, and between the change in wrist position with a 1 s effort versus a 5 s effort. For perceived velocity of movement, there is a significant difference between a 5% effort and a 50% effort.

of effort ($F_{1,5} = 14.8$, p < 0.05). However, there was no significant effect of effort duration on the velocity of perceived movements. Interestingly, the trend was towards slower movements with a longer effort, which is the same as the first experiment (Fig. 3.5). As with the first block, on average subjects indicated that after an effort their hand returned very near (within 0.1 °) to the position that they had indicated their wrist occupied before the effort.

3.4.3 Subject reports after the block

All subjects reported that they had made two distinct levels of effort while paralysed and anaesthetised, and that they perceived definite movement of their phantom hand during efforts. However, one subject who participated in both experiments reported perception of movement only on the first occasion. On the second occasion, the subject said that the phantom hand simply jumped from position to position with no perceivable movement. Three subjects reported that perception was the same in both flexion and extension, while the others reported that it was easier to make an effort in flexion or extension. Five subjects said that the movements started immediately after they started an effort and four reported that their phantom always moved for the whole duration of their effort. The majority of subjects (five out of nine subjects) felt that the phantom movements were like pushing through a viscous substance. The substances suggested by the subjects were oatmeal, honey, wet concrete, water or glue.

3.5 Discussion

We have shown that motor command signals can generate graded sensations of continuous movement in the absence of sensory input. Subjects made no real wrist movements, had no EMG in the wrist flexors or extensors, and had no changes in afferent input related to movement. Yet, subjects not only tracked perceived wrist movements with a pointer but they later reported, in all but one case, that their efforts evoked a distinct continuous movement of the phantom rather than an instantaneous change in its position. Subjects perceived their phantom wrist to move faster if they made bigger efforts and further if they made longer efforts. The results of the control experiment indicate that after training subjects were able to consistently produce efforts of 20% and 40% without feedback.

In the control experiment, subjects made wrist flexion and extension efforts against two loads that were not known in advance. Thus, their voluntary efforts

generated movements of unpredictable displacement and velocity. Under these conditions, subjects indicated reliably the wrist movements with a pointer above their hand. While their performance was not perfect (Fig. 3.3), it was consistent, as shown by the strong linear relation between the actual and perceived wrist position. Subjects tended to overestimate both the change in position and the velocity of the movements. Figure 3.3 shows that the gradient of the relation is \sim 1.3 for perceived position and \sim 1.7 for velocity. It is unlikely that use of the pointer to indicate movements causes this overestimation as subjects accurately indicate wrist position with a pointer when the wrist is moved passively (Gandevia et al., 2006) and indicate similar elbow positions with an arm or a pointer (Gritsenko et al., 2007). Thus, the overestimation most likely represents perception of larger, faster movements than those that occurred. This could be due a contribution of motor command signals to limb position sense (Smith *et al.*, 2009; Chapter 2) and our current results show that there may be a similar effect on perception of limb velocity. However, overestimation of remembered limb position has previously been reported early in passive as well as active elbow movements (Gritsenko et al., 2007) so that overestimation of movement extent and velocity when subjects were intact may be independent of the presence of voluntary effort.

These results on altered position are consistent with recent reports that voluntary efforts can alter the perceived position of a phantom wrist during ischaemic block of the arm and can also influence perceived wrist position during local curarisation (Gandevia *et al.*, 2006; Smith *et al.*, 2009). In contrast, previous studies, in which subjects attempted to move paralysed (McCloskey & Torda, 1975) or paralysed and anaesthetised limbs or digits (Goodwin *et al.*, 1972a), reported that no limb movements were perceived. In these studies, efforts were brief and may not have allowed time to generate illusory movements. In the current study, brief efforts lasting 1s produced perceptions of wrist movement in all subjects, but not on all attempts. In addition, the current study promoted uncertainty about possible wrist movements through prior exposure to trials in which efforts against unexpected loads produced movements that varied from 0 °



Figure 3.7: Comparison of the changes in perceived position and velocity from both experiments. Data for flexion and extension trials have been pooled and the data from one subject who reported perceiving instantaneous changes in position without movements were excluded. A The mean changes in perceived wrist position are plotted against the duration of effort for the four levels of effort (5%, 20%, 40% and 50% maximum). The size of perceived movement of the phantom wrist scales with the level of effort and with the duration of effort. However, the relation is not 1:1. Thus a tenfold increase in voluntary effort does not produce a movement that is ten times bigger, nor does an effort lasting five times longer produce a movement five times bigger. The shape of the curve below 1 s is unknown (dotted lines) but must approach the origin. B The perceived wrist velocity plotted against duration of effort for the four levels of The perceived wrist velocity scales with the level of effort within effort. experiments. The velocity scales inversely with duration of effort. As for position, neither relation is 1:1 and the dotted parts of the curve represent unknown data that must intersect the origin.

to 70 °. The role of motor commands in the ability to track velocities has also been examined by altering the relationship between muscle recruitment and arm velocity through fatigue of the muscle (Allen & Proske, 2006). Passive movements of one arm were tracked by voluntary movements of the other. This ability was altered by muscle vibration but not by fatigue, and it was concluded that motor commands did not contribute. However, the task was not ideal as subjects controlled the speed of their arm with eccentric voluntary contractions. Thus the speed was determined by how quickly their muscles were relaxed voluntarily. Furthermore, comparison of active and passive movements did not allow comparison of motor command between arms.

When subjects made efforts during the ischaemic block, the perception that the wrist moved in the direction of the effort was robust. On average, the size of the movements, that is the change in position with effort, graded with both the level and the duration of voluntary effort. Figure 3.7A shows the data for position from both experiments plotted together (with the data from flexion and extension pooled). However the grading was not a one-to-one ratio. An effort for five times as long (1 s efforts vs. 5 s efforts) did not displace the phantom five times as far. In addition, multiplying the level of effort by ten (5% line vs. 50% line) only increased the size of the phantom movement by 2.5 - 3 times. The curves are plotted as linear, because there are only two data points, but below 1s the data are non-linear, as the curves must pass through the origin. Perceived velocity of the phantom also increased with an increased level of effort (Fig. 3.7B) and graded within each experiment. The poor grading between experiments is probably due to two different subject groups being used. Perhaps the subjects in the second experiment paid closer attention to the velocity of the phantom movements they perceived. Again, a tenfold increase in effort (5% to 50% effort) did not increase perceived speed tenfold, rather the increase was about twofold. In contrast to movement extent, perceived velocity did not increase with increased duration of effort.

Although all subjects perceived movements of their phantom wrist in the direction of effort, they did not have identical experiences. These differences were revealed

both by the movements indicated with the pointer and by subjects' reports after the block. While some subjects perceived uniform movement throughout the efforts, others reported movements at the start of the effort followed by a pause before the return movement on relaxation. Thus, it was not the duration of the effort that was misperceived but rather that movement was not perceived throughout the effort. The cessation of movement during an effort was most obvious with the longest efforts but also occurred with the brief efforts of 1 s duration. This suggests that the phantom wrist movements are not simply reaching the end of their range of motion for longer efforts. There was not a set time limit to the perceived movement (e.g. the first 0.5 s of effort), because longer duration efforts produced larger movements. In addition some subjects reported that there was a delay between when they started the effort and when the phantom began to move, while others reported that the phantom movements started immediately. Those subjects who reported a delay between the beginning of the effort and the phantom movement described a feeling of nothing happening initially, and then their hand began to move.

We argue that subjects perceive movements of the phantom wrist due to a contribution of motor command signals to the sense of limb movement. However, other factors could contribute. As mentioned in the Introduction, a signal of motor command in this context refers to a central signal that is monotonically related to the motoneuronal output. Studies in experimental psychology have considered other perceptions such as will, agency and intention that might also be related to motor command (Jeannerod, 1999). For example, awareness of the intention to act is believed to begin at a time after the selection of a movement but during the preparatory phase and to arise in areas of the brain that are 'higher' than the motor cortex (see Haggard, 2005). However, it seems unlikely that awareness of the intention to act would be sufficient to generate the perceptions of wrist movement in the current experiment. Subjects were asked to make different levels of effort with their wrist flexors and extensors and so they did not plan movements. Thus, awareness of intention might signal timing and level of effort but should not give information on the resultant unplanned wrist movement.

Visual input can also contribute to perceptions of limb movement. Amputees experience phantom movements of their amputated limb when a mirror is used to duplicate a movement of the intact limb in the space occupied by the phantom (Ramachandran & Rogers-Ramachandran, 2000). Our study specifically excluded vision of the ischaemically blocked arm. Although subjects may have visualised movements of their phantom wrist when asked to make voluntary efforts, this is unlikely as subjects were not given any instruction in this regard and were never told to expect their voluntary efforts to produce phantom movements and they did not report visualisation of any movements. Finally, activation of proximal muscles has been linked to the perception of movement of phantom limbs. In the current study, once the ischaemic block was complete, the arm distal to the cuff was paralysed and anaesthetised. However, activity in muscles proximal to the cuff was not excluded and proximal muscles were probably performing their normal postural roles during voluntary efforts with the phantom. Reilly et al. (2006) have shown in amputees that proximal muscles activate differentially for different phantom movements and that ischaemia of muscles in the stump diminishes perceived movement. The interpretation of this and its comparison to acute experimental phantoms is complicated by the fact that amputees probably have undergone cortical remapping (Kew et al., 1994; Schieber & Deuel, 1997; Mercier et al., 2006). It is difficult to see why, during an acute ischaemic block in otherwise normal subjects, activation of a proximal muscle should be responsible for the perception of movement of a distal joint. None of the muscles that were intact or partially intact in our experiments are involved in control of the wrist and afferents activated by proximal contractions would be expected to signal unambiguously forces, changes in position or movements at proximal joints. While it is possible that information from proximal muscles may contribute to the perceptions of phantom movement, it is more likely that motor command signals related to the wrist are the dominant contributor to these perceptions of movement.

What information can be derived from a motor command signal? First, it can signal both the start and end of a voluntary action (McCloskey *et al.*, 1983b).

Second, the direction of the voluntary movement can be determined as this depends upon which muscles are activated (Gandevia & Rothwell, 1987; Gandevia et al., 1990). Finally, the motor command indicates how much of the muscle is activated, that is, how much drive is sent to the muscle to perform the action. Further information about the actions of motor command on the unloaded limbs could be learned from experience. For example, with the assistance of afferent feedback, experience could teach the brain how much force is produced by a muscle for a given motor command. Then, provided the muscle is not fatigued, the brain could control voluntary force based only on the level of motor command. Furthermore, experience could provide information about the weight and inertia of the unloaded limbs and the effects of gravity. This information, along with the relation between muscle force and motor command output, could be stored in a model of the kinematics of the unloaded body. This would indicate how the unloaded limbs behave and move with motor commands, including how fast they move for a given command. Such a model could control the unloaded body using only information derived from motor command signals, although perhaps not perfectly (Balslev et al., 2007). The remaining information required to control the body are the properties of any external loads and the state of the muscles, including the level of muscle fatigue. This information can be derived with the use of afferent information (e.g. Gandevia & McCloskey, 1978).

In the present study, afferent information from below the cuff was blocked from reaching the spinal cord and the motor commands were blocked from reaching the agonist muscles. However, any central model about the effect of motor commands on the limbs should remain. When subjects attempted voluntary efforts with their paralysed and anaesthetised wrist muscles they perceived both movement and displacement of their phantom wrist. This suggests that the motor command signals were still processed by a model of body kinematics and that the output of the model was the perception that the phantom hand moved with a velocity and became displaced from its starting position. Why then did the phantom return to its starting position after subjects stopped making efforts? For the phantom wrist, afferent signals do not change with voluntary efforts or passive

movement but the brain presumably still interprets this unchanging information. With the cessation of the motor command signal, the phantom may revert to a hand position which is the brain's interpretation of the unchanging afferent information. This raises the question of why the phantom moves at all if the afferents continuously signal a static position. Presumably the low unchanging firing rates of the afferent signals are given little weight by the model, so that the motor command information dominates during the voluntary efforts, but afterwards the low-level unchanging afferent signal is all that is left.

Why do subjects not report that the limb moved as if it were unloaded? They describe a feeling of pushing through a viscous substance. It is possible that perceptions were influenced by the control experiment which involved pushing isometrically or against a viscous load. However, a subject volunteered a similar report of pushing through a viscous substance in a previous experiment in which no '*training*' was given (Gandevia *et al.*, 2006). This perception may relate to the motor commands signalling movement and a change of position, while the afferent signals were unchanging. Perhaps these competing signals evoke the sensation of a slower more difficult movement.

In summary, we present two novel findings. First, subjects can perceive the velocity of a phantom limb during voluntary efforts and the velocity of these movements depends on the level of effort, with larger efforts generating larger velocities. Second, the extent of movements of a phantom limb is larger if subjects made voluntary efforts for longer. These results show that motor command signals have an additional role in proprioception: as well as their recently established role in the sense of limb position, they can generate a sense of limb movement.

Chapter 4

Proprioceptive signals contribute to the sense of body ownership

4.1 Abstract

The sense of body ownership, knowledge that parts of our body 'belong' to us, is presumably developed using sensory information. Sensory signals that report events occurring exclusively at the body, such as the sense of touch, seem ideal for this. This sense of ownership can be easily modified by cutaneous signals. For example, an illusion of ownership over an artificial rubber hand can be induced by synchronously stroking both the subject's hand and the rubber hand. Non-cutaneous proprioceptive signals (e.g. from muscle receptors) also exclusively signal events occurring at the body, but their influence on the sense of body ownership is not known. We developed a technique to generate an illusion of ownership over an artificial plastic finger, using movement at the proximal interphalangeal joint as the stimulus. We then examined this illusion in 20 subjects when their index finger was intact and when the cutaneous and joint afferents from the finger had been blocked by local anaesthesia of the digital nerves. Subjects experienced an illusion of ownership over the plastic finger when the digital nerves were blocked. This shows that local cutaneous signals are not essential for the illusion and that input arising proximally, presumably from receptors in muscles which move the finger, can induce a sense of body ownership. We found no evidence that voluntary controlled stimuli induce stronger illusions of body ownership than those induced by passive movement. It seems that the congruence of sensory stimuli is more important to establishing body ownership than the presence of multiple sensory signals.

4.2 Introduction

We know that our body parts 'belong' to us without having to move, contract or otherwise test the body part in question. Presumably the brain develops the map of what belongs to it by using sensory information. However, not all sensory channels are appropriate to do this. For example, we can use vision to see the parts of the body, but we can also see the parts of other bodies so that by itself vision cannot differentiate foreign body parts from those we own. By contrast, touch seems ideal for identification of ownership as any tactile stimuli that are perceived must, by definition, be occurring against the brain's own body. We do not usually perceive tactile stimuli on anything that is not part of our body.

Although this sense of body ownership seems robust, it can be disrupted in a range of clinical conditions including stroke, epilepsy, anorexia nervosa, bulimia, autism, schizophrenia and neuropathic pain (Moseley et al., 2008). Furthermore, it can be easily modified by acute manipulation of sensory input. Perhaps the most well known example of such manipulation is the 'rubber hand illusion', first described by Botvinick and Cohen (1998). This illusion can be generated by synchronously stroking the subject's hand (out of view) and a rubber hand (in view) with the stroking applied to a similar anatomical position. This illusion can also be induced using somatic signals only, that is without visual cues, by moving a blindfolded subject's index finger so that it touches a rubber hand and simultaneously touching the subject's real other hand (Ehrsson et al., 2005). However, the illusion is more vivid if the rubber hand is placed in a posture that the subject's real hand could occupy (Pavani et al., 2000; Austen et al., 2004) and the stimuli are spatially congruent (Costantini & Haggard, 2007). One proposed mechanism for the illusion is the detection of multisensory signals by the premotor, intraparietal and cerebellar regions of the brain (Ehrsson et al., 2004; Ehrsson et al., 2005). Neural activity in primary somatosensory cortex has been linked to body ownership (Schaefer et al., 2006) as well as activity in frontal cortex and the insula (Tsakiris et al., 2007). Once this illusion of ownership of the hand is established, subjects have physiological responses to threats made against the rubber hand (e.g. Armel & Ramachandran, 2003; Ehrsson et al., 2007). The

illusion is not broken by subjective reasoning or explanation by the experimenter. Furthermore there are physiological changes, such as cooling, in the real hand that is 'replaced' by the rubber hand (Moseley *et al.*, 2008).

Production of the rubber hand illusion by cutaneous stroking shows that cutaneous inputs can provide a signal of body ownership. However, touch is not the only sense that reports exclusively about events acting on the body. The other proprioceptive cues from muscle receptors, joint receptors and central command signals also provide information only about what is happening to the body. Could these sensory channels be as important as cutaneous channels in the development of the brain's sense of body ownership? Is cutaneous information essential? A combination of visual and joint movement stimuli has been used previously to investigate the induction of the rubber hand illusion (Dummer et al., 2009), but cutaneous stimuli were not excluded in that study. It is well established that movement of the hand excites input from specialised skin, joint and muscle receptors (e.g. Hulliger et al., 1979; Burke et al., 1988). Although the results of Dummer et al. show that joint movements, in place of tactile stroking, can induce the rubber hand illusion, their results do not reveal whether signals from muscle receptors, joint receptors or central motor command signals have any role in the sense of body ownership. In the study of Dummer et al., signals from cutaneous receptors around the joints were available and may have been the critical input which induced the illusion. Cutaneous signals not only provide information about objects and surfaces touched by the skin, but cutaneous stretch receptors signal movement of the joints (Edin & Johansson, 1995; Collins et al., 2005).

The present study was designed to investigate whether the non-cutaneous proprioceptive signals contribute to the development of the sense of body ownership. As a tool to measure the influence of cutaneous and non-cutaneous proprioceptive signals on the perception of body ownership, we developed a 'plastic finger' illusion. The finger was used because it is feasible to block the digital nerves with local anaesthesia and remove all input from cutaneous and joint receptors. Because the muscles which flex and extend the fingers are in the forearm, proprioceptive signals from muscle receptors remain intact. We hypothesised that proprioceptive cues would be sufficient to induce an illusion of ownership of a finger in the absence of cutaneous information.

4.3 Methods

Twenty healthy subjects (nine male) aged 21-56 participated in the study. Sixteen subjects performed all conditions. Four subjects did not perform two of the control conditions which used incongruent movement and were introduced after these subjects had been tested. All subjects gave informed consent and the experimental procedures were carried out in accordance with the Declaration of Helsinki. The University of New South Wales Human Research Ethics Committee approved the study. All subjects were informed about the experimental procedures but were unaware of the exact experimental hypothesis.

4.3.1 Experimental setup

Subjects sat with their right arm resting in a semi-pronated position on the lower of two tables (Fig. 4.1). The upper table had a rotatable shaft running though it with an axis of rotation that was collinear with the proximal interphalangeal joint of the subject's right index finger. The distal and middle segment of the subject's index finger was wrapped in a piece of neoprene and pushed into a piece of pipe. The pipe was attached to the rotatable shaft via a coupling, which allowed the rotation of the shaft to be either locked to the subject's proximal interphalangeal joint or to move independently. The apparatus prevented movement at the other joints of the finger and the wrist.

A plastic finger, of the type used by magicians, was attached to the top of the rotatable shaft through its proximal interphalangeal joint so that when the shaft coupling was engaged, movement of the plastic finger was synchronised with that of the subject's finger. A set of blocks and pipes were placed in a line 'proximal' to the plastic finger and covered with a towel to provide the visual impression that there was an arm covered by a towel attached to the plastic finger. The same towel also covered the subject's arm to the shoulder and occluded visual input of the rotatable shaft that connected the plastic finger to their own finger. This false



Figure 4.1: Diagram of the experimental setup. The subject sat with their right arm resting on the lower table in front of them. The upper table covered the subject's arm from the elbow down and a towel covered a false arm placed on the upper table, made from appropriately shaped blocks, and the subject's arm up to and including the shoulder. Thus the subject's right arm was not visible from the shoulder down. The towel and false arm were arranged so that it looked as if the towel was simply covering the subject's own arm. A plastic finger, protruded from the end of the towel so that the distal and intermediate segments were visible to the subject. This plastic finger was fixed to a rotating shaft though its proximal interphalangeal joint. This shaft was aligned with the proximal interphalangeal joint of the subject's right index finger and connected to a piece of pipe that held the distal and intermediate segments of the subject's index finger. In this setup the subject's proximal interphalangeal joint was aligned with that of the plastic finger and both could move freely around that axis. The pipe and the positioning of the subject's arm relative to it ensured that the subject's distal interphalangeal joint and metacarpophalangeal joint could not move. The coupling could be released so that the subject's index finger and the plastic finger could move independently, or it could lock so that the movement of the subject's index finger and the plastic finger were congruent. The subject's other fingers were kept in a relaxed curled position. For the two conditions where touch was used as a stimulus instead of movement, the pipe was removed allowing access to the skin of the subject's index finger.

arm was placed in a position so that it was directly over the subject's arm, which was resting on the lower table. The subject's view was limited to the plastic finger and the towel over the false arm.

This study tested if proprioceptive cues, in the absence of tactile cues, could be used to induce an illusion of body ownership over the plastic finger. Furthermore it tested if the illusion was as strong when proprioceptive cues were used compared to when tactile cues were used. In order to do this we stimulated the subject's index finger at the same time as the plastic finger under eight different conditions.

4.3.2 Basic condition

The basic condition was intended to ensure that an illusion of ownership could be induced over an artificial plastic finger using a similar experimental approach to that established for the rubber hand illusion (Botvinick & Cohen, 1998). Using commercially available 12 mm paint-brushes the experimenter synchronously stroked the subject's finger and the plastic finger in a congruent direction for three minutes. The subject could see the stroking of the plastic finger, but not the stroking of their own finger.

4.3.3 Test conditions

There were four test conditions. During all test conditions the coupling on the rotatable shaft that connected the subject's finger to the plastic finger was locked so that the movements of the two fingers were congruent. For the first test condition the subject's index finger was intact. The subject was instructed to keep the hand relaxed while the experimenter held the distal segment of the plastic finger and moved it continuously into flexion and extension though an arc of about 30 ° for three minutes. The subject saw the experimenter moving the plastic finger and also felt (but could not see) their own finger performing exactly the same movement at exactly the same time. The second test condition was similar to the first, except that the subject was instructed to voluntarily flex and extend the proximal interphalangeal joint of their finger through an arc of \sim 30 ° continuously for three minutes. Here the subjects voluntarily moved their finger

and felt it moving, but could not see it moving. What they saw was the plastic finger moving in a manner that was congruent to their own finger movements. The third and fourth test conditions were the same as the first and second conditions, respectively, except that these conditions were performed after a digital nerve block of the right index finger (see below).

4.3.4 Control conditions

Three control conditions were used to ensure that the illusions reported by subjects in the test conditions were due to the congruence of the visual and proprioceptive information. The first of the control conditions repeated the tactile stimulus of the basic condition, but was done after both digital nerves of the subject's index finger had been blocked with local anaesthetic (see below). The second control condition used movement of the proximal interphalangeal joint as the stimulus. However this stimulus was not delivered in a congruent manner. The coupling on the rotatable shaft that connected the subject's finger to the plastic finger (Fig. 4.1) was disengaged so that the two fingers could move independently of one another. The subject was instructed to keep the hand relaxed and the experimenter flexed and extended the subject's right index proximal interphalangeal joint through an arc of $\sim 30^{\circ}$ for three minutes. At the same time the experimenter controlled the movement of the plastic finger to make movements that were similar in velocity and magnitude to the subject's voluntary movement, but were otherwise unrelated. The final control condition was the same as the second control condition, except that the subject was instructed to voluntarily flex and extend their right index proximal interphalangeal joint through an arc of $\sim 30^{\circ}$. Once again the experimenter controlled the movement of the plastic finger to make movements that were similar in velocity and magnitude to the subject's voluntary movement, but were otherwise unrelated. The subject could not see the experimenter's hand controlling the movements of the plastic finger.

4.3.5 Digital nerve block of the index finger

A total of 3 - 4 ml of 1% lignocaine was injected into the medial and lateral side of the index finger 10 mm distal to the metacarpophalangeal joint in order to block both digital nerves. A piece of tape was placed around the index finger just distal to the metacarpophalangeal joint to impede slightly the venous return from the finger and thus prolong the block. The block was clinically complete in 5 to 10 minutes with complete loss of light touch sensation. Light touch was tested intermittently to ensure that the block remained complete. After the experiment the tape was removed and the subject recovered completely within a few hours.

4.3.6 Measurements

To evaluate the strength of the illusion of ownership over the plastic finger the subject was asked to complete a questionnaire. The established nine-item questionnaire (Botvinick & Cohen, 1998) was modified to apply to a finger illusion instead of a hand/arm illusion, and to incorporate the provision of non-tactile instead of solely tactile stimuli (Table 4.1). Others have used a version with only 5 items (e.g. Dummer *et al.*, 2009) but we opted to use the whole question set because we were establishing the illusion under novel conditions and we needed to understand what the subjects were experiencing. For the conditions involving passive or active movement the questions were otherwise the same. The order of questionnaire items was randomised between conditions. Each item had a discrete seven-point scale. Subjects were instructed to circle the 'correct' answer. The conditions in which the digital nerves were blocked were always undertaken after the other conditions. However, the order of both the blocked conditions and the intact conditions was randomised.

4.3.7 Data and statistical analysis

For the responses taken from the questionnaire, each of the seven possible responses to the questions, ranging from 'Disagree strongly' to 'Agree strongly', was given an integer value that ranged from -3 to +3, respectively. A zero value corresponded to a response of 'Unsure'. The data from each subject were pooled

#	Condition	Question
1	Touch	It seemed as if I were feeling the touch of the paintbrush at the location where I saw the plastic finger touched.
	Movement	It seemed as if I were feeling the movement at the location where I saw the plastic finger move.
2	Touch	It seemed as though the touch I felt was caused by the paintbrush touching the plastic finger.
	Movement	It seemed as though the movement I felt was caused by the movement of the plastic finger.
3	Common	I felt as if the plastic finger were my finger.
4	Common	I felt as if my (real) finger were drifting up (towards the plastic finger).
5	Common	It seemed as if I might have more than one right index finger, hand, or arm.
6	Touch	It seemed as if the touch I was feeling came from somewhere between my own finger and the plastic finger.
	Movement	It seemed as if the movement I was feeling came from somewhere between my own finger and the plastic finger.
7	Common	It felt as if my (real) finger were turning 'plasticy'.
8	Common	It appeared (visually) as if the plastic finger were drifting down (towards my finger).
9	Common	The plastic finger began to resemble my own (real) finger, in terms of shape, skin tone, freckles or some other visual feature.

Table 4.1: **The set of questions used in the study.** The nine questions used by Botvinick and Cohen (1998) were adapted to refer to the finger, rather than the hand, and plastic, rather than rubber. Questions 1, 2 and 6 were further modified to create a second version of the question that related to movement rather than touch. Note that after the modification to refer to movement, the meaning of question 2 became ambiguous and subjects stated that it's meaning was not clear. The questions labeled as being a 'Touch' condition were used for the two synchronous touch conditions. 'Movement' questions were used for all six movements conditions. Questions labeled 'Common' were used for all conditions.

within conditions. The data were not normally distributed so the median and interquartile ranges (IQR) were calculated. Where questions were tested to determine if the median answer was greater than zero (see Results, Figs. 4. 2 and 4. 3) a Wilcoxon signed-rank test was used. When comparing passive movement

to active movement, data for the blocked and intact conditions were pooled and when comparing a blocked finger to an intact finger, the data for passive movements and active movements were pooled. Differences between these integer values were used to indicate if subjects had a more positive response to one condition than they did to the other (Fig. 4. 4). Where the median responses to questions for experimental conditions were compared to each other (see Results, Fig 4. 4) a Wilcoxon paired sample test was used to determine if there was a difference between conditions. The threshold for significance was always p< 0.05. Data were analysed using Igor Pro version 6.12 (Wavemetrics, Lake Oswego, OR, USA).

4.4 Results

We investigated if non-tactile proprioceptive cues could reliably induce an illusion of ownership over a plastic finger. We coupled the subject's index finger to an artificial plastic finger so that the two moved in unison. We then flexed and extended the proximal interphalangeal joint passively or had subjects make the same movements voluntarily to induce an illusion of ownership of the artificial finger. Both of these conditions were performed with an intact finger as well as after the digital nerves had been blocked. In addition, we tested key control conditions. During two of these, the movements of the subject's finger and the plastic finger were unrelated and during the third, a touch stimulus was used, but the subject's index finger was anaesthetised.

4.4.1 Basic condition

This basic condition produced a vivid illusion of ownership of the plastic finger in all 20 subjects. This condition involved tactile stimulation by stroking synchronously both the subject's finger and the plastic finger with the same movement. This was then chosen as the benchmark for induction of an illusion of ownership of the finger. This general method reliably induces an illusion of ownership of a rubber hand (Tsakiris & Haggard, 2005). Of the nine questionnaire items, three questions showed a median response that was



Figure 4.2: Questionnaire responses for the group during the 'Intact synchronous touch' condition shown as median (± IQR) (n = 20). The questions are the same as those used by Botvinick and Cohen (1998). Q1: It seemed as if I were feeling the touch of the paintbrush at the location where I saw the plastic finger touched. Q2: It seemed as though the touch I felt was caused by the paintbrush touching the plastic finger. Q3: I felt as if the plastic finger were my finger. Q4: I felt as if my (real) finger were drifting up (towards the plastic finger). Q5: It seemed as if I might have more than one right index finger, hand or arm. Q6: It seemed as if the touch I was feeling came from somewhere between my own finger and the plastic finger. Q7: It felt as if my (real) finger were turning 'plasticy'. Q8: It appeared (visually) as if the plastic finger were drifting down (towards my finger). Q9: The plastic finger began to resemble my own (real) finger, in terms of shape, skin tone, freckles or some other visual feature. The boxes show the interquartile ranges of the group data for the responses to each question and the thick black line indicates the median response. The red boxes show the three questions that showed a positive response (i.e. > 0). These positive responses were significantly greater than zero (p < 0.05) for each of these three questions. Q1 and Q3 were used in the other conditions to measure the presence of an illusion of body ownership. Q2 was not used because its meaning is ambiguous when directly translated to 'movement.' Q5, Q7, Q8 and Q9 showed median responses that were significantly less than zero.

significantly greater than zero (p < 0.05) (Fig. 4. 2). The same three questions have already been seen to indicate the presence of a rubber hand illusion (Giummarra *et al.*, 2010). We excluded question 2 because a simple rewording of this question to make it relevant to movement also gave it ambiguous meaning (see Table 4.1). We used subjects responses in the remaining two questions to determine the presence of an illusion of finger ownership in the subsequent conditions.

4.4.2 Test conditions

The median (\pm IQR) responses to questions 1 and 3 are shown for the four test conditions in Figure 4.3. During all of these conditions the plastic finger was coupled to the subject's right index finger so that both proximal interphalangeal joints moved in unison. When the subject's finger was intact and the movements were passive, 19 (of 20) subjects gave a positive response to question 1 or question 3 with 14 of those giving a positive response to both questions. When the movement was made actively by the subject only 14 subjects gave a positive response to question 1 or 3, with 10 of those subjects giving a positive response to both questions. When the subject's finger was blocked, 17 subjects gave a positive response to question 1 or question 3. If the movements were controlled by the experimenter, 16 of the 17 subjects gave a positive answer to both questions when the movements were made actively by the subject.

Significantly positive median responses (p < 0.05) occurred for question 1 when the movements were passive, that is controlled by the experimenter (Fig. 4.3). A significantly positive group response was found for active movements only when the finger was blocked. We found one significant positive response (p < 0.05) to question 3 which occurred when the subject's index finger was blocked and the movements were imposed on a passive finger. These results are consistent with comments from the subjects which suggested that an illusion of ownership of the plastic finger was easier to induce and more vivid with passive movements and when the finger was blocked. Figure 4.3 shows a trend towards a positive response to question 3 when the finger was intact and the movements were

Q1 It seemed as if I were feeling the touch of the paintbrush/movement at the location where I saw the plastic finger touched/move.



Q3 I felt as if the plastic finger were mine.



Figure 4.3: Median (\pm IQR) responses to questions 1 and 3 for all control and congruent movement conditions. The boxes show the interquartile range of the group data for each question response and the thick black line indicates the median response. Red boxes show data for the experimental conditions where the movements of the plastic finger and the subject's finger were congruent. Passive and active congruent movements were tested for the intact index finger and the index finger after it had both its digital nerves blocked with local anaesthetic. * indicates a response that was significantly greater than zero (i.e. a response of 'Agree somewhat' or higher) (p < 0.05). The white boxes show the data for the three control conditions, IIPM: Intact Incongruent Passive Movement, IIAM: Intact Incongruent Active Movement and BST: Blocked Synchronous Touch. No control condition showed a median positive response for either question. Question 1 had a median response that was significantly positive for all congruent movement conditions except active movement in an intact finger. The only significant positive response for question 3 was for congruent movement of a blocked and passive finger. Thus subjects adopted the plastic finger into the body schema to some degree for all four experimental conditions except for active congruent movements of the intact index finger.

passive, but the result was not significant.

An illusion of ownership of the plastic finger was induced in more subjects and was more vivid, for passive movements than active movements and with a blocked finger rather than an intact finger. We calculated the difference between subjects' responses for both passive movement versus active movement and a blocked finger versus an intact finger (Fig. 4.4). These differences showed that subjects' responses to both questions 1 and 3 were significantly more positive (p < 0.05) when their finger was blocked than when it was not. For passive movement compared to active movement, the response to question 3 was significantly more positive (p < 0.05).

4.4.3 Control conditions

No more than six subjects gave a positive response to question 1 or question 3 for any of the control conditions. The first control condition used the same tactile cues as the basic condition except that the digital nerves of the subject's index finger were blocked, which eliminated tactile cues. This condition did not produce a significant median positive response to questions 1 and 3 (Fig. 4.3), which means that no illusion of finger ownership was experienced. While some subjects reported a 'strange feeling', they did not report any feelings of the basic plastic finger illusion. The remaining two control conditions used movement as the stimulus but this movement was not congruent between the subject's finger and the plastic finger. For these conditions there was not a significant median positive response to questions 1 and 3 (Fig. 4.3). In addition, the subjects gave no indication that they experienced a plastic finger illusion or any other strange perceptions during these two conditions.



Figure 4.4: Histograms of the difference between response of subjects for passive movement versus active movement, and a blocked finger versus an intact finger. A and B show how many subjects had a given difference between responses for passive congruent movement and active congruent movement. Each subject provides two answers as there were two active and two passive conditions. A positive difference indicates that the subject responded with a more positive response for the passive task than the active task. Passive versus active differences for question 3 show a weighting to more positive responses and the median difference is significantly greater than zero (p < 0.05). C and D show how many subjects had a given difference between responses in conditions with a blocked finger and an intact finger. Each subject provides two answers as there were two blocked and two intact conditions. A positive difference shows that subjects provided a more positive response to the question during the digital nerve block. Data from both question 1 and 3 are weighted in favour of a positive difference and the median difference is significantly greater than zero (p < 0.05).

4.5 Discussion

This study provides insight into the physiological mechanisms underlying the sense of body ownership and generation of the body schema. We used congruent movements of the right proximal interphalangeal joint of the subjects' right index finger and an artificial index finger. The combination of visual and proprioceptive stimuli caused the subjects to incorporate the plastic finger into their body schema and report that they felt as if the plastic finger was their finger, consistent with our hypothesis. This study produced one novel and indisputable result. When the digital nerves of the subjects' finger were blocked with local anaesthetic, removing sensory input from skin and joint receptors, the visuo-proprioceptive stimuli still induced an illusion of ownership over the finger. This shows that visuo-tactile cues are not critical for manipulation of the sense of body ownership and thus suggests that they would not be critical for establishing it. Furthermore, non-cutaneous proprioceptive cues, coupled with vision, are sufficient to establish body ownership. These results support the main hypothesis. The remainder of the discussion considers other novel findings of the study.

Congruent movements performed under digital nerve block induced an illusion of finger ownership that was significantly stronger than the illusion of ownership that was induced by congruent movements performed with an intact finger. This result might not be predicted because joint and skin receptors contribute to the perception of joint movement (e.g. Browne et al., 1954; Gandevia & McCloskey, 1976), so that anaesthesia of the finger reduces the proprioceptive information which is congruent with the visual information but strengthens the illusion. However, different classes of skin receptor differ in their contribution to proprioception. While some slowly adapting stretch receptors provide signals of joint movements (e.g. Edin & Johansson, 1995; Collins et al., 2005), some rapidly adapting skin receptors can interfere with proprioceptive judgements. Vibration that excites Pacinian corpuscles reduces proprioceptive ability in the finger (Weerakkody et al., 2009). Thus it may be that blocking the digital nerve removed a component of the finger's cutaneous input that interfered with the proprioceptive input used to establish the illusion of body ownership. However, it is also likely that, despite our best efforts, the signals from skin receptors in the subjects' finger were not perfectly congruent with the visual stimulus. The pipe that held the subject's index finger (Fig. 4.1) was designed to mimic the way the experimenter held the plastic finger, but the tactile input, which the subject

expected on the basis of visual input, and the actual tactile input from the pipe were almost certainly not identical. This slight mismatch in the passive conditions (greater mismatch in active conditions, see below) may impair the adoption of the plastic finger into the body schema. If this is the reason for the less vivid illusion with an intact finger than with the blocked finger, it shows that what is critical to manipulate the sense of body ownership is congruence between sensory stimuli. That is, fewer channels of perfectly congruent sensory information exert a stronger effect than more channels of imperfectly congruent sensory information.

Which of the peripheral signals arising proximal to the finger is likely to be contributing to the illusion of ownership of the artificial finger? The most obvious signals derive from muscle spindle afferents that arise in the extrinsic and intrinsic hand muscles. They encode changes in joint position and movements (Matthews, 1972; Edin & Vallbo, 1990) and their population discharge produces illusory changes in these parameters (e.g. Goodwin *et al.*, 1972a; Gandevia, 1985; Macefield *et al.*, 1990; Wise *et al.*, 1996). However, while Golgi tendon organ afferents are unlikely to be driven powerfully by passive movement (Houk & Henneman, 1967), a role for them and other proximal mechanoreceptors cannot be ruled out.

It has been shown that when subjects voluntarily control the movements used to induce an illusion of body ownership over a rubber hand that the illusion is ~23% stronger than when the movements are passively imposed by the experimenter (Dummer *et al.*, 2009). This is not surprising because the subject had "agency" over the rubber hand. That is the subject had a sense of intending and executing their own actions. This agency may be expected to strengthen the sense of body ownership because we normally have agency over our own body and things in contact with it, for example tools. Previous studies support this position (Tsakiris *et al.*, 2006), but our results do not - active congruent movements (i.e. voluntary movements) produced an illusion that was the same or weaker than passive congruent movements (Fig. 4.4). Perhaps this was due to the greater incongruence between the tactile and visual information in the active conditions. In these conditions the subject's finger was still held by the apparatus, but the plastic finger was not held by the experimenter. However, if this were the only reason for a weaker illusion, then it would be expected that blocking the digital nerves of the finger and removing all tactile information would make the illusion induced by active movements stronger than that induced by passive movements. This did not occur. Furthermore, the data (Fig. 4.3) suggest that during the nerve block the active movements still induced a similar, or weaker, illusion of ownership over the plastic finger than the passive movements. An alternative explanation is that agency may not be critical to establish body ownership because agency is not unique to our body. We can exert agency over tools and other external objects. In contrast, congruence between vision and tactile or proprioceptive input is unique to our body parts as no external object can provide the brain with tactile or proprioceptive signals. Psychology literature has shown that agency and body ownership are dissociable (Longo et al., 2008). Another point to consider in the comparison of passive movements versus active movements is that there is fusimotor activation of muscle spindles in active movements (e.g. Vallbo, 1971; Burke et al., 1976a). This makes the processing of spindle signals more complex and it may change the way in which their population discharge is interpreted (Dimitriou & Edin, 2008a, b, 2010). It is possible that coherent input from populations of spindles in passive muscles is more easily decoded as a useful signal (Prochazka & Gorassini, 1998) which can influence body ownership.

Some subjects reported a strange feeling after they had been set up in the apparatus, but before any stimuli had been presented. In this situation the only information about the plastic finger is from the visual system, signalling that the plastic finger is in a position and posture that could be adopted by the subject's own finger. Importantly however, despite this feeling these subjects did not report that they felt any ownership over the plastic finger. In fact, these anecdotal reports and the results from the control conditions show that visual stimuli alone are not enough to establish the sense of body ownership over the finger. Vision must be coupled with congruent proprioceptive or tactile signals for subjects to
adopt the plastic finger as their own. Of course, that the rubber hand illusion can be induced without visual input (Ehrsson *et al.*, 2005) emphasises the importance of cross-modal congruence rather than visual input.

In summary, we have shown that non-tactile proprioceptive cues contribute to the sense of body ownership and that signals from skin receptors are not required. It seems that the quality of the congruence between vision and tactile or proprioceptive cues is more important than having multiple congruent sensory modes and we find no evidence that voluntarily-controlled stimuli can induce stronger illusions of body ownership than externally-imposed stimuli.

Chapter 5

Overestimation of force during matching of externally-generated forces

5.1 Abstract

To make accurate movements the brain must differentiate between forces it commands and forces imposed by the environment. This requires afferent information and signals related to central commands. If subjects match an externally-generated target force with a self-generated force, they produce a force that is larger than the target. It has been proposed that this is due to simple attenuation of afferent force signals produced by the body's own actions, but the mechanisms are unclear. Four studies of forces applied to the index finger in 14 subjects investigated this force overestimation. We determined which sensory signals are involved, if handedness is important, if overestimation is present at high forces, and which muscle actions can generate it. Subjects overestimate an externally-generated target force by 2-3 N when matching it with a voluntary force using a simple contraction or complex muscle synergy. This 'offset' occurs at low but not high forces. The effect occurs when only cutaneous inputs, or when only combined inputs from muscle and central command sources can signal force. We report a novel central factor that increases the gain, or gradient of the relationship, between the matching and target forces to ~1.20. This increased gain is present only if the target force is received on an active finger and persists after the 'offset' is abolished. It may reflect processing of reactive forces during the target phase of the task. Overall, the previously described simple model of force attenuation cannot explain fully the overestimation of external forces.

5.2 Introduction

Both exteroceptive and proprioceptive senses are important for our interaction with the environment as we must know both how the environment acts on our body and how our body acts on the environment and itself. We perceive how hard our muscles work to perform a task as well as how much force is produced. Forces are detected by afferent information, which comes from tendon organs, signalling the contractile forces of the muscles and skin receptors which signal skin compression. Central information related to the amount of central motor command also provides information about how much the muscle has been activated. This can signal muscle force (e.g. Gandevia & McCloskey, 1977b; Gandevia, 1996; Carson *et al.*, 2002), limb movement (Chapter 4) and position (Walsh *et al.*, 2004; Gandevia *et al.*, 2006; Chapter 2). These central signals may also correct for reafferent sensory 'noise' (Goodwin *et al.*, 1972a; Bays & Wolpert, 2007). A reafferent signal (or reafferance) refers to sensory input produced by the body's own actions, as opposed to an exafferent signal (or exafference) which is sensory input generated by external factors.

If a weight sits on the hand resting on the table, then only skin information is available. Once muscles contract to hold the weight, additional information is available from tendon organs and motor command signals. If subjects are asked to match an external force they produce a larger self-generated force (Shergill *et al.*, 2003; Shergill *et al.*, 2005; Voss *et al.*, 2007). The proposed reason is that the nervous system attenuates the feedback from self-generated forces to reduce the 'noise' of our own actions, making us more sensitive to externally-generated forces. Various mechanisms have been proposed over the years to correct or remove reafferent signals . The original models focussed on visual localisation and kinaesthesia of the eye (Sperry, 1950; von Holst, 1954). Since then the subtraction of reafferent signals has been shown for other sensory systems including the electric sense of electric fish (Bell, 1982), and the vestibular system (Roy & Cullen, 2001; Cullen *et al.*, 2009). This mechanism has also been frequently tested in the somatic domain with cutaneous stimuli (Weiskrantz *et al.*, 1971; Dyhre-Poulsen, 1975; Coquery, 1978; Angel & Malenka, 1982; Starr &

Cohen, 1985; Milne *et al.*, 1988; Jiang *et al.*, 1990; Blakemore *et al.*, 1998; Williams *et al.*, 1998). Most of these studies have focussed on the detection and perceived intensity of electrical stimuli applied to the skin, rather than more natural stimuli, such as compression of the skin when an object is touched. Furthermore, the other somatic signals, such as those from muscle receptors, have not received the same attention.

A model has recently been proposed for the attenuation of self-generated forces (Bays & Wolpert, 2007), but details of the mechanism have not been investigated. It is unclear whether the overestimation manifests as a constant force 'offset' (Shergill et al., 2005; Voss et al., 2007) or whether it includes a 'gradient' (Shergill et al., 2003). It has also been reported that when the target force is received on an active finger the results do not significantly differ from the passive condition (Shergill et al., 2003). However the details of the overestimation effect under these active conditions, when signals from muscle receptors and central sources are available, are unknown. This study consisted of four experiments on matching forces applied to the index finger. The first investigated which sensory signals are involved when subjects overestimate during force matching. The second examined whether the hand to which the target force was applied made a difference. The third compared two different matching actions and also self-generated forces. Because the overestimation effect has only been investigated for small forces, and because subjects cannot produce a larger matching force as they approach their maximum, the fourth experiment tested a wide range of forces.

5.3 Methods

Fourteen healthy subjects (four male) aged 27 - 39 participated in this study. Two (female) participated in all parts, six (2 male) participated in the first three experiments and the other six (2 male) participated in the fourth experiment. All subjects gave informed consent and the experimental procedures were carried out in accordance with the Declaration of Helskinki. The University of New South Wales Human Research Ethics Committee approved the study. The subjects were

informed about the experimental procedures, that is, that they would perform weight matching tasks with their index fingers under various conditions, which were also explained. However the subjects were kept unaware of the precise experimental hypotheses.

5.3.1 Experimental Setup

Figure 5.1 depicts the experimental setup. The test arm, left or right depending upon the experiment, rested supine on a table supported under the forearm from the elbow to the wrist with the back of the hand unsupported. The index finger was held extended with a load cell that was attached to a shaft suspended over the distal segment. The load cell was free to move up and down, or it could be locked into position. The subject was instructed to keep the remaining fingers in a relaxed, slightly flexed position. A support was placed under the index finger if the experiment required a passive test finger. If an active test finger was required the finger support was removed and the subject was instructed to hold their finger in position. When the target force was externally generated, weights were placed on the platform located on top of the load cell shaft. If the target force was to be self-applied, then the subject pushed down on this platform with their contralateral hand. Using the contralateral hand here allowed the index finger receiving the force to remain passive if necessary. This was also the way that subjects produced a matching force with the contralateral hand when required. If the match was to be generated with the test index finger, then the shaft was locked and the subject flexed the index finger isometrically against the load cell. The subject was denied vision of their index finger, their contralateral hand and the apparatus.

5.3.2 Experiment 1: Force matching with the index finger passive, active, or active with a digital nerve block

The purpose of this experiment was to investigate the performance of a forcematching task under conditions in which different sensory information was available. The first condition, *index passive*, used a passive test finger so that only information from skin receptors was available. This is similar to previous studies (Shergill *et al.*, 2003). The second condition, called *index active*, used an



Figure 5.1: **Diagram of the experimental setup.** The subject's forearm rested on a table with the hand protruding off the edge. During experiments in which the subject's index finger was required to be passive, it rested on a support, but in experiments in which 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 initial target force was produced by an external force on the index finger or by a self-generated force made by the contralateral hand (see Methods). The initial target was applied for ~3 s. The subject was asked to generate the matching force either by pushing down on the top of the platform with the contralateral 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.

active finger so that information from skin receptors, muscle receptors and central command signals were available. The third condition used an active test finger with its digital nerves blocked by an injection of local anaesthetic. This is referred to as *index active with digital block*. Under this condition information from muscle receptors and central command signals was available but information from skin and joint receptors in the finger was not. For all three conditions the target force was externally applied with weights on top of the load cell platform (Fig. 5.1) and the subject matched by pushing down on the platform with their

contralateral hand. For each of the three conditions 10 different forces were presented, ranging from 1 N to 10 N in 1 N increments. 10 N is approximately 25% of the maximum voluntary force that can be generated by the finger. Each force was presented five times (total 50 trials) and the order of trials was randomised. Each of the three conditions was tested in a block of 50 trials, in the order of *index passive, index active* then *index active with digital block*.

For each trial, a weight was placed on the subject's finger via the load cell and the experimenter said "here is a force". The subject was given ~ 3 s to judge the force before the weight was removed. Next, the subject was told "apply the same force with your other hand", and the subject used their contralateral hand to push down on the platform to match the force on their index finger. The subject began to generate the matching force within 2 s of the target force being removed. In the two conditions *index active* and *index active with digital block* the subjects were required to maintain the position of their index finger. They were instructed to hold the position of their finger at the start of the conditions in which the index finger was active to support the weight.

5.3.2.1 Blocking the digital nerves of the index finger.

A total of 3 - 4 ml of 1% lignocaine was injected into the medial and lateral side of the index finger 10 mm distal to the metacarpal joint to block both digital nerves. A band was placed around the index finger just distal to the joint to impede slightly the venous return in the finger and thus prolong the block. The block was clinically complete in 5-10 min with complete loss of light touch sensation. Light touch was tested intermittently to ensure that the block remained complete. After the experiment the band around the finger was removed and the subject recovered completely within a few hours.

5.3.3 Experiment 2: Force matching with different hands

This experiment was performed to test for an influence of handedness on the overestimation effect seen in the results of experiment one and so the experimental procedure was similar. There were two conditions, *index passive*

and *index active*. The order of events within a trial was the same as for experiment 1. The target force was always externally-applied by placing weights on the platform and the subject always matched by pushing down on the platform with their contralateral hand. Once again forces ranged from 1 N to 10 N in 1 N increments and were used in randomised 50-trial blocks. However, in this experiment, both conditions were presented to the index fingers of both hands, creating a total of four blocks of trials. The order in which the blocks were presented to subjects was varied. The conduct of each trial and instruction to the subject were the same as for experiment 1.

5.3.4 Experiment 3: Force matching with a self-generated target vs. an externally-generated target

In the previous two experiments all matching forces were generated by the subjects via a complex multi-joint movement with their contralateral hand pushing down on the load cell platform to generate a force on their test index finger (Fig. 5.1). In the third experiment matching forces were generated by the subject simply pushing back on the load cell with their test index finger, after the shaft of the load cell was locked in place. The first purpose of this experiment was to determine if there was any difference in force matching with the 'push-back' matching compared to matching with the contralateral hand used in experiments 1 and 2. The second purpose was to test if the overestimation of force observed in the experiments persisted when the subject was responsible for generating both the target force and the matching force.

This experiment had four different conditions. In the first (*target external, index passive*) the target force was generated by placing weights on the load cell platform as for the previous experiments. As before, the target force was applied to the pad of the index finger with the instruction "here is a force" and the subject was given \sim 3 s to assess the force before it was removed. After the target force was removed the load cell was locked just above the subject's index finger. Then the subject was asked to "apply the same force by pushing back," and the subject flexed isometrically against the load cell to generate the matching force. This first

condition (target external, index passive) was performed with the index finger supported and passive. The second condition (target external, index active) was the same except that the finger was unsupported and active during the presentation of the target force. The third condition (target self-applied, index passive) used a passive finger and the target force was generated by the subject, as follows. On an oscilloscope, the subject received visual feedback of the force applied to the load cell with a line that corresponded to the target force for the trial. The subject was asked to push down on the load cell platform with their contralateral hand to the target force with the words "use your other hand to push to the line." The subject held the target force for ~ 3 s before being told to relax. Then the visual feedback was removed, the load cell was locked into position and the subject was told to "apply the same force by pushing back" and the subject flexed with their index finger to produce the matching force. So both the target force and the matching force were voluntarily controlled by the subject. The fourth condition (target self-applied, index active) was as for condition three except with an unsupported active finger. For this experiment four target forces were used ranging from 2.5 N to 10 N in increments of 2.5 N and each force was presented 5 times making a total of 20 trials for each condition. The order of trials for a condition was randomised and the order of conditions varied.

5.3.5 Experiment 4: Force matching at high forces

The fourth experiment was designed to determine whether the force matching overestimation effect was abolished at forces that were a large percentage of the subject's maximal voluntary contraction (MVC). It is expected that subjects cannot continue to overestimate the target force as it approaches the maximum force available from the index finger. Finger flexion MVC was measured three times and the largest was taken as the subject's maximum. During each attempt subjects received verbal encouragement and were provided with visual feedback of their force. Subsequently, four levels of force were used, 15%, 35%, 55% and 75% of the subject's MVC and each was presented five times (total 20 trials) in each of the three conditions. In all conditions the target force was applied using weights placed onto the load cell platform. In the first condition the index finger

was supported and passive, and the matching force was generated by the subject's contralateral hand pushing down on the load cell platform. The second condition also used a passive index finger but the matching force was generated by the subject pushing back against the load cell that was locked into position. The third condition was the same as the second but the index finger was unsupported and active. The order of trials within a condition was randomised and the order of the three conditions varied. Because of the higher forces used in this experiment subjects were given longer rests between trials to ensure that no fatigue occurred.

5.3.6 Data collection, analysis and statistical methods

The signal from the load cell was amplified and then digitised at 100 Hz by a CED 1401 (Cambridge Electronic Design, UK) and recorded with CED Spike2 v6 software. Target forces were measured as a mean force over the presentation, except in trials where the index finger was active and the target was applied with weights. Here the first 0.5 s was excluded to allow time for the subject to steady the weight. The matching forces were measured as the maximum force the subject applied during the match. Subjects had been instructed to increase their applied force until it reached the desired matching force. Data from experiments 1, 2 and 3 underwent regression analysis to determine the equation for the line of best fit and the statistical significance of that line. Threshold for significance was set at p<0.05. Data from experiment four were pooled into four groups, each corresponding to one of the four target forces. 95% confidence intervals were calculated for both the target and matched forces. Mean data and the gradients and y-intercepts of lines of best fit are reported as means \pm 95% confidence intervals.

5.4 Results

In experiment 1 we determined the ability of subjects to match an externally applied force to their index finger under three conditions in which different sensory information was available from the test finger. Subjects overestimated external forces applied to their finger when they produced a voluntary matching force. We then performed three further experiments to investigate this overestimation in more detail.

5.4.1 Experiment 1: Force matching with the index finger passive, active or active with a digital nerve block

The target force was applied externally by placing weights on the target finger and the subject generated the matching force with the contralateral hand by pushing down on the weight platform. Subjects overestimated the external target force when matching it with a self-generated force in all three conditions. In the *index passive* condition the index finger was supported and remained relaxed so that only information from the skin was available to signal the force. Data from one subject performing this task are shown in Figure 5.2. The subject consistently produced a matching force that was larger than the target force. However, the amount by which the subject overestimated the force did not depend on the target force. There was no change in the gradient of the data away from unity. Similarly, the mean data for the group (Fig. 5.3A) also showed a gradient not different from 1 (1.05 [0.92, 1.18], mean [95% CI]) but a y-intercept of 2.13 N [1.38 N, 2.88 N]. When information from skin receptors was removed by local anesthesia but information from muscle receptors and central signals is present (Fig. 5.3C), there are similar findings, with a gradient of 1.11 [1.0, 1.22] and a y-intercept of 2.53 N [1.88 N, 3.18 N]. In the *index active* case (Fig. 5.3B) the gradient of the data is greater than 1 (1.27 [1.17, 1.37]) but is not different from the other two conditions in this experiment. The y-intercept of the line of best fit is 1.82 N [1.21 N, 2.43 N]. The y-intercepts and gradients for each condition are summarised in Fig 5.4.

5.4.2 Experiment 2: Force matching with different hands

Experiment two tested if the overestimation effect observed in experiment 1 was the same whether subjects used the left or right hand. All subjects were right handed. Results for experiment 2 are similar to the data from experiment 1 (Fig. 5.4, Experiment 1 and 2). Again there is a positive y-intercept for the line of best fit through the pooled data, 3.04 N [2.36 N, 3.72 N] for the *left index passive*



Figure 5.2: Data from a single subject during a 'Target external, index passive, match contralateral' task experiment. An external target force was applied to the subject's passive index finger by a weight for ~3 s. After it was removed the subject matched it by generating a force on the index finger by pushing down with their contralateral hand. There is a significant (p<0.001) linear relation between their matching force and the target force applied to their index finger. This subject consistently applied a matching force that is higher than the target force. The data are offset (open circle [95% CI]) above the line of identity (dashed line) but still have a unity gradient. The inset shows raw data from one trial. The first increase in force is the external target and the second is the matching force produced by the subject with the contralateral hand.

condition, 2.51 N [1.96 N, 3.06 N] for *right index passive*, 2.82 N [2.24 N, 3.40 N] for *left index active*, and 2.36 N [1.81 N, 2.91 N] for *right index active* (Fig. 5.4, upper panel). For the two passive conditions the gradient of the line of best fit for the pooled data is not different from unity (left: 0.95 [0.88, 1.02]; right: 1.03 [0.98, 1.08]; Fig. 5.4, lower panel). For the two active conditions the gradients are 1.15 [1.09, 1.21] and 1.19 [1.13, 1.25] for *left index active* and *right*

index active, respectively. Unlike experiment 1, the gradients of the data for the active conditions are different from the gradients of the passive conditions in addition to being greater than one. The overestimation seen here and in experiment 1 did not depend on whether forces were applied to the left or right index finger (or whether matching forces were produced by the left or right hand).

5.4.3 Experiment 3: Force matching with a self-generated target vs. an externally-generated target

Two subjects were unable to perform the two tasks that required a passive index finger. They found these tasks too difficult and hence their data were excluded. In this experiment the matching force was generated by the subject pushing back against the load cell with the test index finger, rather than the contralateral hand as in the previous experiments. In addition there were two target conditions, either the target was externally-generated with weights, or self-generated by the subject. When the target force was externally-generated (Fig. 5.4, Experiment 3) the results were consistent with data from experiments 1 and 2. That is, subjects matched with a force that was larger than the target force and the data were offset above the line of identity by 2.19 N [0.83 N, 3.55 N] for the target external, index passive condition and 1.50 N [0.77 N, 2.23 N] for the target external, index active condition. Once again, the gradient of the data for the passive finger was not different from unity (0.94 [0.68, 1.20]). While the gradient for the active data was greater than 1 (1.17 [1.02, 1.32]), it was not different from that for the passive condition. When the subjects matched a self-generated target force they were able to do so more accurately and the pooled data are located around the line of identity (Fig. 5.4, broken box). The offsets for the *target self-applied*, *index* passive task (0.22 N [-0.87 N, 1.31 N]) and the target self-applied, index active task (-0.88 [-1.77, 0.01]) are not different from zero. The gradients of the pooled data for these two tasks are not equal to one with the target self-applied, index passive gradient being <1 (0.74 [0.60, 0.88]) and the target self-applied, index active gradient >1 (1.17 [1.05, 1.29]). These two gradients also differ from each other.



Figure 5.3: Group data from Experiment 1 (8 subjects) for 'target external, match contralateral' tasks. Thick lines are the line of best fit for the pooled data shown with a 95% CI (dashed lines). The red thin lines are lines of best fit for data from individual subjects. For all three panels the target force was applied externally with a weight onto the index finger and the subject produced a matching force with the contralateral hand. A shows data from a task in which the index finger was passive and rested on a support. In **B** the index finger was actively held in position by the subject. **C** is the same task as for panel B with the index finger being actively held in position by the subject, but its digital nerves had been blocked with local anaesthetic. The results are similar for all three conditions. On average,

subjects consistently apply a matching force that is greater than the target force. The relation between the matching and target forces is linear for all three conditions (p < 0.001). The data from all three tasks shows a positive y-intercept (~2N, open circles). The gradient for the linear relation in the index passive task (1.05 [0.92, 1.18], mean [95% CI]) and the index active, digital nerves blocked (1.11 [1.00, 1.22]) are not different from unity. The gradient for the index active task is 1.27 [1.17, 2.31]. It is not different from the gradients of the other two tasks.

5.4.4 Experiment 4: Force matching at high forces

The fourth experiment tested the force matching performance of subjects over a wide range of forces from 15% of maximal voluntary contraction (MVC) of index finger flexion up to 75% MVC. The mean MVC was 41.2 N [37.0 N, 45.4 N]. The target force was always applied externally with weights but the matching force was generated with either the contralateral hand or the test index finger. For the *index passive, match contralateral* task an overestimation effect was observed at forces up to ~55% MVC (Fig. 5.5A). During the *index passive, match index-flexion* task, subjects overestimated target forces of 15% MVC and matched accurately a target force of 35% MVC (Fig. 5.5B). However when the target force was 55% or 75% it was matched with a force that was <u>smaller</u>. For the *index active, match index-flexion* condition the subjects matched with a larger force for targets of 15% and 35% MVC, but otherwise were accurate in their matching (Fig. 5.5C).

5.4 Discussion

Subjects overestimate an externally-generated target force when matching it with a self-generated force, a finding consistent with previous reports (Shergill *et al.*, 2003; Shergill *et al.*, 2005; Voss *et al.*, 2007). However, the cause of this overestimation is not as simple as the attenuation of sensory reafference that has been suggested (Bays & Wolpert, 2007). Our novel findings are that this overestimation effect occurs consistently under several conditions at low forces including when we restrict which sensory signals can contribute, but it does not occur consistently at high forces. In addition, there are two components to the



Figure 5.4: The mean y-intercepts and gradients of the overestimation for each condition from Experiments 1, 2 and 3. The upper panel shows the size of the offset component (±95% confidence interval) which was determined from the y-intercept of the mean line of best fit between matching force and target force for each condition in each of the experiments. The lower panel shows the size of the gradient component of the overestimation as a difference (± 95% CI) between the gradient of the mean line of best fit and the line of identity (i.e. observed gradient minus 1). The test finger was either passive (red columns) or active (black columns). In Experiment 1, the test finger was anesthetised in one condition (blue column, no skin). In Experiment 2, the test finger was the left or right index in different conditions. In Experiments 1 and 2, subjects used the contralateral hand to push on the force transducer to produce the matching force on the test finger. In Experiment 3, subjects produced the matching force by pushing back on the transducer with the test finger. In Experiments 1 and 2 and in two conditions in Experiment 3, the target force was externally-generated by weights. In the other two conditions of Experiment 3 (broken box), the target force was selfgenerated by the contralateral hand. An offset of 1.5 - 3 N is present when the subjects match an externally-generated target force, but is abolished when the subjects generate the target force themselves (broken box). A gradient steeper than the line of identity is only present when the subject is required to actively maintain the position of the index finger when the target force is presented (black columns). Gradients shown here as 0.15 - 0.25 more than the line of identity represent total gradients of 1.15-1.25.

overestimation, a constant component (i.e. offset) and one that depends upon the level of force (i.e. a gradient or gain). This separation has not been described before and it appears that previous studies focused on the constant component, as the gain component is only present in some studies (e.g. Shergill *et al.*, 2003; Shergill *et al.*, 2005).

Our findings for the constant component of the force overestimation effect are consistent with previous findings. Apart from two conditions in experiment 3, all conditions involved a subject matching an externally-generated force with a selfgenerated force. When subjects did this, they consistently overestimated the target force by 2 - 3 N, shown as a positive y-intercept with matching force plotted versus target force. This offset is larger than previously reported (e.g. Shergill *et al.*, 2003) but is still abolished when both the target and the matching force were self generated. Furthermore, subjects overestimated their target when force information was available only from skin receptors, only from muscle receptors and central signals, and when all sources were available. Thus, this overestimation is not restricted to one sensory channel and includes somatic signals beyond the cutaneous signals that have been the focus of previous study on sensory attenuation. We found no effect of handedness, suggesting that the effect is not linked to any discrepancy between the sensory or motor abilities of the dominant and non-dominant hands. It was important to asses the effect of handedness because manual performance with the index finger differs with hand dominance (Brouwer et al., 2001).

In our first two experiments the subjects received the target force on their index finger but produced the matching force with their contralateral hand. In the third experiment subjects produced the matching force with the same finger that received the target force. Pushing back with the same finger to match the force



Figure 5.5: Pooled data from Experiment 4 (8 subjects) for target forces that are 15-75% maximum voluntary contraction (MVC). In all panels the target force was externally applied with a weight. Data are shown as means \pm 95% confidence intervals. In **A** the index is passive and the matching force is self-applied with the contralateral hand. Here subjects matched with a higher force than the target for all forces except for 75% MVC. **B** shows the data obtained when the index was passive and supported when the target force was generated by flexing the index finger against the load cell, which had been locked in position. On average, subjects match accurately (35% MVC) or match with a force that is

lower than the target force (55% MVC and 75% MVC). **C** is a task in which the subject actively held the index finger in position and the matching force was generated by flexion of the index finger against the locked load cell. In this task subjects, on average, matched with a force that was higher than the target for forces less than 50% MVC but accurately matched forces that were greater than 50% MVC.

engages similar regions of skin and requires activation of a limited number of muscles. By contrast production of the matching force with the palm of the contralateral hand is more complex and requires the activation of many muscles in the contralateral arm. However, both types of matching produced similar overestimation of the target force. While the matching force must be self-generated for subjects to overestimate the target, it does not matter if the motor action used is complex and uses remote muscles. Furthermore, the amount of overestimation is similar. This may mean that the extra cues are ignored by subjects in favour of matching cues available during both the target presentation and the match. Alternatively, it may mean that any attenuation occurs at high levels when perceptions generated from different signals can be compared.

Previous models describing a force attenuation process (Bays & Wolpert, 2007, Fig 2A) have suggested that the overestimation effect is due to "attenuation" of the reafferent sensory feedback so that this feedback, which is generated when the subject's own action produces the matching force, is perceived with less weight or importance than the exafference. This seems useful as it sensitises us to external perturbations from the environment, about which we have no other information. However, importantly, such attenuation of reafference cannot be complete. Not only can no forward model predicting sensory reafference of self-generated actions be perfect, but more importantly, a complete subtraction of sensory reafference would leave no afferent source for force proprioception. The constant force offset of the overestimation effect observed in the present study suggests that the attenuation of the sensory reafference is independent of the level of force. Thus, the sensory reafference is attenuated by a constant amount and what is left behind to be perceived is dependent on the level of force applied and this signal is therefore useful for proprioception. An alternative explanation would be that the

sensory reafference is subtracted completely and the brain uses another signal for proprioception, but this does not explain the constant component of the overestimation when subjects match an externally-generated force with a selfgenerated one.

Another important implication of the constant component of the overestimation effect is that it implies that a subject would match an external force of 0 N with a self-generated force of 2-3 N. The overestimation has been shown to be present at forces as low as 0.5 N (Shergill *et al.*, 2003) but has not been investigated at even lower forces. We would expect a non-linearity to occur as the target force approaches 0 N so that the matching force versus target force relation intersects the origin. However if the constant component of the force overestimation is due to a constant attenuation of the reafferent signal then a self-generated force of up to 3 N would be attenuated and presumably perceived as a zero force because it is unphysiological for a muscle to generate a negative force (or the perception of such a force).

The experimental task can be split into a target and matching phase. The target phase begins with presentation of the target force, continues with its perception and ends with the subject deciding on their matching goal. The matching phase begins with the initial generation of the matching force and continues though perception of that force, and adjustment until the match is achieved. Attenuation of reafference should influence the perception of force in the matching phase. However, when the target phase is performed with a finger held actively in position, in addition to the constant component discussed above, there is a component that depends on the force level. The gradient between the matching and target force increases from 1.0 to about 1.15 - 1.2, i.e. subjects produce an additional 15 - 20% increase in force at each target level. While significantly different from unity, these increased gradients do not always differ significantly from conditions where the target phase is performed with a passive finger. Similarly Shergill et al. (2003) saw no significant difference between a passive target phase and an active one. However, we consistently found the increased gain when the target phase was active. It persisted when both the target and

matching forces were self generated, abolishing the constant component. If the gradient component was part of the same reafferent attenuation as the constant component, then it should also be abolished when the subject generates both the target and matching forces. Our third experiment (Fig 5.4, broken box, filled column) shows this is not the case.

In experiment 3, the passive and active version of the task were identical during the matching phase. This suggests that the gradient component of the force overestimation, occured during the target phase of the force matching task. In contrast, the model proposed by Bays and Wolpert (2007) to explain the attenuation of reafferent signals puts the attenuation in the matching phase. It may be that the gradient component is completely independent of the constant component (and the reafferent attenuation process proposed by Bays and Wolpert (2007)). When the finger is active during the target phase of the matching task, the force produced by the finger is determined by the external weight, but is controlled through a voluntary motor command. If a subject reacts to the external perturbation of the weight and adjusts their motor command to hold it, then as the motor command is adjusted the exafference due to the external weight should become reafference of the voluntary action holding the weight. If reafference in the target phase is attenuated as in the matching phase then the overestimation would be cancelled out in the same way as when the target force is self generated by the subject. This is not what we observed. Rather we see the preservation of the constant component and the addition of the gradient component. Furthermore if the gradient component is produced in the target phase, it is an accentuation of the force rather than an attenuation. This suggests that there is a difference in the processing of reafference from planned voluntary actions and reactive voluntary actions. Dyhre-Poulsen (1975) observed a similar situation in the detection of vibration on the skin. During ballistic movement of the finger cutaneous sensibility was depressed, but it was enhanced during exploratory movements. During the active target phase our subjects were instructed to hold their finger in position while a weight was lowered onto it. It makes good sense that the brain would enhance sensation of reafference in this situation rather than attenuate it

because the voluntary force has to be matched to an unpredictable external force as it is applied. Further experiments will be needed to determine the physiological mechanism behind the gradient component of force overestimation, but we suggest that it is generated in the target phase and is due to an enhancement of reafference during reactive voluntary tasks.

So far discussion has focused on what happens at forces below $\sim 25\%$ MVC. Previous studies have only examined forces below ~10% MVC. However it is clear that any overestimation when matching an externally-applied target force with a self-applied matching force must be limited by the subject's maximal voluntary force, and results in experiment 4 show that the overestimation seen in earlier experiments is not preserved at high forces. These results are consistent with a previously reported tendency to undershoot high forces during two-arm matching in which both forces are self-generated (Jones & Hunter, 1982). The results from each of our three high-force conditions were different and there may be other effects, in addition to the two overestimation components, at play. Because our task requires remembering the target force for a period of ≤ 2 s, there could be an effect of temporal order occurring at high forces. There is a small effect of temporal order at low forces (Bays et al., 2006) but it is unknown if this is the same at high levels of force. However, if a temporal order effect were present, it should occur in each of the conditions in Experiment 4 (Fig. 5.5). This means that such an effect is not bigger than the 1 - 2 N reduction in the overestimation that is seen when the highest level of force is compared to the lowest in the *index passive, match contralateral* condition when the highest level of force is compared to the lowest level (Fig. 5.5A). In this condition, because the match is made with the larger muscle group of the contralateral arm, the muscles do not approach their maximal voluntary force. When the smaller muscle group, which flexes the index finger, is used in the *index passive, match index-flexion*, there is an underestimation of high forces (Fig. 5.5B). Comparison of these two conditions suggests that in addition to any temporal order effect, there is another process related to the approach of the matching muscle group to its maximum force. In addition, at high forces, when the finger was active during the target

phase the *underestimation* produced by matching with the index finger was reduced (Fig. 5.5B and C). If the overestimation seen at low forces is preserved but overwhelmed by an independent effect at high forces, then the difference between the passive and active tasks may be explained by the presence of the gradient component.

In summary we have found that subjects overestimate an externally-generated target force when matching it with a self-applied voluntary force at low, but not high, levels of force. Furthermore this effect occurs for multiple sensory channels involved in force perception. As well as an offset in the matching force, we report a second novel component that increases the gradient between the matching and target forces. This gradient is consistently present if the target force is received by a finger which is actively holding its position and persists if the constant component is abolished. We suggest that the gradient component is generated in the target phase of the matching task and that it is due to an enhancement of the reafferent signals from the voluntary reactive task. Our results do not exclude the presence of a process that attenuates sensory reafference, but they do suggest that the process is more complicated than a simple linear cancellation or attenuation of reafferent sensory signals.

Chapter 6

General discussion

The broad group of experiments presented in the preceding chapters investigated different aspects of proprioception. A general theme is the role of centrally-generated signals and representations as well as the interaction of these signals and representations with peripherally-derived information. In Chapters 2 through 5 I present some novel contributions to knowledge of proprioception that generate some new questions. This Chapter will discuss these findings and other observations within the broad scope of proprioception as well as suggest some possible avenues for future research.

6.1 Proprioception and body representations

The body schema provides a framework for all proprioceptive information to be integrated and perceived together (see Chapter 4). Rather than having to consider an array of joint angles and velocities, we just perceive the current position of our bodies. This gives us a simplified perception of our body posture and movement control and also stores information about variables about which we have no continuous sensory information, for example the length of the body segments. The body schema has been important to proprioception research because of the influence proprioceptive signals have on it. The influence of sensory signals on the body schema has been used to show the contribution of sensory inputs to proprioception. For example, the classic evidence that muscle spindles contribute to position and movement sense was provided by vibration of the muscle producing changes in the body schema (i.e. illusory movements)(e.g. Goodwin et al., 1972a). Similar illusory movements were used in Chapter 3 to show that central command signals contribute to the sense of movement and velocity. The body schema also represents an integration of all proprioceptive information. As research on proprioception moves deeper into understanding how the signals involved interact with each other, insight may come from knowing how these signals interact with the body schema, as ultimately it represents the part of proprioception that we perceive.

6.2 Central signals of motor command

The role of centrally-generated command signals in proprioception has been controversial (see Chapter 1). The only way central signals were thought to directly contribute to proprioception was in providing information about effort and heaviness. Otherwise the role of central signals was indirect, as corollary discharges cancelling out sensory reafference. Over recent years that view has been revised following evidence that centrally-generated signals provide information about limb position. The study in Chapter 3 presents the first evidence that central command signals also provide information about limb movement and velocity. However central commands do not signal absolute limb position, so in order to provide information about variables they must be decoded by calibrated information.

The only information available from a motor command sent to a muscle is the start time and duration of the muscle activation, which muscles were activated, and how much those muscles were activated. Information about which muscles were activated, and how strongly, tells the brain which joints are involved in the movement and in which direction they should move. However, in order to determine the velocity of a movement from a motor command the brain must also know how the body responds to motor commands and in which direction the gravity vector is acting. Information about how the body responds to motor commands could be learned from experience and stored, being updated as the relation between motor commands and joint movements changes. The body's orientation to gravity can be provided by the vestibular system and vision. Hence, using only information about motor commands and body kinematics the brain could judge the duration, magnitude and velocity of limb movements. In contrast, to know the position of the limbs after a movement the brain needs to know the initial position. This is not information that motor commands or a model based on motor commands can provide. This information must come from peripheral proprioceptors, or vision. Furthermore, central commands can only provide information about voluntary movements, that is, actions that the brain initiates. They can provide no information about movements of the body that are due to

external influences. Again this information must come from peripheral receptors or, in some cases, from vision.

Centrally-generated command signals have shortcomings, like all proprioceptive signals. They also do not provide any information that peripheral signals cannot. Limb movements can be signalled by muscle, skin and joint receptors, the sense of effort could be generated by muscle spindles (Luu, B and Fitzpatrick, R, unpublished observations) and even the timing of the commands could be determined from afferent information. Furthermore, calibrated information about body kinematics could easily become uncalibrated, through muscle fatigue or environmental influences external to the body. So why use central signals in proprioception? One reason is speed of information. Any information coming back from the periphery occurs in response to an event, and then has to travel back to the brain before it can be known. In contrast, information about the command generating a voluntary movement is available as the command is issued (McCloskey et al., 1983a). It could even be available earlier, when the desired voluntary action has been selected and the command needed to realise that action has been determined, but not yet sent out to the muscle. So while information about motor commands is not unique, its early availability and access to internal models of the body are an advantage over information from the periphery.

6.3 Fine motor control with poor proprioception

An observation common to all the studies presented in this thesis as well as other studies on proprioception, is that perhaps surprisingly people are not very good at proprioceptive tasks. My first experiments investigating proprioception showed that under control conditions when subjects were asked to match the angle of their elbows they consistently made errors of up to 5° (Walsh *et al.*, 2004). Observations presented in Chapters 2, 4 and 5 are consistent with this view. Subjects are unable to accurately indicate the position of their wrist or the movements it makes nor can they accurately match the forces applied to their finger. It is said that the role of proprioception is to tell us what our body is doing, and where it is in space. If subjects make errors of as much as 10° (Fig.

3.3) when asked to indicate their wrist position, do they really know where their wrist is? As in Chapter 3 there are usually strong correlations between the actual situation and what subjects report, but how bad subjects are at psychophysical proprioception tasks still stands out. Despite these seemingly large errors we are capable of very fine motor tasks. If during motor tasks we had a 5 $^{\circ}$ error in perception of wrist angle we would not be able to feed ourselves without constant visual feedback. If there is a 3 N error in knowing how much force we apply with our fingers (as suggested in Chapter 5) we could not handle delicate objects, such as a flower, without dropping or crushing it. Yet we do these things without a problem, even when the task is novel.

There appears to be a disconnection between fine motor ability and performance in specific proprioceptive tasks. It has the feel of an observer effect, where proprioception provides the accurate information required for motor control, but trying to "observe" that information introduces an error to it. We are not normally aware of the individual angles of our joints, we are just aware of the position of our body. We are not aware of the speeds of the individual movements of each joint, we are just aware that our limb is moving from this position to that one. Similarly, we do not perform precision motor tasks by consciously controlling angles, velocities and forces of individual joint and muscles. We hold, push and move objects. In contrast, experiments on proprioception typically require subjects to consciously report (or match) individual positions, velocities and forces. These experimental tasks are quite unphysiological. Furthermore, they focus on one "sub-sense" of proprioception, while the brain must consider all proprioceptive information in sensorimotor tasks. Despite the disparity between fine motor control and psychophysical tasks, psychophysical experiments are useful. They are excellent to study the specific role of specific signals in proprioception. For example, investigation of the contribution of muscle spindle signals to the sense of position.

6.4 Many signals make proprioception work

Unlike other senses proprioception utilises multiple signals from multiple sources. This means that it is not only important to know what each of these signals do, but how these signals interact with each other. Chapter 2 and Chapter 5 both looked at the interaction of information from central command signals with afferent information. The results of Chapter 2 showed an interaction between thixotropic muscle conditioning (see Chapter 1) and voluntary muscle contraction. The results from Chapter 2, in combination with previous work (Smith et al., 2009), were interpreted to mean that the brain weights the multiple sources of sensory information available to it. This suggests that the brain favours the signals that are more reliable at a given time, or during a given task, over those that are not. All of the sensory signals that contribute to proprioception are specialised in some way to detect a particular type of information, be it muscular tension, or joint angle. However each also has its shortcomings. As examples, the activation of intrafusal muscle fibres can make muscle spindle signals ambiguous, and cutaneous receptors signal skin stretch due to both joint movement and forces applied to the skin. How does the brain deal with these signals? One way could be by having multiple signals provide information on a single variable. For example, information about joint angle comes from muscle spindles, skin receptors, joint receptors and motor command signals. The combination of signals could cover some of the shortcomings of particular signals, but how the brain combines these signals is key to how it accurately determines joint angle.

It is not known how all the signals that signal joint angle interact with each other, but there are a few possibilities. One is the weighting system mentioned above and in Chapter 2. If the brain reduces the importance of signals which are not accurate during the current task, then the accuracy of joint angle detection should increase. The brain would listen to the signals that are in their "*sweet spot*" and performing best, while ignoring those that are compromised. Signals in their "*sweet spot*" could be operating at the steepest part of their stimulus response curve, or operating at the highest data rate, or both. However to do this the brain must be able to tell which signals are compromised. This could be determined from firing rates. Signals that have strong consistent firing rates, or consistent changes in firing rate over a time or physiological range, could be favoured over those signals that have low and intermittent firing rates. This mechanism is simple and linear in nature. An alternative, and more non-linear, way is that the brain could learn from experience that a combination of sensory signals indicates a specific situation. This mechanism does not require the brain to overtly favour or ignore signals dependent on their reliability during the task because it is assumed that each sensory signal will behave in a similar way each time a particular situation occurs. The unreliability of a signal is itself useful information. These two mechanisms are not that different. The differences are in how they are conceptualised and how compromised signals are used. The brain may use a combination of the two, using the information that a signal has an intermittent firing rate, and then ignoring its input. Another consideration is that in addition to all the sensory signals contributing to proprioception there will be other influences, like the goal of the current motor task and success in achieving that goal.

6.5 Models of proprioception

Chapter 5 also investigated an interaction between motor commands and peripheral information, but the mechanism investigated is proposed to reduce the impact of sensory noise, rather than combine multiple sensory channels into a coherent sensation. Bays and Wolpert (2007) propose that when we generate a voluntary force, the sensory information due to our own action of generating the force (i.e. the reafference) is attenuated. The purpose of attenuating the reafference is to accentuate the sensory information due to external influences (i.e. exafference). This model was investigated in Chapter 5, which presents novel findings and discusses what they mean for the model. One of the problems with Bays and Wolpert's model (Fig. 1.4) is that it shows all the reafference being subtracted completely. This is consistent with earlier reafferent subtraction models (e.g. von Holst, 1954), but in these earlier models the reafference which was subtracted did not need to be perceived. For example, von Holst (1954) said

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reafference from sensory cells in the eye muscles did not generate a perception of the objects moving through the visual field and was therefore subtracted out. However, in the Bays and Wolpert model the subtracted reafference does need to be perceived because it generates the signal of force proprioception. There are other difficulties with the model. Force sensation derives from multiple signals, some of which have roles outside force detection. Do these signals always get attenuated? The attenuation of a force or movement has meaning. An attenuated force is smaller and an attenuated velocity is slower, but what about an attenuated joint angle? A subtraction-based model can work for force sensation but does not conceptually fit proprioception as a whole. Any model describing a proprioceptive mechanism needs to take into consideration the integration and processing of multiple signals that have multiple roles. The model needs to be appropriate to all physiological motor tasks and also needs to integrate with higher systems like task planning and goal achievement.

The Bays and Wolpert (2007) model fits with one physiological observation but seems to violate others. The model presented in Figure 6.1 is a '*work in progress*' model and suggests how information may flow during movement control. It processes afference with a "sensory weighting" component rather than a reafferent subtraction because the weighting is more generally applicable to proprioception. The attenuation of sensory signals during movement is evident in several sensory channels (see Chapter 5, Introduction), but it is not yet clear if this is a general phenomenon or a specific one. Models like this are useful for conceptualising and communicating ideas and experimental findings, but care must be taken not to fixate on an explanation derived from a model. A physiological mechanism derived from experimental evidence is more important.

6.6 Moving forward with proprioception research

The work presented in this thesis raises some new questions. Some of these questions involve how proprioceptive signals interact with each other to produce a perception. Chapter 2 proposed that the brain weights the multiple sensory signals available to to it, but how does it do so? A lot is known about which



Figure 6.1: A model representing how sensory information may flow during a motor task. A motor task begins with a goal that is determined by higher thought processes, for example, get a glass of water. This goal may require many movements to complete. The model suggests that selected goal enters a motor planning process. Motor planning requires information about the *current state* of the body, which is based on sensory information. Based on the selected goal and the current state, motor planning can determine if the goal has been achieved and, if the goal has not been achieved, determine the next movement. For a movement to occur a motor command must be generated and issued to the body. To determine the motor command required, motor planning needs information about body kinematics, that is, how the body reacts to motor commands. Presumably the brain goes through a calculation/simulation process using information about body kinematics and the state the body will be in after a movement (sensory predictor) to determine a motor command. The motor planning process provides three outputs, the motor command to achieve the desired movement, the expected state after the movement, and the central sensory information, the latter is the 'information from motor command signals' referred to in this thesis. The motor command acts on the body, as do external influences from the world and the body produces afferent input from many sources (large arrow). The afferent input is combined with the central sensory information in a sensory weighting process and a new state, the state of the body after the movement is complete, is produced. Some signals may have their sensory reafference reduced, or removed and this is indicated by the sensory weighting process receiving the expected state. The new state becomes the current state and is used in conjunction with central sensory signals to update the model of the body kinematics. If the new current state does not match the selected goal then motor planning will calculate a new movement and the process will repeat iteratively until the selected goal is achieved.

signals contribute to proprioception, what information they provide and when they provide it. Knowing when a given signal contributes, or is compromised, could be exploited to begin to understand how the brain weights the information that it receives. The experiments in Chapter 3 showed for the first time that information about motor commands contributes to the sense of movement and velocity, but how do these central commands interact with the signals from muscle spindles, skin and joint receptors that also contribute? Information from motor commands is fast, but requires a calibrated model to provide information about limb movements. Presumably this model is generated using afferent feedback, but how is it kept up to date as the body grows and changes, or as muscles fatigue? Is it the same calibrated model that is used to predict sensory feedback and control reafferent sensory noise? Is this model the body schema? Other questions relate to the brain areas involved in generating and processing the central commands signals. Where in the brain do these central command signals come from? Are they related to the sense of effort? Are they generated by the same process that drives the motor cortex? Techniques such as functional magnetic resonance imaging and transcranial magnetic stimulation may be used to investigate these points. Many studies have used imaging to identify brain regions associated with proprioception (e.g. Dettmers et al., 1995; Naito et al., 1999; Naito & Ehrsson, 2001; Naito et al., 2002). The discovery that central signals of motor command contribute to the sense of position and the sense of movement and velocity is an important one, but it is just the beginning of learning how these signals contribute.

Another set of questions are posed by Chapter 5, which showed that the previously reported overestimation of external forces consisted of two parts. The constant component and the gradient component. The constant component could be applied in a model similar to the one proposed by Bays and Wolpert (2007), but the gradient component could not. Chapter 5 suggested that the gradient was being generated during the target phase and was due to an enhancement of reafference rather than an attenuation, but the details of how the gradient component is generated needs to be investigated. Chapter 5 also raised the question, why do subjects begin to underestimate' external forces at high levels of

force? Discussion of those results suggested that a temporal order effect may contribute, but an additional independent effect is also present. What is this independent effect? What impact does it have on any processing of reafferent signals at high forces? At the opposite end of the force scale, the constant component implies a non-linearity in force matching ability at forces below 0.5 N. Knowing whether a 3 N constant overestimation of external forces continues as forces approach zero may shed light on the perception of external versus voluntary forces as well as attenuation of reafference signals.

Proprioception is complex and far from fully understood. The findings presented in this thesis contribute to the understanding of proprioceptive mechanisms. Furthermore this work has defined new avenues of continuing research to understand this sense which is so critical to our movement control. Ultimately improved understanding of proprioception should lead to improved understanding of how the brain controls movement of the body in health and in disease.
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